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N° 1

SHORT COMMUNICATION

Effect of the Water Extract of *Galega officinalis L.* on Human Platelet Aggregation *in vitro*

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***Galega officinalis L.* is a traditional medicinal plant from Bulgaria. It was found that the aqueous extract of *Herba Galegae* suppressed platelet aggregation *in vitro* induced by adenosine diphosphate, epinephrine, thrombin and collagen. The compounds with antiaggregating action have not as yet been isolated from *Galega officinalis*.**

Keywords: plant extract; *Herba Galegae*; *in vitro*; platelet aggregation

INTRODUCTION

The effect of various natural, synthetic and pharmaceutical compounds on platelet aggregation is of interest in the search for new medicinal substances and preparations (Mashkovski, 1988).

Galega officinalis is a plant used in traditional medicine for treatment of *diabetes mellitus*. Biologically active alkaloids, exhibiting a hypoglycaemic effect, were isolated from *Herba Galegae* (Hoppe, 1975; Petkov, 1982). There are data (Petkov, 1982) indicating that the plant extract has an anticoagulation effect. In connection with this, we studied the effect of water, ethanol and chloroform extracts of *Herba Galegae* on platelet aggregation *in vitro*. It was found that only the aqueous extract suppressed platelet aggregation.

MATERIAL AND METHODS

Plant material. The aerial parts of *Galega officinalis* at flowering stage were collected between May and August 1992 in different parts of Thrace, Bulgaria. The plant was verified by the Department of Botany, Faculty of Pharmacy (University of Sofia, Bulgaria).

Extraction. Aqueous extracts were obtained by maceration of 2 g dry matter in 20 mL distilled water for 20–24 h at 18°–20°C. The fresh extract was filtered twice and the effect on platelet aggregation studied immediately.

Isolation of human platelets. Blood was taken from volunteers who had received no medication for 15 days prior to blood collection. Blood was collected in disposable syringes at a ratio of 1 part 3.8% trisodium citrate and 9 parts venous blood (Zucker, 1989). Platelet-rich plasma (PRP) was prepared by centrifugation ($180 \times g$ for 10 min) and diluted to 300×10^6 platelets per mL with autologous platelet-poor plasma ($1800 \times g$ for 15 min).

Platelet aggregation. Aggregation was studied with a spectrophotometer set to operate at wavelength 600 nm and the results were recorded on an electronic recorder [XY-Recorder en dim 620. 02, VEB, Germany] (Born, 1962).

Reagents. Adenosine 5'-diphosphate (ADP) at a concentration of 1×10^{-3} M from Reanal (Hungary); epinephrine (1×10^{-4} M) and collagen (2 mg/mL) from Sigma Chemical Ltd (USA); human thrombin (8 units/mL) from the Research Institute of Haematology and Blood Transfusion (Sofia, Bulgaria) were used as aggregating agents.

Drugs. Sodium salicylate ($C_7H_5NaO_3$) at a concentration of 40 mg/mL in physiological saline, pH 7.4; verapamil (2.5 mg/mL); heparin (15 U/mL); dipyridamole

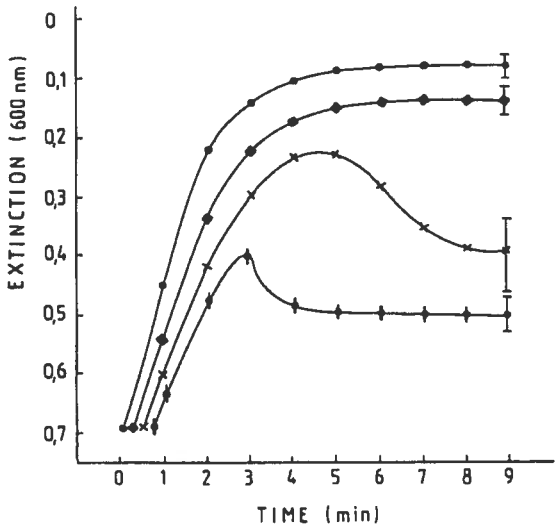

Figure 1. *In vitro* effect of 20 µL (×) and 40 µL (◆) aqueous extracts of *Herba Galegae*, containing 22.5 ± 2.6 mg/mL average dry matter and of a 20 µL aqueous solution of 40 mg/mL sodium salicylate (◆) as a basis for comparison of platelet aggregation of 400 µL platelet-rich plasma by adenosine diphosphate. For control (●) the aggregation of 400 µL PRP was used, after the addition of 20 µL ADP (1×10^{-3} M). Values are means of ± maximum standard errors for 10 independent experiments.

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№ 2

An Effect of *Galega officinalis* L. Extract on Platelet Aggregation in Rats

Atanas T. Atanasov

ABSTRACT. The effect of aqueous extracts of *Galega officinalis* L. on platelet aggregation was studied by examining the blood from rats given an intravenous application of extract in the caudal vein. Treatment of test animals with extract at a ratio of 1 part extract (25.1 ± 3.8 mg/ml dry substance) per 40 parts blood, suppressed platelet aggregation as compared with untreated controls. Suppression of aggregation was lost by 3 h after injection of extract. The components with antiaggregating activity have not identified. *[Article copies available from The Haworth Document Delivery Service: 1-800-342-9678.]*

KEYWORDS. Anticoagulation, herba galegae, medicinal plant.

INTRODUCTION

Experimental studies of plant extracts on platelet aggregation are relevant in any search for new substances that may be used in the treatment of patients with disturbed homeostasis. *Galega officinalis* L. is a plant used with a traditional medicine system of Bulgaria (6) and India (5) in treatment of diabetes mellitus because the extract has hypoglycemic effects. Evidence also exists indicating the extract has anticoagulating activity (6). Recent experimental results (1) have suggested aqueous extracts of this plant suppress *in vitro* platelet aggregation induced by aggregating agents such as adenosine diphosphate, epinephrine, thrombin, and collagen.

In this study, platelet aggregation in plasma from rats treated *in vivo* with aqueous extracts of the *Galega officinalis* L. was investigated.

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EFFECT OF LOCAL COOLING ON SKIN TEMPERATURE RESTORATION TIME FOR FINGERS OF THE UPPER EXTREMITIES

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Abstract—Finger skin temperature (T_{sk}) changes after cold immersion were studied in 114 clinically healthy persons (60 men and 54 women) aged 18 to 70 from Stara Zagora (42°28′N, −1h 42′E, altitude of 220 m), Bulgaria. The aim of this study was to measure T_{sk} changes and analyze temporal dynamics for restoration of the initial T_{sk} of fingers after cooling. We applied cooling on the 3rd and 4th fingers of both hands of 15 persons (8 men and 7 women) for 2.5 min within a temperature range from 2°C to 14°C inclusive. A cold-induced vasodilatation response in the water temperature range 2–8°C was hypothesized while we were not completely sure of the type of reactions after cooling in the range 10–14°C. The reactions to 2–8°C were vasodilatatory and similar to those reported by other investigators (Wenger *et al.*, 1975; Zanzov, 1985) using the classical method. When the old cold-induced vasodilatation (CIVD) test was modified to 2.5 min of finger cooling in water at 4°C (CI test—a *cold-induced test*), the maximum time needed for restoration of initial T_{sk} of both 3rd and 4th fingers of both hands of all 114 persons was found to be 8.5 min and the mean time was between 5–6 min. The new CI test at 4°C causes neither harm nor unbearable pain and might be used in monitoring the impact of environmental temperature changes on normal subjects for purposes of applied and/or occupational physiology as well as in clinical practice.

Key Word Index: Finger skin temperature; cold-induced test; restoration time; thermal environment; Bulgaria

INTRODUCTION

Variability in the effects of ambient temperature changes upon the human body may be indicative of the extent of its acclimatization to thermal stresses, or of some pathological condition. The changes in skin temperature (T_{sk}) and, by implication, changes in hand blood flow, occurring in response to local cooling have been used as indicators of cold acclimatization (Budd, 1964; Naidu and Sachdeva, 1993). In one such procedure, the so called 'cold-induced vasodilatation test', the hands are immersed for 5 min in a bath of water at 12°C. The time it takes after removal from the bath for hand T_{sk} to return to its pre-immersion value is then recorded. The T_{sk} is measured at intervals of 3 min at the level of *toruli tactiles* of fingers (Wenger *et al.*, 1975; Zanzov, 1985). The normal recovery time is 10 to 20 min, but when there is impairment to the blood circulation, the time may be 30 to 50 min or even longer. The variability of the normal recovery time limits the reliability of the test since there are incidental fluctuations in T_{sk} during long recovery periods which make small changes in the blood supply to the palms and fingers more difficult to detect. Another technique was used by Naidu and Sachdeva (1993) to study the occurrence of cold-acclimatization in members of an Antarctic expedition. A hand was immersed up to the wrist in water of 0°C for 2 min and the T_{sk} recorded within 30 s after its removal. Since this test was almost certainly painful, and recovery was measured over such a short period, the validity of the test may be doubted. Also, no study by now has attempted, especially in Bulgarians, to give detailed description of temporal dynamics of cold-induced T_{sk} changes. The objective of the study reported here was to find

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This work was initiated in 1993 when Dr Dimitrov was with the Department of Environmental Biology at the University of Manchester, Manchester, U.K.

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Inhibiting and disaggregating effect of gel-filtered *Galega officinalis* L. herbal extract on platelet aggregation

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Abstract

The in vitro inhibiting and disaggregating effect on platelet aggregation of a gel-fractionated herbal extract from *Galega officinalis* L. is examined. The obtained Sephadex G-25 filtered fraction was 35–36 times more active than the crude extract. The threshold concentration at which this fraction inhibits platelet aggregation (5–10% inhibition) by 50 μM adenosine 5′-diphosphate (ADP) is 4.5–5 μg per 1 ml platelet-rich plasma (PRP). At a concentration of 35 μg/ml PRP the fraction inhibits 50% of aggregation by ADP and at a concentration of 125 μg/ml PRP fully inhibits the aggregation of PRP by ADP. At a concentration of 40 μg/ml PRP the fraction inhibits initiation of platelet aggregation by 0.18 mg/ml collagen and at 50 μg/ml PRP inhibits the initiation of aggregation by 0.7 units/ml thrombin. The G-25 filtered fraction shows a strong disaggregating effect on aggregated PRP. At a concentration of 65–75 μg/ml PRP, the fraction is able to disaggregate the 50–53% of aggregated platelet-rich plasma by 50 μM ADP, and 25% of aggregated PRP by 0.18 mg/ml collagen.

Keywords: *Galega officinalis* L.; Extract; Inhibition; Platelet aggregation

1. Introduction

Galega officinalis L. is a plant used in the traditional medicinal system of Bulgaria, Italy and India (Chopra et al., 1956; Petkov, 1982) in the treatment of diabetes mellitus. A biologically active alkaloid galegine, exhibiting a hypoglycemic effect in vivo was isolated from *G. officinalis* (Reuter, 1963; Hoppe, 1975). In healthy normoglicemic volunteers galegine at a dose of 2–4 mg/kg body mass leads to reduction of blood glucose, which begins after 3–4 h and continues for about 9 h. A hypoglycemic effect is observed in patients with diabetes mellitus (Benigni et al., 1964). The plant extract appears to have an anticoagulation effect (Erspamer, 1943; Petkov, 1982). Recent experimental results (Atanasov, 1993, 1994) show that the 2.25% crude aqueous extracts of this plant at a dose of 1.0–2.5 mg/ml platelet-rich plasma (PRP) suppress in vitro platelet aggregation induced by aggregating agents such as adenosine 5′-diphosphate (ADP), epinephrine, thrombin and collagen. The IC_{50} (50% inhibition effect) for aggregation by 50 μM

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Nitric oxide and free stable nitroxyl radicals in the mechanism of biological action of the spin-labeled compounds

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Summary A comparison of more important physical, chemical and biological properties of the nitric oxide (NO) and free stable nitroxyl radicals (nitroxides) on the base of their structural similarity is made in the article. The active moiety in the nitroxide molecule represents a sterically hindered nitric oxide. The mechanisms of biological action of the nitroxides and especially of their derivatives with antitumor agents from the groups of nitrogen mustards, nitrosoureas, aziridines and triazenes (spin-labeled compounds) is explained through the biological activities of sterically hindered NO. Similarly to NO, nitroxides also can react with superoxide anion radical (O_2^-), they possess superoxide dismutase (SOD) mimetic action. While the interaction of NO with O_2^- yields very toxic peroxynitrite ($ONOO^-$), its formation is strongly limited in the presence of a nitroxide. It is known that the nitrosourea antitumor drugs, like lomustine (CCNU) and carmustine (BCNU), showed high general toxicity, one of the reasons for that probability is the formation of NO, and subsequently of $ONOO^-$, during their metabolism. The biological investigations of the nitroxides showed their considerably lower general toxicity that could be explained with the SOD-mimetic action of the nitroxide present in their molecule. © 2001 Harcourt Publishers Ltd

INTRODUCTION

The intensive study of the nitric oxide (NO) during the last 20 years accumulated many data about its biological action (1–4). According to the chemical structure of NO (more correctly nitrosonium NO^+), it can be formed by the removal of one electron. According to their chemical structure the free stable nitroxyl radicals (nitroxides) represent a sterically hindered nitric oxide (Fig. 1).

A large number of spin-labeled antitumor compounds from the groups of nitrogen mustard (5,6), aziridines (7), nitrosoureas (8) and triazanes (9) have been synthesized and studied. A considerably lower general toxicity of the spin-labeled antitumor compounds than their diamagnetic analoges was established and, what is more, the spin-labeled nitrosoureas have been proven to be powerful antimelanomic agents (10). An attempt to explain some mechanisms of the biological action of the spin-labeled antitumour compounds by comparison of some properties of NO and nitroxides is made in the present article.

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Some biological properties of nitric oxide

Interest in nitric oxide as a chemical affecting human life has increased over the last 20 years, first through its damaging effects (2,4). The last were associated with the yielding of peroxynitrite ($ONOO^-$) through the direct reaction of nitric oxide (NO) with superoxide anion radical (O_2^-). Peroxynitrite is a potent oxidant capable of:

- directly oxidizing protein and non protein sulfhydryls

N° 6

Vascular Endothelium

Source and Target of Inflammatory Mediators

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EFFECTS ON HERBAL EXTRACT OF GALLEGA OFFICINALIS ON PLATELED AGGREGATION

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Gallega officinalis L. is a plant used in the traditional medicinal system of Bulgaria, Italy and India in the treatment of diabetes mellitus. The in vitro inhibiting and disaggregating effect on plateled aggregation of gel-fractionated herbal extract from Gallega officinalis is studied. The threshold concentration at which this fraction inhibited plateled aggregation (5-10% inhibition) by 50 mcM ADP was 4.5 – 5 mcg/ml plateled rich plasma (PRP). At a concentration of 35 mcg/ml PRP the fraction inhibited 50% of aggregation by adenosine-5-diphosphate (ADP) and at a concentration of 125 mcg/ml PRP fully inhibits the aggregation of PRP by ADP. At a concentration of 40 mcg/ml PRP the fraction inhibits initiation of plateled aggregation by 0.18 mg/ml collagen and at 50 mcg/ml PRP inhibited the initiation of aggregation by 0.7 units/ml trombin. The fraction showed a strong disaggregating effect on aggregated PRP. The obtained results permitted us to conclude that the isolations of biological active compound from this extract and study its effects would help clarify and minimize some complications of diabetes mellitus on blood coagulation and plateled aggregation.

N° 7

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Changes of the power coefficient in the '*metabolism–mass*' relationship in the evolutionary process of animals

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Abstract

The power coefficient k decreases along evolution in an allometric relationship between the oxygen consumption rate and the body mass of animals. This theoretical study investigated the role of the power coefficient k and its behavior along evolution. The animals were organized in three groups according to the values of the power coefficient k as follows: (I) from unicellular *Prokaryotes* to *Eukaryotes*; (II) from *Mytilus* and *Annelida* to Pisces; (III) from *Reptilia* to *Mammals* and *Aves*. At the beginning of each animal group (stage), the value of k was close to 0.9–1.0 and at the end of the stage it was close to 0.67–0.70. Exponential sharp increase of the power coefficient k was observed during the biological transition from Protozoa to simply organized Metazoa and in the transition from Poikylothermic to Homothermic organisms (e.g. from Pisces to Reptilia). Also, when using the periodogram regression analysis, a cyclic (periodic) pattern in this increase was observed (i.e. period $T \approx 8$–11 units, $P < 0.05$). It was postulated that the power coefficient k, as with the coefficient a, might represent the increase of complexity of animal organization within each group.

Keywords: Relationship 'metabolism–mass'; Evolution of animals; Cyclicity; Transformations

1. Introduction

The energetics of organisms is strongly dependent upon their mass (Brody, 1945; Kleiber, 1961; Prosser, 1977; Schmidt-Nielsen, 1984; Gillooly et al., 2001). The relationship between the mass W of an organism and the rate of metabolism Vo_2 (*quantity of oxygen consumed per unit of time*), or the intensity of metabolism vo_2 (*quantity of oxygen consumed by unit of mass per unit of time*), is represented by the allometric dependence: $Vo_2 = aW^k$ and $vo_2 = aW^{k-1}$, where a and k are coefficients being characteristic for each group of animals. The coefficient a represents the rate of metabolism of a conventional organism with a mass equal to 1 kg. It is used for comparing the standard metabolism of organisms with different

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№ 8

Antiplatelet Aggregation Activity of a Fraction Isolated from *Galega officinalis* L.

Atanas Todorov Atanasov
Bojidar Tchorbanov

ABSTRACT. A fraction isolated from a crude aqueous extract of *Galega officinalis* L. and purified by column chromatography inhibit platelet aggregation in platelet-rich plasma. The active fraction of the extract, molecular weight of 100-140 kDa, appeared to be a polysaccharide-protein complex. Aggregation of platelets initiated by 25 μM ADP was inhibited 50 percent by 11.2 μg/ml of the fraction. Aggregation of platelets initiated by 100 μg/ml collagen and 0.8 U/ml thrombin was completely inhibited by 16 μg/ml and 18.3 μg/ml, respectively.

KEYWORDS. Blood clotting, medicinal plant

INTRODUCTION

Galega officinalis L. is widely grown and used in a traditional medicine system of East Europe, Italy, Bulgaria, and India for the treatment

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Anti-Platelet Fraction from *Galega officinalis* L. Inhibits Platelet Aggregation

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ABSTRACT

A fraction from crude extract of *Galega officinalis* L. was purified by gel filtration on Sephadex G-25, Sepharose 4B, and ion-exchange chromatography on diethylaminoethyl (DEAE)–cellulose. The fraction with molecular weight 100–140 kDa appears to have a polysaccharide nature, including protein. The fraction inhibits platelet aggregation initiated by 25 μM adenosine 5′-diphosphate (ADP), 100 μg/ml collagen, and 0.8 U/ml thrombin with the 50% inhibiting concentration (IC_{50}) being 11.2 μg/ml for ADP, and the IC_{100} being 15.1 μg/ml for collagen and IC_{100} 19.6 μg/ml for thrombin.

INTRODUCTION

GALEGA OFFICINALIS L. is a plant that is widely grown and used in a traditional medicine system of East Europe, Italy, Bulgaria, and India in the treatment of diabetes mellitus.[1] *G. officinalis* is a food component for animals and humans in Italy.[2] The plant increases lactation humans and animals.[3] More than 15 biologically active substances are isolated from *G. officinalis*, including galegine, hydroxygalegine, peganine, vasicinone, lutein (alkaloids), pentahydroxyflavone 5-glucoside, luteolin, galuteoline, luteolin 5-glucoside (glucosides); flavonoids, glucoside saponins, and γ-γ dimethylallylamidine.[3–8]

Experimental investigations have shows that the crude aqueous extracts[9] and gel-fractionated extract of the plant suppress platelet aggregation induced by adenosine 5′-diphosphate (ADP), epinephrine, thrombin, and collagen and disaggregated platelet clumps in platelet-rich plasma.[10] The aqueous extract of *G. officinalis* suppressed platelet aggregation *in vivo* in rats after intravenous injection of aqueous extract (90–100 mg/kg body weight) in the caudal vein.[11]

MATERIALS AND METHODS

Plant material

The aerial parts of *G. officinalis* at flowering stage were collected between May and August, 2000, in different parts of Thrace, a region of Bulgaria. The identification of the plant was verified by Dr. I. Asenov (Taxonomist), Department of Botany, Faculty of Pharmacy, University of Sofia, Bulgaria, where voucher No 12186 is on deposit.

Preparation of the extract

Crude aqueous extracts were obtained by maceration of 200 g dry matter in 2,000 ml dis-

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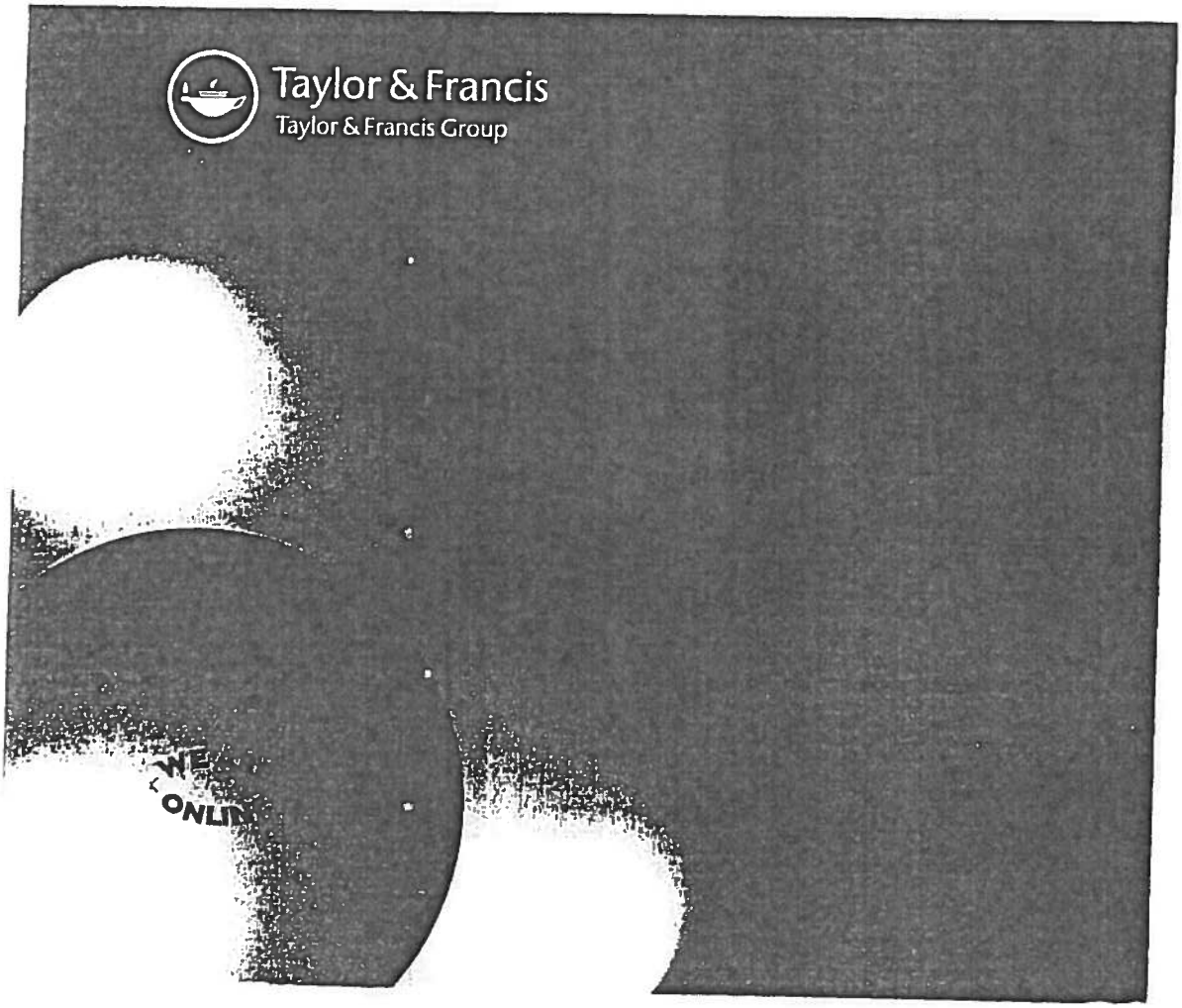

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Time Periods in the Nasal Cycle During Night Sleep

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Abstract

The periodic congestion and decongestion of nasal venous sinuses and the alternation of airflow from one side of the nose to the other are referred to as a 'nasal cycle' in the literature. The aim of this study was to detect the nasal cycle during sleep in normal subjects and describe existing time periods and their sequence and patterns. We studied 58 records of the nasal cycle over 6–9 hours of sleep in six healthy volunteers and revealed that the cycle could be described as a combination of 1 to 4 discrete ultradian periods with various length: 1.0–1.5 h (mean 78.6 min), 2.5–3.0 h (168.3 min), 4.0–4.5 h (260.3 min) or 5.5–6.0 h (347.5 min). The distribution of the discrete time periods was multi-modal and the mean lengths of periods were 'multiples' of a basic period of 85.4 min (≈1.5 h) which was very close to the mean length of the sleep cycle (≈1.5 h). In all subjects, during any of the REM stages of the sleep, an alternation of the airflow through the nostrils was observed. In about 75% of all cases, the switch of the flow between the nostrils occurred during the second or following REM stages of the sleep thus shaping a nasal cycle that contained mainly periods of 3.0 or 4.5 hours. We suggest a novel classification of the nocturnal nasal cyclicity and hypothesis that there is a relationship between the nasal cycle and the sleep cycle which, like other cyclic physiological phenomena with ultradian rhythmicity, expresses a pattern of 'lateralisation' that is synchronous with changes in the sleep cycle.

Keywords: Nasal cycle, time periods, sleep cycle, ultradian rhythms, chronobiology.

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Nasal and sleep cycle – possible synchronization during night sleep

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Nasal and sleep cycle – possible synchronization during night sleep

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Summary Regular cyclic changes in nostril airflow due to a nasal congestion and decongestion are known in literature as nasal cycle. Registration of breathing from each nostril separately gives possibility to registrate moments of alternative change of airflow of nostrils and periods of nasal cycle. This registration during night sleep shows that the length of these periods are about 1.5 h, 3.0 h and 4.5 h. The length of these periods are multiple of mean length of sleep cycle – about 1.5 h. The alternative change of airflow through nostrils occurs through some of REM stages of the sleep. This shows, that during the night sleep becomes synchronization of nasal and sleep cycles in some of the REM phases of sleep. As a result – length of periods of the nasal cycle are one or more length of sleep cycle.

INTRODUCTION

Most of the normal subjects show regular cyclic changes in nostril airflow. These spontaneous cyclical activity due to a nasal congestion and decongestion are known in literature as nasal cycle (1). The nasal cycle can be demonstrated in most ansleep adults (2,3) and sleeping humans (4). Other cyclical phenomena showing lateralization synchronous with the nasal cycle have been reported in humans. They include electrocortical activity (5,6), sweating (7), pupil size, conjunctival capillary diameter (8) and even cognitive performance (9).

HYPOTHESES

Scientific interests are directed to the question – whether sleep and nasal cycle are synchronized like discussed above cyclical phenomena?

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METHOD

Three healthy males, aged 21 (No. 1), 35 (No. 2) and 47 (No. 3) years, volunteered as subjects. The subject entered into a bio-climatic chamber at 20:00 h and go to sleep at 22:00 h, dorsally. The airflow temperature from each nostril separately (nostril respiration) was measured using two thermistors inserted in cylinder with diameter 1 cm. The cylinders are inserted slightly in the nostrils and fixed to the nose by a facemask. The signals from thermistors amplifies and registered as the method used from Canter (10) and Mirza et al. (11). The sleep stages are registrated by left or right nostril respiration at speed paper 240–600 mm/h. The REM stages of sleep are registrated by Cheyne-Stokes-like pattern respiration. The nasal cycle and periods of this cycle are registrated at speed paper 20 mm/h.

RESULTS

On Figs. 1–5 are shown records of the nasal cycle of the subjects N1, N2 and N3. The alternative changes of dominant airflow through nostrils occurs through periods with length near to 1.5 h, 3.0 h and 4.5 h (see figure legends). On Fig. 6a and b are shown the records of the sleep cycles of the subject N2. The change of the dominant airflow through nostrils occurs during REM stages

N = 12

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Nitroxyl radicals and malignant pigment melanoma

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Nitroxyl radicals and malignant pigment melanoma

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Summary Our studies showed that the spin-labeled (SL) compounds (free stable nitroxyl radical derivatives) accumulate predominantly in pigment melanoma and some of them possess high antimelanoma activity (100% curability of tumor bearing animals) and lower general toxicity. Taking into account our results we describe a proposed mechanism of the spin-labeled accumulation in melanoma, their antimelanoma activity and lower toxicity.

INTRODUCTION

Perspective for clinical use are antitumor compounds with tumorspecific action and low general toxicity. The spin-labeled antitumor compounds synthesized by us accumulate predominantly in pigment melanoma in comparison with healthy tissues and other tumors (1). We explain the mechanism of this selective accumulation with the SOD-mimic action of SL. The present work is closely connected with our other article published recently in Medical Hypotheses (2).

RESULTS AND DISCUSSION

We consider that superoxide anion radical ($O_2^{\cdot}$) plays a significant role in the melanoma pathogenesis. Some studies showed that melanoma cells produce large amounts of superoxide anion radicals and moreover, it is implicated in the mechanism of metastasis (3). The melanin itself, generating in the pigment melanoma, is a good $O_2^{\cdot}$ scavenger (4), and with its absence in both apigment and depigment melanomas their high malignancy could be explained.

We propose that the accumulation of SL compounds in the pigment melanoma tissue is connected with a superoxide-dismutase (SOD) mimic action of SL compounds, established by us (5), and other authors (6). The spin-labeled derivatives of antitumor therapeutics like nitrosoureas and triazenes synthesized by us realize their SOD mimic action, in contrast to enzyme SOD, by an oxyreducing process going according to Scheme 1, where R = O, OH, NH_2 or nitrosourea and triazene residues.

The low water solubility of the nitroxyl (I) established by us in comparison with the corresponding hydroxyl amine (II) is the probable reason for the detection by the ESR technique and accumulation of SL compounds in the melanoma tissue, where a big amount of $O_2^{\cdot}$ is producing. The high antimelanoma activity of the spin-labeled triazenes (SLT) and spin-labeled nitrosoureas (SLNU) (7) probably is due to their accumulation in pigment melanoma. Another probable reason for the high antimelanoma effect especially of SLNU is the formation of the greatly cell toxic peroxynitrite ($ONOO^-$) by interaction of $O_2^{\cdot}$ with nitric oxide ($NO^{\cdot}$), liberating from nitrosourea antitumor drugs during their biotransformation, according to the scheme:

$$NO^{\cdot} + O_2^{\cdot} \rightarrow ONOO^{\cdot}$$

$$ONOO^{\cdot} + H^+ \rightarrow HONOO$$

$$HONOO \rightarrow {}^{\cdot}OH + \dot{N}O_2$$

These species are potentially toxic as they can react with and alter the structure of cellular or extracellular macromolecules such as unsaturated fatty acid, proteins and DNA.

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The linear alometric relationship between total metabolic energy per life span and body mass of poikilothermic animals

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Abstract

A linear relationship exists between total metabolic energy per life span PT_{ls} (kJ) and body mass M (kg) of 54 poikilothermic species (Protozoa, Nematoda, Mollusca, Asteroidae, Insecta, Arachnoidae, Crustacea, Pisces, Amphibia, Reptilia and Snakes): $PT_{ls} = A^*_{ls} M^{1.0838}$, where P (kJ/day) is the rate of metabolism and T_{ls} (days) is the life span of animals. The linear coefficient $A^*_{ls} = 3.7 \times 10^5$ kJ/kg is the total metabolic energy, exhausted during the life span per 1 kg body mass of animals. This linear coefficient can be regarded as relatively constant metabolic parameter for poikilothermic organisms, ranging from 0.1×10^5 to 5.5×10^5 kJ/kg, in spite of 17-degree differences between metabolic rate and body mass of animals. A linear relationship between total metabolic energy per life span and body mass of only 48 poikilothermic multicellular animals (without Protozoa) is: $PT_{ls} = A^*_{ls} M^{0.9692}$ with linear coefficient $A^*_{ls} = 2.34 \times 10^5$ kJ/kg. Since a power relationship exists between the rate of metabolism and body mass of animals of the type: $P = aM^k$ (a and k are the alometric constants), an empiric rule could be formulated, that life span is a time interval for which the total metabolic energy per life span becomes proportional to body mass of animals and power coefficient k becomes ≈1.0.

Keywords: Total metabolic energy; Life span; Poikilothermic animals

1. Introduction

The bioenergetic studies on poikilothermic, mammals, and aves (Hemmingsen, 1950, 1960; Zeuthen, 1953; Heusner, 1985; Kleiber, 1961; Schmidt-Nielsen, 1984) have shown that the rate of oxygen consumption P (kJ/day) is related to the body mass M (kg) as expressed by the equation of type: $P = aM^k$. Zotin and Lamprecht (1996) have shown that the coefficient a grows with increasing complexity of animal's organization during the evolutionary process and that there is a relationship between the values of the coefficient a and the place of animals along the evolutionary tree.

Atanasov and Dimitrov (2002) showed that the power coefficient k changes with the complexity of animals during the evolutionary process and three evolutionary branches have been formed according to the

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Prognosis of Prolongation and Reduction of Human Pregnancy Duration, Using Alometric Relation Between Length of Pregnancy, Body Mass and Metabolism of Mammals

Atanas Todorov Atanasov

Using the relationship between length of pregnancy T(day), body mass M(g) and basal metabolism of mammals from type: $T=7.5451\ M^{0.26R9}$ and $T.P/M=A_{pr}$, where, P (kcal/day)-rate of metabolism, A_{pr}(kcal/kg)-total metabolic energy of mother during pregnancy, per 1 kg body mass, a method for calculation the prolongation and reduction of pregnancy duration was proposed.

Key words: Prognosis, length of pregnancy, body mass, metabolism

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known, but it is possible that this agent inhibits NF-kB activation by modulation of binding of NF-kB with DNA or affecting unknown mechanisms in the nuclear translocation of NF-kB [3].

Given the above facts, I speculate that VPA may prove to be a novel addition to the treatment armamentarium of this severe and often untreatable disease.

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Possible metabolism – body weight effect on prolongation and reduction of the pregnancy duration

A method for calculating the prolongation and reduction of pregnancy duration is proposed. The method is based on the alometric relationship between the extent of pregnancy, body weight and metabolism of pregnant women.

Hypothesis and calculations

The prognosis of changes in pregnancy duration is of extreme significance for the survival of the newborn. Data of Hytten [1] show that the normal pregnancy duration is expected at a mean increase in body weight of mother of about 25–30%. The oxygen consumption of the maternal organism also increases by 25–30% [2], but this is not reported in the gynecological practice as factor acting upon pregnancy duration. Atanasov shows [3,4] that there exists a relationship between length of pregnancy – T_{pr} (day), body weight – M (kg) and metabolism – P (kcal/day) of a pregnant woman from type: $T_{pr} = A_{pr}/(P/M)$, where $A_{pr} = T_{pr}\ (P/M)$ – is the total metabolic energy for 280 days per 1 kg body weight of a mother. This relationship shows that the pregnancy duration depends both on the body weight and metabolism of a woman. According to data of Hytten [1] and Allaly [2], the equal increase of the body weight and metabolism of a pregnant women with 25–30% leads to keeping her metabolism per unit of body mass before – $(P/M)_{norm}$ and after conception – $(P/M)_{pr}$. This hypothesis gives us the possibility to analyse three cases of pregnancy, taking into consideration the changes in the metabolism and body weight of women after conception.

Case one (normal length of pregnancy)

The body weight and metabolism after conception increase proportionally, so that $(P/M)_{pr} = (P/M)_{norm}$. Provided before pregnancy the woman's weight is $M = 60$ kg and her metabolism is $P = 1800$ kcal/day, the value of normal metabolism per unit mass $(P/M)_{norm}$ would be 30 (kcal/day kg). For the same pregnant woman (with a mean increase in the body weight 12.5 kg from 60 to 72.5 kg and in metabolism with 25% from 1800 to 2250 kcal/day) [3,4], the value of $(P/M)_{pr}$ will also be 30 (kcal/day kg), i.e. $(P/M)_{pr} = (P/M)_{norm.} =$ 30 kcal/day kg. From the equation $A_{pr} = T_{pr} \cdot (P/M)_{norm\ =\ pr}$ it is possible to calculate the total metabolic energy of a mother during 280 days period of pregnancy: $A_{pr} = [30$ (kcal/day kg) × 280 days] = 8400 kcal/kg.

Case two (shorter length of pregnancy)

The metabolism P increases faster than the increase in the body weight M and $(P/M)_{pr} > (P/M)_{norm.}$ As a

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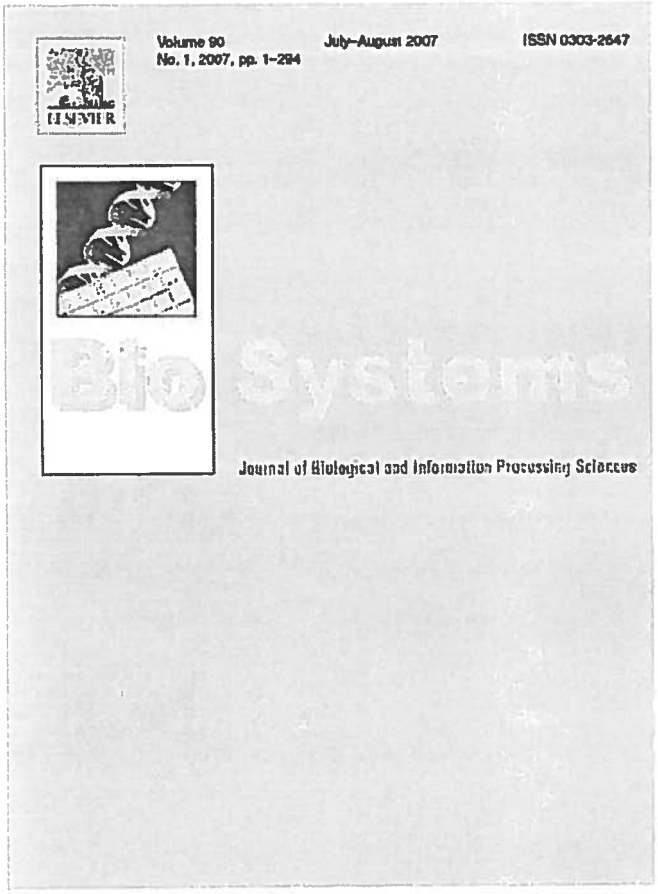

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The linear allometric relationship between total metabolic energy per life span and body mass of mammals

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Abstract

The aim of this study is to establish and calculate the exact allometric relationship between the total metabolic energy per life span and the body mass in a wide range of mammals with about six orders of magnitude variation of the body mass of animals. The study shows that it exists a linear relationship between the total metabolic energy per life span PT_{ls} (kJ) and the body mass M (kg) of 95 mammals (3 monotremes, Subclass Prototheria, 16 marsupialis (Subclass Theria, Infraclass Metatheria) and 76 placentals (Subclass Theria, Infraclass Eutheria)) from type: $PT_{ls} = A_{ls}{}^{+}M^{1.0511}$, where P (kJ/day) is the basal rate of metabolism and T_{ls} (days) is the mean life span of animals. The linear coefficient $A_{ls}{}^{+} = 7.158 \times 10^5$ kJ/kg is the total metabolic energy, exhausted during the life span per 1 kg body mass of the animals. The mean values of the total metabolic energy per life span, per unit body mass (A_{ls}) for orders from Subclass Prototheria and Theria (Infraclass Metatheria) and orders Xenarthra, Pholidota, Soricomorpha, Rodentia (Infraclass Eutheria) varied negligible in interval $(4.656–5.80) \times 10^5$ kJ/kg. The coefficient A_{ls} grows from $(7.68–8.36) \times 10^5$ kJ/kg in Lagomorpha and Artiodactyla (Eutheria) to $(10.58–12.64) \times 10^5$ kJ/kg in orders Carnivora, Pinnipeda and Chiroptera (Eutheria). A_{ls} grows maximum to 18.5×10^5 kJ/kg in Primates. Thus, the values of coefficient A_{ls} differ maximum four-fold in all orders. Across the all species the values of A_{ls} are changes about one order of magnitude. Consequently, our survey shows that the changes of the body mass, basal metabolic rate and the life span of animals are three mutually related parameters, so that the product $A_{ls} = (PT_{ls})/M$ remains relatively constant in comparison to 1 million fold difference in body mass and total metabolic energy per life span between mammals.

Keywords: Mammals; Basal metabolic rate; Life span; Total metabolic energy

1. Introduction

The patterns existing between the other fundamental characters of living organisms and her body mass are generally described as a power function. The bioenergetic studies on animals (Hemmingsen, 1960; Kleiber, 1961; Schmidt-Nielsen, 1984; McNab, 1988; Speakman, 2005; Nagy, 2005) have shown that the rate of oxygen consumption P (kJ/day) is related to the body mass M (kg) as expressed by the equation of type $P = aM^k$, where a and k are allometric parameters. The study of this fundamental equation continues on theoretical and experimental level, concerning the effects of physical and physiological factors on metabolic rate: temperature (Gillooly et al., 2001), an allometric cascade that links the cellular and the whole animal metabolism (Darveau et al., 2002), changes of the power coefficient in equations $P = aM^k$ in evolutionary process of animals (Atanasov and Dimitrov, 2002), membranes and the setting of energy demand (Hulbert and Else,

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The Near to Linear Allometric Relationship Between the Total Metabolic Energy per Life Span and the Body Mass of Aves

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Abstract: The aim of this study is to establish and calculate the allometric relationship between the total metabolic energy per life span and the body mass in Passerine and Nonpasserine birds for maximum and life span in captivity. The study shows that it exists near to linear relationship between the total metabolic energy per life span PTls (kJ) and the body mass M (kg) of birds from the type: $PT_{ls} = A^0_{ls}M^k$, where P (kJ day^{-1}) is the basal metabolic rate, Tls (day) is the life span (maximum or life span in captivity) and A^0_{ls} (kJ kg^{-1}) is the total metabolic energy, exhausted during the life span per 1 kg body mass of birds. The received results show that for all birds, the power coefficient (k) in the 'lifespan metabolism-mass' relationship fall in the interval 0.8776-0.934 (for maximum and life span in captivity). For maximum life span the power coefficient k for all birds is 0.904 ($R^2 = 0.976$) and separately for Passerine it is 0.935 ($R^2 = 0.987$), for Nonpasserine it is 0.926 ($R^2 = 0.98$). The linear coefficient A^0_{ls} for all birds is 26.866×10^5 kJ kg^{-1} and separately for Passerine it is $36,728\times10^5$ kJ kg^{-1}, for Nonpasserine it is 25.199×10^5 kJ kg^{-1}. Possibly, the linearity between lifespan metabolic energy and body mass expresses a general allometric law in animal energetics, since it is valid for Poikilothetms, Mammals and approximately for Aves.

Key words: Aves, basal metabolic rate, lifespan, total metabolic energy

INTRODUCTION

The patterns existing between the other fundamental characters of living organisms and their body mass are generally described as a power function. The bioenergetic studies on Aves (Hemmingsen, 1960; Kleiber, 1961; Schmidt-Nielsen, 1984) have shown that the basal metabolic rate (P) in birds is related to the body mass (M) as expressed by the equation of type $P = aM^k$, where a and k are allometric parameters.

Lasiewski and Dawson (1967) divide the birds into 2 big groups, respectively basal metabolic rate: Passeriformes (with higher metabolic rate) and Nonpasseriformes (with smaller metabolic rate). Lasiewski and Dawson have found that for all birds the basal metabolic rate (P, kcald^{-1}) is related to the body mass (M, kg) as $P = 86.4M^{0.668}$, separately for Passerine as $P = 129M^{0.724}$ and for Nonpasserine as $P = 78.3M^{0.723}$.

On the contrary, Rezende *et al.* (2002) analyzed and compared the scaling of basal and maximal thermogenic metabolic rates in Passerine and Nonpasserine birds using conventional and phylogenetic methods. They found no statistical differences in the scaling of avian (Passerine and Nonpasserine) energetics.

Aschoff and Pohl (1970a, b) divide the birds into duirnal and nocturnal, respectively basal metabolic rate too. If the period of the normal activity of the birds is signed by • and period of relaxation is signed by •, Aschoff and Pohl for Passerine birds have received $P_{\bullet} = 140.9M^{0.704}$ and $P_{\bullet} = 114.8M^{0.726}$. For Nonpasserine birds have received $P_{\bullet} = 91.0M^{0.729}$ and $P_{\bullet} = 73.5M^{0.734}$, respectively (where P in kcal d^{-1}; M in kg).

Bennett and Harvey (1987) have received that the basal metabolic rate in all birds is proportional to body surface i.e. power coefficient k in 'metabolism-mass' relationship is near to 0.67.

Speakman (2005) have analysed data for basal metabolic rate in birds and have received the same result. The 'metabolism-mass' relationship for all birds is from the type $P = 3.4M^{0.671}$ with $R^2 = 0.958$ (where P in kJ d^{-1} and M in g). The power coefficient 0.671 showed that the basal metabolism is propotional to body surface.

Nagy (1987, 2005) measuring field metabolic rate in birds using the doubly labeled water method have received the similar power coefficient, but 3-fold higher linear coefficient $P = 10.5M^{0.681}$ with $R^2 = 0.938$ (where P in kJ d^{-1}; M in g).

REVIEW PB

SYNTHETIC AND NATURAL PEPTIDES AS ANTITHROMBOTIC AGENTS - A VIEW ON THE CURRENT DEVELOPMENT

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ABSTRACT

A view on the current development of synthesis as well as isolation of antithrombotic agents of peptide origin is presented. The structure and action of several anticoagulant peptides/proteins isolated from animal sources during the last 20 years are described. The synthesis of peptide mimetics manifesting even weaker anticoagulant activity is discussed as a main studies purpose. Compounds of both polysaccharides and peptide origin possessing inhibition of platelet aggregation isolated from microbial, animal and plant origin are summarized. Current investigations on a fraction (MW 100-120 kDa) isolated from goat's rue (Galega officinalis L.) appears to have a polysaccharide nature, including a protein part that is presented with special attention due to the high anti-aggregating activity, especially initiated by adenosine diphosphate, collagen and thrombin.

Keywords: antithrombotic agents, anticoagulants, trombin inhibitors, antiaggregants, natural and synthetic peptides, antiaggregants, *Galega officinalis* L.

Introduction

Antithrombotic agents are widely used in the medicine for treatments of hemostatic impairments such as coronary angioplasts, coronary thromboembolisms, myocard heart attack, pulmonary embolism, etc. Haemostasis is a key process whose correct functioning is an important defence 1process activated in case of injury of the blood system. Coagulation is a defence function of the organism that has to be strictly regulated. After the bleeding is stopped, a number of limiting self-regulatory mechanisms are initiated. This process is accompanied by a series of enzyme reactions described in 1964 as an enzyme cascade (44).

The living organisms have natural mechanisms to overcome clotting processes, the thrombolytic processes and other physiological disorders. This is affected *via* different substances with defence function called antithrombocytes. They include inhibitors of thrombin, factor Xa, Factor IXa, factors participating in the extrinsic and intrinsic pathways of the coagulation cascade (13).

The inhibitors of serine proteinases are a large class of proteins which is divided into families according to their structure and mechanism of action. Most inhibitors of coagulation factors of the intrinsic pathway are members of the *serpin* family. On the other hand, inhibitors of the extrinsic pathway such as hirudin and antistasin are classified as members of the family of Kunitz type inhibitors (39).

It is well recognized now that the success for the prevention and the treatment of arterial diseases closely relates with the necessity for better anti-thrombus therapy to avoid the clots complications. The crucial role of the thrombin in the pathophysiological mechanisms of anticoagulant and antiaggregation processes has been clearly demonstrated (13) in numbers of studies published in the last ten years (**Fig. 1**).

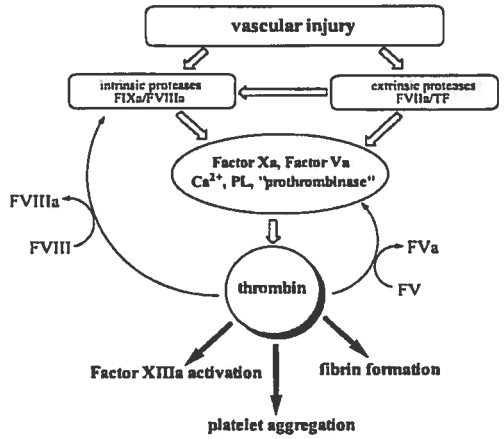

Fig. 1. Simplified scheme of the coagulation-aggregation system connection

Thrombin is a serine protease included in the blood coagulation cascade which in the same time also plays a key role in the process of thrombin-induced platelet aggregation. In eighties, after disclosing the close relationship between the two processes: aggregation and coagulation, it was revealed that a numbers of natural anticoagulants display antiaggregation properties, due to their ability to inhibit the thrombin (11, 58). In this global context some previous investigations on the fragment analogues of decorsin, protein with well established antiaggregation properties reveal that it possess anticoagulant activities too (62, 63, 84).

Natural inhibitors of serine proteases

In the last 20 years a number of proteins and peptides with different molecule mass and well established anticoagulation

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INHIBITING EFFECT OF DESALTED EXTRACT FROM *GALEGA OFFICINALIS L.* ON PLATELET AGGREGATION

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SUMMARY

The inhibiting and disaggregating effect of desalted and fractionated herbal extract of Galega officinalis L. on platelet aggregation in vitro is studied. At a concentration of 35 μg/ml in a platelet-rich plasma (PRP) the fraction inhibits 50% of aggregation by ADP and at 125 μg/ml PRP it inhibits fully the aggregation of PRP by ADP. At a concentration of 40 μg/ml PRP the fraction inhibits the initiation of platelet aggregation by collagen and at 50 μg/ml PRP inhibits the initiation of aggregation by thrombin. At a concentration of 65 μg/ml PRP the fraction can disaggregate 50% of the aggregated platelet-rich plasma by ADP and 25% of aggregated PRP by collagen.

Keywords: *Galega officinalis L.*, extract, inhibition, platelet aggregation

INTRODUCTION

Galega officinalis L. is a plant used in the traditional medicinal system of Bulgaria and Italy1 in the treatment of diabetes mellitus. Galegine, a biologically active alkaloid, exhibiting a hypoglycemic effect in vivo, was isolated from Galega officinalis[2]. Recent research[3,4] has shown that the 2.25% crude aqueous extracts of this plant in a dose of 1.0-2.5 mg/ml PRP suppress in vitro platelet aggregation induced by aggregating agents such as ADP, epinephrine, thrombin and collagen. Introduced in the caudal vein of rats in a ratio of one part 2.5% extract per 40 parts blood, the crude extracts of *Galega officinalis L.* suppress in vivo platelet aggregation in rats for 2.5-3.0 hours[5]. The aqueous extract of *Galega officinalis L.* has a synergic effect on platelet aggregation in common with anti-aggregant agents such as aspirin, dipyridamol, ticlopidine, sulfin-pyrazone, indobufenum, digoxin, theophyline and other drugs with similar action[6]. Biologically-active compounds with anti-aggregating action had not been isolated from *Galega officinalis L.* up to 1990.

MATERIALS AND METHODS

Plant material and preparation of extract. The aerial parts of *Galega officinalis L.* (*Herba Galegae*) at flowering stage were collected and used. The crude aqueous extract was obtained by maceration of 150 g dry matter in 2000 ml distilled water for 20-24 hours at 18-20°C. The fresh extract was corrected to pH 7.0 with NH_3 and centrifuged at 150 g after 1 hour. The supernatant was filtered and concentrated at a temperature below 35°C to extract with dry matter about 165-170 mg/ml.

Gel-filtration on Sephadex G-25. The concentrated extract (10 ml) was applied to column (600 mm x 55 mm) equilibrated with NH_3 buffer, pH 7. The column was

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Pharmacologie

EFFECT OF NITROXYL RADICALS ON HUMAN PLATELET AGGREGATION IN VITRO

Z. Raikov, A. Atanasov

(*Submitted by Academician E. Golovinsky on December 12, 1999*)

Introduction. A comparison of more important physical, chemical and biological properties of nitrogen oxide ($NO^{\cdot}$) and free stable nitroxyl radicals (nitroxides) on the reason of their structural similarity was made in our recent article [1]. Like $NO^{\cdot}$, nitroxides exhibit superoxide anion ($O_2^{\cdot}$) scavenging activity and so, they exert superoxide dismutase (SOD) mimetic action [2].

Bearing in mind, on the one hand, the structural similarity of $NO^{\cdot}$ and nitroxides and, on the other hand, $NO^{\cdot}$ inhibition on platelet aggregation [3-5], we aimed to study the effect of some nitroxides on platelet aggregation in vitro and to compare it with those of some drugs. The results of this investigation are presented in the article.

Materials and methods. REAGENTS AND DRUGS. Adenosine 5′-diphosphate (ADP) and Cadaverine are from Reanal (Hungary); Dipyridamol, Aspirin, Sodium salicylate ($C_7H_5NaO_3$) from Pharmachim (Bulgaria). Nitroxyl free radicals were from Aldrich.

ISOLATION OF HUMAN PLATELETS. Blood was taken from volunteers who had received no medication for 15 days prior to blood collection. Blood was collected in disposable syringes at a ratio of 1 part 3.8% trisodium citrate and 9 parts venous blood [6]. Platelet-rich plasma (PRP) was prepared by centrifugation (180 × g for 10 min) and diluted to 300×10^6 platelets per 1 ml autologous platelet-poor plasma (1800 × g for 15 min).

PLATELET AGGREGATION. Aggregation was studied by a spectrophotometer set to c rate at wavelength 600 nm, and the results were recorded on an electronic recorder [XY-recorder en dim 620 02 VEB, Germany].

The absorption change that takes place during the aggregation of 400 μl platelet-rich plasma compared with platelet-poor plasma (whose absorption was taken as zero) after adding 20–50 μl aggregating agents (2 μM ADP and 0.2 U/l thrombine—final concentration) at 37 °C and a rate at stirring of 1000 rpm was the basis of measurement for aggregating effects [8]. The substances studied were added to the rich platelet plasma with stirring and after 5 min aggregating agents (ADP or thrombine) were added.

Results and discussion. The nitroxides whose effect on platelet aggregation was studied are presented in Fig. 1.

The effects on the platelet aggregation of three nitroxides from the group of 4-R-(2,2,6,6-tetramethyl-piperidine-1-oxyl) [TMPO] expressed by the compound concentration inhibiting 50% of the aggregation ($IC_{50\%}$), are presented in Table 1. IC_{50} of some drugs commonly used as antiaggregating agents are presented in Table 1, too.

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ORIGINAL ARTICLES

Experimental Investigations

ANTI-AGGREGATION ACTIVITY OF CRUDE WATER EXTRACT OF GALEGA OFFICINALIS L. FRACTIONATED ON SEPHADEX G-25 AND SEPHAROSE 4B

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SUMMARY

The present study describes a method for preparation of biologically active fraction from crude water extract of *Galega officinalis* L. by gel filtration on Sephadex G-25 and Sepharose 4B. In an in vitro experiment (at a dose of 12.0±0.45 μg/ml) fractionated extracts inhibited adenosine diphosphate (ADF) induced platelet aggregation by 50%. Inhibitory effects on collagen (0.18 mg/ml) and thrombin (0.7 U/ml) induced platelet aggregation were observed at doses of 0.18±0.65 μg/ml and 20±0.82 μg/ml, respectively. The optimum activity was observed at a temperature of 30-42°C. It was found that the fraction contained 15.23% protein. As shown by amino acid analysis several amino acids (alanine, glycine, valine, lysine, asparagine, arginine and serine) accounted for 50% of its protein content. These amino acids formed tri- and tetrapeptides (RGD, RGDS, KRDS, RGDS), which inhibited platelet aggregation. The RGD and AGVD fibrinogen amino acid sequences responsible for the recognition and binding to the glycoprotein IIb/IIIa receptors consisted of the same amino acids.

Key words: *Galega officinalis L., fractionation, inhibitory effect, platelet aggregation*

INTRODUCTION

The herbal plant Galega officinalis L. is a major part of the Bulgarian and Italian traditional medicine. It has been used in the treatment of diabetes mellitus[1]. More than 15 biologically active substances have been isolated from Galega officinalis L.: alkaloids[2], flavonoids[3], glucosides[4], saponins[5], etc. Lipids, proteins and cellulose are also detectable in the plant by phytochemical analysis[6]. Platelet aggregation inhibitors have not been isolated so far. Previous experiments[7,9] have shown that Gallega officinalis L. water extracts inhibit in vitro and in vivo platelet aggregation induced by ADF, epinephrine, thrombin and collagen. Desalinated on Sephadex G-25 fractionated water extract from G. officinalis L. is 35 to 36 times more potent platelet aggregation inhibitor than the crude water extract[9,10].

This study was focused on: 1. development of a method for fraction purification; 2. identification of the biologically active substances; 3. investigation of its effects on platelet aggregation.

MATERIALS AND METHODS

Plant material

The epigeous parts of the plant were collected during the flowering season (May through August, Thracian valley, Bulgaria). The plant was identified at the Department of Botany, Academy of Medicine, Sofia (voucher specimen 12186).

Correspondence and reprint request to: A. Atanasov, Department of Biophysics, Medical Faculty, Thracian University, Stara Zagora
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ДОКЛАДИ

НА БЪЛГАРСКАТА АКАДЕМИЯ НА НАУКИТЕ

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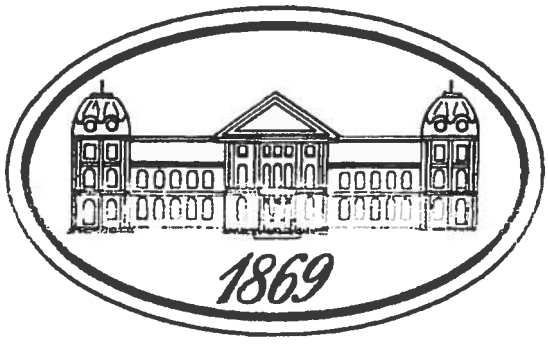

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CHIMIE
Biochimie

ON THE CHEMICAL COMPOSITION OF A FRACTION FROM *GALEGA OFFICINALIS* L. WITH ANTI-AGGREGATING ACTIVITY ON PLATELET

A. Atanasov, B. Tchorbanov*

(*Submitted by Academician E. Golovinsky on March 17, 2003*)

Abstract

The chemical composition of a purified fraction from *Galega officinalis* consists of about 74% polysaccharide and 23% protein part. The inhibiting effect of the fraction on platelet aggregation induced by adenosine 5′-diphosphate and collagen was higher than activity of theophylline (30 times) and of aspirin (140 times), respectively.

Key words: *Galega officinalis* L., chemical composition, anti-aggregating activity on platelet

Galega officinalis L. is a plant used in the traditional medicine for treatment of *diabetes mellitus*. Recent results by ATANASOV [1,2] show that crude aqueous extract of this plant suppresses in vitro and in vivo platelet aggregation induced by aggregating agents such as adenosine 5′-diphosphate, epinephrine, thrombin and collagen. The isolation of a fraction (molecular mass of 100–140 kDa) from *G. officinalis* L. exceeding the activity of the known anti-aggregants is described in our previous work [3].

The aim of this study is to carry out an additional purification of the fraction; to clarify the chemical composition by amino-acid analysis, near-infrared spectrometry as well as to demonstrate its biological activity.

Materials and methods. Fraction from *Galega officinalis* L. with anti-aggregating activity on platelet aggregation isolated according to [3] with inhibiting concentration (IC_{50} of 11 μg/ml platelet-rich plasma) was used in this study. The lyophilized desalted material (24 mg) from DEAE-Cellulose column was applied on a Sephadex G-100 (52 × 1.6 cm) column, equilibrated with 0.01 M Tris-HCl, pH 7.3. The active fraction was eluted by the start buffer at flow rate of 16 ml per hour and it was desalted on a Sephadex G-25 column and lyophilized.

The protein content of the active fraction was determined by the method of BRADFORD [4] as well as by amino acid analysis. The amino-acid composition of the fraction was determined after 24 h hydrolysis at 110 °C with 5.7 M HCl on an Amino acid analyzer T 339 M (Microtechna, Prague).

This paper was presented on the 3rd Bulgarian Symposium on Peptides, May 17–19, 2002, Panichishte, SW Rila Mountain region, Bulgaria.

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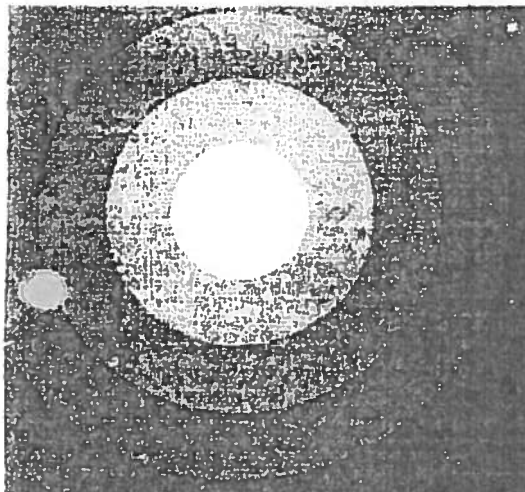

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Регистрация на дишането, сънните и носни цикли на човек

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АБСТРАКТ

Хипотеза. Регистрацията на амплитудата на дишането отделно през лявата и дясна ноздра дава възможност при подходяща скорост на записа да се регистрират сънните и носни цикли

Метод. Регистрацията на дишането от всяка ноздра се извършва при скорост на записа - 7500 mm/h, регистрацията на сънните цикли при скорост на записа- 240-600mm/h, а регистрация на носните цикли при скорост на записа- 20-60mm/h.

Резултати. Представена е методика и апаратура, с която са направени записи на дишането, сънните и носни цикли на човек.

Заключение. Методиката дава възможност едновременно да се регистрират дишането, сънните и носни цикли на хора през деня, по време на сън и при отоларинголожки интервенции.

Ключови думи: дишане, сънен цикъл, носен цикъл.

Pro Otology - Supplement: 81-83, 2003

ABSTRACT

Registration of Breating, Sleep and Nasal Cycles for Human.
At. Atanasov.

Hypothesis: Registration of amplitude of breathing trough left and right nostril separately make possible registration of sleep and nasal cycles, by change of speed of record

Method: Registration of breathing from each nostril must be made at speed of record- 7500mm/h, for registration of the sleep cycles, at speed of record - 240-600mm/h and for registration of the nasal cycle, at spped of paper – 20 - 60mm/h.

Results: In manuscript is presented the method, aparatures and the records of breathing, sleep and nasal cycles for human.

Conclusion: The method give possibility to registrate the breathing, sleep and nasal cycles during daytime, sleep and rhinology intervention.

Key words: Breathing, Sleep cycle, Nasal cycle.

Pro Otology - Supplement: 81-83, 2003

ВЪВЕДЕНИЕ

Температурната разлика на издишвания въздух от лявата и дясна ноздра, поради различното назално съпротивление в норма е от 1(С до 3(С (1, 2). При алтернативната смяна на проходимостта и назалното съпротивление на ноздрите, температурата на издишваните от тях въздушни потоци се сменя алтернативно. Сменят се и обемите на издишвания въздух от двете ноздри. В норма разликата в обемите на дихателния въдух през ноздрите е средно 1.0-3.5 пъти като с толкова се променя и количеството на издишваната с въздуха топлина. Измерването на температурната разлика и на количеството топлина, съдържаща се в издишвания от ноздрите въздух, дава възможност за едновременна регистрацията на дишането, назалния и сънните цикли (3, 4).

МЕТОД

Температурата на издишвания и вдишван от ноздрите въздух се измерва отделно с помощта на два термистора, инсталирани на пътя на въздушните потоци. Термисторите са монтирани в маска, която се закрепва върху носа на изследваното лице - Фиг.1(А, В).

В маската - два отворени цилиндъра с диаметър 1cm са леко вмъкнати в отворите на ноздрите и служат за насочване на дихателните потоци към термисторите.Тези два цилиндъра са вмъкнати в по-голям цилиндър с дължина 3,5cm и диаметър 1,5cm. Двата термистора са монтирани в големия цилиндър, коаксиално на ноздрите и техните въздушни потоци. Сигналът от всеки термистор се усилва с електронен усилвател с чувствителност 4-20 mV/1(С и регистрира от XY пишещо устройство (5, 6). Температурата на издишваният от ноздрите въздух е близка до телесната температура, а температурата на вдишвания от ноздрите въздух е равна на стайната температура. Това изисква температурата на стаята по време на измерванията да не се променя в рамките на (1-2(С. Записващото устройство мо-

Bulgarian Journal of Veterinary Medicine (2004), **7**, Suppl. 1, 29–33

ISOLATION AND CHEMICAL COMPOSITION OF A FRACTION FROM *GALEGA OFFICINALIS* L., INHIBITING PLATELET AGGREGATION

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Summary

Atanasov, A., B. Tchorbanov, Zh. Tsokeva and V. Spassov, 2004. Isolation and chemical composition of a fraction from *Galega officinalis* L., inhibiting platelet aggregation. *Bulg. J. Vet. Med.*, **7**, Suppl. 1, 29–33.

A fraction from crude extract of *Galega officinalis* L. has been purified by chromatography on Sephadex G-25, Sepharose 4B, DEAE-Cellulose and Sephadex G-100 column. The final purification factor of the fraction was 120. The peak in elution profile after Sephadex G-150 showed a molecular weight of 100-140 kDa. Active fragments with lower molecular mass were also detected. The isolated fraction appeared to have a polysaccharide nature, including 23 % of protein. The amino acid analysis of the fraction showed a protein content composed from almost all amino acids. The fraction compounds inhibited platelet aggregation induced by 25 μM ADP, 100 μg/mL collagen and 0.8 U/mL thrombin with IC_{50} 9.3 μg/mL for ADP and with IC_{100} 12.8 μg/mL and 15.1 μg/mL for collagen and thrombin respectively.

Key words: amino acid composition, extract, *Galega officinalis* L., platelet aggregation, polysaccharide-protein fraction

INTRODUCTION

Galega officinalis L. is a plant wide distributed in East Europe, Italy and Bulgaria. The plant is used in the traditional medicine of these countries in the treatment of *diabetes mellitus* (Benigni *et al.*, 1972). Over 15 biologically-active substances are isolated from *Galega officinalis*: alkaloids, flavonoids, glucosides, saponin and others. The biologically active alkaloid *galegine* (exhibiting a hypoglycaemic effect *in vivo*) was also isolated from *Galega officinalis* (Hoppe, 1975). Recent experimental results of Atanasov (1994) showed that *in vitro* the crude extract suppress platelet aggregation induced by ADP, thrombin and collagen. In this paper we report the purification and characterization of a final active fraction from crude extract of *Galega officinalis* L.

MATERIAL AND METHODS

Plant material, preparation of the extract and isolation of the active fraction

The aerial parts of *Galega officinalis* at flowering stage were collected in different parts of Trakia (Bulgaria). Crude extracts were obtained by maceration of 200 g dry matter in 2000 mL distilled water (pH 8 adjusted with sodium hydrogen carbonate) for 20–24 hours at 18–20 °C. Fresh ex-

Bulgarian Journal of Veterinary Medicine (2005), 8, No 1, 13–22

ALLOMETRIC RELATIONSHIP BETWEEN THE LENGTH OF PREGNANCY AND BODY WEIGHT IN MAMMALS

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Summary

Atanasov, A. T., 2005. Allometric relationship between the length of pregnancy and body weight in mammals. *Bulg. J. Vet. Med.*, **8**, No 1, 13–22.

The relationship between the length of pregnancy and the body weight in mammals – Metatheria and Placentalia, including 17 orders of animals with body weights ranging from 8 g to 15 t was investigated. It was found out that an allometric relationship existed, that could be described by the equation $T = 7.545 \times M^{0.2689}$, where T – pregnancy length in days, M – body weight in grammes, 7.545 – allometric coefficient, 0.2689 – power allometric coefficient.

Key words: body weight, length of pregnancy, mammals

INTRODUCTION

There are numerous scientific reports about allometric relationships between animal body weight and a number of physiological parameters (Kleiber, 1961; Schmidt-Nielsen, 1984; McNab, 1988) – the rate and frequency as traits of physiological and biochemical processes, metabolism rate (Ballard *et al.*, 1969), the biological half-life of various drugs (Lashev & Pashov, 1992; Lashev *et al.*, 1992, 1995; Pashov *et al.*, 1997; West *et al.*, 2002) etc.

From the point of view of practical and theoretical medicine, allometric relationships regarding the innate processes in animals are particularly interesting. Having studied numerous birds with body weights ranging from 2.5 g (colibri) to 1000 kg (epiornis) Rann & Ar (1974) revealed an allometric relationship between the incubation time and egg weight whereas Rahn *et al.* (1975) showed the link between incubation time and the weight of parent birds.

The studies upon the pregnancy in large varieties of animal species are scarce (Atanasov, 2004, 2005). With this connection, we investigated the presence of an allometric relationship between the body weight of mammals and the length of pregnancy as well as the influence of genotype on such a correlation.

MATERIALS AND METHODS

The data for the studied mammal species, their body weight and pregnancy lengths were collected from review papers (Walker, 1968; Markov, 1980; Grant, 1980; Maurice, 1962; Naumov & Kuzyakina, 1971) and original articles. The present investigation included 105 animal species from the Mammalia class from Metatheria and Placentalia subclasses and the following orders: Marsupialia, Insectivora, Chiroptera, Edentata, Pholidota,

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БЪЛГАРСКА МЕДИЦИНА, ТОМ XII, БР. 5 • 2004 • BULGARIAN MEDICINE, VOL. XII, N 5

ЛИНЕЙНА ЗАВИСИМОСТ МЕЖДУ ПЪЛНАТА МЕТАБОЛИТНА ЕНЕРГИЯ ЗА ЕДИН ЖИВОТ И ТЕЛЕСНАТА МАСА ПРИ ПОЙКИЛОТЕРМНИТЕ ЖИВОТНИ

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LINEAR RELATIONSHIP BETWEEN THE TOTAL METABOLIC ENERGY PER LIFE SPAN AND THE BODY MASS OF POIKILOTHERMIC ANIMALS

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Рецензент на статията: доц. д-р Ив. Таневб дбн

РЕЗЮМЕ. *При 54 пойкилотермни животни от различни класове и групи: Protozoa, Nematoda, Mollusca, Asteroidae, Insecta, Arachnoidae, Crustacea, Pisces, Amphibia, Reptilia и Snakes е установена линейна зависимост между пълната метаболитна енергия изразходвана за един живот $P.T_k$ (kJ) и масата M(kg): $P.T_k = A_k.M$. Коефициентът $A_k = 2,85.10^4$ kJ/kg е пълната метаболитна енергия за един живот на 1 kg телесна маса. P(kJ/day) - скоростта на метаболизма, T_k - продължителността на живота на организмите. В сила е зависимостта $P.T_k \leq A_k(max).M$, където максималната стойност на коефициента $A_k(max) = 5,0.10^4$ kJ/kg е горната енергетична граница за пойкилотермните видове.*

КЛЮЧОВИ ДУМИ: *метаболитна енергия, продължителност на живота, пойкилотермни животни.*

INTRODUCTION. Handbooks of bioenergetics (1,2) show that the relation between oxygen consumption rate of animals and their body mass is expressed by the equation: $P = aM^k$, where P is the quantity of oxygen consumed or heat production per unit time (kJ/day), M - body mass of animals (kg), a and k - alometric coefficients. If T_k - is longevity of animals, the quantity - ($P.T_k$) is the total metabolic energy of animals per life span. The aim of this study is to establish the relationship between total metabolite energy per life span of poikilithermic animals and her body mass.

DATA AND METHODS. The study researches 54 poikilothermic species from different types and classes. Data for rate of basal metabolism P, body mass M and life span T (year, day, hours) of animals are collected from other scientific sources (1,2,3,4,5). The total metabolic energy per life span - $P.T_k$ (kJ) is calculated as product from velocity of metabolism P (kJ/day) and life span-T_k(day) for each animal. The total metabolic energy per life span per 1 kg body mass $A_k = (P.T_k)/M$, kJ/kg is calculated as a ratio of ($P.T_k$) and body mass M. A statistic package is used for calculations (5).

Data for body mass M, velocity of metabolism P and life span Tls of animals are: [Animal (name), body mass - M (kg), velocity of metabolism - P (kJ/day), life span - T_k (hour, day, year)]: *Protozoa* (1a). Bacteria, 1.10^{-15} kg, 48.10^{-12} kJ/day, 1 day; (1b). Bacteria, 1.10^{-15} kg, 240.10^{-12} kJ/d, 1d; (2). Azotobacter chroococcum, 1.10^{-15} kg, $4,82.10^{-10}$ kJ/d, 1d; (3a). Flagellata and Mastogophora, 1.10^{-13} kg, $14,47.10^{-10}$ kJ/d, 7d; (3b). Flagelata and Mastogophora, 1.10^{-13} kg, $28,94.10^{-10}$ kJ/d, 7d; (4). Saccharomyces cereviseae, 2.10^{-14} kg, $36,17.10^{-11}$ kJ/d, 7d; *Nematoda:* (5). Clymenella torquata, 50.10^{-6} kg, $7,1.10^{-3}$ kJ/d, 8y; (6). Clymenella mucosa, 109.10^{-6} kg, $13,93.10^{-3}$ kJ/d, 8y; (7). Climenella zonalis, 23.10^{-6} kg, $3,6.10^{-3}$ kJ/d, 8y; (8). Soil warm, 1.10^{-8} kg, $0,724.10^{-6}$ kJ/d, 10y; (9). Ascaris, $0,01.10^{-3}$ kg, $2,412.10^{-3}$ kJ/d, 5y; *Mollusca:* (10). Ancylus, $0,02.10^{-3}$ kg, $1,707.10^{-3}$ kJ/d, 10y; (11). Octopus, $0,02.10^{-3}$ kg, $2,7.10^{-3}$ kJ/d, 10y; (12). Lymnaea, $0,02.10^{-3}$ kg, $2,316.10^{-3}$ kJ/d, 10y; (13). Molusca, $3,10^{-3}$ kg, 0,1733 kJ/d, 10y; *Asteroidae:* (14). Asterias, 10.10^{-3} kg, 1,93 kJ/d, 7y; *Arthropoda (Insecta, Arachnoidae):* (15). Aranei (Phidiphor), $0,337.10^{-3}$ kg, $24,12.10^{-3}$ kJ/d, 8y; (16). Aranei (Achaeranea), $0,073.10^{-3}$ kg, $12,54.10^{-3}$ kJ/d, 6y; (17). Aranei (Phidippus), $0,568.10^{-3}$ kg, $25,48.10^{-3}$ kJ/d, 10y; (18). Porcellio, $0,082.10^{-3}$ kg, $3,8.10^{-3}$ kJ/d, 10y; (19). Lepisma-insecta, $0,0125.10^{-3}$ kg, 0,85 kJ/d, 7d; (20). Drozofila-insecta, $1,2.10^{-6}$ kg, $8,4.10^{-5}$ kJ/d, 21 d; *Arthropoda (Crustacea):* (21). Emerita, 15.10^{-3} kg, $795,96.10^{-3}$ kJ/d, 10y; (22). Orcomella, $2,39.10^{-3}$ kg, 203.10^{-3} kJ/d, 10y; (23). Laborchestia, $0,27.10^{-3}$ kg, $22,92.10^{-3}$ kJ/d, 10y; (24). Orconectes, 14.10^{-3} kg, 1,013 kJ/d, 10y; *Osteichthytes (Pisces):* (25). Cyprinus (Cyprinus carpio), 0,074 kg, 3,21 kJ/d, 12y; (26). Notothenia, 0,2 kg, 5,4 kJ/d, 24y ; (27). Chaenocephalus, 0,2 kg, 6,07 kJ/d, 24y; (28). Scyliorhinus, 0,149 kg, 4,3 kJ/d, 18y; (29). Mugil, 0,149 kg, 7,188 kJ/d, 18y; (30). Lampetra, 0,037 kg, 1,749 kJ/d, 12y; (31). Girella, 0,070 kg, 4,42 kJ/d, 12y; (32). Anguilla, 0,040 kg, 1,698 kJ/d, 12y; (33). Bagarius bagarius, 0,147 kg, 6,52 kJ/d, 25y; (34). Salvelinus alpinus, 0,112 kg, 11,075 kJ/d, 12y; (35). Catostomus catostomus, 0,070 kg, 3,678 kJ/d, 12y; (36). Ictalurus (Amiurus nebulosus), 0,127 kg, 4,288 kJ/d, 28y; *Amphibia:* (37). Frog (Rana), 32.10^{-3} kg, 0,852 kJ/d, 36y; (38). Frog (Acris), 30.10^{-3} kg, 1,447 kJ/d, 25y; (39). Salamandra atra, $13,4.10^{-3}$ kg, 0,482 kJ/d, 20y; *Reptilia:* (40). Agamidae (Amphibolurus), 373.10^{-3} kg, 25,18 kJ/d, 10y; (41). (Dipsosaurus), 64.10^{-3} kg, 0,965 kJ/d, 10y; (42). (Anolis), 5.10^{-3} kg, 0,281 kJ/d, 10y; (43). (Lasepta), $6,3.10^{-3}$ kg, 0,744 kJ/d, 10y; (44). Tortoise (Chrysemys), 0,25 kg, 4,48 kJ/d, 30y; (45). Tortoise (Pseudemys) 0,25 kg, 13,5 kJ/d, 30y; (46). Sauria (Iguana), 0,785 kg, 58,7 kJ/d, 20y; (47). Crocodile (Alligator), 49 kg, $1,83.10^{3}$ kJ/d, 40y; *Reptilia (Snakes):* (48). Boidae, 1,0 kg, 10 kJ/d, 30y; (49). Boidae, 10,0 kg, 100 kJ/d, 30y; (50). Colubridae, 0,080 kg, 1 kJ/d, 14y; (51). Piton, 5 kg, 17 kJ/d, 30y; (52). Eunectes, 11,3 kg, 114,5 kJ/d, 30y ; (53). Natrix, 0,084 kg, 2,834 kJ/d, 14y; (54). Grass-snake, 3,27 kg, 28,4 kJ/d, 30y.

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THE TOTAL METABOLIC ENERGY PER LIFE SPAN OF THE MAMMALS IS LINEAR PROPORTIONAL TO THE BODY MASS WITH LINEAR COEFFICIENT (7±0.5)x10^{5}kJ/kg

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ABSTRACT

Over a wide range of living species (90 mammals from mouse to elephant) was shown that there is positive correlation between the total metabolic energy per life span PT_{ls} (kJ) (rate of methabolism, kJ/day x life span, day) and body mass M(kg) from type: $PT_{ls} = A^{+}_{ls} M^{1.0358}$ (R=0.98, n=90) with mean linear coeficient A^{+}_{ls}= 6.7x10^{5}kJ/kg. Real slope of correlation line of total metabolic energy per life span on mass may be near to 1.0. The total metabolic energy per life span (per 1 kg body mass) - A_{ls} have a characteristic values for other orders of mammals, ranging from 3 x10^5 kJ/kg to 30 x10^5 kJ/kg, despite of 6 orders of magnitude in rate of metabolism and the body mass of animals. The value A_{ls} is the ' energy capacity of 1kg' living body mass. The study shows that 1 kg body mass of mammals consumes nearly equal amount of metabolic energy during all life. Exhausting of this energy amount leads to biological death.

Key words: rate of metabolism, metabolic energy, body mass, life span

INTRODUCTION

The power relationship between the rate of metabolism P and body mass M of animals is expressed by the law of Kleiber (1, 2): $P=aM^k$, where a, k-are alometric constants characteristic for every class and order of animals (3.4). The attempt to explain the decrease of the intensity of metabolism P/M , that is observed with the increase of the body mass of the animals continue of experimental and theoretical level (5,6), becouse this power dependence is fundamental for energetics of living organisms. The introducing of the life span T_{ls} as a parameter (6, 7, 8, 9) give possibility to calculate the total metabolic energy per life span of animals in function of body mass.

DATA AND METHOD

The data for the rate of metabolism P(kJ/day) , body mass of species M(kg) are given from original scientific sourses (11, 12, 13, 14, 15, 16). The calculating data for the total metabolic energy per life span P T_{ls}(kJ) and for the total metabolic energy per life span (per 1 kg body mass)- A^{+}_{ls}(kJ/kg) for 90 mammals are given from original publications (7, 8, 9). The data for life span T_{ls}(day) are given from (17).

Data for body mass M, rate of metabolism P and life span T_{ls} of Mammals are: [Animal (name), body mass-M(kg), rate of metabolism-P(kJ/day), life span-T_{ls}(year)]: **class PROTHOTHERIA-order Monotremata** (1).Tachiglossus aculeatus, 2.5kg; 301.5kJ/d; 10 years;(2).Ornithorhynchus anatinus, 1.3kg; 228.6kJ/d; 8y;(3).Zaglossus bruijni, 10.3kg; 593.78kJ/d; 19y; ;**class METATHERIA- order Didelphoidea** (4).Lutreolina crassicaudata, 0.812kg; 198.3kJ/d; 7y; (5).Didelphis marsupialis, 1.329kg; 298.66kJ/d; 8y; **order Dasyurida** (6).Antechinus macdonnellensis, 0.0141kg; 9kJ/d; 2y; (7).Antechinus stuarti, 0.0365kg; 17.6kJ/d; 3y;
(8).Antechinomus laniger, 0.0085kg; 5.166kJ/d; 2y; (9).Dasyuroides burnei, 0.089kg; 37.35kJ/d; 3y;(10).Isodon macroorus, 1kg; 200.9kJ/d; 6y; (11). Perameles nasuta, 0.645kg; 152, 46kJ/d; 5.5y; (12).Planigale maculata, 0.0131kg; 9.64kJ/d; 2y; (13). Sminthopsis crassicaudata,

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LINEAR ALLOMETRIC RELATIONSHIP BETWEEN TOTAL METABOLIC ENERGY PER LIFE SPAN AND BODY MASS OF TERRESTRIAL MAMMALS IN CAPTIVITY

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Summary

Atanasov, A.T., 2006. Linear allometric relationship between total metabolic energy per life span and body mass of terrestrial mammals in captivity. *Bulg. J. Vet. Med.*, 9, No 3, 159–174.

The biocnergetic studies on animals have shown that basal metabolic rate P (kJ/d), is related to the body mass M (kg) of animals as expressed by the equation: $P = aM^k$, where a and k are allometric coefficients. The aim of this study was to investigate the allometric relationship between the total metabolic energy per life span $P_{ls} = PT_{ls}$, where T_{ls} is the life span, and the body mass of terrestrial mammals in captivity. Using statistical analyses it was shown that in 86 terrestrial mammals (Prototheria, Metatheria and Eutheria), a linear relationship between total metabolic energy per life span (PTls, kJ) and body mass (M, kg) existed: $PT_{ls} = A^{+}_{ls} M^{0.968}$, where T_{ls} (d) is the life span of animals in captivity in days, calculated from formula of Sacher $T_{ls}(y) = 11.8 \times M^{0.20}$ and the linear coefficient $A^{+}_{ls} = 11.407 \times 10^5$ kJ/kg is the total metabolic energy, expended during the life span per 1 kg body mass of animals with physical dimension of "potential". This linear coefficient can be regarded as relatively constant metabolic parameter for all terrestrial mammals, in spite of 6-degree differences between basal metabolic rate and body mass of animals. A mean values of linear coefficient $\bar{A}_{ls}$ for 13 studied orders (Monotremata, Didelphimorphia, Dasyuromorphia, Peramelemorphia, Diprotodontia, Xenarthra, Pholidota, Rodentia, Lagomorpha, Artiodactyla, Carnivora, Chiroptera, Primates) grow from 5.6×10^5 kJ/kg in Didelphimorphia to 18.1×10^5 kJ/kg in Monkeys. It was shown that from the view of classical physics, the basal metabolic rate could be expressed as: $P = (A_{ls} a_{ch} M)/R_{ch}$, where A_{ls} – total metabolic energy per life span, per 1kg body mass, R_{ch} = body (volume/surface) ratio of organisms and $a_{ch} = R_{ch}/T_{ls}$ (m/s) – characteristics speed with values $5 \times 10^{-10} \div 2 \times 10^{-11}$ (m/s). The conventional 'metabolic force' $F_{met} = P/a_{ch} = (A_{ls}M)/R_{ch}$, related to basal metabolic rate P, was expressed as a function of metabolic potential (A_{ls}), body mass (M) and conventional length (R_{ch}), which is characteristics length for every organism.

Key words: force, gravitation, life span, mammals, metabolic energy

INTRODUCTION

The pattern existing between various fundamental characters of living organisms and their body size or mass are generally described as a power function called 'allometric'. The bioenergetic studies on poikilothermic, mammals and aves (Hemmingsen, 1960; Kleiber, 1961; Hofman, 1983; Heusner, 1985; McNab, 1988; Gillooly *et al.*, 2001) have shown that the basal metabolic rate (P, kJ/d) is related to the body mass (M, kg) as expressed by the equation of the type $P=aM^k$. The biological meaning of linear and power coefficients a and k is connected with evolutionary range of animals (Zotin & Lamprecht, 1996; Atana-

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THE NEAR TO LINEAR ALLOMETRIC RELATIONSHIP BETWEEN TOTAL METABOLIC ENERGY PER LIFE SPAN AND BODY MASS OF NONPASSERINE BIRDS

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Summary

Atanasov, A. T., 2007. The near to linear allometric relationship between total metabolic energy per life span and body mass of nonpasserine birds. *Bulg. J. Vet. Med.*, **10**, No 4, ... – ...

The bioenergetic studies on animals have shown that the basal rate of metabolism P(kJ/d) is related to the body mass M (kg) of the animals as expressed by the equation $P=aM^k$, where a and k are allometric coefficients. The aim of this study was to investigate the allometric connection between the total metabolic energy per life span PTls (kJ) and the body mass M (kg) of nonpasserine birds (with Tls – life span in days). Using statistical analyses it was shown that a near to linear relationship existed between the total metabolic energy per life span and the body mass of nonpasserine birds (class Aves), belonging to 23 orders (Struthioniformes, Rheiformes, Casuariiformes, Apterygiformes, Sphenisciformes, Procellariiformes, Pelecaniformes, Ciconiiformes, Anseriformes, Charadriiformes, Columbiformes, Falconiformes, Galliformes, Gruiformes, Psittaciformes, Cuculiformes, Strigiformes, Caprimulgiformes, Apodiformes, Coliiformes, Trogoniformes, Coraciiformes and Piciformes) of the type: $PT_{ls}= A^0_{ls} \times M^{0.939}$ with correlation coefficient of $R^2=0.97$. The linear coefficient $A^0_{ls} = 29.4\times10^5$ kJ/kg is the total metabolic energy, exhausted during the life span per 1 kg body mass of birds. This linear coefficient can be regarded as a relatively constant metabolic parameter for nonpasserine birds, in spite of 10^5 fold differences between the body mass of birds. The mean values of linear coefficient $\bar{A}_{ls}$ for the 23 studied orders differed 4.65 times between big birds (order Struthioniformes) and small birds (order Psittaciformes), since $\bar{A}_{ls}$ grew from 12.5×10^5 kJ/kg in order Struthioniformes to 58.13×10^5 kJ/kg in order Psittaciformes. The mean $\bar{A}_{ls}$ values for 23 orders were nearly multiple to 3×10^5kJ/kg. The energy of 3×10^5kJ/kg was exhausted from 1 kg body mass of big and small birds for the periods when the sexual maturity was reached.

Key words: basal rate of metabolism, life span, nonpasserine birds, total metabolic energy

INTRODUCTION

The patterns existing between body size or mass and the other fundamental features of living organisms are generally described by a power function called an 'allometric' one.

The bioenergetic studies on poikilothermic animals, mammals and birds (Hemmingsen, 1960; Kleiber, 1961; Schmidt-Nielsen, 1984; Heusner, 1985; McNab, 1988; Chen & Li, 2003; Agutter & Wheatley, 2004; Speakman, 2005) have shown that the basal rate of metabolism P(kJ/d) is related to the body mass M(kg) as expressed by an equation of type $P=aM^k$. The biological meaning of the linear coefficient a and the power coeffi-

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Original Contribution

THE ALLOMETRIC RELATIONSHIPS BETWEEN GRAVITATIONAL CONSTANT, MAX PLANCK CONSTANT AND BODY MASS, SIZE, GENERATION TIME, DENSITY AND SPEED OF GROWTH IN PROKARYOTES

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ABSTRACT

The study shows that there is an allometric relationship between the gravitational constant, the Planck's constant and the body mass, size, generation time, density and the speed of growth in prokaryotes. The allometric relationships are received on the basis of Max Planck's ratios between the gravitational constant $G=6.673x10^{-11}(N.m^2/kg^2)$, the Planck's constant $h=6.6262x10^{-34}$ (J.s) and the speed of light $c= 2.9979x10^8$ m/s. Max Planck and other theoretical physicists have calculated the fundamental physical quantum for mass: $M=(h.c/G)^{1/2}=2.176x10^{-8}$ kg, length: $L=(h.G/c^3)^{1/2}=1.616x10^{-35}$m, time: $T=(h.G/c^5)^{1/2}=5.389x10^{-44}$s, and density: $\rho=M/L^3\approx1.10^{97}$, kg/ m^3, using G, h and c constants in these ratios. If in Planck's relations we replace the speed of light 'c' with speed $v_{cell}= (8\pm0.16)x10^{-11}$m/s, equal to linear growth of prokaryotes, during multiplication of cells by binary fission: $v_{cell}=M_{cell}/(\rho_{cell}L_{cell}^2T_{gt})\approx L_{cell}/T_{gt}$ (where M_{cell}-body mass of cells in kg, ρ_{cell} -body density of cells in kg/m^3, L_{cell} - body length of cells in m, T_{cell}- generation time between multiplication in s), we can get the values for mass, size, generation time and the density, that is typical for small prokaryotes (Bacteria, Mycoplasmatales, Rickettsiales, Chlamydae).

Key words: Gravitational constant, Planck's constant, Prokaryotes, mass, size, density, generation time, allometric relationships.

INTRODUCTION

The pattern existing between the other characters of living organisms (metabolic, respiration and enzyme rate, heart and respiration frequency, organ weight, life span) and their body size or mass are generally described as a power function called 'allometric' The allometric equation was studied on theoretical and experimental level about 100 years ago, concerning mainly the connection between oxygen consumption and body mass of animals (Kleiber, 1961; Schmidt-Nielsen, 1984; Speakman, 2005; Nagy, 2005), aging and longevity in Mammals (Cutler, 1984); relationship between the total metabolic energy per life span and the body mass in animals (Atanasov, 2005a, b, c; 2006 a, b, c; 2007); the effect of temperature on metabolic rate (Gillooly et al., 2001), an allometric cascade that links the cellular and the whole animal metabolism (Darveau et al., 2002), changes of the linear and power coefficient in 'metabolism-mass' relationships (Zotin and Lamprecht, 1996; Atanasov and Dimitrov, 2002), membranes and the setting of energy demand (Hulbert and Else, 2005), re-calculation of 'metabolism-mass' equations using 'field metabolic rate' data (Speakman et al., 2002;Chaui-Berlinck et al., 2005; Speakman and Selman, 2003; White and Seymour, 2005; McLean and Speakman, 2000; Speakman et al., 2003, 2004; Selman et al., 2005).

Missing in the cited literature above are surveys on the relationship between the integral biological and physical characteristics of living organisms (such as body mass, body volume, body surface, body density) and fundamental physical constant of Universe.

From four fundamental physical forces and interactions (gravitational, weak, electrostatic and nuclear) the main role in the metabolic processes of the living world play the gravitational and electromagnetic

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THE CHANGE OF POWER COEFFICENT IN 'METABOLISM-MASS' RELATIONSHIP ACROSS LIFE'S TAXONS DURING EVOLUTION: PREDICTION FOR 'MASS-DEPENDENT METABOLIC MODEL'

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ABSTRACT

In this work we have to show that during the increasement of the order in the organisms from Unicellular to Plants, Poikilotherms and Homeotherms, the power coefficient in 'metabolism-mass' relationship $P=aM^k$ changes from taxa to taxa varying between the optimal value of k=0.85-0.90. The organisms with high complexity and differentiation (non-continuously growing organisms) are characterized with values of exponent k lower than 0.85-0.90. The organisms with low complexity, differentiation, and high growing processes (continuously growing organisms) are characterized with value of exponent k higher than 0.85-0.90. The ontogenetic organism has values of k around 0.85-0.90. Here, we presented for first time a new "mass-dependent metabolic model" based on connection between power coefficient k and growing processes.

Key words: metabolism, exponent, poikilotherms, mammals, aves, mass-dependent metabolism.

INTRODUCTION

Bioenergetics is connected with evolution of organisms. Handbooks of bioenergetics show that the basal metabolic rate (P, J/s) of animals is connected with their mass (M, kg) by the equation

$$P = aM^k \quad (1)$$

The coefficient a means a mass-specific metabolic rate for an organism with unit body mass (1g or 1kg). The biological mean of power coefficient (exponent) k is trouble.

Organismal complexity is positively correlated to body size (1, 2). Both size and complexity have increased throughout the evolutionary history of life (3, 4, 5).While these patterns are widely accepted, the mechanisms behind the evolution of organismal complexity are poorly understood (6). However, there is not any standard definition of complexity. McShea (7) provides several definitions for biological complexity. These include: the number of different parts within a hierarchy (genes, cells, organs, etc.), the number of interactions between parts in this hierarchy, the number of parts for a particular spatial or temporal scale and the number of interactions between parts in a spatial or temporal scale. Some conceptual models have linked the evolution of organismal complexity, measured by the number of cell types, with increasements in the body size of the organism (1, 2). Other conceptual models have connected the evolution of metabolic intensity, the mass specific rate of energetic processing for a given body mass, with body size (5, 8). However, none of these approaches have considered the mechanistic linkage between the number of cell types, body size and metabolic intensity. Interestingly, body size, complexity and metabolic intensity have all increased throughout macroevolution (9, 10). In the contrary, Makarieva et al. (11) have showed that the mean mass-specific metabolic rate is strikingly similar across life's major domains and has an evidence for life's metabolic optimum.

The scaling of basal metabolic rate with body mass (eqn. 1) has long been a controversial

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IN VITRO ЕФЕКТ НА ВОДНИТЕ ИЗВЛЕЦИ НА НЯКОИ ЛЕЧЕБНИ РАСТЕНИЯ ОТ БЪЛГАРСКАТА ФЛОРА ВЪРХУ ТРОМБОЦИТНАТА АГРЕГАЦИЯ

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РЕЗЮМЕ: *Разработен е високочувствителен метод за регистриране на потискащи тромбоцитната агрегация съставки в извлеците на лечебни растения. С помощта на същия метод са идентифицирани 10 лечебни растения, които съдържат такива съставки. Извлеците на две лечебни растения - Galega officinalis L. и Punica granatum L. потискат в значителна степен тромбоцитната агрегация. При останалите осем - Agrimonia eupatoria L., Cydonia oblonga Mill., Arctostaphyllos uva-ursi L. (Sprend.), Geum urbanum L., Dryopteris filix-mas (L.) schott, Corylus avellana L., Ephedra distachya L., Primula officinalis L. потискането е незначително, но в замяна на това извлеците на тези лечебни растения показват лектиноподобно действие, което се изразява в силно нарушаване на колоидния стабилитет на серумните и плазмени протеини и аглутиниращо действие върху еритроцитите на плъха и човека. Пет от тези лечебни растения не са регистрирани в научната литература като лектинсъдържащи.*

КЛЮЧОВИ ДУМИ: *лечебни растения, водни извлеци, in vitro, тромбоцитна агрегация.*

УВОД: Въздействието на различните природни и синтетични химични субстанции върху тромбоцитната агрегация представлява интерес за практиката във връзка с търсенето на нови лекарствени средства, необходими за лечението на заболявания, свързани с нарушения на хомеостаза (1). Един проблем, свързан с търсенето и идентифицирането на съставки, потискащи тромбоцитната агрегация в извлеците на лечебните растения, е ниската концентрация на тези съставки в извлеците. Това налага да се търсят експериментални условия, при които тромбоцитната суспензия, идентифицираща наличието на такива съставки, да бъде максимално чувствителна към потискащото им действие. В нашите експерименти това беше постигнато като използвахме плъша тромбоцитна плазма, разредена с разтвор на Хенкс без Ca^{2+} в подходящо съотношение, което я прави 5-6 пъти по-чувствителна към потискащи фактори в сравнение с човешката тромбоцитна плазма със същото съдържание на тромбоцити в плазмата.

МАТЕРИАЛИ И МЕТОДИ

Лечебните растения бяха получени комерсиално и идентифицирани в Катедрата по ботаника при Фармацевтичен факултет - София (България). Всички растения са събирани между май и септември по време на цъфтеж - 1992 година в различни части на Тракийската низина. Водните извлеци се получаваха чрез мацерация на 2 g сух материал от

IN VITRO EFFECT OF WATER EXTRACTS OF SOME MEDICINAL PLANTS FROM BULGARIAN FLORA ON PLATELET AGGREGATION

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SUMMARY: *A high-sensitive method for registration of compounds with inhibitory effect on platelet aggregation in water extracts from medicinal plants is elaborated. With the help of the same method 10 medicinal plants, containing those compounds are identified. Water extracts from two medicinal plants: Galega officinalis L. and Punica granatum L. inhibit considerably platelet aggregation. The other eight extracts of: Agrimonia eupatoria L., Cydonia oblonga Mill., Arctostaphyllos uva-ursi L. (Sprend.), Geum urbanum L., Dryopteris filix-mas (L.) schott, Corylus avellana L., Ephedra distachya L., Primula officinalis L. provide slight inhibition but in spite of that the extracts of these plants show lectin-like action, expressed by strong disturbance of colloidal stability of plasma and serum proteins and agglutinatory effect on rat and human erythrocytes. Five of these medicinal plants are not registered in scientific literature as lectin-containing.*

KEY WORDS: *medicinal plants, water extracts, in vitro, platelet aggregation.*

The effect of different natural and synthetic chemical substances on platelet aggregation is interesting for practice in connection with the search for new medicinal substances for treating patients with disrupted homeostasis [1]. One of the problems connected with searching and identification of compounds with inhibitory effect on platelet aggregation is their low concentration in plant extracts. This requires searching for experimental conditions, where platelet suspension identifying these compounds must be maximum sensitive to their inhibitory effect. In our experiments this was attained by using rat platelet-rich plasma diluted with solution of Hank's free of Ca^{2+} in suitable proportions. This made it 5 - 6 times more sensitive to inhibitory factors in comparison with human platelet-rich plasma containing the same platelets.

MATERIAL AND METHODS

Medicinal plants were received commercially and verified at Botany Department, Pharmacy Faculty - Sofia (Bulgaria). All plants were collected at different parts of the Thracian plain, Bulgaria, from May till September 1992 during their flowering stage. The water extracts were obtained by maceration of 2 g dry matter in 20 ml physiological saline (0.15 M solution of sodium chloride, pH 7.4) for 24 hours at 18-20°C (Table 1). Fresh extracts had been filtered twice, before studying the effect on platelet aggregation. The blood necessary for investigation on platelet aggregation [2] was taken under narcosis (15 mg sodium pentobarbital per 100 g body weight) from albino Wistar rats by means of an intracardial puncture. For a definite

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PNEUMATIC EJECTOR FOR INTRODUCTION OF MICROAMOUNTS OF CHEMICAL SUBSTANCES WITH AIR UNDER PRESSURE

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A block-scheme of pneumatic ejector for introduction of microamounts of substances with air under pressure is presented. Single ejector meetings are described in detail. Technical data about its components are given.

Key-words: pneumatic ejector, chemical substances, scheme, components.

It is sometimes necessary to introduce substances in minimal amounts (micro-, nano- and picoliters) in small volumes (cells, organs, and tissues) in biological and medical practice. For that purpose, different methods for pressure ejection of substances with air under pressure [1], by means of iontophoresis [2], etc. are elaborated. Every method possesses its advantages and disadvantages enabling its application in some or other cases [3, 4].

In the present work we offer a technical performance of a pneumatic ejector where chemical substance is put into a given area by means of short-acting pressure impulse of air under pressure. Scheme of ejector is demonstrated on fig. 1.

We shall describe every part of the ejector one by one.

1. Flask with inert gas under pressure

A flask with argon or nitrogen under pressure provided with a reducing valve is used. The chemical composition of the gas must not influence upon tissues. Work pressure is between 100 and 500 kPa. Rubber impregnated

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ELECTRONIC CIRCUIT OF DIFFERENTIAL APPLIANCE FOR SPECTROPHOTOMETERS OF «SPEKOL» TYPE FOR AUTOMATIZED RECEIPT AND RECORDING OF DIFFERENTIAL AGGREGOGRAM

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A circuit for differentiation of the initial signal of spectrophotometers of «SPEKOL» type is presented. The circuit is universal according to its capacities and can, therefore, be used for studying the kinetics of thrombocyte aggeregation, erythrocyte haemolysis, enzyme reactions, etc.

Key-words: differential appliance, circuit, aggregogram, thrombocytes.

The ratio between light permeability of thrombocyte-rich plasma and that of thrombocyte-free one is measured and graphically registered in order to evaluate thrombocyte aggregation capacity [1, 2]1 The change of this value designated as degree of thrombocyte aggregation reflects the course of aggregation process under the influence of a given aggregation inductor (ADP, adrenalin, collagen, etc.). After inductor supplementation to the plasma with thrombocytes at 37 °C and centrifugation of about 1000 g min ^{1} the change of light permeability Q % of the plasma during the aggregation process is registered. Light permeability value of thrombocyte rich plasma (approximately $200 - 300.10^{9}$ cells/l) in a «SPEKOL» adjusted with htrombocyte-poor plasma is considered 0 per cent of aggregation (or Q_0). Maximal lightening of plasma containing functionally normal thrombocytes after their aggregation under the aforementioned conditions is considered 100 per cent of aggregation (or Q_{max}). Interval between Q_0 and Q_{max} is divided into 10 parts of 10 per cent each. Aggregation degree is defined as:

$$A = \frac{Q - Q_a}{Q_{max} - Q_0} \ 100\ \%,$$

СЪЮЗ НА НАУЧНИТЕ МЕДИЦИНСКИ ДРУЖЕСТВА В БЪЛГАРИЯ
ДРУЖЕСТВО ПО БИОМЕДИЦИНСКА ФИЗИКА И ТЕХНИКА

МАТЕРИАЛИ

НА ШЕСТАТА НАЦИОНАЛНА КОНФЕРЕНЦИЯ ПО БИОМЕДИЦИНСКА ФИЗИКА И ТЕХНИКА С МЕЖДУНАРОДНО УЧАСТИЕ

София, 22 - 24 октомври 1992

DEVICE FOR MEASURING THE PLATELET AGGREGATION ON THE BASIS OF SPECTROPHOTOMETER "SPECOL -21" AND THE POSSIBILITIES FOR WORKING WITH IT

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The diagnosis of number of diseases, accompanied by disturbaces of the haemostasis necessitates to measure the degree and the rate of the platelet aggregation.

For this aim the mostly used method is Born's photometric [Born G.V., Nature, 1962, vol.194, p927] or subsequently elaborated impedance method [Cardinal D.C., Flower R.J., J. Pharmacol. Meth., 1980, vol.3, p.135]. In scientific literature can be observed different modification of these two methods, in which different laboratory apparatus are used.

At the present time the apparatus applied for studying the platelet aggregation is composed of spectral colorimeter " Specol -21", X-Y typing device "Specord", thermostatic apparat - hydro-thermostat and agitator-laboratory homogenisator with regulated revolutions for mixing of platelet suspension. The combination of separate apparatus into one siatem is represented in the figure.

One of the advantages of "Specol -21" is the availability of thermostatic devise, built in the apparatus for maintaing the temperature of the solution in the cuvet and also free access to the cuvet allowing the stirring of suspenaion to be accomplished with the help of laboratory homogenesator, equiped with a long mettalic axis, which terminates with plexiglass cap with right angle section 1X2 millimeter, dirsotly submerged in the platelet suspension. The end of the plexiglass cap must be located above the level of the optical ray of the spectrophotometer. The observation and the registration of the aggregation process can be accomplished by the changes in the optical density / E - extinction units/ or by the light photopermeability / Q, % /.

After preparation of platelet suspension, which contains a definite quantity of platelets / 200-300.10^6 in 1 ml/ according to the standard methods /Born G.V., Nature, 1962; Cardinal D.C. et all., J. Pharmacol. Meth., 1980/, the spectral colorimeter is adjusted against the plasma without platelets at a wavelength 550-600 nm in the cuvet with a width of 0,3 cm. In these conditions the introduction of 20 μl aggregating agent - 1.10^{-3} M adenosine diphosphate to 400 μl platelet plasma at 37°C temperature and rate of mixing of platelet 800-900 revoluti-

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НА ШЕСТАТА НАЦИОНАЛНА КОНФЕРЕНЦИЯ ПО БИОМЕДИЦИНСКА ФИЗИКА И ТЕХНИКА С МЕЖДУНАРОДНО УЧАСТИЕ

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APPLICATION OF TURBIDIMETRY AND VISUAL MICROSCOPICALLY METHOD FOR DETERMINATION OF THE PARAMETERS OF PLATELET AGGREGATION IN SCIENTIFIC INVESTIGATION

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For studing of platelet aggregation frequently is used Born's turbidimetric method, in which the increase of the photopermeability or the decrease of the optical density/extinction/ of platelet-rich plasma is registered.This change in photopermeability or optical density occurs as a result of reducing the amount of the free platelets in the plasma in the process of aggregation [Born G.V., Nature, 1962, vol.194, N 4832, p. 927].The necessary platelet-rich plasma for studing the platelet aggregation is obtained from venous blood, after removing the erythrocytes by standard method [Lisichkov T., Disorders of hemostatis, Sofia, Medicina, 1987].The plasma is adjusted up to 200-300.10^6 platelets in 1 ml.For initiation of aggregation process 50 µl aggregating agent /2.10^{-4} mol/L adenosine diphosphate, 1.10^{-4} mol/L epinephrine, 2 mg/ml collagen, thrombin and etc./ is added in the cuvet, which contains 500 µl platelet-rich plasma.In the process of aggregation the initial number Nmax of free platelets in plasma gradually decreases, as it reaches to a certain minimal number Nmin at the end of aggregation process.The reducing of the platelets in the plasma isaccompanied by degreasing of the extinction from value Emax at the beginning of the aggregation process up to value Emin at the end of aggregation process - Fig. / 1 curve/So that Nmax number of platelets in plasma correspond to the value of the extinction Emax, and Nmin number of platelets in plasma correspond to the value of the extinction Emin. The degree A, % of platelet aggregation, and rate V, extinc.units/min of platelet aggregation are calculated on the basis of the change of the extinction E in the process of aggregation and the time T, min which the process takes.[Howard M.A., Sawers R.J., Finkin B.C., Blood, 1973, vol.41, N5, p.667] by the relations: A =(Emax-Emin)/ Emax .100 % and rate . V =(Emax- Emin)/T ,extinc. units/min, where by Emax is the maximal value of the extinction at the beginning of the aggregation process, Emin is the minimal value of the extinction at the end of the aggregation process, T - is the duration of the aggregation process in minutes.

The determination of A, % and V on the basis of the number of the free platelets in plasma is accomplished by the relations [Tarasova N.I.

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THE DILATATION COLD WATER TEST OF THE FINGERS OF UPPER LIMBS

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One of the methods in the medical practise for the evaluation of the blood supply and the thermoregulation of the palms and the fingers is the cold water test[Wenger C.B., M.F. Roberts, E.R. Nadel, J.A. Stolwijk. Thermoregulatory control of ainger blood flow, J. Appl. Physiol, 38, 1975, p.78 ; Chronic arterial insufficiency of the extremites, Edited by Prof. Iv. Zanzov, St.Publ.House "Medicina i Fiskultura", Sofia, 1985, Bulgaria]. The technical implementation of the classical cold test is done by cooling the hands for 5 min in water bath at 12°C and measuring the time for restoration of initial temperature of the fingers throuh interval of 3 min at the level of pulp of the fingers.As the normal time for restoration of the temperature is regarded as the time between 10 and 20 minutes at avorage temperature of the fingers 28,5°C.During functional disturbance of the arterial supply the restoration takes a longer period of time 35-50 min. or more.One of the insufficiency of this method is relatively long time interval /from 10 to 50 min or more/ during which the skin temperature changes, by which it is difficult to register small changes /better or worse/ in the state of blood supply to the palms and fingers, which is important for the control of the treatment during the application of different drugs. For further improvement of this method, were studied the cold reactions of the fingers, after cooling them in the interval of temperatures from 2°C to 18°C for 2,5 min.The restoration of the initial temperature of the fingers was measured with a thermometer on the basis of "thermopair" with sizes 0,25 X 0,25 mm through intervals from 0,5 to 1 min on the level of the pulp of the fingers, with exactly 0,25 C.The cooling of the fingers is accomplished in a small container with the size 8X 8X 8 cm., by submerging every finger separately up to the second joint.During the time of cooling the water is mixed with agitator for better heat-exchange.The restoration of initial temperature of the third and fourth fingers/middle, ring fingers/ is represented graphically in Figure 1.From the figure it can be seen, that the curve of restoration of the initial temperature of these fingers, after cooling them from 2°C to 8°C is from the dilatation type with one and same slope, which shows the maximum rate of the restoration of initial temperature of the fingers.The curves of the restoration of the temperature after cooling at 10°C, 12°C, and 14°C can be characterized as

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РАЗПРЕДЕЛЕНИЕ НА ТЕМПЕРАТУРАТА ВЪРХУ НОРМАЛНА ТЪПАНЧЕВА МЕМБРАНА

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Summary. Dimov P D (Department of Otorhinolaryngology, Higher Medical Institute, 11 Armeiska str., Stara Zagora 6000 Bulgaria) and Atanasov A T. Distribution of local temperature on a normal tympanic membrane. Annual of the Higher Medical Institute of Stara Zagora [Bulgaria] 1996; 5: 11-12. The temperature of 33 tympanic membranes was measured by a direct touch of 'cooper-constantan' thermocouple (connected to a sensible millivoltmeter type 'V 540 Meratronik') to the membrane under surgery microscope. For studying the temperature distribution, seven zones on the tympanic membrane were conditionally chosen. It was found that the average temperature of the normal tympanic membrane was under 37°C. Differences were seen in the average local temperature among the seven zones.

Key words: *tympanic membrane, local temperature, millivoltmeter, thermocouple*

В медицинската литература има оскъдни данни за изменение на температурата на тъпанчевата мембрана [1, 2]. Известно е, че възпалителните и невъзпалителни заболявания на ухото протичат с промяна в локалната температура.

Целта на нашето изследване е да установим нормалните граници на локалното изменение на температурата при здрава тъпанчева мембрана.

МАТЕРИАЛ И МЕТОДИ

Обект на нашето обследване бяха 33 нормални тъпанчеви мембрани: 18 -- при мъже и 15 -- при жени. Целият контингент беше подложен на отоскопично изследване под операционен микроскоп 'Karl Zeis' за предварителна преценка на състоянието на мембраната. Бяха измерени локалните температури на следните седем зони: 1. Предно-горен квадрант; 2. Предно-долен квадрант; 3. Задно-долен квадрант; 4. Задно-горен квадрант; 5. Парс фласида на тъпанчевата мембрана; 6. Процесус бревис малеи; 7. Умбо на тъпанчевата мембрана. Измерването се извършваше под операционен микроскоп с директно допиране на мед-константанова термодвойка (Ф =0.2 mm) до предварително набелязаните точки от седемте зони. Термодвойката беше свързана към чувствителен миливолтметър тип 'V 540 Meratronik'. Чувствителността на така импровизирания електро-медицински термометър беше 0.2°C. Непосредствено преди и след всяко измерване, показанията на уреда се калибрираха с помощта на два термостата, единият от които беше настроен на 35°C, а другият -- на 40°C. Всички отоскопични и термометрични данни от изследванията бяха отбелязани на отделни листове и обработени статистически.

РЕЗУЛТАТИ И ОБСЪЖДАНЕ

Беше изчислена средната температура поотделно на всяка една от седемте зони на изследваните тъпанчеви мембрани(вж. Табл. 1).

Получените резултати показват, че има разлика в индивидуалните температури на тъпанчевата ципа на всеки пациент поотделно, като вариациите около средната температура на тъпанчето за едно ухо не надхвърлят 0.3°C.

Изчислените средни стойности на температурата в определените седем зони показват, че различните точки се характеризират с индивидуална температура, като последната нараства към 5, 6 и 7 точки. Температурата е най-висока в последните три точки. Средната обща температура на цялата тъпанчева мембрана при мъжете е 36.64°C, а при жените -- 36.81°C. Локалното разпределение на температурата в измерените седем точки при женските уши е по-висока от съответните точки при мъжете с около 0.2°C. Времето за замерване на локалната температура в седемте точки на тъпанчевата мембрана под микроскоп беше средно около 4 минути. Редно е да се изтъкне, че изследването се извършваше без анестезия.

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МЕДИЦИНСКИ ФАКУЛТЕТ - ТРАКИЙСКИ УНИВЕРСИТЕТ
FACULTY OF MEDICINE THRACIAN UNIVERSITY

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ЦИКЛИЧНИ ВАРИАЦИИ В ЧЕСТОТАТА НА РАЗПРОСТРАНЕНИЕ НА МОЗЪЧНО-СЪДОВАТА БОЛЕСТ В СТАРА ЗАГОРА (БЪЛГАРИЯ) ЗА ПЕРИОДА 1985-1988 Г.

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Summary. Dimitrov B D (Department of Social Medicine and Public Health, Higher Medical Institute, 11 Armeiska str., Stara Zagora 6000 Bulgaria), Atanasov A T and Guechev A G. Cyclic variations in the incidence rate of cerebro-vascular disease in Stara Zagora (Bulgaria) for the period 1985-1988. ***Annual of the Higher Medical Institute of Stara Zagora [Bulgaria] 1996; 5: 23-24.*** *Epidemiological study on monthly incidence of acute cerebro-vascular disease (CVD code -- ICD9, Dx:430-437) was carried out in The Stara Zagora Regional Clinical Hospital (cases registered from March 1985 to December 1988 incl.). All patients were 180 (aged 61.8 ± 10.5; 57.2% men, 42.8% women; 77.7% ischaemic, 22.3% hemorrhaged stroke). For particular study, the type of stroke was ignored. The periodogram regression analysis (PRA) revealed different cycles in monthly incidence rate variations of CVD for this region of Bulgaria (period T=2, 2.75 and 6.25 months, p<0.05). Phase-correlation analysis (PCA) and sigma-method were applied to explore statistical associations of monthly heliomagnetic index Rz with monthly incidence of CVD. PCA revealed insignificant temporal associations with a lag-period ΔT as follow: ΔT=+5 months (R=-0.30, p>0.05) and ΔT=-2 months (R=+0.21, p>0.05).*

Key words: *monthly solar activity, cyclicity, ecological analysis, stroke, incidence variations*

Редица автори са установили достоверни, макар и слаби, статистически връзки на електромагнитните излъчвания от естествен и антропогенен произход с различни болести на органите на кръвообращението [1, 2, 3, 6]. Известно е, че електромагнитните феномени (геомагнитно поле, слънчева радиация и др.) показват циклична активност [1]. От друга страна, описана е и годишна цикличност (сезонност) във възникването на сърдечно-съдови нарушения [3] и настъпването на мозъчни инсулти [5] в различни страни по света. Съществува ли в България подобна цикличност в регистрирането на болести на органите на кръвообращението? Може ли да се опише отношението между такава цикличност и циклите в хелиомагнитната активност, което по-нататък да се използва за целите на епидемиологичните проучвания?

Целта на настоящото изследване е (i) да даде статистическа оценка на вариациите в месечната заболяемост от мозъчно-съдова болест (МСБ) в гр. Стара Загора за периода 1985-1988 г., и (ii) да определи вероятността за статистически асоциации на заболяемостта с месечните стойности на 11-годишния слънчев индекс Rz (Волфово число).

МАТЕРИАЛ И МЕТОДИ

Заболяемостта от мозъчно-съдова болест (МКБ 9, No.430-437) беше проучена на базата на броя на острите случаи, регистрирани по обръщаемост в Неврологично отделение на ОРБ - Стара Загора в интервала от м. март 1985 г. до м. декември 1988 г. (N = 46 месеца). Като *нестандартен израз показател за заболяемостта* беше изследвана честотата на разпространение на 100000 души от населението по месеци. Като *фактор* в анализа бяха използвани месечните стойности на индекса Rz на 11-годишния слънчев цикъл, взаимствани от международния информационен бюлетин на НОАА (Solar and Geophysical Data -- Prompt Reports, NOAA, USA, 1988). За целта на проучването бяха приложени следните методи: вариационен анализ, алтернативен анализ, периодограмен регресионен анализ (ПРА) и фазово-корелационен анализ (ФКА) [4]. Двата статистически анализа за изследване на динамични редове са използвани успешно при изучаване на слънчево-климатични и хелиоепидемиологични връзки [4].

РЕЗУЛТАТИ И ОБСЪЖДАНЕ

За посочения интервал от 46 месеца са установени 180 случая с инсулт (n=180). Средната възраст на пациентите е 61.8 ± 10.5 г., а разпределението по пол -- 103 мъже (57.2%) и 77 жени

Том 1, Tome 1 1988

ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ-СТАРА ЗАГОРА

ANNUAIRE DE L'INSTITUT SUPERIEUR DE MEDECINE DE STARA ZAGORA

София · 1990 · Sofia

ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ — СТАРА ЗАГОРА
Том I
1988
ANNUAIRE DE L'INSTITUT SUPERIEUR DE MEDECINE DE STARA SAGORA
Tome I
1983

ГРАФИЧЕСКО ПРЕДСТАВЯНЕ НА СКОРОСТНИЯ ПРОЦЕС НА АГРЕГАЦИЯ НА ТРОМБОЦИТИ

АТАНАС Т. АТАНАСОВ

Катедра по физика и биофизика

При изследване на агрегационната способност на тромбоцитите се измерва и графично се регистрира промяната на светопропускането на плазма, богата на тромбоцити, с ле инициация на тромбоцитната агрегация с помощта на даден фактор, наречен индуктор (АДФ, адреналин, колаген и др.). Графичният запис на процеса по същество е интегрален запис (интегрална агрегограма), който отразява нарастването на степента на агрегация в тромбоцитната суспензия след прибавянето на индуктора. Предложен е метод за построяване на диференциална агрегограма, която отразява скоростния процес на агрегация на тромбоцитите. Въведени са някои показатели на диферен циалната агрегограма.

Ключови думи: тромбоцити, агрегация, интегрална и диференциална агрегограма.

За оценка на агрегационната способност на тромбоцитите се измерва и графично се регистрира отношението на светопропускането на богата на тромбоцити плазма към светопропускането на плазма, лишена от тромбоцити [1, 2]. Промяната на тази величина, която се означава като степен на агрегация на тромбоцитите, е свързана с протичането на агрегационния процес в плазмата под действието на даден агрегационен индуктор (АДФ, адреналин, колаген и др.). Графичният запис на процеса по същество е интегрален запис — интегрална агрегограма, която отразява нарастването на степента на агрегация в тромбоцитната суспензия в зависимост от времето (фиг. 1, *а*).

Допълнителна информация за агрегационната функция на тромбоцитите може да даде и динамиката на процеса, т. е. зависимостта, която показва начина, по който се променя скоростта на агрегация на тромбоцитите в зависимост от времето (фиг. 1, *б*). Тази закономерност може да се разглежда като диференциална крива (диференциална агрегограма), която описва промяната на парциалната агрегация с течение на времето.

Диференциалната агрегограма може да се построи на базата на данните от графическия запис на агрегометъра. През равни интервали от време ΔT се отчита степента на агрегация A_i на тромбоцитите от момента

СЪЮЗ НА УЧЕНИТЕ В БЪЛГАРИЯ
клон СТАРА ЗАГОРА
КЛУБ НА МЛАДИЯ УЧЕН

ОСМА НАЦИОНАЛНА КОНФЕРЕНЦИЯ

СЪВРЕМЕННИ ТЕНДЕНЦИИ В РАЗВИТИЕТО НА ФУНДАМЕНТАЛНИТЕ И ПРИЛОЖНИ НАУКИ

5-6 Юни 1997 г.

EIGHTH NATIONAL CONFERENCE
"MODERN TENDENCIES IN THE DEVELOPMENT
OF FUNDAMENTAL AND APPLIED SCIENCES"
5-6 June 1997, Stara Zagora, Bulgaria

A PHENOMENON OF DOMINANT NASAL PASSABILITY OF THE LEFT NOSTRIL IN DIURNAL PERIOD AND DOMINANT NASAL PASSABILITY OF THE RIGHT NOSTRIL IN NOCTURNAL PERIOD

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Abstract

Nasal passability of left and right nostrils were studied in diurnal and nocturnal periods. Dominant left nasal passability in 72.4% from all cases during day and dominant right nasal passability in 51.9% during night was established. Domination of left nostril is related to the active brain state and domination of right one - to the relaxed brain state.

Key words: nasal passability, day-night, active and passive brain state.

Introduction

The nasal passability is one of the most important conditions for the normal respiratory function. Problems with air flow transition through the nostrils is an important health issue discussed since the time of ancient Indian medicine and especially in Yoga practice [2]. Respiratory exercises in Yoga practice are aimed at actively controlling the respiratory process as a condition for better health and vitality. The emphasis in Yoga practice is put on the normal nasal passage and, especially on transition of air flow through the left and right nostril separately. According to this practice, regular change of nasal passability of nostrils every 2-2.5 hours is biological rhythm that is a criterion for good health. Also, air flow transition through the left or right nostril was associated with different aspects of metabolism of the organism.

The aim was to perform experiments to study diurnal and nocturnal (during sleep) patterns of the nasal passage, separately for each nostril,

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Семинар по Отология и Невро-Отология

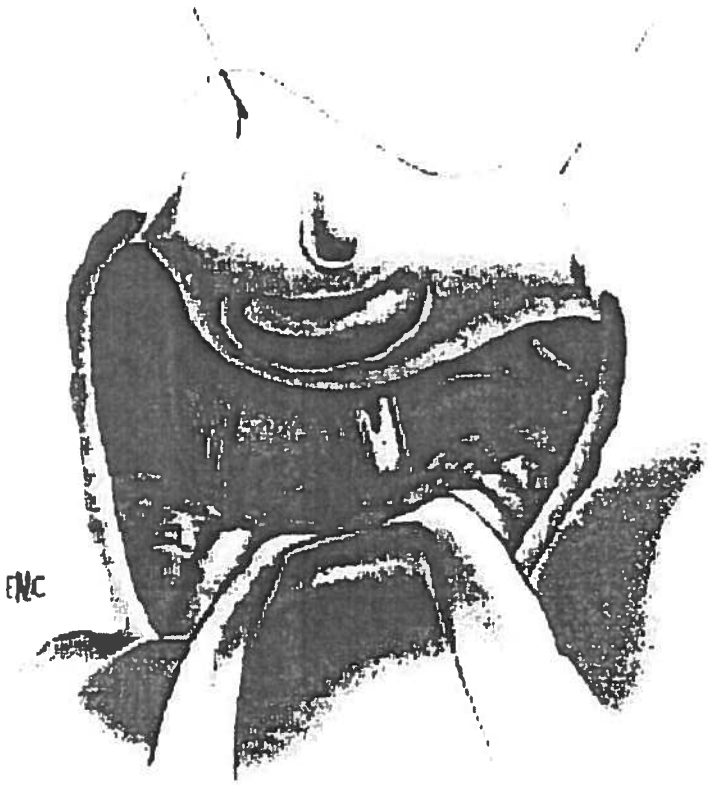
2-ри Видеосеминар Стара Загора, България

19-20 Май 2000 г.

Seminar on Otology and Neuro-Otology

2-nd Videoseminar Stara Zagora, Bulgaria

May 19-20, 2000



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АЗОТЕН ОКИС И НИТРОКСИЛИ. МЕХАНИЗЪМ НА ДЕЙСТВИЕ НА СПИН-БЕЛЯЗАНИ ПРОТИВОТУМОРНИ ВЕЩЕСТВА

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NITRIC OXIDE AND NITROXIDES. MECHANISM OF ACTION OF SPIN-LABELED ANTITUMOR DRUGS

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РЕЗЮМЕ

В публикацията се сравняват най-важните физически, химически и биологични свойства на азотния окис (NO) и свободните стабилни нитроксилови радикали (нитроксиди). Активната функция на нитроксидните молекули е стерично запречения азотен окис. Използван е оригинален подход за обяснение на механизма на биологичната активност на нитроксидите и най-вече на техните производни, притежаващи антитуморен остатък от групата на азотния иприт, нитрозоуреите, азиридините и триазените (спин-белязани вещества) чрез биологичната активност на NO-групата. Подобно на азотния окис, нитроксилите могат да реагират със супероксид анион радикали, т.е. притежават супероксид дисмутаза (SOD) миметично действие.

Докато взаимодействието на азотния окис със супероксид анион радикала води до силно токсичния пероксинитрид ONOO-, то неговото образуване е силно ограничено в присъствието на нитроксиди.

Известно е, че нитрозоурейните лекарства като ломустин (CCNU) и кармустин (BCNU) показват висока обща токсичност една от причините за която вероятно е отделянето на NO и последващото образуване на ONOO по време на техния метаболизъм.

Биологичните изследвания на синтезираните от нас нитрозоуреи показват значително по-ниска обща токсичност, която може да бъде обяснена със SOD-миметичното действие на нитроксиловия остатък в тяхната молекула.

В тази публикация се очертават перспективите за бъдещи изследвания на нитроксилите с цел потвърждаване на тяхната NO-активност.

Ключови думи: азотен окис, нитроксил

ABSTRACT

A comparison of more important physical, chemical and biological properties of the nitric oxide (NO) and free stable nitroxyl radicals (nitroxides) on the base of their structural similarity is made in the present article. The active moiety in the nitroxide molecule is a sterically hindered nitric oxide. An original approach is used for explanation of the mechanisms of biological action of the nitroxides and especially - of their derivatives with antitumor agents from the groups of: nitrogen mustards, nitrosoureas, aziridines and triazenes (spin-labeled compounds) through the biological activities of NO. Similarly to NO, nitroxides also can react with superoxide anion radical (O_2), they possess superoxide dismutase (SOD) mimetic action. While the interaction of NO with O_2 yields very toxic peroxynitrite (ONOO-), its formation is strongly limited in the presence of a nitroxide. It is known that the nitrosourea antitumor drugs, like lomustine (CCNU) and carmustine (BCNU), showed high general toxicity, one of the reasons for that probably is the formation of NO and subsequently - of ONOO- during their metabolism. The biological investigations of the synthesized by us spin-labeled nitrosoureas showed their considerably lower general toxicity that could be explained with the SOD-mimetic action of the nitroxide, present in their molecule. In the article are outlined perspectives for further investigations of the nitroxides with aim to confirm our supposition that they possess NO activities.

Key words: nitric oxide, nitroxides

МЕДИЦИНСКИ ФАКУЛТЕТ
ТРАКИЙСКИ УНИВЕРСИТЕТ
СТАРА ЗАГОРА

ЮБИЛЕЙНА НАУЧНА КОНФЕРЕНЦИЯ

с международно участие

"20 години ВМИ - МФ – СТАРА ЗАГОРА"

ТОМ 1

МЕДИКО-БИОЛОГИЧНИ НАУКИ

ПРОФИЛАКТИЧНА МЕДИЦИНА И ОБЩЕСТВЕНО ЗДРАВЕ

Редактори: Проф. д-р Николай Лазаров, дмн
Доц. д-р Юлияна Маринова, дм

СТАРА ЗАГОРА
18-20 октомври 2002

МИКРОКАЛОРИМЕТРИЧНО И ТЕРМИЧНО ИЗСЛЕДВАНЕ НА ИЗОЛИРАНА ОТ *GALEGA OFFICINALIS* L.` ФРАКЦИЯ, ИНХИБИРАЩА ТРОМБОЦИТНАТА АГРЕГАЦИЯ

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MICROCALORIMETRIC AND THERMAL STUDY OF *GALEGA OFFICINALIS* L. FRACTION, INHIBITING PLATELET AGGREGATION

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ABSTRACT. A fraction of the water extract from the herb *Galega officinalis* has been isolated that strongly inhibited platelet aggregation by 25 μM ADP by one IC_{50} 9.3±0.25 μg/ml lyophilized fraction. The fraction disaggregated previously aggregated platelet rich plasma by 25 μM ADP by one IC_{50} 15±0.40 μg/ml lyophilized fraction. In this study the thermal properties of the fraction were tested. The fraction (1.2% solution in 20 mM phospate buffer, pH 7.4) was heated in a home-made scanning microcalorimeter and demonstrated thermal denaturation at 70-90°C. In another array the capability of the fraction to inhibit platelet aggregation and disaggregate previously aggregated platelet rich plasma was increasingly subdued after 20 min exposure to various temperatures from 20 to 98°C. The data obtained allowed calculation of the enthalpy of heat denaturation (65±5 kJ/mol) and the denaturation temperature (65°C) of the active fraction.

Key words: platelet aggregation; *Galega officinalis*; heat denaturation.

Galega officinalis L. е растение, използвано за лечение на diabetes mellitus [6]. Над 15 съединения са изолирани от *Galega officinalis* L.: алкалоиди [9], флавоноиди [10], глюкозиди [8], сапонини [7] и др. Изследванията на Атанасов [1, 2] показват, че водните извлеци на растението потискат *in vitro* и *in vivo* тромбоцитната агрегация, индуцирана с аденозиндифосфат, адреналин, тромбин и колаген.

№ 45

РИЛСКИ СИМПОЗИУМ

15-16 Октомври 2003 г.

Стара Загора, Старозагорски минерални бани

Сборник доклади

"Профилактика на социално значими заболявания"

Международна година на инвалида в Европейския съюз
"2003 - Европейска година на хората с увреждания"

Под редакцията на доц. д-р Павел Димов
и колаборацията на д-р Петър Руев, доц. Веска Шошева и д-р Анелия Ботева

EAONO

Европейска Академия по
Отология и Невро-Отология

Рилският симпозиум "Профилактика на социално значими заболявания" е акредитиран от СНМЕ.
Съвет за кредитна оценка за продължителна медицинска квалификация София, клон на U.E.M.S. с оценка 7 кредита.

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Регистрация на дишането, сънните и носни цикли на човек

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АБСТРАКТ

Хипотеза. Регистрацията на амплитудата на дишането отделно през лявата и дясна ноздра дава възможност при подходяща скорост на записа да се регистрират сънните и носни цикли

Метод. Регистрацията на дишането от всяка ноздра се извършва при скорост на записа - 7500 mm/h, регистрацията на сънните цикли при скорост на записа- 240-600mm/h, а регистрация на носните цикли при скорост на записа- 20-60mm/h.

Резултати. Представена е методика и апаратура, с която са направени записи на дишането, сънните и носни цикли на човек.

Заключение. Методиката дава възможност едновременно да се регистрират дишането, сънните и носни цикли на хора през деня, по време на сън и при отоларинголожки интервенции.

Ключови думи: дишане, сънен цикъл, носен цикъл.

Pro Otology - Supplement: 81-83, 2003

ABSTRACT

Registration of Breating, Sleep and Nasal Cycles for Human.

At Atanasov

Hypothesis: Registration of amplitude of breathing trough left and right nostril separately make possible registration of sleep and nasal cycles, by change of speed of record

Method: Registration of breathing from each nostril must be made at speed of record- 7500mm/h, for registration of the sleep cycles, at speed of record - 240-600mm/h and for registration of the nasal cycle, at spped of paper – 20 - 60mm/h.

Results: In manuscript is presented the method, aparatures and the records of breathing, sleep and nasal cycles for human.

Conclusion: The method give possibility to registrate the breathing, sleep and nasal cycles during daytime, sleep and rhinology intervention.

Key words: Breathing, Sleep cycle, Nasal cycle.

Pro Otology - Supplement: 81-83, 2003

ВЪВЕДЕНИЕ

Температурната разлика на издишвания въздух от лявата и дясна ноздра, поради различното назално съпротивление в норма е от 1(С до 3(С (1, 2). При алтернативната смяна на проходимостта и назалното съпротивление на ноздрите, температурата на издишваните от тях въздушни потоци се сменя алтернативно. Сменят се и обемите на издишвания въздух от двете ноздри. В норма разликата в обемите на дихателния въдух през ноздрите е средно 1.0-3.5 пъти като с тодкова се променя и количеството на издишваната с въздуха топлина. Измерването на температурната разлика и на количеството топлина, съдържаща се в издишвания от ноздрите въздух, дава възможност за едновременна регистрацията на дишането, назалния и сънните цикли (3, 4).

МЕТОД

Температурата на издишвания и вдишван от ноздрите въздух се измерва отделно с помощта на два термистора, инсталирани на пътя на въздушните потоци. Термисторите са монтирани в маска, която се закрепва върху носа на изследваното лице - Фиг.1(A, B).

В маската - два отворени цилиндъра с диаметър 1cm са леко вмъкнати в отворите на ноздрите и служат за насочване на дихателните потоци към термисторите.Тези два цилиндъра са вмъкнати в по-голям цилиндър с дължина 3,5cm и диаметър 1,5cm. Двата термистора са монтирани в големия цилиндър, коаксиално на ноздрите и техните въздушни потоци. Сигналът от всеки термистор се усилва с електронен усилвател с чувствителност 4-20 mV/1(C и регистрира от XY пишещо устройство (5, 6). Температурата на издишваният от ноздрите въздух е близка до телесната температура, а температурата на вдишвания от ноздрите въздух е равна на стайната температура. Това изисква температурата на стаята по време на измерванията да не се променя в рамките на (1-2(C. Записващото устройство мо-

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NONINVASIVE APPARATUS FOR MEASUREMENT OF BREATHING FLOW THROUGH THE NOSTRILS AND COMPUTERIZED DETERMINATION OF NASAL AND SLEEP CYCLES IN HUMAN

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ABSTRACT

In human breathing nasal cycles have recently been found that are related to the sleep cycles, cyclic hemispheric electrical activity and blood supply to brain and to some nasal-pharyngeal disorders. With the aim to investigate nasal and sleep cycles an apparatus for continuous (up to 12 hours) and non-invasive measurement of the air flow through nostrils was constructed. A facial mask was used combined with air flow detectors whose analog signal was amplified, discretizied and stored in computer. The measurement is carried out during sleep or muscle activity and could help the early diagnostics of some nasal-pharyngeal disorders.

Key words: *nasal and sleep cycle, computerized diagnostics, nasal-pharyngeal disorders.*

УВОД

При алтернативната смяна на проходимостта и назалното съпротивление на ноздрите, въздушни потоци през тях също се сменят алтернативно. Сменят се алтернативно обемите на вдишвания и издишван въздух през двете ноздри. В норма разликата в обемите на дихателния въдух през ноздрите е около 1.0-3.5 пъти. Регистрацията на дишането , чрез измерване на разхода на въздуха отделно през лявата и дясна ноздра, дава възможност при промяна на скорост на записа от 7500 mm/h на 240-600mm/h и на 20-60mm/h , да се регистрират едновременно дишането, сънните и носни цикли на човек.Това е методика подобна на използваната от Атанасов и съавт. (1,2,3) за едновременна регистрация на дишането, назалните и сънни цикли при хора.

МЕТОД

Дишането се измерва по разхода на вдишвания и издишван въздух през всяка ноздра поотделно. За тази цел е разработен нов метод за измерване на разход на въздуха, показан на Фиг.1. В средата на пластмасова тръбичка е поставен нагревател (2), по който тече много слаб ток (около 10 mA) с ниско напрежение (около 3 v). Отделената топлина загрява преминаващия въздух и създава температурна разлика DT между въздушния поток преди и след нагревателя. Тази температурна разлика се измерва с диференциална термодвойка (1) от типа мед/константан, чието напрежение се усилва няколкостотин пъти от правотоков усилвател. Изходното напрежение на усилвателя се преобразува в правоъгълни

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ЕЛЕКТРОНЕН ТЕРМОМЕТЪР ЗА ЛАБОРАТОРНИ И МЕДИЦИНСКИ ИЗСЛЕДВАНИЯ

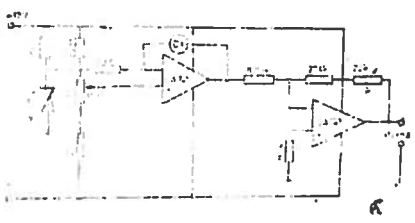
АТАНАС Т. АТАНАСОВ

Катедра по физика и биофизика

Представена е схема на прецизен електронен термометър с термисторен измерителен елемент. Термометърът се отличава с голяма чувствителност и обхват и може да бъде използуван като универсален медицински и лабораторен прибор за точни измервания на температурата на различни по големина участъци на човешкото тяло. Особено подходящ е за измерване на кожната температура.

Ключови думи: термометър, термистор.

В лабораторната и медицинската практика често се налага да се измерват температури с голяма точност. За тази цел съществуват различни по конструктивно и схематично решение термометри [1, 2]. Предлагаме една схема, изпълнена с операционни усилватели UA 741 PC, производство на САЩ. Измерителният елемент е термистор, включен в обратната връзка на първия операционен усилвател (фиг. 1). Диапазонът от измервани температури е от 0 °C до 100 °C, а чувствителността на схемата е от 0,05 °C до 0,1 °C (10 mV на 1 °C). При по-високо захранване схемата може да се включи в пишещи устройства без собствен усилвател.



Фиг. 1

В зависимост от площта на използувания термистор могат да се измерват температури на различни по големина участъци от човешкото тяло. Термометърът е особено подходящ за измерване на кожната температура.

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VII.9. THE ALOMETRIC RELATIONSHIPS BETWEEN LENGTH OF PREGNANCY, BODY MASS AND METABOLISM OF MAMMALS

Atanas Todorov Atanasov

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Summary We studied relationship between length of pregnancy T(day) and body mass M(g) of 105 mammals from *Metatheria* and *Placentalia* with mass ranging from 10g to 15t. We established alometric relationships from type: $T=7.5451\ M^{0.2689}$ and $T.P/M=Const(A_{pr})$., where P (kcal/day)-metabolism, 7.5451- alometric coefficient, 0.2689-degree alometric coefficient, $A_{pregnancy}$-constant.

INTRODUCTION

For the birds is established alometric relationship between the metabolism of birds and their body mass (1) and between duration of incubation time of eggs and mass of the birds (2). For the mammals is established just alometric relationship between metabolism and their body mass (3). In this sense our interest is directed to the question, is there alometric relationship between length of pregnancy and body mass of the mammals?

METHOD AND DATA

We collected data for 105 mammals from specialized scientific encyclopedia (4,5). In this manuscript are given data for 20 mammals: mouse (body mass 21g; length of pregnancy 19-20day), scorpio hamster (50g, 33d), rat(250g, 25d), hamster(400g, 30d), squirrel(750g, 41d), guinea-pig(510g, 68d), hedgehog(800g, 49d), rabbit(3.5kg, 50d), cat(5kg, 62d), dog(10kg, 62d), leopard(32kg, 90d), sheep(49kg, 148d), human(60kg, 280d), llama(100kg, 360d), deer(300kg, 200d), camel(460d, 400d), horse(500kg, 350d), giraffe(1000g, 430d), rhinoceros(1500kg, 440d), elephant (3500kg, 630d). Statistic software is used for computing of the relationships (6).

RESULTS

On the Fig.1A is shown relationship between length of pregnancy and body mass of 105 mammals. On Fig 1B is shown the same relationship for 20 mammals. The graphic relationship on Fig.1A approximated with function from type: $T=7.545M^{0.2689}$ (7,8) with correlation coefficient 0.899±0.043 and standard deviation of regression 0.177, where T-length of pregnancy(days), M-body mass of the mammals(grams), 7.545-alometric coefficient, 0.268-degree alometric coefficient. The value of F factor is 435.45 ($p<0.000001$). This shows that the relationship between length of pregnancy and body mass of the mammals isn't due to the random variation of data. The same relationship for body mass M(in kg) is: $T=48M^{0.2689}$.

Brody (3) in studies about metabolism and mass of mammals "from mouse to elephant" obtains alometric relationship between speed of metabolism P(kcal/day) and body mass M(kg) from type: $P=70M^{0.734}$. This relationship per unit mass is: $P^*=70M^{-0.266}$, where $P^*=P/M$. Absolute value (-0.266) of the degree coefficient in this relationship is close to the absolute value of the degree coefficient (0.2689) in the relationship $T=48M^{0.2689}$. From two relationships we obtain theoretic connection between length of pregnancy T(d), metabolism P(kcal/d) and body mass M(kg) of all mammals: $T.P/M= Const\ (A_{pr})$. For mouse A_{pr} is 5.10^3 kcal/kg, for elephant - $6.52.10^3$kcal/kg and for human -$8.1.10^3$ kcal/kg.

HYPOTHESIS

Equation $T.P/M=Const(A_{pr})$, obtained by statistics analysis of data for 105 mammals keeps validity about different groups and individuals of mammals.

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ЕДИН ОБЩ АЛОМЕТРИЧЕН ЗАКОН: ТОТАЛНАТА МЕТАБОЛИТНА ЕНЕРГИЯ ЗА ЕДИН ЖИВОТ НА СТУДЕНОКРЪВНИТЕ ЖИВОТНИ, МЛЕКОПИТАЕЩИТЕ И ПТИЦИТЕ Е ЛИНЕЙНО ПРОПОРЦИОНАЛНА НА ТЕЛЕСНАТА ИМ МАСА

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ONE GENERAL ALOMETRIC LAW: THE TOTAL METABOLIC ENERGY PER LIFE SPAN OF THE ANIMALS (POIKILOTHERMIC, MAMMALS, AVES) IS LINEAR PROPORTIONAL TO THE BODY MASS

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ABSTRACT

Over a wide range of living species from Poikilothermic to Mammals and Aves was shown that there is positive correlation between total metabolic energy per life span and body mass (R=0.97, n=185).Real slope of correlation line of total metabolic energy per life span on mass may be near to 1.0. So, for all living species exist the general law: the total metabolic energy per life span is linear proportional to the body mass.

Key words: *rate of metabolism, metabolic energy, body mass, life span*

The power relationship between the rate of metabolism P and body mass M of animals is expressed by the law of Kleiber (1,2): $P=aM^k$, where a, k-are alometric constants characteristic for every class and order of animals (3,4). The attempt to explain the decrease of the intensity of metabolism P/M , that is observed with the increase of the body mass of the animals continue of experimental and theoretical level (5,6), becouse this power dependence is fundamental for energetics of living organisms. The introducing of the life span T_{ls} as a parameter (7, 8, 9, 10) give possibility to calculate the total metabolic energy per life span of animals in function of body mass.

DATA AND METHOD

The data for the rate of metabolism P(kJ/day) , body mass of species M(kg) are given from original scientific sourses (11, 12, 13, 14, 15, 16, 17, 19, 20). The calculating data for the total metabolic energy per life span P T_{ls}(kJ)

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ТЕЛЕСНАТА МАСА(M) И ОБЕМА(V) ОТНЕСЕНИ КЪМ ПРОИЗВЕДЕНИЕТО НА ТЕЛЕСНАТА ПОВЪРХНОСТ(S) И ПРОДЪЛЖИТЕЛНОСТТА НА ЖИВОТА(T_{LS}) НА ЖИВОТНИТЕ СА ОТНОСИТЕЛНО ПОСТОЯННИ ВЕЛИЧИНИ: $M/(S.T_{LS})\approx 5X10^{-7} \div 0.2X10^{-8}$(KG/M².S) И $V/(S.T_{LS})\approx 5X10^{-10} \div 0.2X10^{-11}$ (M/S)

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THE RATIO OF THE BODY MASS(M) AS WELL AS THE BODY VOLUME(V) OF ANIMALS TO PRODUCT OF THE BODY SURFACE(S) AND LIFE SPAN(T_{LS}) ARE RELATIVELY CONSTANT PARAMETERS: $M/(S.T_{LS})\approx 5X10^{-7} \div 0.2X10^{-8}$(KG/M².S) AND $V/(S.T_{LS}) \approx 5X10^{-10} \div 0.2X10^{-11}$ (M/S)

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ABSTRACT

The ratio of the body mass M(kg) as well as the body volume V(m^3) of animals (Poilothermic, Mammals and Aves) to product of the body surface S(m^2) and life span T_{ls}(s) are relatively constant parameters $a_{mch}=M/ST_{ls}=5'10^{-7}$ë$0.2'10^{-8}$ (kg/m^2 s) and $a_{vch}= V/ST_{ls} = 5'10^{-10}$ ë $0.2'10^{-11}$ (m/s) respectively.

The parameters a_{mch} and a_{vch} are the intensity of increasing of the body mass and the volume for time period equal to the life span. These parameter are connected with rate of metabolism P(J/s) by the equation $P/S=A_{ls}a_{mch}$. The coefficient A_{ls} (the total metabolic energy per life span, per unit body mass) can be received from author's established general relationship: $PT_{ls}=A_{ls}M$, between the total metabolic energy per life span PT_{ls} (J) and the body mass M(kg) of animals.

Key words: a ratio, body mass, surface, life span

INTRODUCTION

The bioenergetic studies on animals (Hemmingsen, 1950, 1960; Heusner, 1985; Kleiber, 1961; Schmidt-Nielsen, 1984) have shown that the rate of oxygen consumption P(kJ/day) is related to the body mass M(kg) as expressed by the equation of type: $P = aM^k$. In previous works, Atanasov (2005, a, b, c) inserted the life span (T_{ls}) of animals as a parameter, showing that the relationships between the total metabolic energy per life span ($P T_{ls}$) and body mass over a broad number of animals (Poikilothermic, Mammals and Aves) is expressed by the equation with power coefficient **k** near to 1.0 with variation ±0.8: [1] $P T_{ls} = A_{ls} M^{1\pm 0.8}$, where A_{ls} is relatively constant parameter. Brody (1962) shows, that between the rate of basal metabolism P(kJ/d) and the body surface S(m^2) exists a linear relation from type: [2] P/S=k (const.) , where k (const.) is relatively constant parameter. From relation [1] and [2] we received: [3] $kST_{ls}=A_{ls}M^{1\pm 0.8}$ and [4] $k/A_{ls} = M^{1\pm 0.8}/(ST_{ls})$, where k/A_{ls} =const. Because the

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СЪЩЕСТВУВА ЛИ СКОРОСТ НА БИОЛОГИЧНИТЕ ПРОЦЕСИ В ЖИВИТЕ ОРГАНИЗМИ СВЪРЗАНА С ОТНОШЕНИЕТО НА ОБЕМА(V), ПОВЪРНОСТТА(S) И ПРОДЪЛЖИТЕЛНОСТТА НА ЖИВОТА(T_{LS}) ИМ: $V/ST_{LS} = 5Ґ10^{-10} \div 0.2Ґ10^{-11}$ (M/S)

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DOES THE SPEED OF BIOLOGICAL PROCESS, RELATED TO RATIO BETWEEN BODY VOLUME (V), BODY SURFACE (S) AND LIFE SPAN (T_{LS}): $V/ST_{LS} = 5Ґ10^{-10} \div 0.2Ґ10^{-11}$ (M/S) EXIST IN LIVING ORGANISMS

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ABSTRACT

The ratio of the volume V(m^3) and body surface S(m^2) of living organism L_{ch}=V/S (m) is "characteristic lenght", so that the parameter a_{vch} =V/ST_{ls} (T/s/-life span) have a meaning of "characteristic speed" with values 5´10^{-10}ë0.2´10^{-11} (m/s). The values of a_{vch} are very near to passive ion permeability through cell membranes. The keeping of speed a_{vch} can be connected with synchronization of the ratio between the body volume, surface and life span during growth and life of living organisms.

Key words: *a speed, mass, surface, life span, living organisms*

INTRODUCTION

The bioenergetic studies on animals (Hemmingsen, 1950, 1960; Heusner, 1985; Kleiber, 1961; Schmidt-Nielsen, 1984) have shown that the rate of oxygen consumption P(kJ/day) is related to the body mass M(kg) as expressed by the equation of type: $P = aM^k$. In previous works, Atanasov (2005, a, b, c) inserted the life span (T_{ls}) of animals as a parameter, showing that the relationships between the total metabolic energy per life span (PT_{ls}) and body mass over a broad number of animals (Poikilothermic, Mammals and Aves) is expressed by the equation with power coefficient **k** near to 1.0 with variation ±0.8: [1] $P T_{ls} = A_{ls} M^{1\pm0.8}$, where A_{ls} is relatively constant parameter. Brody (1962) shows, that between the rate of basal metabolism P(kJ/d) and the body surface S(m^2) exists a linear relation from type: [2] P/S=k (const.) , where k (const.) is relatively constant parameter. From relation [1] and [2] we received: [3] $kST_{ls} = A_{ls} M^{1\pm0.8}$ and [4] $k/A_{ls} = M^{1\pm0.8}/(ST_{ls})$, where k/A_{ls} =const. Because the coefficients k and A_{ls} are relatively constant parameters, the relation $M^{1\pm0.8}/(ST_{ls})$ will be constant too. Since the body mass M(kg) and the body volume V(m^3) are connected with relation: M=rV, where r=1050-1100 (kg/ m^3) is the diapason of body density of Poikilothermic, Mammals and Aves, the relation $V^{1\pm0.8}/(ST_{ls})$ will be relatively constant.

The aim of this study is to calculate the $V/(ST_{ls})$ ratio for wide number of animals- Poikilothermic, Mammals and Aves.

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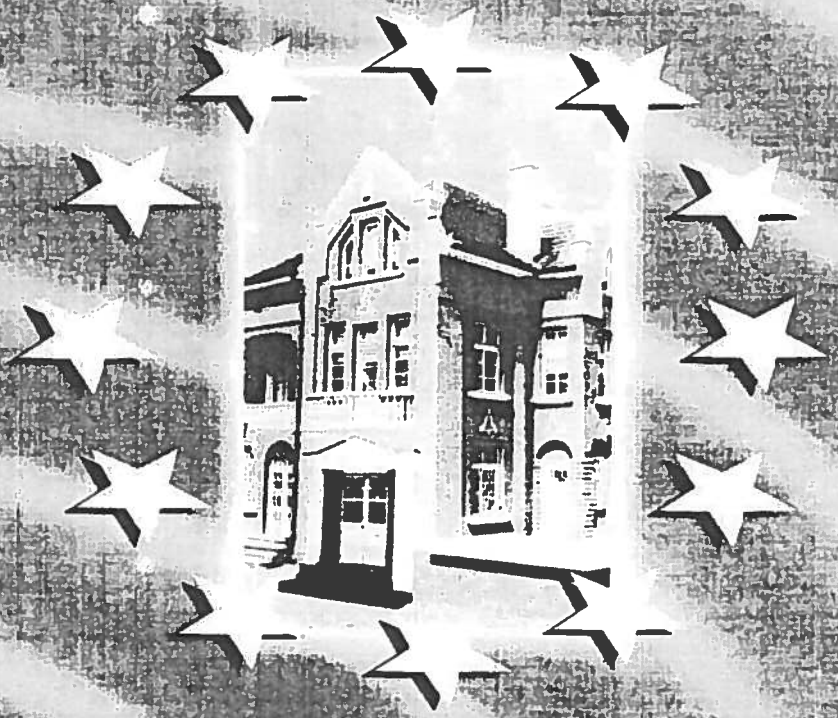
СЪЮЗ НА УЧЕНИТЕ СТАРА ЗАГОРА
UNION OF BULGARIAN SCIENTISTS,
STARA ZAGORA

Международна научна конференция Стара Загора, 7 - 8 юни 2007 г.
International science conference Stara Zagora, June 7 - 8, 2007

Предизвикателствата пред науката във връзка с членството на България в ЕС
Challenges for Bulgarian Science in This Country's EU Membership



Том VII
Хуманна медицина

Volume VII
Medicine

DOES THE ALLOMETRIC RELATIONSHIPS BETWEEN GRAVITATIONAL CONSTANT, MAX PLANCK'S CONSTANT AND BODY MASS, SIZE, GENERATION TIME, DENSITY AND SPEED OF GROWTH IN PROKARYOTES EXIST?

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ABSTRACT

In this work is shown that from the Max Planck's ratios for mass $M=(h.c/G)^{1/2}$ kg, length $L=(h.G/c^3)^{1/2}$ m, time $T=(h.G/c^5)^{1/2}$ s and density $c=M/L^3$ kg/m^3 (where $G=6.673x10^{-11}$ N.m^2/kg^2 is gravitational constant, $h=6.6262x10^{-34}$ J.s is Planck's constant, $c= 2.9979x10^8$ m/s is speed of light) we can receive the body mass $M_{cell}=(h.v_{cell}/G)^{1/2}$ kg, body size $L_{cell}=(h.G/v_{cell}^3)^{1/2}$ m, generation time $T_{cell}=(h.G/v_{cell}^5)^{1/2}$ s and body density $c_{cell}= M_{cell}/L_{cell}^3$ kg/m^3 of Prokaryotes (Bacteria, Mycoplasmatales, Rickettsiales and Chlamydae), if we replace the speed of light 'c' with speed of linear growth of cells ' v_{cell}'. The general conclusion is made, that possibly the connection between biological characteristics of Prokaryotes and physical constant in Universe exist.

Key words: *Gravitational constant, Planck's constant, Prokaryotes.*

INTRODUCTION

The pattern existing between the other fundamental characters of living organisms and her body size or mass are generally described as a power function called 'allometric'. From four fundamental physical forces and interactions in physics -gravitational, weak, electrostatic and nuclear (Eddington, 1948; Bueche, 1982) the main role in metabolic processes of living world play gravitational and electromagnetic interactions. The electromagnetic interactions, that is the base of biochemical reactions in cells are located in small spatial area with size about protein and membrane length (i.e. about 2ч8 nm) and realized for the time about 10^{-3}ч10^{-6} seconds (Westerhoff and van Dam, 1987; Rubin, 1987). Gravitational interactions act into full area of cell's mass and volume and can be interpreted like a integral forces, acting continuously in individual space during lifetime of cells. The gravitational studies concern: biology of size and gravity (Yamashita and Baba, 2004; Brown, 1991), self-organization of microtubule, cells, tissues and biological systems in gravitational field (Fujiwara, 2004; Tabony et al., 2002; Vunjak et al., 2002). However, the intimate mechanism of gravitational interactions in living cells are insufficiently studied (Gabova et al., 1991; Mashinsky, 2001).

The gravitational constant $G=6.673x10^{-11}$(N.m^2/kg^2), Planck's constant $h= 6.6262x10^{-34}$ (J.s) and speed of light $c= 2.9979x10^8$ (m/s) are fundamental physical constants in Universe (Dyson,1972). Max Planck and others theoretical physicists were connected gravitational constant (G), Planck's

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Съюз на учените - Стара Загора
Stara Zagora Union of Scientists

Научна конференция с международно участие
"Стара Загора '2004"
3 – 4 юни 2004 г.

Scientific conference with international participation
"Stara Zagora '2004"
June 3 – 4, 2004

Том IV
Хуманна медицина
Част 1. Клетъчна и молекулярна биология и микробиология. Физиология и фармакология

Volume IV
Human medicine
Part 1. Clinical and molecular biology, microbiology. Physiology and pharmacology

THE ALOMETRIC RELATIONSHIPS BETWEEN DURATION OF PREGNANCY, BODY MASS AND INTENSITY OF METABOLISM OF MAMMALS: METATHERIA AND PLACENTALIA

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ABSTRACT

We studied relationship between duration of pregnancy T(day), body mass M(g) and intensity of metabolism P (kcal/day.g) of 105 mammals from Metatheria and Placentalia with body mass ranging from 10g to 15t. We established alometric relationships from type: $T=7.5451\ M^{0.2689}$ and T.P=K(const.), where 7.5451- alometric coefficient, 0.2689-degree alometric coefficient, , K-constant with values from 1.5 to 8.5.

Key words: *alometric relationships,duration of pregnancy, body mass, metabolism*

УВОД

В научната литература съществуват различни алометрични зависимости за бозайници и птици. Rann и At (Rann and At, 1974) изследвайки птици с маса от 2,5g (колибри) до 1000kg(епиорнис) са показали, че съществува алометрична зависимост между времето на инкубация и масата на яйцата и между времето на инкубация и масата на птиците-родители(Rahn et al., 1975). Също за бозайници и птици са получени алометрични зависимости между метаболизма и тяхната маса (Brody et al., 1934; Lasiewski and Dawson, 1967). Интерес представлява дали съществува алометрична завсимост между продължителността на бременността и телесната маса на бозайниците. Подобно проучване до настоящия момент в научната литература няма.

МАТЕРИАЛ И МЕТОДИ.

Данни за изследваните бозайници, тяхната маса и продължителността на бременността им са взети от обзорни научни трудове (Марков, 1988; Наумов, Кузякина, 1971) и са дадени в Таблица 1. В проучването са включени 105 животни от групата на бозайниците (Mammalia).

Статистически соуфтерен пакет 'Статистика' беше използван за изчисляване на вида на зависимостта "продължителност на бременността–телесна маса на бозайниците" и останалите статистически параметри (Atanasov&Dimitrov, 2002).

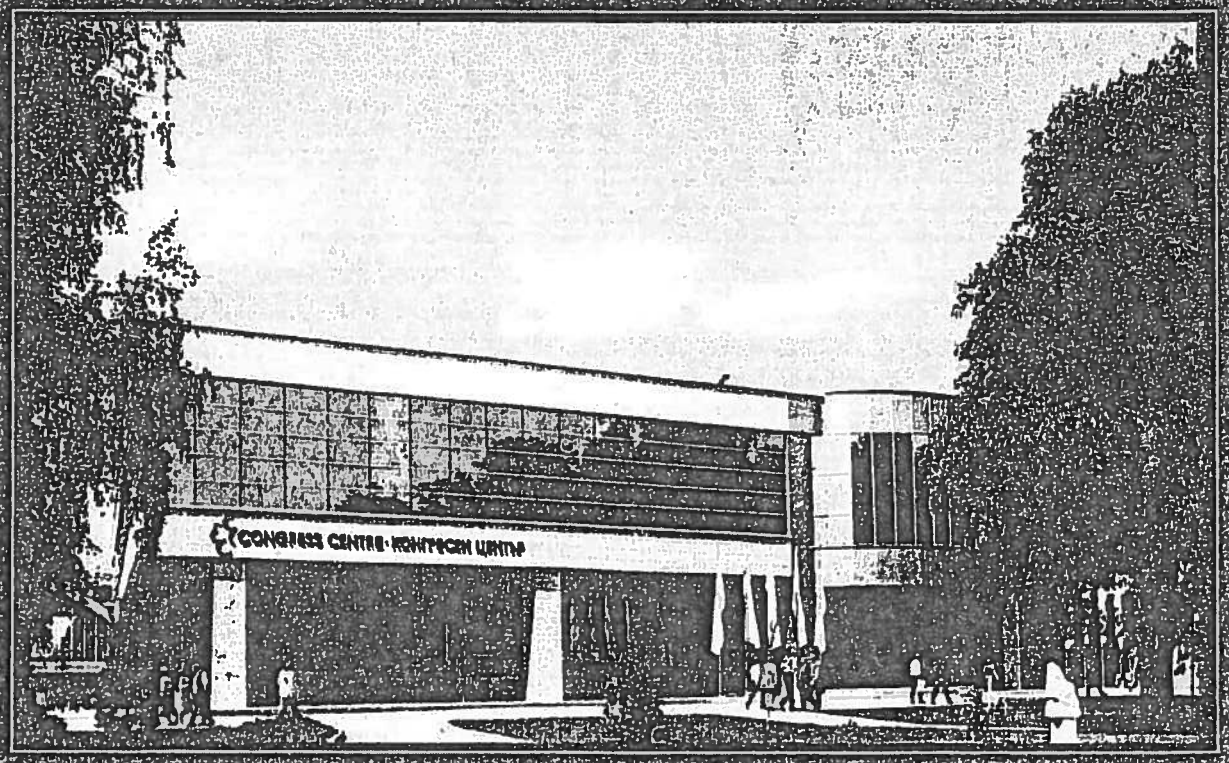
ЮБИЛЕЙНА НАУЧНА СЕСИЯ

60 г. МЕДИЦИНСКИ УНИВЕРСИТЕТ - ПЛОВДИВ

10 - 11 Ноември 2005

Пловдив

СБОРНИК РЕЗЮМЕТА



приложено антидотно лечение пациентите преживяха интоксикацията и са изписани в добро здраве.

Ключови думи: *Нуреле Дурбан, фосфорорганично отравяне, антидотно лечение*
Тип представяне: *научно съобщение*

ЕДНА ОБЩА АЛОМЕТРИЧНА ЗАКОНОМЕРНОСТ: ТОТАЛНАТА МЕТАБОЛИТНА ЕНЕРГИЯ ЗА ЕДИН ЖИВОТ НА ЖИВОТНИТЕ /СТУДЕНОКРЪВНИ, МЛЕКОПИТАЕЩИ И ПТИЦИ/ Е ЛИНЕЙНО ПРОПОРЦИОНАЛНА НА ТЕЛЕСНА ИМ МАСА

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Въведение: Степенната зависимост между скоростта на метаболизма P и телесната маса M на животните се изразява със закона на Клейбер $P=aM^k$, където a и k-са алометрични коефициенти, характерни за всеки клас и група животни. Въвеждането на продължителността на живота T_{ls} като параметър дава възможност да се изчисли тоталната метаболитна енергия, консумирана от животните в продължение на един живот във функция от тяхната телесна маса. **Цел:** Целта на представеното проучване е, да се намери функционалната зависимост между тоталната метаболитна енергия за един живот и телесната маса на 185 животни. **Материали и методи:** Данните за скоростта на метаболизма P(kJ/day), телесната маса M(kg) и продължителността на живота T_{ls}(day) за отделните индивиди са взети от обзорни научни публикации и книги. Изчислените стойности на тоталната метаболитна енергия за един живот P T_{ls} (kJ) и тоталната метаболитна енергия за един живот /за 1 kg телесна маса/ A_{ls}(kJ/kg) за 54 студенокръвни индивида, 90 млекопитаещи и 41 птици са взети от оригиналните публикации на автора. **Резултати** : За широк спектър от индивиди / Poikilothermic, Mammals, Aves / с разлики в скоростта на метаболизма и телесната маса 18 порядъка е показано, че съществува линейна зависимост / $P\ T_{ls} = A_{ls}\ M$ / между тоталната метаболитна енергия за един живот /$P\ T_{ls}$ / и телесната маса на животните /M/, с корелационен коефициент R=0.97 и n=185. Наклонът на кривата "тотална метаболитна енергия-телесна маса" е близък до 1.0. **Заключение:** За живите организми съществува обща закономерност, която се изразява в това, че тоталната метаболитна енергия, изразходвана от животните за един живот е линейно пропорционална на тяхната телесна маса

Ключови думи: *скорост на метаболизма, метаболитна енергия, телесна маса, продължителност на живота*
Тип представяне: *научно съобщение*

ГОТОВИ ЛИ СМЕ ДА ПОСРЕЩНЕМ КОНГО-КРИМСКАТА ХЕМОРАГИЧНА ТРЕСКА ВЪВ ВАРНЕНСКИ РАЙОН

Н. Вълканова, Цонко П. Паунов, А. Костова, С. Станева*, Р. Константинов*
*УНС по Епидемиология, МУ-Варна, *РИОКОЗ, Варна, България*

След десетилетия на отсъствие от Варненска област и липсата на регистрирани клинични случаи, Конго-кримската хеморагична треска се завърна.
От активното природно огнище в Бургаски регион заболяването се разпространява на Север и по наши наблюдения всяка година се обхващат нови населени места, които по административно-териториално делене попадат във Варненски район. По тази причина заболелите се насочват за консултация към Инфекциозна клиника на Варненската университетска болница.

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МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ
СССР

ГОСУДАРСТВЕННАЯ
ЦЕНТРАЛЬНАЯ НАУЧНАЯ
МЕДИЦИНСКАЯ БИБЛИОТЕКА

117418, Москва, ул. Красикова, 30
Тел. 128-33-46

Тел. 120-65-78

Уважаемый тов. А.М. Атанасов

Направленная Вами рукописная работа Графическое изображение скоростного процесса агрегации тромбоцитов принята на депонирование и зарегистрирована в Гос. центр. науч. медицинской библиотеке за № Д-23404 от 3.06. 1993 г.

Библиографическое описание настоящей рукописи будет опубликовано в Текущем указателе научной медицинской литературы. "Справка о депонировании рукописи" высылается по запросу автора. Просьба вести переписку по адресу: 117866 ГСП-7 г.Москва Ул. Красикова, д. 30. Гос. центр. науч. мед. б-ка. Комната 326. Сектор депонирования.

При направлении рукописной работы на депонирование необходимо вложить её в картонную папку.

Руководитель Отдела комплектования отечественной [illegible]
Матвеенкова Л.А.

РЕЗЮМЕ

ГРАФИЧЕСКОЕ ИЗОБРАЖЕНИЕ СКОРОСТНОГО ПРОЦЕССА АГРЕГАЦИИ ТРОМБОЦИТОВ

Атанасов, А. Т.

Графическая запись процесса агрегации тромбоцитов представляет собой интегральную запись /интегральную агрегограмму/, отражающая нарастание агрегации в тромбоцитной суспенсии.Дополнительную информацию об агрегационной функции тромбоцитов может дать и динамика процесса т.е. зависимость, показывающая способ изменения скорости агрегации тромбоцитов в зависимости от времени.Эту зависимость по существу является дифференциальной кривой /дифференциальной агрегограммой/.Автор предлагает графический способ построения дифференциальной агрегограммой, на базе данных графической записи агрегометра.

Том 1, Tome 1 1988

ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ-СТАРА ЗАГОРА

ANNUAIRE DE L'INSTITUT SUPERIEUR DE MEDECINE DE STARA ZAGORA

София · 1990 · Sofia

ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ — СТАРА ЗАГОРА
Том I 1988
ANNUAIRE DE L'INSTITUT SUPERIEUR DE MEDECINE DE STARA ZAGORA
Tome I 1968

ЕЛЕКТРОНЕН ТЕРМОМЕТЪР ЗА ЛАБОРАТОРНИ И МЕДИЦИНСКИ ИЗСЛЕДВАНИЯ

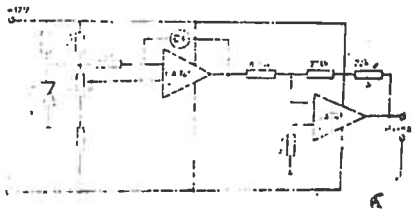
АТАНАС Т. АТАНАСОВ

Катедра по физика и биофизика

Представена е схема на прецизен електронен термометър с термисторен измерителен елемент. Термометърът се отличава с голяма чувствителност и обхват и може да бъде използуван като универсален медицински и лабораторен прибор за точни измервания на температурата на различни по големина участъци на човешкото тяло. Особено подходящ е за измерване на кожната температура.

Ключови думи: термометър, термистор.

В лабораторната и медицинската практика често се налага да се измерват температури с голяма точност. За тази цел съществуват различни по конструктивно и схематично решение термометри [1, 2]. Предлагаме една схема, изпълнена с операционни усилватели UA 741 PC, производство на САЩ. Измерителният елемент е термистор, включен в обратната връзка на първия операционен усилвател (фиг. 1). Диапазонът от измервани температури е от 0 °C до 100 °C, а чувствителността на схемата е от 0,05 °C до 0,1 °C (10 mV на 1 °C). При по-високо захранване схемата може да се включи в пишещи устройства без собствен усилвател.



Фиг. 1

В зависимост от площта на използувания термистор могат да се измерват температури на различни по големина участъци от човешкото тяло. Термометърът е особено подходящ за измерване на кожната температура.

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ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ - СТАРА ЗАГОРА

ANNUAL OF THE HIGHER MEDICAL INSTITUTE OF STARA ZAGORA

МЕДИЦИНСКИ ФАКУЛТЕТ - ТРАКИЙСКИ УНИВЕРСИТЕТ
FACULTY OF MEDICINE - THRACIAN UNIVERSITY

Стара Загора - 1996 - Stara Zagora

ЕФЕКТ НА ВОДНИ ИЗВЛЕЦИ ОТ БЪЛГАРСКИ ЛЕЧЕБНИ РАСТЕНИЯ, СЪДЪРЖАЩИ ДЪБИЛНИ ВЕЩЕСТВА, ВЪРХУ ТРОМБОЦИТНАТА АГРЕГАЦИЯ

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Summary. Atanasov A T (Department of Physics and Biophysics, Higher Medical Institute, 11 Armeiska str., Stara Zagora 6000 Bulgaria) and Spasov V. Effect of water extracts from medicinal plants containing taninum on platelet aggregation. Annual of the Higher Medical Institute of Stara Zagora [Bulgaria] 1996; 4: 9-10. Searching for new chemical substances influencing on platelet aggregation is a very important endeavour for medical practice. The in vitro effect of water extracts from 18 plants on aggregation of platelets in female rats was investigated. Following a literature search, plants with high content of taninum were chosen. An inhibition of platelet aggregation from water extracts of Agrimonia eupatoria L.; Arctostaphylos uva-ursi L. Sprend; Corylus avellana L.; Cydonia oblonga Mill.; Dryopteris filix-mas (L.) Schott; Ephedra distachya L.; Geum urbanum L.; Primula officinalis (L.) Hill.; and Punica granatum L. was established. The analysis on literature data indicated these plants contained about 10% taninum except Cydonia oblonga Mill. and Primula officinalis (L.) Hill. Few plants with content of taninum over 10% did not have any effect on the platelet aggregation.

***Key words:** taninum, medicinal plant, platelet aggregation*

Дъбилните вещества са високомолекулярни полимерни съединения с молекулна маса от 500 до 20000 D. В зависимост от химичния им строеж, K. Freudenberg ги разделя на хидролизиращи се и кондензирани танини. В състава на българските лечебни растения се съдържат танини и от двете групи.

В настоящата работа е направено скринингово проучване на 18 лечебни растения с високо съдържание на дъбилни вещества. Изследван е ефектът на водните извлеци върху тромбоцитната агрегация.

МАТЕРИАЛ И МЕТОДИ

Изследваните лечебни растения са: *Agrimonia eupatoria L.* (herba) -- до 5% катехини, до 8% галотанини; *Achillea millefolium L.* (herba) -- до 2.8%; *Alchemilla vulgaris L.* (herba, rhizoma) -- около 10% танини, производни на галовата и елаговата киселина; *Arctostaphylos uva-ursi L. Sprend* (folia) -- около 20% галотанини; *Cotinus cogygria Scop.* (folia) -- 15-25% галотанини; *Corullus avellana L.* (cortex) -- около 10% танини; *Cydonia oblonga Mill.* (folia); *Dryopteris filix-mas (L.) Schott* (rhizoma) -- до 10% филикс дъбилна киселина; *Ephedra distachya L.* (herba) -- до 10% пирокатехини; *Geum urbanum L.* (radix, rhizoma) -- до 30% танини; *Juglans regia L.* (folia) -- до 4-5% танини; *Hypericum perforatum L.* (herba) -- до 10% катехинови дъбилни вещества; *Lavandula angustifolia Mill.* (flores) -- до 12% танини; *Ocimum basilicum L.* (herba) -- до 5% танини; *Primula officinalis (L.) Hill.* (folia); *Punica granatum L.* (cortex) -- до 25% танини; *Rosmarinus officinalis L.* (folia) -- до 8% танини; *Rubus sp. diversa* (folia) -- от 5 до 14% танини; *Symphytum officinale L.* (radix) -- до 6.5% танини; *Vaccinium myrtillus L.* (folia) -- 20% танини в листата и до 10% танини в плодовете [1, 3].

Водните извлеци бяха получени чрез накисване (мацерация) на 2 g сух материал в 20 ml дестилирана вода за 20-24 h при 18-20°C. Свежият извлек беше прецеден двукратно през филтърна хартия и ефектът му върху тромбоцитната агрегация беше изследван веднага. Използвахме метода на Born [5], модифициран от Атанасов [4]. Богатата на тромбоцити плазма от бели плъхове (Wistar) беше стандартизирана до 250000-300000 тромбоцита в 1 микролитър с помощта на разтвор на Hanks без калций: NaCl - 8 g; KCl - 4 g; $MgSO_4 . 7 H_2O$ - 0.1 g; $MgCl . 6 H_2O$ - 0.1 g; $Na_2HPO_4 . 12 H_2O$ - 0.15 g; глюкоза - 1 g; дестилирана вода - до 1000 ml. За изследване на ефекта на водните извлеци върху тромбоцитната агрегация, към 300 ml богата на тромбоцити плазма се добавяше 17-23 ml воден извлек от всяко лечебно растение. Като агрегиращ агент се използваше 20 ml аденозиндифосфат -- 1.10^{-3} M (Reanal, Hungary). Способността на извлеците да аглутинират клетки и еритроцити беше проверена, както върху 2% еритроцитна суспензия, така

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LENGTH OF PERIODS IN THE NASAL CYCLE DURING 24-HOURS REGISTRATION

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ABSTACT

The periodic congestion and decongestion of the nasal venous sinuses and an alternation of airflow from one side of the nose to the other are known in literature as 'nasal cycle'. It is established that nasal cycle during 24-hours refistration contains from 4 to 8 time full periods with length varies from 0.80 h to 5.75 h. The mean length of all full periods is 2. 80±0.17h. The mean length of full periods of left nostril is 3.07h and the mean length of periods of right nostril is 2.43h. The result sugest, that have any assymetry in lenght of periods of airflow trought left and right nostrils about 40 min. The longer periods of left nostril can be connected with higher metabolic and functional activity of brain and human organism during active work.

Key words: nasal cycle, periods of nostril.

INTRODUCTION

The spontaneous cyclical activities due to a nasal congestion and decongestion are known in literature as 'nasal cycle,. Mirza et al.(1997) find in nasal cycle periods lengths ranging from approximately 1 to 5 hours during day. Gilbert (1989) finds longer mean estimated period in nasal cycle during day with time-duration 4.5+/-1.0 hours (range 3.5 - 6.0 h). Winkler et al. (1994) characterize daily nasal cycle as a chaotic ultradian rhythm with a period ranging from 1h 15min to 3h 20 minutes. In investigation of the nasal cycle during day (Lenz et al., 1985) measured a nasal cycle in 80% of 40 healthy individuals with a mean period of 2.5 h. Atanasov et al.(2003) characterize nasal cycle during night sleep as ultradian rhythms with periods, that is myltiplied to the length of sleep cycle(1.5h). In conection with this we try to characterize nasal cycle during 24-hour registration, using more parameters on the time.

METHOD, SUBJECTS AND STATISTICAL ANALYSIS

Temperature difference of inspirated and expirated air of each nostril detected by two thermistors, using mask. Signal of thermistors multiplies by electronic amplifier and registers by XY-recorder. The same method is used for investigation of nasal cycle during night sleep (Atanasov et al., 2003).

Subjects were ten right-handed, healthy males (medical students and doctors), non-smoking, non-obese, non-snoring. The subjects aged - N1: 18 years, N2: 20 years, N3: 21 years, N4: 25 years, N5: 29 years, N6: 31 years, N7: 38 years, N8: 40 years, N9: 42 years and N10: 45 years. The subjects did not have a history of chronic rhinitis, none were on medications. Registration

ГОДИШНИК НА ВИСШ МЕДИЦИНСКИ ИНСТИТУТ - СТАРА ЗАГОРА
ТОМ V 1992г.

ИН ВИТРО ЕФЕКТ НА ВОДНИТЕ ИЗВЛЕЦИ НА ЖАБЛЕКА ВЪРХУ ТРОМБОЦИТНАТА АГРЕГАЦИЯ В СЪЧЕТАНИЕ С НЯКОИ ЧЕСТО ИЗПОЛЗВАНИ ЛЕКАРСТВЕНИ СРЕДСТВА

Атанас Тодоров Атанасов

Представени са резултатите от изследванията за потискащия ефект на водните извлеци на Жаблека върху тромбоцитната агрегация при самостоятелно прилагане и в съчетание с различни лекарствени средства от групата на противовъзпалителните, сърдечните гликозиди, наркотизиращите средства и местните анестетици. Показано е наличието на синергизъм между редица лекарства и водните извлеци на Жаблека, който се изразява в значителен потискащ ефект върху тромбоцитната агрегация в условия ин витро.

Ключови думи: тромбоцитна агрегация, Жаблек

Жаблеката е била използвана при лечението на захарния диабет благодарение на хипогликемичното си действие/1, 2/. Показано е противовъзпалителното, диуретично и лактогонно действие на растението /3, 4/. В нашите експерименти установихме, че в условия ин витро водните извлеци на Жаблека притежават значителен антиагрегантен ефект при директното прибавяне на малки количества извлек към тромбоцитната суспензия. Съчетаното прилагане на водните извлеци на Жаблека с някои често използвани лекарствени средства / в това число и антиагреганти/ води до значително по-силен сумарен потискащ ефект върху тромбоцитната агрегация отколкото при прилагането на извлека и лекарствата поотделно. Подчертаваме, че получените резултати в условия ин витро не трябва

ГОДИШНИК НА ВИСШ МЕДИЦИНСКИ ИНСТИТУТ - СТАРА ЗАГОРА
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СПОСОБ ЗА ОТПРЕПАРИРАНЕ НА ОПАШНАТА ВЕНА ПРИ БЕЛИ ПЛЪХОВЕ ЗА МНОГОКРАТНО ИЗПОЛЗВАНЕ

Атанас Тодоров Атанасов

Рецензент: к.т.н.доц. С. Марков
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Предложен е способ за отпрепариране с цел многократно използване на венозен участък от опашната вена при бели лабораторни плъхове.Методът позволява многократно кръвовземане или инжекции на отпрепарираният венозен участък.

Ключови думи: способ, вена, отпрепариране.

В лабораторната и научно-изследователска работа често се налага да се взема кръв от малки животни / в случая бели лабораторни плъхове/, като за тази цел са предложени различни способи [1,2].В настоящата работа предлагаме един способ за отпрепариране на венозен участък от опашната вена при бели лабораторни плъхове, който цели да олекчи тази процедура, а от друга страна да позволи многократно и за дълго време / дни или седмица/ да бъде използван венозният участък.Обикновено при взимането на кръв или при инжекцията на даден препарат в опашната вена на плъхове се изисква значителен опит за да бъдем сигурни в попадението на иглата във вената, поради малките размери и подвижността на самата вена.За някои научно-изследователски нужди, като - изследване на тромбоцитната агрегация и кръвосъсирването, това трябва да стане прецизно за да не се променят параметрите на кръвта и кръвните елементи.Предложеният способ отстранява тези трудности.

Вените лягат да станат по видими, чрез потапяне на опашката в плитък разтвор на натриев сулфид за 5 минути.Това прави кожата бяла и розова и промазва кератинираните клетки.

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6th International Symposium on Spin Trapping

ugust 27-31, 2000

arseille, France – Palais du Pharo

Nitric oxide and nitroxides. Inhibition of platelet aggregation in vitro

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Keywords: nitric oxide, nitroxyls, spin-labeles, superoxide anion radical, platelet aggregation

A comparison of more important physical, chemical and biological properties of the nitric oxide (NO) and free stable nitroxyl radicals (nitroxides) on the base of their structural similarity is made in the present article. The active moiety in the nitroxide molecule is a sterically hindered nitric oxide. An original approach is used for explanation of the mechanisms of biological action of the nitroxides and especially - of their derivatives with antitumor agents from the groups of: nitrogen mustards [1], nitrosoureas [2], and triazenes [3] (spin-labeled compounds) through the biological activities of NO. Similarly to NO, nitroxides also can react with superoxide anion radical (SAR), they possess superoxide dismutase (SOD) mimetic action. While the interaction of NO with SAR yields very toxic peroxynitrite (ONOO-), its formation is strongly limited in the presence of a nitroxyl. It is known that the nitrosourea antitumor drugs, like lomustine (CCNU) and carmustine (BCNU), showed high general toxicity, one of the reasons for that probably is the formation of NO and subsequently - of ONOO- during their metabolism. The biological investigations of the synthesized by us spin-labeled nitrosoureas showed their considerably lower general toxicity that could be explained with the SOD-mimetic action of the nitroxide, present in their molecule. In the article are outlined perspectives for further investigations of the nitroxides with aim to confirm our supposition that they possess NO activities.

We have found that nitroxyls possess inhibiting effect on the platelet aggregation which is comparable to this of aspirin, cadaverin and verapamil.

Although nitroxyls contain hindered NO-group they inhibit the platelet aggregation just like NO. The precursors and the derivatives of nitroxyls, without NO-group do not show such activity.

So we consider that concepts like "Radical Therapy" and "NO-mimetic Compounds" have to be introdused in the literature.

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6th CMAPSEEC

6th Conference on Aromatic and Medicinal Plants of Southeast European Countries

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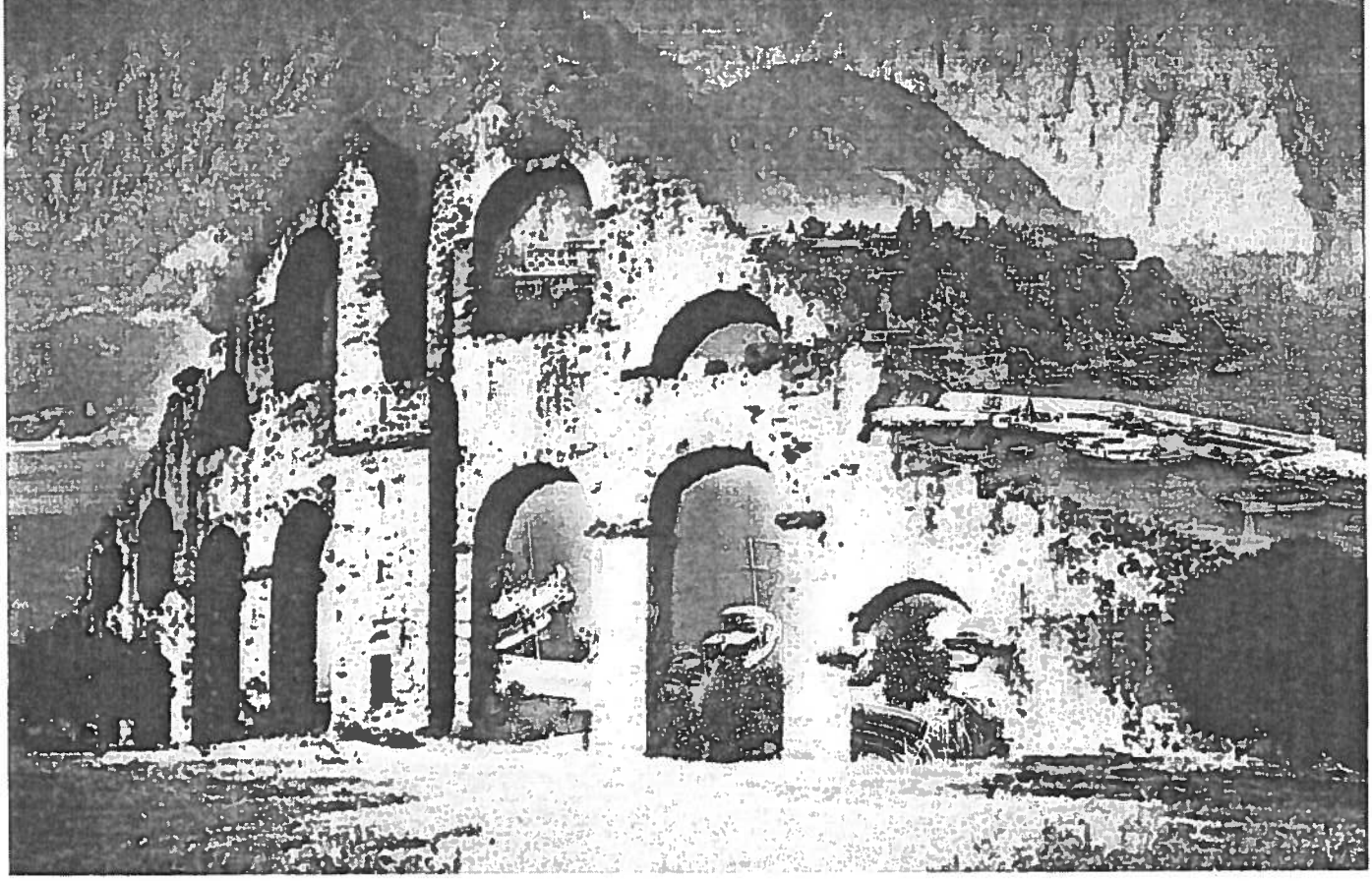

A fraction from *Galega officinalis* manifesting anti-aggregating activity on human platelet aggregation *in vitro*

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Abstract

Biologically-active substances inhibiting platelet aggregation isolated from medicinal plants are summarized. An extract from the medicinal plant goat rue – *Galega officinalis* L. (*Fabaceae, Leguminosae*) manifested powerful anti-aggregating activity. An original scheme for isolation of an active fraction was developed to obtaining of a purified active fraction demonstrating anti-aggregating activity. The fraction inhibits human platelet aggregation initiated by 25 μM adenosine 5'-diphospate, 100 μg/ml collagen, and 0.8 U/ml thrombin with IC_{50} being 11 μg/ml for ADP, and IC_{100} being 15 μg/ml for collagen 20 μg/ml for thrombin, respectively.

Study by flow cytometric assays with monoclonal antibodies CD62P-FITS, specific for P-selectin expression in activated platelet shows that the fraction's active compounds disrupted the fibrinogen bridges between the platelets, responsible for the irreversible aggregation. The isolation of anti-aggregating fraction from *Galega officinalis* L. appears an interesting scientific topic in area of the medical practice.

Keywords: *Galega officinalis* L., anti-aggregating activity, isolation

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Scientific Research

Diagnostic Strategies and Treatment for Ewing's Sarcoma

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ABSTRACT

Ewing's sarcoma is an enigmatic malignancy of progenitor cell origin, driven by transcription factor oncogenic fusions. About 85% of ESFT cases harbor the t(11;22) translocation and express the fusion protein EWS-FLI. Both bone marrow-derived human Mesenchymal stem cells and Neural crest stem cells are permissive for EWS-FLI1 expression that initiates transition to ESFT-like cellular phenotype. Diagnosis of Ewing's tumor is based on pathologic and molecular findings. The hypoxia enhances the malignancy of ESFT invasive capacity. An $ALDH^{high}$ subpopulation of Ewing's sarcoma cells, capable of self-renewal, tumor initiation and resistant to chemotherapy *in vitro*, are not resistant to YK-4-279. Intensive high-dose chemotherapy followed by stem-cell reconstitution was used for ESFT patients in second remission. Plerixafor in combination with G-CSF is an effective enhance stem cell mobilization regimen for stem cell collection with lowest success rate in patients with neuroblastoma. The ESFT-derived antigens EZH2(666) and CHM1(319) are suitable targets for protective allo-restricted human CD8(+) T-cell responses against non-immunogenic ESFT. Primitive neuroectodermal features and MSC origin are both compatible with G(D2) aberrant expression and explore G(D2) immune targeting in ESFT.

Keywords: Ewing's Sarcoma Family of Tumors; Cancer Stem Cells; Immunotherapy; Hematopoietic Progenitor Cell Transplant; Diagnostic Strategies; ESFT Therapy

1. Introduction

Ewing's sarcoma family of tumors (ESFT) are aggressive bone tumors in adolescents and young adults, but chemotherapy-sensitive and patients with metastatic disease often achieve remission.

The EWS Fusion Proteins are potent promoter-specific transcriptional activators, due to EWS-Activation-Domain (EAD) and a DNA binding domain from the fusion partner. They interact with other proteins required for mRNA biogenesis and induce tumorigenesis by perturbing gene expression. Around 85% of Ewing's tumours carry the most frequent EWSR1-FLI-1 fusion (**Table 1**).

Anti-cancer agents (DHR-related peptides and other small molecules) targeted against the N-terminal part of EAD, may possess therapeutic potentialities against Ewing's sarcoma as inhibitors of EAD-mediated trans-activation and also as immunogenic agents [1].

2. Diagnostic Strategies for Ewing's Sarcoma

Ewing's sarcoma family tumors (ESFTs) are aggressive tumors of putative stem cell origin for which prognostic biomarkers and novel treatments are needed [2]. Diagno-

Table 1. EWS associated chromosomal translocations in ESFT.

ESFT	EWS fusion gene	Chromosomal translocation
Angiomatoid fibrous histocytoma	EWS-ATF1	t(12,22)
	EWS-CREB1	t(2;22)
Clear cell sarcoma	EWS-ATF1	t(12;22)(q13;p11)
	EWS-CREB1	t(2;22)
Desmoplastic small round cell tumor	EWS-WT1	t(11;22)(p13;q12)
Ewing's sacoma or primitive neuroectodermal tumor	EWS-FLI1	t(11;22)(q24;q12)
	EWS-ERG	t(21;22)(q22;q12)
	EWS-ETV1	t(7;22)(p22;q12)
	EWS-ETV4	
	EWS-FEV	t(17;22)(q12;q12)
	EWS-E1AF	t(2;22)(q33;q12)
Extraskeletal myxoid chrondrosarcoma	EWS-NR4A3	t(9;22)
	EWS-TAF2N	t(9;17)
Myxoid chrondrosarcoma	EWS-CHN	t(9;22)(q22;q12)
Myxoid liposarcoma	EWS-CHOP	t(12;22)(q13;q12)
	EWS-CHOP	t(12;22)(q13;q12)

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Method for Tentative Evaluation of Membrane Permeability Coefficients for Sodium and Potassium Ions in Unicellular Organisms

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ABSTRACT

The membrane permeability coefficient for sodium and potassium ions in unicellular organisms can be calculated using the data for cell volume, surface and mean generation time during growth and dividing of cells by binary. Accordingly theory of proposed method, the membrane permeability coefficients for passed trough outer cell membrane sodium and potassium ions, is equal to the volume of unicellular organism divided to product between cell surface and mean generation time of cells. The calculated by this way diapason of values overlaps with experimentally measured diapason of values of permeability coefficient for sodium and potassium ions. The deviation between the theoretically calculated and experimentally measured values of permeability coefficient does not exceed one order of magnitude.

Keywords: Prokaryotes; Eukaryotes; Permeability Coefficient; Sodium; Potassium; Ion

1. Theory of Method

The ion permeability of the plasma membrane has been recognized as an important problem in cell function. The main ions in cell physiology are protons, sodium, potassium and chloride ions, because of their participation in the building of transmembrane ions gradients, the support of cell potentials and energetics mechanisms in cells [1-4]. Permeability may be defined phenomenological as the amount of substance transported across a unit area in unit time as the result of a unit force [5,6]. Permeability of given solutes is characterized by the permeability coefficient, measured by the amount of solute passing in unit time through unit area of membrane under the influence of unit concentration gradient [7]. The dimension of permeability coefficient is in meter per second if membrane area is given in m^2, cell volume in m^3 and concentration of solutes is given in mol per liter [8].

A guiding principle in the estimation of the permeability coefficient is that the cell boundary acted as a lipid-like phase through which the penetrating solute diffused. A simple hypothesis based on Fick's laws of diffusion is that the instantaneous rate of uptake of the solutes (ds/dt) through the semi-permeable bounding membrane, into a vesicle (liposome or cell) of volume (V), is represented as the product of the surface area (S) of vesicle, the difference in solute concentration between the interior (Cin) and exterior (Cex) compartments (Cex − Cin), and the permeability coefficient (P) that connect the diffusion coefficient of solutes, thickness of membrane and relative solubility of substances in water-oil phases [9].

The relevant equations are:

$$ds/dt = PS(Cex - Cin) \quad (1)$$

and

$$dCin = ds/V \quad (2)$$

where Cex and Cin are function of the time.

When cell surface area S, cell volume V and exterior concentration Cex (because of big exterior volume) are constant, these two equations simplify to:

$$dCin/dt = (PS/V)(Cex - Cin) \quad (3)$$

After integration we receive for concentration Cin(t) in vesicle after time t :

$$\begin{aligned}&[Cex - Cin(t)]/[Cex - Cin(0)]\\ &= \exp[(-PSt)/V]\\ &= \exp(-kt)\end{aligned} \quad (4)$$

where Cin(0) is the concentration of solute in vesicle at the moment t = 0.

The equation (PSt)/V = kt represents the connection between permeability coefficient P(m/s) and the first-

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Calculation of vibration modes of mechanical waves on microtubules presented like strings and bars

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Abstract: The study describes a physical model of vibrating microtubules in living cells, presented as strings and bars. Calculated are proper-frequencies of first four vibration modes of transverse and longitudinal waves on microtubules. For microtubules with length 1-30μm and shear modulus 5.0×10^6 N/m^2 the proper-frequencies of standing transverse waves fall in diapason of 1×10^3 - 5×10^7 Hz. For microtubules with same length and Young's modulus 10^8–10^9 N/m^2 the proper-frequencies of standing longitudinal waves fall in diapason of 5×10^6 - 3×10^9 Hz. These calculated diapasons of frequencies overlap with experimentally registered diapasons of frequencies of mechanical and electric vibrations in bacteria, yeast cells, erythrocytes, infuzorii and soma cells. Some theoretical problems related to the present model are discussed.

Keywords: Microtubules, String, Bar, Frequency, Transverse, Longitudinal, Waves

1. Introduction

The living cells and their structures have vibrations in all frequency diapason - mechanical, acoustical, electrical, electromagnetic, ultraviolet, infrared and visible [1, 2, 3, 4]. By vibration, the living cells can transfer mass, energy and information (signals) between them and inside [5, 6]. Endogenous mechanical and electromechanical vibrations of some cell structures like membranes and microtubules may have fundamental function in organization of living organisms, including intensity of biochemical reactions, cell growth and building of morphological structures, cellular transport, long range control of cellular functions and sensor functions in cells [7, 8, 9, 10, 11]. The microtubules determine the topology of the cells during the entire cell cycle [12, 13]. Certain authors attribute the participation of microtubules in the logical functions of the brain and consciousness [14, 15]. The possibility that microtubules carry power and information by mechanical and electromechanical vibration of their building macromolecules is under investigation. In this regard various theoretical models have been made, connecting the modes of measured vibrations emitted by the cells with the function of the microtubules. In the same sense, the aim of this study is i) to calculate the modes of mechanical vibrations in microtubules, using model in which they are presented as strings and bars and ii) to compare the calculated frequencies with experimentally measured frequencies of mechanical and electromechanical vibrations and signals emitted from living cells.

2. Experimentally Registered Mechanical and Electrical Vibrations and Signals Emitted from Living Cells

The experimentally registered vibrations and signals are received predominantly on some type of cells (bacteria, yeast, infuzorii, erythrocytes and soma cells). Experimentally measured frequencies of mechanical and electrical vibration in these types of cells don't exceed 10^7 Hz, despite of that the calculated frequencies in theoretical models of other authors reach till to 10^{11} Hz [7, 16, 17, 18]. However, the external electric and electromagnetic fields (microwaves) with frequencies 10^5 -10^{11} Hz have clear expressed non-thermal biological effect on cells, tissues and organisms [19, 20, 21] showing that the cells and their structures are capable of absorbing and resonate the vibration in this frequency range.

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Scientific Research

Length of Periods in the Nasal Cycle during 24-Hours Registration

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Abstract

The periodic congestion and decongestion of the nasal venous sinuses and an alternation of airflow from one side of the nose to the other are known in literature as "nasal cycle". It is established that nasal cycle during 24-hours registration contains from 4 to 8 time full periods, length of which varies from 0.80 h to 5.75 h. The mean length of all full periods is 2.80 ± 0.17 h. The mean length of full periods of left nostril is 3.07 h and the mean length of periods of right nostril is 2.43 h. The result suggests that there is any asymmetry in length of periods of airflow trough left and right nostrils about 40 min. The longer periods of left nostril can be connected with higher metabolic and functional activity of brain and human organism during active work.

Keywords

Nasal Cycle, Periods of Nostril, Sleep Cycle

1. Introduction

The spontaneous cyclical activities due to a nasal congestion and decongestion are known in literature as "nasal cycle". Mirza *et al.* [1] find in the nasal cycle periods lengths ranging from approximately 1 to 5 hours during day. Gilbert [2] finds longer mean estimated period in nasal cycle during day with time-duration 4.5+/−1.0 hours (range 3.5 - 6.0 h). Winkler *et al.* [3] characterized daily nasal cycle as a chaotic ultradian rhythm with a periods ranging from 1 h 15 min to 3 h 20 minutes. In investigation of the nasal cycle during day Lenz *et al.* [5] measured a nasal cycle in 80% of 40 healthy individuals with a mean period of 2.5 h. Atanasov *et al.* [5] firstly characterized nasal cycle during night sleep as ultradian rhythms with periods that multiplied to the length of sleep cycle (1.5 h). Atanasov and coworkers [6] showed that the switch from left to right nostril's domination airflow (and reverse) occurs only during REM phases of the night sleep. Ten years later Kimura *et al.* [7] received similar result.

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ARE THE CENTRIOLES SENSORY CENTRES IN LIVING CELLS? IMPACT TO MECHANISM OF CANCER (A HYPOTHESIS)

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Abstract. In this manuscript the hypothesis that the main function of centrioles is due of sensor centres is developed. The centrioles receive sensor information from microtubules as 'intracellular' sensor antennas and from primary cilia as 'extracellular' sensor antennas, initiating cellular effector activities and reactions - regulation of cell proliferation, differentiation, migration, cell polarity and tissue morphology. It is possible the centrioles play a role of epigenetic centre and switch genes' program(s) in cells as effector reaction.

The function of centrosome, centrioles, cilia and microtubules. The two major properties of the centrosome are its capacity to reproduce by duplication and its ability to nucleate microtubules (1). Centrioles are the cylindrical structures found within the centrosomes of animal cells (a pair of centrioles form the core of centrosome) and at the core of the mitotic spindle pole. The absence of centrioles in the centrosome from other eukaryotic organisms leads to the domination view that the centriole's pair is not relevant to centrosome activity (2). This raises the question: what is the real function of centrioles? One of the main centriole functions is to form the cilia and flagella. The cilia can exist in two main structural forms with different functions: motile cilia and non-motile (primary) cilia. The primary cilium is a generally non-motile cilium that occurs singly on most cells in the vertebrate body. Recent findings reveal that the primary cilium is an antenna displaying specific receptor relaying signals to the cell body (3). Microtubules are the main constituents of the cellular cytoskeleton together with microtubule associated proteins, intermediary and actin filaments. Microtubules are dynamical instability structures because they lead to reorganization of the cytoskeleton and, therefore, cellular morphology and functions. However, in highly differentiated cells like neurons there is a stable population of cytoskeletal microtubules. In most cells the majority of microtubules emanates from a microtubule-organizing center (centrioles) and radiates to the membrane and other structures of the cells (4).

The presence of centrioles is obviously useful for all cellular sensory functions. If we regard the sensor functions of eukaryotic cells in an evolutionary way, we will observe that the appearance of microtubules, centrioles and cilia in cells is accompanied by increasing of the metabolic and sensor activity of cells, as well as complexity of sensing functions. The presence of centrioles correlates strictly with the presence of cilia throughout the eukaryotic phylogeny. The absence of cilia in higher land plants, fungi and red algae is accompanied by lack of centrioles or basal bodies. The presence of cilia in

Scaling of volume to surface ratio and doubling time in growing unicellular organisms: Do cells appear quantum-mechanical systems?

Atanas Todorov Atanasov

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Scaling of Volume to Surface Ratio and Doubling Time in Growing Unicellular Organisms: Do Cells Appear Quantum-Mechanical Systems?

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Abstract. The scaling of physical and biological characteristics of the living organisms is a basic method for searching of new biophysical laws. In series of previous studies the author showed that in Poikilotherms, Mammals and Aves, the volume to surface ratio $V \times S^{-1}$ (m) of organisms is proportional to their generation time T_{dt}(s) via growth rate v (m s^{-1}): $V \times S^{-1} = v_{gr} \times T^{r}$. The power and the correlation coefficients are near to 1.0. Aim of this study is: i) to prove with experimental data the validity of the above equation for Unicellular organisms and ii) to show that perhaps, the cells are quantum-mechanical systems. The data for body mass M (kg), density ρ (kg/m^3), minimum and maximum doubling time T_{dt} (s) for 50 unicellular organisms are assembled from scientific sources, and the computer program 'Statistics' is used for calculations. In result i) the analytical relationship from type: $V \times S^{-1} = 4.46 \cdot 10^{-11} \times T_{dt}$ was found, where $v_{gr} = 4.46 \times 10^{-11}$ m/s and ii) it is shown that the products between cell mass M, cell length expressed by V/S ratio and growth rate v_{gr} satisfied the Heisenberg uncertainty principle i.e. the inequalities $V/S \times M \times v_{gr} > h/2\pi$ and $T_{dt} \times M \times v_{gr}^2 > h/2\pi$ are valid, where $h = 6.626 \times 10^{-34}$ J·s is the Planck constant. This rise the question: do cells appear quantum-mechanical systems?

Keywords: Unicellular organisms, Heisenberg uncertainty principle, Planck constant.
PACS: 03.Quantum mechanics.

INTRODUCTION

The scaling of physical and biological characteristics of the living organisms is a basic method for searching of new allometric relationships. In series of studies the author showed that in multicellular Poikilotherms, Mammals and Aves the volume to surface ratio $V \times S^{-1}$ (m) of animals is proportional to their generation time T_{dt}(s) via growth rate v (m s^{-1}) of organisms: $V \times S^{-1} = v_{gr} \times T^{r}$. The power and the correlation coefficients are near to 1.0 [1]. The rate of 'volume to surface ratio growth' of organisms, expressed by coefficient v_{gr}, has a dimension of speed and values, ranging in the window of 10^{-9}-10^{-12} (m s^{-1}) [1, 2]. In later studies [3, 4] the author showed that the rate of growth of organisms is a relatively constant parameter, changing 10^2 folds only, in comparison to 10^{12} fold difference between their body mass. In this reason, the scaling of volume to surface ratio and doubling time in unicellular organisms is of great theoretical and practical interest for biologist and biophysics.

AIM OF THE STUDY

The aim of the study is: i) to prove with experimental data the validity of the equation $V \times S^{-1} = v_{gr} \times T_{dt}$ between the volume to surface ratio $V \times S^{-1}$ and the doubling time T_{dt} in unicellular organisms and ii) to show that perhaps, the cells are quantum-mechanical systems.

METHOD

The data for body mass M (kg), density ρ (kg/m^3), minimum and maximum doubling time T_{dt} (s) of the cells are assembled from scientific publications and sources. The formula for calculation of the volume/surface ratio is given from previous publication of the author [1]: $V/S = M^{0.33}(\rho \times k)^{-1}$, where k is a constant with value corresponding to the geometry of the body [5]. For Viruses ρ=1200 kg m^{-3} and k= 0.0542. For Prokaryotes and Eukaryotes the cell density and the coefficient k are respectively ρ=1100 kg m^{-3} and k= 0.0542. The growth rate v_{gr} is calculated for the mean doubling time T_{mean} of cells.

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Allometric relationships between the length of pregnancy and body parameters in mammals

A. T. Atanasov, M. Todorova, D. T. Valev, and R. Todorova

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Allometric Relationships between the Length of Pregnancy and Body Parameters in Mammals

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Abstract. In this manuscript we investigated the presence of allometric relationships between the length of pregnancy and the body parameters in mammals. The relationships between the length of pregnancy T (d) and the square of body length H^2 (m^2), body surface S (m^2), body mass to surface ratio M/S (kg/m^2) and body-mass index (BMI) (M/H^2) were investigated in mammals: Metatheria and Placentalia, including animals with body mass ranging from 8g in Common shrew to 15t in Killer whale. In result, the found power equations are: $T = 114.3\ (H^2)^{0.352}$; $T= 120.4\ S^{0.38}$; $T = 9.147\ (M/S)^{0.757}$ and $T = 17.6\ BMI^{0.605}$. The study showed that the M/S ratio and BMI are nearly equivalent characteristics in relation to length of pregnancy.

Keywords: Mammals, pregnancy, mass to surface ratio, body mass index
PACS: 87. Biological and medical physics.

INTRODUCTION

There are numerous scientific reports about allometric relationships between animal body mass and a number of physiological parameters in animals – the rate and frequency of physiological and biochemical processes, metabolic rate, lifespan and others [1, 2, 3, 4]. From this point of view, of a considerable interest for practical and theoretical medicine appear to be the relationships between the length of pregnancy and the body parameter in animals. In previous works Atanasov [5, 6] showed the allometric link between the length of pregnancy and the body mass in Mammals. In this study we investigate the presence of allometric relationship between the length of pregnancy and the body parameters in mammals- body length, body surface, body mass to surface ratio and body mass index.

THE AIM OF THE STUDY

The aim of the study is to show the equivalency between the body mass index (BMI) and mass to surface ratio (M/S) as characteristics to pregnant mammals.

MATERIALS AND METHODS

The data for the 103 studied mammal species (from Common shrew to Killer whale), their body mass, body length and pregnancy length were collected from the review papers [6, 7, 8, 9] and original articles. The body surface S (m^2) were calculated by formula $S=0.1M^{0.67}$, where body mass M is given in kg [4]. The present study included 103 animal species from the Mammalia class (Metatheria and Placentalia). The relationships were calculated by means of a statistical software package (Statistica), licensed in the Space Research Institute (Bulgarian Academy of Sciences, Stara Zagora). The scaling exponents of functions were estimated using the least squares linear regression as well as the correlation coefficient between the length of pregnancy and body parameters, the root mean square error and the level of significance of regression, using the F-criterion and 95% confidence interval. A similar methodological approach was successfully used earlier in the study and modeling of the other allometric

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Scaling of Total Metabolic, Gravitational and Heat Energy of Living Organisms, Earth and Sun

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Abstract: The gravitational energy, total metabolic energy and heat energy of living organisms, Earth and Sun are scaled. Statistical analyses have shown that nearly a linear relationship between the total metabolic energy per lifespan of Poikilothermic organisms (P_{ls}, kJ), total heat energy (THE_E, kJ) of the Earth and the body mass (M, kg) of Poikilotherms and Earth (M_E, kg) in log-log plots holds: $P_{ls}= 1.696\times10^5\ M^{0.949}$ with $R^2= 0.996$. A similar relationship between the total metabolic energy of Homoitherms Mammals and Aves (P_{ls}, kJ), the total heat energy of Sun (emitted over Earth surface per Earth's lifespan) (THE_S, kJ), and body mass (M, kg) of Mammals, Aves and Earth (M_E, kg) holds: $P_{ls} = 10.2\times10^5\ M^{1.023}$ with $R^2= 0.996$. The metabolic potential of living organisms, gravitational and heat potential of Earth and Sun are scaled too. The gravitational and 'heat' potential of Earth are emerging as a lower limit of lifespan metabolic potentials of unicellular organisms, while the gravitational and 'heat' potential of Sun are emerging as an upper limit of lifespan metabolic potentials of multicellular organisms (Poikilotherms, Mammals and Aves). The relationships between mass-energy characteristics of living organisms, Earth and Sun show that gravitational and heat energy of Earth and Sun determine maximum and minimum total metabolic energy (per lifespan) of living organisms, while the gravitational and 'heat' potentials of Earth and Sun determine their maximum and minimum lifespan metabolic potentials.

Keywords: Total Metabolic, Gravitational, Heat, Energy, Earth, Sun

1. Introduction

All living organisms in biosphere, from small unicellular prokaryotes to big multicellular animals and plants live in a spatial area of gravitational fields of Earth, Sun, Moon and other planets from Solar System, as well as in the area of their light and heat emission. The gravity is a constant force throughout the evolution of Earth that acts on mass of living organisms and produced weight of the mass. Thus, gravity is fundamental factor which affects the evolution of organisms [1, 2]. From physical point of view the gravitational fields of Earth and Sun are characterized by their gravitational potentials (Fix, 1995), given by the equations:

$$\Gamma_E=-GM_E/R_E \quad (1a),$$

and

$$\Gamma_S = -G\ M_S\ /R_{ES} \quad (1b),$$

where Γ_E (J/kg) is the gravitational potential of Earth equal to 0.625×10^8 J/kg on Earth's ground, Γ_S (J/kg) is the gravitational potential of Sun equal to 8.85×10^8 J/kg on Earth's ground, G is the fundamental gravitational constant of Universe (6.673×10^{-11} Nm^2/kg), M_E is the mass of Earth (5.97×10^{24}kg), M_S is the mass of Sun (1.99×10^{30}kg), R_E is the radius of Earth (6.4×10^6 m) or distance R_{ES} between Earth and Sun (1.5×10^{11} m).

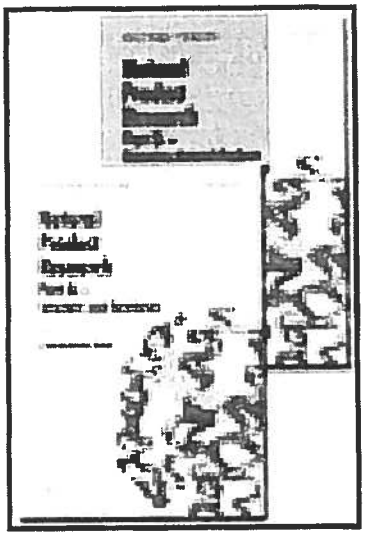
Because the gravitational potential is defined as work of gravitational force to moves unit mass from given point of field to infinity [3], the gravitational energy of given organism in gravitational field of Earth and Sun can be calculated as a product between mass of organisms (M) and gravitational potentials of Earth (Γ_E) and Sun (Γ_S) on Earth's ground:

$$GE_E= \Gamma_E \times M \quad (2a)$$

and

$$GE_S=\Gamma_S\times M \quad (2b)$$

In these equations the gravitational potentials of Earth (Γ_E) and Sun (Γ_S) on Earth's ground have constant values, while the body mass (M) of living organisms vary 23 orders of



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Haberlea rhodopensis: pharmaceutical and medical potential as a food additive

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Possible determination of the physical parameters of the first living cells based on the fundamental physical constants

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Abstract

Here is developed the hypothesis that the cell parameters of unicellular organisms (Prokaryotes and Eukaryotes) are determined by the gravitational constant (G, $N \cdot m^2/kg^2$), Planck constant (h, J·s) and growth rate of cells. By scaling analyses it was shown that the growth rate v_{gr}(m/s) of unicellular bacteria and protozoa is relatively constant parameter, ranging in a narrow window of $10^{-12} - 10^{-10}$ m/s, in comparison to the diapason of cell mass, ranging 10 orders of magnitudes from 10^{-17} kg in bacteria to 10^{-7} kg in amoebas. By dimensional analyses it was shown that the combination between the growth rate of cells, gravitational constant and Planck constant gives equations with dimension of mass $M(v_{gr})=(h \cdot v_{gr}/G)^{½}$ in kg, length L(vgr)=(h·G/vgr3)12 in meter, time T(vgr)=(h·G/vgr5)12 in seconds, and density ρ((vgr)=vgr.3.5/hG2 in kg/m3. For growth rate v_{gr} in diapason of 1×10^{-11} m/s – 1×10^{-95} m/s the calculated numerical values for mass ($3\times10^{-18} - 1\times10^{-16}$ kg), length (5×10^{-8}

-1×10^{-5} m), time (1×10^{2} -1×10^{6} s) and density (1×10^{-1} – 1×10^{4} kg/m^3) overlaps with diapason of experimentally measured values for cell mass (3×10^{-18} -1×10^{-15} kg), volume to surface ratio (1×10^{-7} -1×10^{-4} m), doubling time (1×10^{3} -1×10^{7} s), and density (1050 – 1300 kg/m^3) in bacteria and protozoa. These equations show that appearance of the first living cells could be mutually connected to the physical constants.

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Possible determination of the physical parameters of the first living cells based on the fundamental physical constants

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Possible Determination of the Physical Parameters of the First Living Cells Based on the Fundamental Physical Constants

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Abstract. Here is developed the hypothesis that the cell parameters of unicellular organisms (Prokaryotes and Eukaryotes) are determined by the gravitational constant (G, $N{\cdot}m^2/kg^2$), Planck constant (h, J·s) and growth rate of cells. By scaling analyses it was shown that the growth rate v_{gr}(m/s) of unicellular bacteria and protozoa is relatively constant parameter, ranging in a narrow window of $10^{-12} - 10^{-10}$ m/s, in comparison to the diapason of cell mass, ranging 10 orders of magnitudes from 10^{-17} kg in bacteria to 10^{-7} kg in amoebas. By dimensional analyses it was shown that the combination between the growth rate of cells, gravitational constant and Planck constant gives equations with dimension of mass $M(v_{gr})=(h{\cdot}v_{gr}/G)^{1/2}$ in kg, length $L(v_{gr})=(h{\cdot}G/v_{gr}^{1})^{1/2}$ in meter, time $T(v_{gr})=(h{\cdot}G/v_{gr}^{5})^{1/2}$ in seconds, and density $\rho(v_{gr})\ v_{gr}^{15}/hG^2$ in kg/m^3. For growth rate v_{gr} in diapason of 1×10^{-11} m/s - $1\times10^{-9.5}$ m/s the calculated numerical values for mass ($3\times10^{-18} - 1\times10^{-16}$ kg), length (5×10^{-8} -1×10^{-5} m), time (1×10^{3} -1×10^{6} s) and density (1×10^{-1} - 1×10^{4} kg/m^3) overlaps with diapason of experimentally measured values for cell mass ($3\times10^{-18} - 1\times10^{-15}$ kg), volume to surface ratio (1×10^{-7} -1×10^{-4} m), doubling time (1×10^{3} -1×10^{7} s), and density (1050 – 1300 kg/m^3) in bacteria and protozoa. These equations show that appearance of the first living cells could be mutually connected to the physical constants.

Keywords: Unicellular organisms, growth rate, Planck constant, gravitational constant
PACS: 03.Quantum mechanics.

INTRODUCTION

Scaling of physical and biological characteristics of the living organisms and dimensional analyses are the basic methods for searching of new alometric (empiric) relationships. In series of studies the author showed that in unicellular organisms and in multicellular Poikilotherms, Mammals and Aves the volume to surface ratio V/S (m) is proportional to generation time T_{gt}(s) *via* growth rate v_{gr} (m/s) of organisms:

$$V/S = v_{gr} \times T^{1.0} \quad (1)$$

The powers and the correlation coefficients in Eq.(1) are near to 1.0 [1, 2]. The rate of 'volume to surface ratio growth' of organisms, expressed by coefficient v_{gr}, has a dimension of speed, and values, ranging in a narrow window of 10^{-9}-10^{-12} (m/s) [3]. In later study [4] the author has showed that the growth rate of unicellular organisms is a relatively constant parameter, changing 10^2 folds only, in comparison to 10^{10} fold difference between the body mass of bacteria (1×10^{-17} kg) and amoebas (1×10^{-8} kg). The physical analog of Eq.(1) appears to be a connection between the distance L(m), speed v(m/s) and time T(s) of a given moving physical object i.e.:

$$L(m) = v(m/s) \times T(s) \quad (2)$$

The analogy between Eq.(1) and Eq.(2) give a possibility to regard growth rate of living organisms as physical characteristics (speed) and to combine with other biological and physical constants, using dimensional analyses [5, 6]. The idea to combine the physical and biological constants and parameters has not analog in scientific literature and appears to be a new method in mathematical physics. The aim of the study is: 1) to combine growth rate v_{gr} (m/s), gravitational constant G ($N{\cdot}m^2/kg^2$) and Planck constant h (J·s), and by dimensional analyses to receive new equations with dimension of mass, length, time and density, and 2) to calculate numerical values for mass, length, time and density for growth rate typical for unicellular organisms, and 3) to compare calculated and experimental values for cell mass, length, doubling time and density.

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Lifespan metabolic potential of the unicellular organisms expressed by Boltzmann constant, absolute temperature and proton mass

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KEYWORDS

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Protons
Nucleons
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Total energy calculations

ABSTRACT

The unicellular organisms and phages are the first appeared fundamental living organisms on the Earth. The total metabolic energy (E_{ls}, J) of these organisms can be expressed by their lifespan metabolic potential (A_{ls}, J/kg) and body mass (M, kg): $E_{ls} = A_{ls} M$. In this study we found a different expression - by Boltzmann's constant (k, J/K), nucleon mass (m_{p+}, kg) of protons (and neutrons), body mass (M, kg) of organism or mass (M_s) of biomolecules (proteins, nucleotides, polysaccharides and lipids) building organism, and the absolute temperature (T, K). The found equations are: $E_{ls} = (M/m_{p+})kT$ for phages and $E_{ls} = (M_s/m_{p+})kT$ for the unicellular organisms. From these equations the lifespan metabolic potential can be expressed as: $A_{ls} = E_{ls}/M = (k/m_{p+})T$ for phages and $A_{ls} = E_{ls}/M = (k/3.3m_{p+})T$ for unicellular organisms. The temperature-normated lifespan metabolic potential (A_{ls}/T, J/K·kg) is equals to the ratio between Boltzmann's constant and nucleon mass: $A_{ls}/T = k/m_{p+}$ for phages and $A_{ls}/T = k/3.3m_{p+}$ for unicellular organisms. The numerical value of the k/m_{p+} ratio is equals to 8.254×10^3 J/K·kg, and the numerical value of $k/3.3m_{p+}$ ratio is equal to 2.497×10^3 J/K·kg. These values of temperature-normated lifespan metabolic

potential could be considered fundamental for the unicellular organisms.

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5.

Physics International

Original Research Paper

Possible Physical Determination of the Mass, Size, Doubling Time and Density of the Unicellular Organisms Based on the Fundamental Physical Constants

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Abstract: In manuscript the hypothesis 'that the mass, size, doubling time and density of the unicellular organisms (Prokaryotes and Eukaryotes) are determined by the gravitational constant (G, $N \cdot m^2/kg^2$), Planck constant (h, $J \cdot s$) and growth rate v_{gr} (m/s)' is investigated. By scaling analyses it is indicated that the growth rate of the unicellular organisms ranges in a narrow window of 1.0×10^{-11}–1.0×10^{-10} m/s, in comparison to 10 orders of magnitudes difference between their mass. Dimension analyses demonstrates that the combination between the growth rate of unicellular organisms, gravitational constant and Planck constant provides the equations with dimension of mass $M(v_{gr}) = (h \cdot v_{gr}/G)^{1/3}$ in kilogram, length $L(v_{gr}) = (h \cdot G/v_{gr}^3)^{1/4}$ in meter, time $T(v_{gr}) = (h \cdot G/v_{gr}^5)^{1/6}$ in seconds and density $\rho = v_{gr}^{3.5}/hG^2$ in kg per 1 m^3. For values of growth rate in numerical diapason of 1.0×10^{-11}–$1.0\times10^{-9.5}$ m/s, the calculated numerical values for mass (3.0×10^{-18}–1.0×10^{-16} kg), length (5.0×10^{-8}–1.0×10^{-5} m), time (1.0×10^{2}–1.0×10^{6} s) and density (1.0×10^{-1}–1.0×10^{4} kg/m^3) overlap with diapason of experimentally measured values for cell mass (3.0×10^{-18}–1.0×10^{-15} kg), volume to surface ratio (1.0×10^{-7}–1.0×10^{-4} m), doubling time (1.0×10^{3}–1.0×10^{7} s) and density (1050-1300 kg/m^3) in both bacteria and protozoa.

Keywords: Prokaryotes, Eukaryotes, Planck Constant, Gravitational Constant

Introduction

The origin of the first unicellular organisms on the Earth is one of the enigmas in the life sciences. There are many hypotheses for the origin of bacteria-ranging from astrophysical bases of Universe (Ehrenfreund *et al*., 2002) and self-reproducing coacervates (Oparin, 1973; Colgate *et al*., 2003; Vasas *et al*., 2012) to the first mitotic cells (Sagan, 1967; Ratcliff *et al*., 2012; Montagnes *et al*., 2012). Recently, the quantum-mechanical effects (Patte, 1967; Pati, 2004; Davies, 2008; Tamulis and Grigalavicus, 2010; Fleming *et al*., 2011) and the anthropic principles that implies that Universe must be consistent with the existence of life (Carr and Rees, 1979; Hoyle and Wickramasinghe, 1999; Vidal, 2010; Kamenshchik and Teryaev, 2013) need to be extended into the understanding of life. In the present approach we developed the hypothesis for possible physical determination of the mass, size, doubling time and density parameters of the unicellular organisms on the Earth. The growth rate of unicellular organisms (v_{gr}, *m/s*) is represented as a speed of their volume to surface ratio growth (V/S, *m*) for corresponding doubling time (T_{db}, *s*) of organisms (Atanasov, 2007; 2012a; 2014):

$$v_{gr} = V/(S \times T_{db}) \quad (1)$$

The diapason growth rate of unicellular Prokaryotes and Eukaryotes ranges in a narrow window between 1.0×10^{-11}-1.0×10^{-10} m s^{-1}, in comparison to 10 orders of magnitudes difference between the cells mass (Atanasov, 2012b). The connection between volume to surface ratio and mean doubling time T_{mean}(*s*) of phages, bacteria and protozoa could be approximated by a linear function:

$$V/S = v_{gr} \times T_{mean} \quad (2)$$

with correlation coefficient near to 1.0 (Atanasov, 2014).

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Free

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Thermodynamics of the living organisms. Allometric relationship between the total metabolic energy, chemical energy and body temperature in mammals

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KEYWORDS

Thermodynamics

Zooplankton

Membrane biochemistry

ABSTRACT

The study present relationship between the total metabolic energy ($E_{TME(c)}$, J) derived as a function of body chemical energy (G_{chem}, J) and absolute temperature (T_b, K) in mammals: $E_{TME(c)} = G_{chem}$ (T_b/T_n). In formula the temperature T_n =2.73K appears normalization temperature. The calculated total metabolic energy $E_{TME(c)}$ differs negligible from the total metabolic energy E_{TME}(J), received as a product between the basal metabolic rate (P_m, J/s) and the lifespan (T_{ls}, s) of mammals: $E_{TME} = P_m \times T_{ls}$. The physical nature and biological mean of the normalization temperature (T_n, K) is unclear. It is made the hypothesis that the kT_n energy (where k= 1.3806×10^{-23} J/K -Boltzmann constant) presents energy of excitation states (modes) in biomolecules and body structures that could be in equilibrium with chemical energy accumulated in body. This means that the accumulated chemical energy allows trough all body molecules and structures to propagate excitations states with kT_n energy with wavelength in the rage of width of biological membranes. The accumulated in

PDF

biomolecules chemical energy maintains spread of the excited states through biomolecules without loss of energy.

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Is applicable thermodynamics of negative temperature for living organisms?

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KEYWORDS

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Electrical resistivity
Zooplankton
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ABSTRACT

During organismal development the moment of sexual maturity can be characterizes by nearly maximum basal metabolic rate and body mass. Once the living organism reaches extreme values of the mass and the basal metabolic rate, it reaches near equilibrium thermodynamic steady state physiological level with maximum organismal complexity. Such thermodynamic systems that reach equilibrium steady state level at maximum mass-energy characteristics can be regarded from the prospective of thermodynamics of negative temperature. In these systems the increase of the internal and free energy is accompanied with decrease of the entropy. In our study we show the possibility the living organisms to regard as thermodynamic system with negative temperature

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Journal Name

Original Research Paper

BACTERIA AS QUANTUM CLOCKS

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Abstract: In this study we investigated the biological application of Wigner's inequalities for smallest quantum clock. We showed that the mass, size and doubling time of bacteria satisfied the Wigner's inequalities for quantum clock. Data on 17 bacteria with mass 1×10^{-17}-1×10^{-15} kg, size 0.3-50μm and doubling time 1×10^{3} - 1×10^{5} seconds confirmed the hypothesis of Pešić that possibly the living bacteria appear to be the smallest quantum clocks in the Nature.

Keywords: time, quantum clock, Wigner inequality, bacteria,

Introduction

The application of quantum mechanics to biological systems is of great interest for theoretical and experimental areas of biological sciences. One spatial case of application of quantum mechanics is to examine the living cells and bio-molecules as 'quantum clocks'. The 'quantum clock' is a concept developed by Winger and Salecker (Wigner 1957, 1972) for the non-living physical systems. Later this concept was applied for black hole (Barrow, 1996), living cells (Pešić, 1993) and cellular enzymes (Goel, 2008).The Pešić model of bacteria as 'quantum clock' is supported on inequalities of Wigner (Salecker and Wigner, 1958) for a smallest clock with maximum size 'L' and mass 'M'. Based on quantum mechanical considerations these scientists found that the longest time (T) for a clock that can remain accurate is presented by 'the first inequality':

$$T<M\lambda^2/\hbar \quad (1),$$

where $\hbar = 1.05\times10^{-34}$ J·s is the Planck's constant, and λ is the spread in position of the clock during time T. The smallest time interval that a clock can accurately measure (τ) is presented 'by the second inequality':

$$\tau>(T/\tau)(\hbar/Mc^2) \quad (2),$$

where 'c' is the speed of the light and T/τ is the number of tick of the clock, during the time.

Pešić (1993) first considered the possibility of extending the concept of the clock to biological systems. He observed that in the case of mycoplasmas with cell mass $M=8\times10^{-17}$(kg) and reproduction (doubling) time T=50(min) the calculated λ is greater than 0.07μm. The calculated value of λ is near to the experimentally measured diameter of the mycoplasma of 0.3μm. The conclusion of Pešić was that the cell parameters of mycoplasmas are consistent with inequality (1) and the mycoplasmas actually behave as Wigner clocks with accuracy of 10^{-16}s. Against this concept there is opportunity (Brualla, 2013). Brualla concluded that the current experimental evidence does not support the validity of Wigner inequalities in a biological context. Thus, this problem remains open for resolution. In this work we support the biological application of Wigner's inequalities by wide range of experimental data on Prokaryotes (bacteria).

Working Hypothesis

During growth and dividing of cells by binary the cellular parameters (mass, size and form) of the mother and the daughter cells differ slightly, because of the genetic program in the cells. Genetic program determines the cellular mass and size of the daughter cell, but does not determine the doubling time for which the mother's cell grows and divided by binary. The duration of the doubling time depends on many external parameters (temperature, food sources, pH, ion composition of environment, type of power source) and other factors, which are not under genetic control of the mother's cell. In this sense the doubling time of the cells appears to be non-defined and relatively random parameter that could be changed in given defined time interval. This time interval must be around the quantum limit of longest doubling time for cellular division. This is possibly as living cells work principally as quantum clocks. This means that during bacterial growth the cell size changes continuously similarly to the spread 'λ' in

Science Publications

TRANSDERMAL DELIVERY OF DEXAMETHASONE AND DICLOFENAC MIXURE IN THE TREATMENT OF LATERAL EPICONDYLITIS BY ULTRAPEEL TRANSDERM IONTO SYSTEM

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Background: Lateral epicondylitis (tennis elbow) is an inflammatory-degenerative disease affecting the insertion point (*epicondylus lateralis humeri*) of the extensor and supinator of the wrist, fingers and the palm. In lateral epicondylitis treatments generally used physiotherapy techniques and heat therapy, complete immobilization with a splint, massage, electro, ultrasound and laser therapy, tens, steroid injections, systemic administration of nonsteroidal and anti-inflammatory drugs, phonophoresis, iontophoresis, muscle stimulation, acupuncture and others.

Aims: The authors study combined effect of dexamethasone and diclofenac mixture on lateral epicondylitis after application by dermoelectroporation with Ultrapeel Transderm Ionto System.

Study Design: Experimental study

Methods: 38 patients (21 males and 17 females) aged from 28 to 52 years, diagnosed with lateral epicondylitis participated in this study. A mixture of 75mg/3ml Sodium Diclofenac, 2ml/0.5ml Dexamethasone Sodium and 1.5ml saline was administered by dermoelectroporation. Each patient was treated 3 folds for 3 days period. The efficacy of drug treatment was evaluated by pain threshold measurment in the affected by the condylitis elbow before each transdermal administration of drugs and at 30 days after first administration.

Results: A statistically significant pain relief in affected elbow, near to healthy contralateral elbow at 30 days after the first treatment was achieved in patients.

Conclusion: Based on the received results it is thought that dermoelectroporation (combined with dermabrasion) could be a preferable way of administering anti-inflammatory drugs in inflammatory-degenerative conditions related to the musculoskeletal system, such as myotendinosis.

Keywords: Epicondylitis, dermoelectroporation, dexamethasone, diclofenac, pressure algometry.

INTRODUCTION

Lateral epicondylitis (tennis elbow) is an inflammatory-degenerative disease affecting the insertion point (*epicondylus lateralis humeri*) of the extensor and supinator of the wrist, fingers and the palm. The manifestation of the conditions is characterized by pain in the anterior shoulder muscles, loss of the grasping activity and impaired outward rotation (supination) (1).The epicondylar are becomes sensitive and painful when pressure is applied, and the pain irradiates distally along the forearm muscles. The patients have difficulty in performing their routine daily activities when using the affected arm. In lateral epicondylitis treatments generally given using physiotherapy techniques, ice application and heat therapy, complete immobilization with a splint, massage, electro, ultrasound and laser therapy, tens, SWD, steroid injections, systemic administration of nonsteroidal and anti-

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Preface of the Session 'Application of New Physical Theories, Methods and Technics in Biology and Medicine'

Atanas Todorov Atanasov

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Preface of the Session 'Application of New Physical Theories, Methods and Technics in Biology and Medicine'

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Small description of the symposium. The early 21st century is characterized by the rapid development of biophysical and biomedicine sciences. In biology and medicine continuously are found application new physical theories, methods, technics and other scientific approaches. As new physical theories we can regard these theories explaining new empiric relationships and laws between others biological and medical characteristics of human and living organisms. In this scientific area fall application of quantum mechanics and thermodynamics in life processes, metabolic theories, cancer theories, empiric and statistical relationships between cellular and organismal characteristics. As new scientific methods and technics we can take these ones, which have not been used so far, but are recently developed by various researches. As example, we can take some computerized methods and technics in physics, electronics, radiology and X-ray technics developed for medical purpose. As a new mathematical method in biology and medicine we can take predominantly method of scaling and empiric (alometric) relationships between other biological and biomedical characteristics of human and living organisms.

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Birth date: 15.01.1954, Trakietz (Haskovo); **Education**: 1979 MSc, Faculty of Physics, Sofia University "St. Kliment Ohridski", Bulgaria; **First specialty** "Radiophysics and electronics", **Second specialty** "Biophysics", Sofia University, Bulgaria; **Specialization**: 1979-1982, Neurophysiology of brain, Institute of neurobiology, Bulgarian Academy of Sciences; **Work experience**: 2012-Associate professor of physics and medical technics; **Affiliation:** Department of Physics and Biophysics, Medical Faculty, Thracian University of St. Zagora, Bulgaria; **Teaching Experience:** Medical Physics, Medical Biophysics, Medical Technology and New Technologies in Medicine; **Publications** / full text / - 98; **Basic research interest:** isolation of biologically-active compounds from Bulgarian medicinal plans, study of nasal and sleep cycles, allometric (empiric) laws and relationships in biology and biophysics; transdermal introduction of drugs with pulsed electric field .

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SOME EMPIRICAL CORRELATIONS BETWEEN THE THERMODYNAMIC PROPERTIES OF HYDROGEN CYANIDE, WATER AND ACETYLENE MOLECULES AND THEIR INFRARED SPECTRA

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ABSTRACT. A new method for calculating vibrational modes in the infrared region of the spectrum is proposed. The method is based on the thermodynamic parameters of the molecules- standard molar Gibbs free energy change of molecular formation ΔG_f^0 (kJ/mol), standard molar enthalpy change of molecular formation ΔH_f^0 (kJ/mol) and standard molar entropy of molecule S^0 (J/mol·K). From these thermodynamics parameters the vibrational modes can be calculated using $T_G = \Delta G_f^0/S^0$ and $T_H = \Delta H_f^0/S^0$ (in K) as 'apparent' temperatures. After equation of thermal energy kT_G and kT_H (where k is Boltzmann constant) to energy of electromagnetic quanta hf_G and hf_H (where f is frequency in Hz), it can calculate the wavenumbers (in cm^{-1}) of vibrational modes as: kT_G/ch and kT_H/ch (where c is the speed of light and h is the Planck constant).

Key words: IR spectrum, Gibbs free energy, enthalpy, entropy

INTRODUCTION

1. Main infrared regions. The molecules can vibrate in many ways, and each way is called a 'vibrational mode'. In terms of wavenumbers of vibrational modes the infrared spectral region spans from 33 to 12820 cm^{-1} [1, 2]. The entire infrared range is divided into 3 areas: near-infrared (12820-4000 cm^{-1}), mid-infrared (4000-400 cm^{-1}), far-infrared (400-33 cm^{-1}).The near- infrared region is poor in specific absorptions. Consist of overtones and combination bands resulting from vibrations in the mid-infrared region of the spectrum. The mid-infrared region provides structural information for most organic molecules. The far-infrared region has been less investigated than the other two regions. It has been used with inorganic molecules. The low energies of infrared quanta is not sufficient to cause electronic transitions but they are large enough to cause changes in the frequency and amplitude of molecular vibrations. Infrared spectra have been represented as percent of transmittance versus either the wavenumber of the wavelength. The use of wavenumbers (expressed in cm^{-1}) is standard, with the use of wavelength (expressed in nm or μm). On Figure 1 are given the main selected IR frequencies.

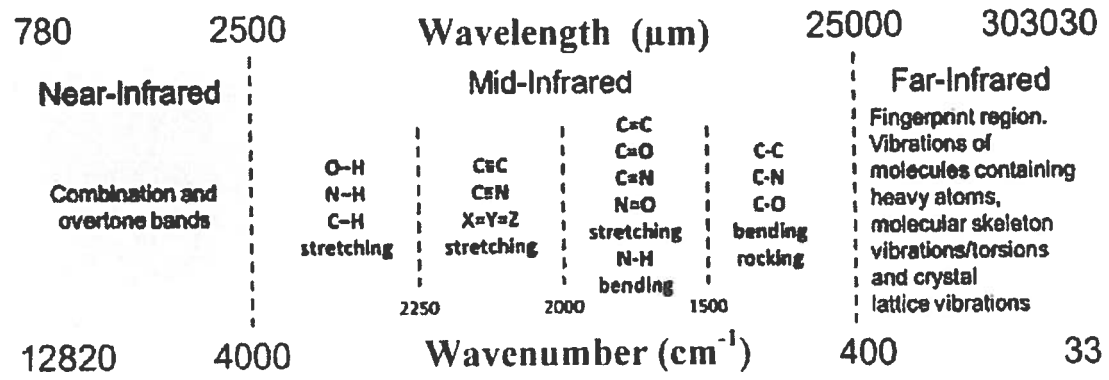

Fig.1. Main Infrared Regions

Bulgarian Journal of Veterinary Medicine (2009), **12**, Suppl. 1, 47–56

ONE GENERAL SCALING LAW IN ANIMAL ENERGETICS: THE TOTAL METABOLIC ENERGY PER LIFESPAN OF MULTICELLULAR ANIMALS IS LINEARLY PROPORTIONAL TO THE BODY MASS

A. ATANASOV

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Summary

Atanasov, A., 2009. One general scaling law in animal energetics: The total metabolic energy per lifespan of multicellular animals is linearly proportional to the body mass. *Bulg. J. Vet. Med.*, **12**, Suppl. 1, 47–56.

The aim of this study was to establish and calculate the relationships between the total metabolic energy per lifespan and the body mass in a wide range of animal species (multicellular poikilotherms, mammals and birds) with about 8 order of magnitude variation between the body mass. The study showed that there was a linear relationship between the total metabolic energy per lifespan Pls (kJ) and the body mass M (kg) of multicellular poikilotherms, mammals and avian species (n=272) from the type: $Pls=Als\times M^{1.02}$ with $R^2=0.906$ and $Als=13.7\times10^5$ kJ/kg. The linear coefficient Als is the total metabolic energy, exhausted during the lifespan of animals, per 1 kg body mass. The linearity between the total metabolic energy per lifespan and the body mass of multicellular animals allowed us to express the total metabolic energy per lifespan as a function of the number of body cells *N* and the mean body mass *m* of a single cell, building the organism: $P_{ls} = A_{ls} \times M = A_{ls} \times N \times m$.

Key words: animal energetics, lifespan, multicellular, total metabolic energy

INTRODUCTION

The patterns existing between the other fundamental characters of living organisms and there body mass are generally described as a power function. The bioenergetic studies on Poikilotherms, Mammals and Aves (Hemmingsen, 1960; Kleiber, 1961; Schmidt-Nielsen, 1984) have shown that the basal metabolic rate (P, kJ/d) in animals is related to the body mass (M, kg) as expressed by the equation of type:

$$P = aM^k \qquad (1)$$

where *a* and *k* are allometric coefficients

In multicellular poikilotherms *k* varied in the interval 0.6÷0.94 (Prosser, 1977; Schmidt-Nielsen, 1984), in mammals *k* varied within the interval 0.602÷0.772 (Heusner, 1991; Kleiber, 1961; McNab, 1988) and in birds – within 0.67÷0.734 (Lasiewski & Dawson, 1967; 1969; Bennett & Harvey, 1987).

The allometric relationships between the lifespan of living organisms (T_{ls}, y) and the body mass (M, kg) in other evolutionary groups has expressed as power equations:

$$T_{ls} = bM^n \qquad (2)$$

where *b* and *n* are allometric coefficients

Bulgarian Journal of Veterinary Medicine (2009), **12**, Suppl. 1, 57–66

ONE GENERAL SCALING LAW IN BIOLOGICAL SPACE AND TIME: THE VOLUME/SURFACE RATIO OF LIVING ORGANISMS IS LINEARLY PROPORTIONAL TO THEIR LIFESPAN

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Summary

Atanasov, A., 2009. One general scaling law in biological space and time: The volume/surface ration of living organisms is linearly proportional to their lifespan. *Bulg. J. Vet. Med.*, **12**. Suppl. 1, 57–66.

The volume/surface ratio (V/S, m) in Poikilotherms, Mammals and Aves is linearly proportional to the lifespan (Tls, s): $V/S = a_{vst}$ Tls, where the linear coefficient $a_{vst} \approx 1x10^{-10} \div 4x10^{-13}$ m/s has a dimension of speed. This shows that the animal space and time are mutually connected, so that the coefficient a_{vst} appears a constant parameter, in comparison to 21 orders of magnitude variation between body mass of organisms. The biological sense of a_{vst} is the speed volume/surface growth in cells, during multiplication by binary.

Key words: aves, ammals, poikilotherms, volume/surface ratio

INTRODUCTION

The body size, the body mass, the lifespan and the biological speed in living organisms fall in the area of classical physics. In SI (Scientific International) metrical system, from viruses and bacteria to big animals the linear size of organisms fall in diapason from $1x10^{-8}$m to $1x10^{2}$ m, the body mass fall in diapason from about $1x10^{-19}$kg to $1x10^{4}$kg, the generation time in unicellular and lifespan in multicellular organisms fall in diapason from about 20 min to $3x10^{2}$ years and the speed of biological processes fall in diapason from the speed of linear cells growth $\sim 1x10^{-12}$m/s (Atanasov, 2007a) to the speed of a nerve impulse $\sim 1x10^{2}$m/s (Glaser, 1983). In previous works Atanasov (2006a, 2006b) shows that volume (V, m^3), surface (S, m^2) and life span (Tls, s) in living organisms are mutually connected so that the ratio between volume and (surface x lifespan) appears a constant parameter a_{vst} with the dimension of speed:

$$a_{vst} = V/(S.Tls) = 1x10^{-9} \div 1x10^{-13} \text{ m/s} \quad (1)$$

The constant a_{vst} has a biological sense of speed of linear or volume/surface growth of cells during multiplication by binary (Atanasov, 2007a). The equation (1) shows that between the volume/surface ratio and the lifespan, a linear connection from the type exists:

$$V/S = a_{vst} Tls \quad (2)$$

where 'vst' means 'volume-surface-lifespan' ratio.

The aim of this study is to receive the exactly mathematical relationship between the volume/surface ratio and the lifespan in a wide number of Poikilotherms, Mammals and Aves (207 species) with about

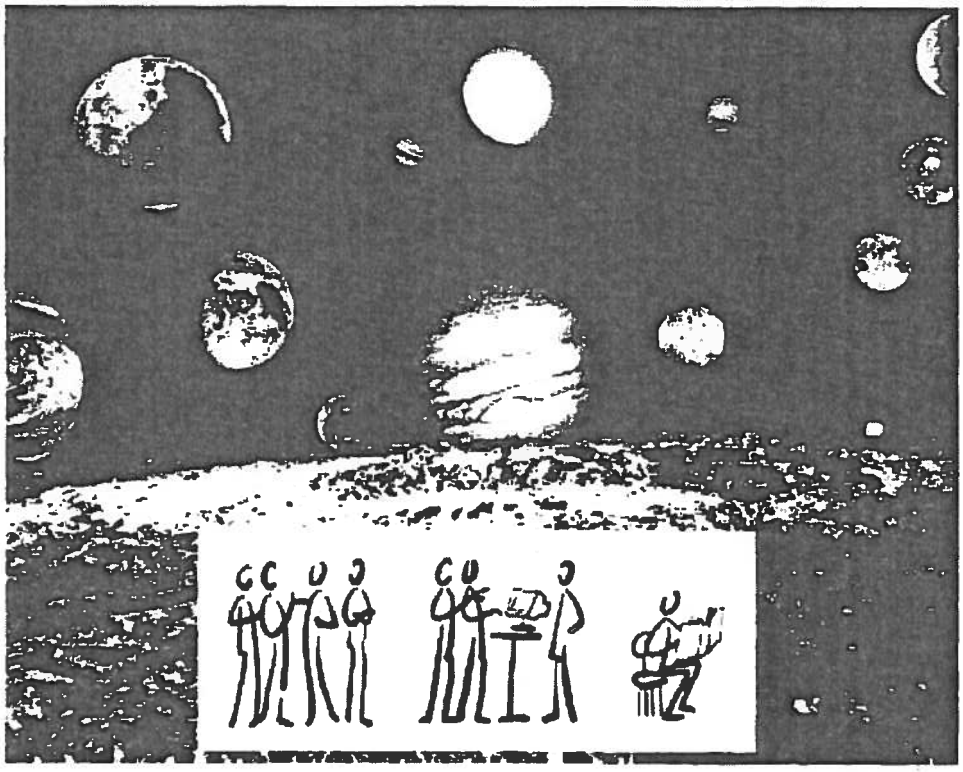
№ 84

Технически университет София

Департамент по приложна физика

Дни на физиката 2010

Сборник популярни и научни доклади



София, 14 - 17 Април 2010 г.

PROBABLE PHYSICAL DETERMINATION OF THE MASS, SIZE, GENERATION TIME AND RATE OF GROWTH IN MOST SIMPLE LIVING CELLS (PROKARYOTES)

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Abstract. Prokaryotes represent the minimal 'quanta' of matter that can be considered 'alive'.Integrated physical characteristics in Prokaryotesmost are tested – cell mass M_{cell}, linear size L_{cell}, generation time T_{gt} and linear speed of growth v_{cell}. In this work we have received three relationships with dimension of mass M_{cell} (kg) = $(h.\ v_{cell}/G)^{1/2}$, linear size L_{cell} (m) = $(h.G/\ v_{cell}^3)^{1/2}$ and time T_{cell}(s) = $(h.G/\ v_{cell}^5)$ after combination of speed of growth of Prokaryotes in the range of $v_{cell}=3.0x10^{-11}–1.4x10^{-9}$ m/s with gravitational constant $G = 6.673x10^{-11}$ $N.m^2/kg^2$ and Planck constant $h = 6.6262x10^{-34}$ J. From these relations we can calculate the minimum mass (M_{cell}), length (L_{cell}) and generation time (T_{cell}) of Prokaryotes.

Key words: prokaryotes, gravitational constant, Planck constant, rate of growth

1. Увод

Огромните разлики в масите, размерите и времето на живот на живите организми поставя въпроса - съществуват ли минимални и максимални характеристики на живите организми и от какво зависят тези характеристики? Прокариотите са най-просто устроените безядрени клетки, възникнали преди 3 милиарда години в процеса на биологичната еволюция [1]. Към тях се отнасят около 3000 бактерии – fig. 1. Бактериите имат минимални клетъчни маси, клетъчни размери и и генерационно време време за удвояване на клетката чрез делене. Микоплазмата е най-малката бактерия способна да живее и самостоятелно да се размножава в естествена и изкуствена хранителна среда.

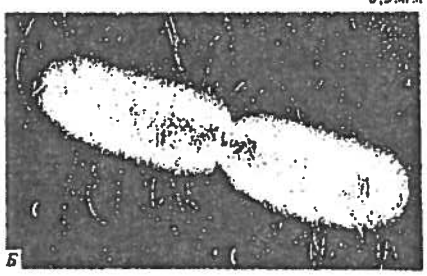

Fig. 1 *Scheme of doubling bacteria.*

Микоплазмата има клетъчна маса около 1×10^{-17} kg и среден размер на клетката около 1×10^{-7} m. При неутрално pH клетъчното съдържание на микоплазмата би имало не повече от 2 водородни йона [2]. В толкова малък

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Original Contribution

SCALING OF BIOLOGICAL SPACE AND TIME: VOLUME TO SURFACE RATIO IN LIVING ORGANISMS IS PROPORTIONAL TO LIFESPAN

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ABSTRACT

The manuscript presents a relationship between volume to surface ratio and biological time (generation time and lifespan) in 223 organisms (Unicellular organisms, Poikilotherms, Mammals and Aves) with 22 order of magnitude variation between body mass. The study shows that in unicellular and multicellular organisms the volume to surface ratio $V\times S^{-1}$ (m) is proportional to generation time and lifespan T_{ls}(s) as: $V\times S^{-1} = a_{vst}\times T_{ls}^{\ 0.915}$ with correlation coefficient R^2=0.931. The coefficient a_{vst}=8.993×10^{-11}(m·s^{-1}) has a dimension of speed and appears relatively constant parameter in comparison to 22 orders of magnitude variation between body mass of organisms. On cellular level a_{vst} has a biological sense of speed of volume/surface ratio change, during growth and multiplication of cells by binary. The equation between volume/surface ratio and lifespan relates to some scientific problems, connecting with body size, form and time in living organisms.

Key words: scaling, organism, mass, volume, surface, space, time

INTRODUCTION

The body mass, the body size (length, volume, surface), the lifespan and generation time are basic physical and physiological characteristics of living organisms. From physical point of view these characteristics as well as the speed of biological processes fall in the scientific area of classical physics [1]. From a small viruses with mass 1.0×10^{-20} kg to big whales with mass 1.0×10^{5} kg the body mass range about 24-25 orders of magnitude [2]. The body sizes range 10 orders of magnitude from viruses (about 1.0×10^{-8} m) to big whales (1.0×10^{2} m) [3]. The lifespan range 6 orders of magnitude from about 20min generation time in bacteria to 3.0×10^{2} years and more lifespan in tortoises [4]. The speed of biological (biochemical and physiological) processes ranges about 14 orders of magnitude-from the linear speed of cell growth (1.0×10^{-9} – 1.0×10^{-12} m·s^{-1}) [5] to the speed of nerve impulses (1.0×10^{2} m·s^{-1}) [3, 6]. The body density of living organisms falls in a very small interval, from about 1070 kg·m^{-3} in animals to 1100-1250 kg·m^{-3} in bacteria and viruses [7]. Because of the mass, size, lifespan, generation time and speed of organism's processes fall in the area of classical physics, this predict the validity of physical equations connecting space and time *via* speed in biological processes. Reasons for this conclusion give us the received from Bonner [8, 9] linear relationship between total length (L_t) and generation time (T_{gt}) across species, ranging in size from bacteria to sequoia tree and whales. Bonner presents this relationship in graphic form only, but in the physical terms this relationship presents the connection between organism's length L_t(m) and generation time T_{gt} (s) *via* speed v(m·s^{-1}):

$$L_t = v\times T_{gt} \qquad (1)$$

Similarly to body length, the volume to surface ratio ($V\times S^{-1}$) of organisms has a dimension of linear length too. Because of this finding, the volume/surface ratio of organisms can be connect with their generation time *via* given speed (for example 'a_{vst}'), characterizing the life processes. Indeed, from dimensional point

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Original Contribution

ALLOMETRIC SCALING OF TOTAL METABOLIC ENERGY PER LIFESPAN IN LIVING ORGANISMS

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ABSTRACT

The purpose of the study is to establish and calculate the relationship between the total metabolic energy per lifespan and the body mass of Ectotherms, Mammals and Aves (n=278 living organisms) with 21 orders of magnitude variation between their body mass- from Bacteria to *Elephas maximum and Struthio camelus.*

The study shows the existence of a linear relationship between the total metabolic energy per lifespan P_{ls} (kJ), and the body mass M (kg) of all species from type: $P_{ls}=A_{ls}M^{1.0787\pm0.11}$ with R^2=0.980, coefficient A_{ls}=15.18×10^{5}kJ/kg, standard error of the exponent SE=±0.11 and 95% confidence interval of the exponent (0.968 - 1.188). The same relationship for Ectotherms, Mammals and Aves without Protozoa (n=260) is of type: $P_{ls}=A_{ls}M^{1.0089\pm0.042}$ with R^2=0.897, A_{ls} =14.16×10^5 kJ/kg, SE= ±0.042, and 95% confidence interval of exponent (0.967-1.051). In all combinations between Ectotherms, Mammals and Aves the exponent is near to 1.0. The linear coefficient A_{ls} is the total metabolic energy, exhausted during the lifespan per 1kg body mass of given organism and appears to be relatively constant parameter, because of rising 10 times only from Ectotherms to Mammals and Aves, despite of 21 orders of magnitude difference between body mass of organisms.

Key words: scaling, metabolic energy, lifespan, ectotherms, mammals, aves

INTRODUCTION

The patterns existing between the fundamental characters of living organisms and their body mass are generally described as a power function. The bioenergetic studies of Kleiber [1], Brody et al. [2], Zeuthen [3], Hemmingsen [4], Kleiber [5], Schmidt-Nielsen [6], McNab [7], Heusner [8], Niklas [9], Nagy [10] and da Silva and Barbosa [11] on Ectotherms, Mammals and Aves have shown that the basal metabolic rate (P, kJ/d) in animals is related to the body mass (M, kg) by the equation:

$$P=aM^k \quad (1)$$

where a is the normalization constant, and k is the allometric scaling exponent. One of the most important points of controversy in the scientific discussion about the power function is focused on the value of the scaling exponent.

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Some researchers consider the power function (1) with exponent k=0.75 as a universal scaling law, generalized to all living organisms and forms of life (Hemmingsen [4], Kleiber [5], Feldman and McMahon [12], West et al. [13-14], Banavar et al. [15], Savage et al. [16]). On the other hand, several recent studies provided evidences, supporting certain variability in the exponent of the allometric scaling law (Riisgård [17], Dodds et al. [18], Bokma [19], Agutter and Wheatley [20], Glazier [21], Reich et al. [22], White and Seymour [23], White *et al.* [24]).

The values of the scaling exponent k have been studied in other experimental conditions for all animal groups.

Zeuthen[3] and Hemmingsen [4] show that the exponent k is equal to 0.75 in unicellular Eukaryotes. As a hole, unicellular organisms (Eukaryotes and Prokaryotes) showed isometric scaling with exponent k =1.0 [25].

Accordingly to Galvão [26], Ultsch [27], Prosser [28], Schmidt-Nielsen [6], Tudge [29]

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EWING'S SARCOMA STEM CELL

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ABSTRACT

Ewing's sarcoma family of tumors (ESFTs) are round cell tumors of bone and soft tissues, afflicting children and young adults. Ewing's sarcoma cell of origin may be a bone marrow primitive pluripotent cell, a neuroectodermal cell or a MSC. Bone marrow-derived human MSCs are permissive for EWS-FLI1 expression that initiates transition to ESFT-like cellular phenotype. ESFT are genetically related to NCSC, permissive for EWS-FLI1 expression and susceptible to oncogene-induced immortalization. Endogenous *Ews* gene is indispensable for stem cell quiescence. Downregulation of miRNA-145 is implicated in CSC development in ESFT. An $ALDH^{high}$ subpopulation of Ewing's sarcoma cells, resistant to cytotoxic chemotherapeutic agents, is capable of self-renewal and tumor initiation, is a promising target for ESFTs therapy. Prognostic biomarkers and novel treatments are needed for the highly aggressive ESFT.

Key words: Ewing's sarcoma family of tumors, Cancer stem cells, Ewing's sarcoma stem cells, Mesenchymal stem cell; Neural crest stem cells; Immunotherapy, Hematopoietic progenitor cell transplant; Diagnostic strategies.

Abbreviations: ESFT (Ewing's sarcoma family of tumors); Mesenchymal stem cell (MSC). Bone marrow-derived human mesenchymal stem cells (BM-MSC); Neural crest stem cells (NCSC); high expression of aldehyde dehydrogenase ($ALDH^{high}$); Hematopoietic stem progenitor cells (HSPCs)

EWING'S SARCOMA

Sarcomas are about 1% of cancers in patients of all ages. The poorly differentiated tumors are aggressive and metastasize early to lung, bone marrow, and other tissues. Described from James Ewing in 1921, Ewing's Sarcoma, the bone tumor in adolescents and young adults, is still a cryptic malignancy. Ewing's sarcomas are highly aggressive round cell tumors of bone and soft tissues that afflict children and young adults. The majority of these tumors (in 85% of cases) harbor the t(11;22) translocation and express the fusion protein EWS-FLI. The members of the TET protein family include the EWS protein, the FUS/TLS protein, the TATA-binding protein (TBP)-associated factor (TAFII68/TAF15) and the Drosophila cabeza/SARF protein. Although *EWS* is a frequent target of chromosomal translocations, found in most Ewing' sarcoma patients, the role of native *EWS* remains largely unknown. The tumors are genetically characterized by expression of fusion oncogenes resulting from chromosomal translocations involving *EWSR1* (*EWS*), *FUS/TLS* and *FLI1* or other ETS transcription factor (Table 1) [1]. The *EWS-ETS* fusion gene is critically important for maintaining the tumor phenotype of the disease. ESFT is a chemotherapy-sensitive cancer, and even patients with metastatic disease commonly achieve remission. Despite this, 25% of patients with a localized tumor and 70% of patients with metastases develop a recurrence and die of their disease.

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POSSIBLE ROLE OF CENTRIOLES AS SENSOR CENTER IN CELLS

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ABSTRACT

In manuscript is proposed the hypothesis that the centrioles play role of sensor center in cells. The cilia and microtubules can regard as extracellular and intracellular sensor 'antennas' of centrioles by which they detect and controlled the cellular status.

Key words: centrioles, sensor, antennas, cilia, flagella.

INTRODUCTION

1. Centrosome, centriole, cilia and microtubules

The centrosome was discovered a century ago (1). The two major properties of the centrosome is its capacity to reproduce by duplication and its ability to nucleate microtubules.

Centrioles are the cylindrical structures found within the centrosomes of animal cells (a pair of centrioles forms the core of centrosome) and at the core of the mitotic spindle pole, which also act as basal bodies to nucleate formation of cilia and flagella. The replication and separation of centrioles during cell division is synchronous with the cell cycle. The absence of centrioles in the centrosome from other eukaryotic organisms has lead to the domination view that the centriole's pair is not relevant to centrosome activity. This view is also based on the fact that centrioles can be dispensable for spindle assembly, for example during the female meiosis some species (2). This arise the question, what then is the real function of centrioles, if they aren't needed for mitosis?

The other main function of the centrioles is to form the cilia and flagella. The cilia can exist in two main structural forms with different functions: motile cilia and non-motile (primary cilia). The primary cilium is a generally non-motile cilium that occurs singly on most cells in the vertebrate body. Recent findings reveal that the primary cilium is an antenna displaying specific receptors and relaying signals from these receptors to the cell body (3). Primary cilia contain a '9+0' axoneme, consisting of nine outer doublet microtubules but lacking the central pair of microtubules that is found in the '9+2' axoneme of most motile cilia (4). Microtubules control the beating of cilia and flagella, locomotor appendages of some cells, but they differ in their beating patterns. The spite of their ubiquity, the function of primary cilia is very poorly understood. Three major hypotheses for their function have been made. The first is that they are vestigial organelles inherits from an ancestor whose cells had motile cilia, and that they now have no purpose (5). A second hypothesis is that they are involved in controlling the cell cycle (6). Until recently, there has been no experimental evidence in support of these hypotheses. Recently, many observations have provided strong support for the hypothesis that primary cilia have a sensory function (3). Microtubules are the main constituents of the cellular cytoskeleton together with microtubule associated proteins, intermediary and actin filaments. Microtubules are dynamical instability structures because of it leads to reorganization of the cytoskeleton and therefore cellular morphology and

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ALOMETRIC RELATIONSHIPS BETWEEN THE BODY-MASS INDEX, MASS TO SURFACE RATIO AND THE LENGTH OF PREGNANCY IN SOME MAMMALS (Metatheria and Placentalia)

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ABSTRACT

Body mass index (BMI) is characteristics in human physiology represented by the ratio between the body mass and the square of body height, i.e. BMI = Mass/Height^2. In the case of animals (mammals) the BMI can be defined by the length of the body i.e. BMI = Mass/Legth^2. In manuscript is showed existence of relationship between the body mass M(kg), length L(m), surface S(m^2), body mass to surface ratio M/S (kg/m^2) as well as body mass index BMI(kg/m^2) and the length of pregnancy T (days).

Key words: body mass index, length, surface, pregnancy, human, veterinary medicine.

INTRODUCTION

Body mass index (BMI) is a physiological characteristics represented by the ratio of body mass and the square of body height, i.e. BMI = Mass/Height^2. Body mass index is characteristics often used for purpose of diagnostics in Human medicine (1). But BMI is not well developed like prognostic characteristics in Veterinary medicine. In case of mammals the BMI can be defined by the length of the body i.e. BMI = Mass/Legth^2. The field of Veterinary medicine contained wide spectrum of animals (Poikilotherms, Mammals and Aves) with wide spectrum of characteristics: body mass, length and lifetime characteristics (lifespan, length of pregnancy, during puberty, during excretion of drugs) that differs some orders of magnitude between them. However, the connection between BMI and these characteristics is not study. The aim of the work is to investigate the alometric relationship between the body mass, body length, body surface, body mass to surface ratio and the body mass index and the length of pregnancy in Mammals.

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MATERIALS AND METHODS

The data for the 103 studied mammal species Metatheria and Placentalia (from Common shrew to Killer whale), their body mass, body length and pregnancy length were collected from the review papers (2-5). The body surface S (m^2) were calculated by formula $S=0.1M^{0.67}$, where the body mass M is given in kg (6, 7).The body length of animals H (m) was given to be from head to tail i.e. the length of head plus length of spinal cord, without length of the tail.

RESULTS

The relationships between the body mass M (kg), square of body length H^2 (m^2), body length H (m), body surface S (m^2), body mass to surface ratio M/S (kg/m^2) and body-mass index M/H^2) as a function of length of pregnancy T(d) are given on **Table 2**. On **Figure 1** are compared relationships of BMI, M/S ratio as functions of the length of pregnancy T.

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ALOMETRIC RELATIONSHIPS BETWEEN VOLUME TO SURFACE RATIO, GENERATION TIME, MASS-CORRECTED METABOLIC RATE AND LIFESPAN METABOLIC POTENTIAL OF LIVING CELLS IN MODEL FOR SWITCH OF GENE PROGRAMS FROM GROWTH TO DIFFERENTIATION AND APPOPTOSIS

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ABSTRACT

The works of the other scientists have showed that the change of the size and form of the cells can leads to change of their mass-energy and spatial-time characteristics, as well as to switch gene programs of the cells from growth to differentiation and to apoptosis. In this direction the idea for control of metabolic, spatial-time and signaling pathways in cells *via* manipulation of volume to surface ratio (namely shape and size of the cells) is developed in manuscript. The base for such manipulation and control on cellular functions is existence of linear relationship between the volume to surface ratio (V/S, m) and generation time (T_{gt}, s) in unicellular organisms (n=18): $V/S=a_{vsi}T_{gt}^{1.0975}$ (R^2=0.815) and existence of nearly to inversely-linear relationship between the volume to surface ratio and mass-corrected metabolic rate (P^*=P/M, J/s.kg) in unicellular organisms (n=18): $V/S = b_{vsm}/P^{*0.8796}$ (R^2=0.70). The found relationships showed that the metabolic rate and the generation time of the cells are strongly connected to their volume to surface ratio. Thus, the manipulation of volume to surface ratio leads to changes of the basal metabolic rate and generation time of the cells, and this can switch their gene programs from growth to differentiation and to apoptosis. The proposed model is based on universality of the alometric relationships simultaneously for unicellular organisms (bacteria, protozoa) and for soma cells of the multicellular organisms.

Key words: alometric, living cells, gene programs, metabolism, generation time.

INTRODUCTION

The works of the other scientists have showed that the change of size and form of the cell can leads to change of their mass-energy, spatial-time and informational characteristics (gene programs). The idea for control of metabolic, spatial-time and signaling pathways in cells *via* manipulation of size and shape of cells is developed in others theoretical and experimental works. On prokaryotic bacterial cells Donachie and Begg (1) experimentally demonstrated an existence of connection between form and size of the cells and their gene programs . On *Escherichia coli* mutants the authors have showed that transition from rod-shape to spherical and ellipsoidal-shape form of cells lead to change of their generation time and growth rate. However, the authors do not fully explain the intimate mechanism. A similar connection between cell size, growth rate and generation time in *Escherichia coli* and *Azotobacter agilis* is demonstrated by experiments of Harvey, Marr and Painter (2). On eukaryotic cell (capillary endothelial cells) Ingber and co-workers (3, 4) showed that the change of cell shape with same volume can switch gene programs of cells from growth to differentiation and apoptosis –**Figure 1**. Ingber and Folkman (4) have showed that cell shape is the most critical determination of cell function, at least in the present of optimal growth factors and high extracellular matrix binding. Thus, cell shape *per se* appears to govern how individual cells will respond to chemical signals in their microenvironment, as first proposed by Folkman and Moscona (5). Ingber and Jamieson have proposed that this

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ORIGINAL ARTICLES

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ANTI-PLATELET FRACTION ISOLATED FROM *GALEGA OFFICINALIS*

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Summary. A fraction from crude extract of *Galega officinalis* has been purified by column chromatography on Sephadex G-25, Sepharose 4B, DEAE-Cellulose and Sephadex G-100. The final purification factor of the fraction is 120. The peak in elution profile after Sephadex G-150 shows a molecular weight of 100-140 kDa. The isolated fraction appears to have 74% polysaccharides and 23% of proteins. No loss of activity of the final fraction is observed after storage for several months at 4 °C and in lyophilized condition. The fraction compounds inhibit platelet aggregation induced by ADP, collagen and thrombin.

Key words: *Galega officinalis, antiplatelet fraction*

INTRODUCTION

Galega officinalis is a plant wide distributed in Yeast Europe. The plant is used in the traditional medicine in the treatment of *diabetes mellitus* [1]. About 20 biologically – active substances are isolated from *Galega officinalis*: alkaloids, flavonoids, glucosides, saponin and others. Phytochemical analyses gave positive results for lipids, protein and cellulose [2]. The biologically active alkaloid *galegine* (exhibiting a hypoglycaemic effect in vivo) was isolated from *Galega officinalis* [3]. The experimental results of Atanasov shown that the crude aqueous extracts [4, 5], and the fractions from gel-chromatography on Sephadex G-25, Sepharose 4b and ion-exchange chromatography on DEAE-Cellulose suppress platelet aggregation *in vitro* and *in vivo* induced by ADP, epinephrine, thrombin and collagen [6, 7]. In this paper we report the purification and characterization of all active fractions purified by 4 steps from crude extract of *Galega officicnalis*.

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BIOLOGIE

Biotechnologie

MECHANISM OF ACTION OF A FRACTION ISOLATED FROM textitGALEGA OFFICINALIS L., STUDIED BY FLOW CYTOMETRY ASSAYS WITH MONOCLONAL ANTIBODIES AGAINST P-SELECTIN EXPRESSION

Atanas Atanasov

(*Submitted by Academician A. Atanassov on May 4, 2016*)

Abstract

Galega officinalis L. is a plant used for the treatment of *diabetes mellitus*. A fraction from crude extract of the plant has been purified by chromatography on Sephadex G-25. The preliminary analyses of the fraction show that it consists of about 23% protein and 74% polysaccharides. The fraction is a strong inhibitor of platelet aggregation induced by adenosine 5′-diphosphate. The mechanism of action of fraction was studied using flow cytometry assays with monoclonal antibodies CD62P-FITC, specific for P-selectin. The experimental results clearly documented action of fraction like inhibitor of the P-selectin expression molecules on platelet surface-a support of platelet adhesion. Possibly the fraction is antagonist of GPIIb/IIIa receptors for fibrinogen, since it has a strong disaggregating effect on aggregated by ADP platelet-rich plasma.

Key words: *Galega officinalis* L., fraction, ADP, platelet aggregation, flow cytometry

Introduction. *Galega officinalis* L. is a plant used in the traditional medicine system of Bulgaria and Italy for the treatment of *diabetes mellitus*. A preliminary analysis has shown that the plant contains lipids, proteins and polysaccharides [1]. The recent experimental results of Atanasov [2, 3] show that the water extract of this plant suppresses in vitro and in vivo the platelet aggregation induced by adenosine 5′-diphosphate (ADP), epinephrine, thrombin and collagen.

EFFECT OF WATER EXTRACTS OF TANNINS-CONTAINING BULGARIAN PLANTS ON RAT PLATELET AGGREGTION

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ABSTRACT

The search of a new chemical substances influencing platelet aggregation is a very important endeavor for medical practice. The *in vitro* effect of water extract from20 tannins-containing plants from Bulgarian flora on rat platelet aggregation was investigated. The water extracts of 9 medicinal plants: *Agrimonia eupatoria* L.,*Arctostaphylos uva-ursi* L. Sprend, *Corylus avellana* L, *Cydonia oblonga* Mill, *Dryopteris filix-mas* (L.) Schott, *Ephedra distachya* L., *Geum urbanum* L., *Primula officinalis* (L.) Hill and *Punica granatum* L. inhibited platelet aggregation, initiated by adenosine diphosphate. The analysis of literature data indicated these plants contained between 10% and 30% tannins, except of *Primula officnalis* (L.) Hill.

Key words: *medicinal plant, tannin, platelet aggregation, rat.*

INTRODUCTION

Tannins are from 500 to 20 000 D high-molecular polyphenolic compounds with a bitter taste. Accordingly to their chemical structure K. Freudenberg divided tannins into hydrolysable and condensed. A number of Bulgarian medicinal plants are rich in tannins, which are regarded as the active principle. The water-soluble nature of tannins allows easy extraction and is useful in various applications in the chemical and pharmaceutical industry. Plants containing tannins have predominantly astringent, hemostatic, antiseptic and toning properties. The platelet functions play a central role in the processes of blood clotting and many cardiovascular diseases associated with change of platelet activity (Andrioli *et al.*, 1996; Fabre and Gurney, 2010). For correction of the platelet activity can used substances isolated from foods (green tea, garlic and tomato) and medicinal plants (Atanasov, 1994; Mekfi *et al.*, 2006; Rahman and Billington, 2000; Dutta-Roy *et al.*, 2001; Sagesaka-Mitane *et al.*, 1990). Thus, the alternative medicine appears additional source for searching of healing remedies. In this direction, the recent investigations are directed to isolation of tannins-containing substances, including medicinal plants (Haouari. *et al.*, 2006; Mekfi *et al.*, 2006; Mosa *et al.*, 2011).Wide spectrum of plants from Bulgarian flora contain from 10 to 20% tannins (Asenov *et al.*, 1989; Petkov, 1982). The main tannins containing plant accordingly to Bulgarian pharmacopeia are: *Agrimonia eupatoria* L. (herbal material) –up to 5% catechins, and up to 8% gallotannins; *Achillea millefolium* L. (herbal material) – up to 2.8%; *Alchemilla vulgaris* L. (herbal material, rhizome) – about 10% tannins with high content of gallic and ellagic acid; *Arctostaphylos uva-ursi* L. (Sprend) (folia)- about 20% gallotannins; *Cotinus cogigria Scop.* (folia) – 15-20% gallotannins; *Corylus avellana* L. (cortex)- about 10% tannins; *Cydonia oblonga* Mill. (folia); *Dryopteris filix-mas* (L.) Schott (rhizome) – up to 10% fillixic acid; *Ephedra distachya* L. (herbal material) – up to 10% pyrocatechins; *Geum urbanum* L. (radix, rhizome) – up to 30% tannins; *Juglans regia* L. (folia)- up to 5% tannins; *Hypericum perforatum* L. (herbal material) – up to 10% catechins; *Lavandula angustifolia* Mill. (flores) – up to 12% tannins; *Ocimum basilicum* L. (herbal matrial)-up to 5% tannins; *Primula officnalis* (L.) Hill. (folia); *Punica granatum* L. (cortex) – up to 25% tannins; *Rosmarinus officinalis* L. (folia) – up to 8% tannins; *Rubus sp. diversa* (folia) – from 5% to 14% tannins; *Symphytum officinale* L. (radix) – up to 6.5% tannins; *Vaccinium myrtillus* L. (folia, juice) – up to 20% tannins (Asenov *et al.*, 1989; Petkov, 1982).The aim of the study is to test the effect of water extracts of these Bulgarian tannin- containing medicinal plants on rat platelet aggregation.

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SENSITIVITY OF HUMAN AND RAT PLATELET-RICH BLOOD PLASMA TO DRUGS INHIBITING PLATELET AGGREGATION

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Summary

Atanasov, A. T., S. Radev & R. T. Todorova, 2017. Sensitivity of human and rat platelet-rich blood plasma to drugs inhibiting platelet aggregation. *Bulg. J. Vet. Med.*, **20**, Suppl. 1, 175–179.

A method for obtaining blood platelets from albino rats (Wistar) was developed. The study showed that rat platelets were 2–3 times more sensitive to drug with anti-aggregating action in comparison to human platelets. The proposed method expands the ability of spectrometric methods to investigate platelet aggregation in terms of substances such as tannins and lectins that cause turbidity of blood plasma.

Key words: drug, human, platelet aggregation. rat, sensitivity

INTRODUCTION

Blood platelets play an important role in vascular diseases. This fact supports research in the development of new antiplatelet and antithrombotic agents. In this sense, in the screening studies for effects of drugs and multi-component systems on platelet aggregation, it is appropriate to use platelet-rich plasma (PRP) with high susceptibility to inhibitory or stimulatory effect on platelet aggregation. This is particularly important in the study of medicinal plant extracts, which are multi-component system or mixture of chemicals and natural products, in which the concentration of biologically active substances is particularly low. It is well known that the platelets derived from blood of men and the small mammals (mouse, rat, guinea pig) often have very different responses to inhibitory agents (Sinakos & Caen, 1967; Soloviev *et al.* 1999). However, this problem has only been partially explored. The aim of the study is to develop a method for production of highly sensitive PRP from small mammals, without a substantial modification of the initial mammalian blood plasma. As a suitable object we chose albino (Wistar) rats, which are widely distributed laboratory animals (Zapadnjuk, 1983). An additional argument in favour of rats as platelet donor is based on comparison between morphological characteristics of human and rat blood cells. The comparison indicates that the number of free blood platelets in blood of

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EFFECT OF *HABERLEA RHODOPENSIS* ORAL INTAKE ON HEALTHY VOLUNTEERS

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Summary

Todorova, R., R. Radev & A. T. Atanasov, 2017. Effect of *Haberlea rhodopensis* oral intake on healthy volunteers. *Bulg. J. Vet. Med.*, **20**, Suppl. 1, 95–99.

Haberlea rhodopensis (HR) is a Bulgarian endemic resurrection plant. The biological properties of HR plant extracts range from the *in vitro* antioxidant and antibacterial effect on bacterial cultures, to the *in vivo* antioxidant and radio-protective effects on animals. The aim of the present study was to investigate the *in vivo* effect of dried *Haberlea rhodopensis* on the blood line of healthy humans after oral application of the drug. The effect on the human blood parameters was studied two hours after oral administration of a HR lyophilised drug (9 g in compressed gelatin capsules) to healthy volunteers (3 males and 3 females). The percentage change in the total number of blood cells (red blood cells, white blood cells, platelets) vary between 4 and 21%. The absolute number of neutrophils in all studied subjects increased from 19% to 44.18% compared to the control values, taken before the drug intake. The data indicate a strong stimulating effect of the dry plant on the neutrophils count of the human blood. This is an evidence that HR dry drug contains substances that activate neutrophils, associated with the systemic immunity.

Key words: blood parameters, *Haberlea rhodopensis*, immunity, *in vivo* effect on humans, neutrophils

INTRODUCTION

The flower of *Haberlea rhodopensis* (HR) was found in 1834 in Rhodopi Mountain and was named after the Hungarian botanist Carl Constantin Haberle. HR was used in the traditional medicine to treat animal diseases. HR extracts are biologically active: the alcoholic extracts of HR possess strong antioxidant and antimicrobial activities (Ionkova *et al.*, 2008; Radev *et al.*, 2009). Inhibition of the bacterial growth was more pronounced on *S. aureus* than on Gram-negative strains *P. aeruginosa* and *E. coli* (Radev *et al.*, 2009). Higher correlation was found between total flavonoid content and free radical scavenging effect of HR extracts, measured by means of the DPPH discoloration assay, than total tannins and scavenging activity (Ionkova *et al.*, 2008). The antioxidant activity of total extract of HR *(Friv.)* can be attributed to some phytochemicals as flavonoides and anthocyanins (strong scavenging and antioxidant agents) (Radev *et al.*, 2009). The HR extract stimulates the antioxidant skin defences and extracellular matrix protein synthesis (Dell'Acqua & Schweikert, 2012). The HR extracts possess *in vitro*

Alometric Relationships between the Body Parameters of Mammals (from *S. araneus* to *B. musculus*). Impact on Parameters of *Homo sapiens*

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The body mass index (BMI) is a physiological characteristics represented by the ratio of body mass and the square of body height. Body mass index is characteristics often used for purpose of diagnostics in Human medicine, but is not developed like prognostic characteristic in Veterinary medicine. In manuscript we investigated the alometric relationships between the body parameters (mass , square of body length, body surface, body mass to surface ratio, body mass index and length of pregnancy) in 103 mammals (*Metatheria* and *Placentalia*) with impact on parameters of *Homo sapiens*.

Keywords: Mammals, mass to surface ratio, body mass index, anthropology.

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N 97

Some physicochemical characteristics of anti-platelet fraction isolated from *Galega officinalis* L.

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Some physicochemical characteristics of a 100-140 kDa fraction isolated from *Galega officinalis* L. were studied. The water soluble fraction inhibits platelet aggregation initiated by ADP, thrombin and collagen. The enzyme-treated fraction changes negligible inhibiting effect on platelet aggregation. The isolated fraction appears to have a polysaccharide nature, including 23 % protein. No loss in the activity of the fraction after storage for several months at 4 °C in N_3H-H_2O solution with neutral pH, and after freesing of liophilized fraction at -10 °C. The fraction shows maximum activity in the temperature diapason of 10°C-42°C and pH diapason of pH 5.5-9.8. The micro-calorimetric analyses show two protein subunits in the fraction. Anti-platelet fraction may find application in medicine, similarly to dextrans.

Key words: *Galega officnalis* L., isolation, anti-platelet fraction, characteristics

INTRODUCTION

Galega officinalis L.

L. is a medicinal plant wide spread in West Europe, Italy and Bulgaria. The plant has been used in a traditional medicine system in treatment of *diabetes mellitus* [1, 2]. Over 15 biologically-active substances are isolated from *Galega officinalis*: galegine, hydroxygalegine, peganine, vasicinone, lutein (alkaloids), penthahydroxyflavone 5-glucoside, luteolin, galuteoline, luteolin 5-glucoside (glucosides); flavonoids, glucosidessaponins and γ-γ dimethylallylamidin [3, 4]. The previous experimental investigations of Atanasov et.al indicate that the 100-140 kDa fraction isolated from *G. officinalis* has wide spectrum of effects on platelet and blood-plasma functions [5, 6] as :

- Inhibition of platelet release reaction [3]
- Inhibition of spontaneous platelet aggregation [3]
- Inhibition of platelet aggregation initiated by ADP, thrombin and collagen [5, 6]
- Inhibition of platelet aggregation initiated by free-radical compounds [3]
- Inhibition of spontaneous blood-plasma coagulation [3]

In vivo inhibition of platelet aggregation after intravenous injection in animals [7]

In manuscript are presented some physicochemical characteristics of fractions from *Galega officinalis*, which are important for biomedical approach on living organisms.

EXPERIMENTAL

Platelet aggregation measurement and fraction's activity

Blood was taken from volunteers (3 males and 3 females aged 20-23 years) wich was not treated with medicine for 15 days prior to blood collection. Blood was collected in disposable syringes and diluted at a ratio of 1 part 3,8 % trisodium citrate and 9 parts venous blood. Platelet-rich plasma (PRP) was prepared by centrifugation (180 x g for 10 min) and diluted to 300 x 10^6 platelets per ml with autologous platelet-poor plasma (1800 x g for 15 min). The platelet aggregation was studied by a photometric method according Born and Zucker [8]. The extinction change that takes place during the aggregation of 400 µl platelet-rich plasma compared with platelet-poor plasma (whose extinction was taken as zero) after adding aggregating agent at final concentration 25 µM ADP, 100 µg/ml collagen or 0.8 U/ml thrombin at 37°C was the basis of measurement of the aggregating effect. Aggregation (A) is calculated by the formula:

$$A.\,\% = (E_o - E_{sample})/(E_o - E_{plasma}).100\%.$$

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DOES THE VOLUME / (SURFACE·LIFESPAN) RATIO IN LIVING ORGANISMS IS CORRELATED TO MINIMUM MEMBRANE PERMEABILITY OF THEIR CELLS?

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ABSTRACT

The existence of a correlation between volume/(surface·lifespan) ratio and minimum membrane permeability of cells in living organisms was found. The study shows that the volume/(surface·lifespan) ratio $V/(S \cdot T_{ls})$ (m/s) in unicellular and multicellular organisms can be connected with minimum membrane permeability of cells P_{min}(m/s) with relation from type: $V/(S \cdot T_{ls}) = C\ P_{min}$ with correlation coefficient R=0.4 -0.5. The non-dimensional coefficient C varies from 0.1- 1.0 in unicellular organisms to 10-100 in animals. Both, $V/(S \cdot T_{ls})$ ratio and P_{min} have a same dimension (meter per second) and their values fall in a same window of 1.0×10^{-9}(m/s) - 1.0×10^{-13}(m/s). The received result allows the minimum membrane permeability of cells in organisms to be tentatively calculated using data for their volume, surface and lifespan.

Key words: membrane permeability, volume to surface ratio, lifespan, generation time, living organisms.

INTRODUCTION

The body mass and size (body length, surfaced, volume), the lifespan (generation or doubling time) and speed of biological processes of unicellular and multi-cellular living organisms fall in the area of classical physics [1, 2]. The mass of living organisms from viruses (1.0×10^{-20} kg) to big whales (1.0×10^{5} kg) range about 25 orders of magnitude [3]. The body size from viruses (about 1.0×10^{-8} m) to big whales (1.0×10^{2} m) range 10 orders of magnitude [4]. The lifespan from 20min generation time in bacteria to 3.0×10^{2} years lifespan in tortoises range 6 orders of magnitude [5]. The speed of biological processes ranges about 14 orders of magnitude, from speed of cell size growth (1.0×10^{-9}–1.0×10^{-12} m/s) to speed of nerve impulses (1.0×10^{2} m/s) [2, 4, 7]. Only body density of living organisms falls in a very small interval, from 1070 kg/m^3 in animals to 1100-1250 kg/m^3 in bacteria and viruses [7, 8]. This predicts the validity of basic physical equations connecting space and time *via* speed in biology. The received for living organisms relationships [2, 9] between volume/surface ratio (V/S) and lifespan (T_{ls}) (or generation time T_{gt}) *via* speed (a_{vst}) supports this idea:

$$V/S=a_{vst}\times T_{gt} \quad (1)$$
$$V/S=a_{vst}\times T_{ls} \quad (2)$$

The equation (1) related to unicellular organisms, while the equation (2) related to animals. The abbreviation 'vst' means 'volume-surface-time' ratio.

The volume to surface ratio (V/S) of organisms has a dimension of linear length and this ratio divided to lifespan has a dimension of speed or membrane permeability (a_{vst} m/s). For example, the volume V (m^3) to surface S(m^2) has a dimension of linear length L(m):

$$L(m)=V(m^3)/S(m^2) \quad (3)$$

While the ratio between length L(m) and lifespan T_{ls}(s) has a dimension of speed or membrane permeability a_{vst}(m/s):

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EXP.11. INHIBITING EFFECT OF DESALTED EXTRACT FROM *GALEGA OFFICINALIS L.* ON PLATELET AGGREGATION

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Key words: medicinal herbs, Galega officinalis L., platelet aggregation, ADP

Introduction: Extracts from the medicinal herb *Galega officinalis L.* have shown anti-aggregating effects on human and mammalian platelets.

Aim: The aim of this study was to examine the inhibiting and disaggregating effect of desalted and fractionated herbal extract of *Galega officinalis L.* on platelet aggregation *in vitro*.

Material and methods: Desalted fraction from the extract of the herb *Galega officinalis L.* was obtained by routine laboratory procedures. The extract was found to be pure and of high quality.

Results and discussion: The obtained desalted fraction from the extract was 35-36 times more active than the crude extract. The threshold concentration at which the obtained fraction inhibits platelet aggregation, causing 5-10% inhibition by adenosine 5'-diphosphate (ADP), is 4.5-5 mg per 1 ml platelet-rich plasma (PRP). At a concentration of 35 mg/ml PRP, the extract inhibits 50% of aggregation with ADP and, at a concentration of 125 mg/ml PRP, the fraction inhibits fully the aggregation of PRP by ADP. The threshold concentration at which the desalted fraction inhibits platelet aggregation, causing 5-10% inhibition by collagen and thrombin, is 10 mg/ml PRP. At concentration of 40 mg/ml PRP, the fraction inhibits fully the initiation of platelet aggregation by collagen and, in 50 mg/ml PRP it inhibits fully the initiation of aggregation by thrombin. The desalted fraction shows a strong disaggregating effect on aggregated PRP. At concentration of 65 mg/ml PRP, the fraction is able to disaggregate 50% of PRP as aggregated by ADP and, 25% of PRP as aggregated by collagen.

THE ALLOMETRIC RELATIONSHIP BETWEEN C-VALUE DIAPASON IN PROKARYOTES AND EUKARYOTES AND THE ORDER OF THEIR COMPLEXITY

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ABSTRACT

In this work we have to show that during the increasing of the order of the organismal complexity in evolution the genome size of the evolutionary groups varies around one optimal mean diapason of C-values (between 1÷3pg), that is common for all groups (Bacteria, Protozoa, Plants, Poikilotherms, Mammals, Aves). During the increasing of the organismal complexity in evolution the C-value diapason (Cvmax/Cvmin ratio of groups) is close approximately to this common mean diapason, that is near to the C-values diapson in birds.

***Key words**: genome size, C-value, organismal complexity, evolution.*

INTRODUCTION.

Mass is the most fundamental property of living cells and organisms. In this sense the amount of DNA contained within the cells is fundamental property too. The C-value of the genome size in cells has been given as mass in picogram (pg) of DNA per haploid nucleus (Mirsky and Ris, 1951). The C-values of animal genome sizes vary extensively, with existing estimates ranging more than 3300-fold, from 0.04 pg in the placozoan *Trichoplax adhaerens* to 133 pg in the marbled African lungfish *Protopterus aethiopicus* (Gregory, 2005)

In most Vertebrate groups the C-values of genome size varied from about minimum 2-fold to maximum 126-fold. In Jawless Fishes the genome sizes range less than 4-fold in the superclass Agnatha, from 1.3 pg in the southen brook lamprey, *Ichthyomyzon gagei* to 4.6 pg in the hagfish *Myxine garmani*.In Cartilaginous Fishes the genome sizes range from about 2.7 pg in the yellow guitarfish, *Rhinobatos schelegelii* to more than 17.1 pg in the angular roughshark, *Oxynotus centrina*. In Chondrostean Fishes the genome size range from about 1.5 pg to 6.5 pg. In Teleost Fishes the genome soze range more than 11-fold, from about 0.4 pg in tetraodontid pufferfishes to 4.4 pg in the masked corydoras, *Corydoras metae*. In Lobe-Finned Fishes, three genera of lungfishes are recognized, each inhabiting a different continent.These include the South American lungfish (*Lepidosiren paradoxa*) the Australian or Queensland lungfish (*Neoceratodus forsteri*), and a few species of African lungfishes (*Protopterus spp.*), all of wich possess extraordinarily large genomes. The smallest among them is that of *Neoceratodus forsteri*, at 50 pg to highest 133 pg in *Protopterus annectens*. In Amphibians genom size range more than 120-fold from 0.95 pg to 120 pg. In Reptiles and Mammals genome size range about 5-fold, from 1.1 pg to 5.4 pg in Reptiles and from 1.7 pg to 8.4 pg in mammals. The range of genome size in Aves is minimum, in comparison to others animal groups, from 1 pg to 2.2 pg i.e.about 2-fold only.

In most Invertebrate groups the C-values of genome size varied from about minimum 9-fold to maximum 340-fold. In Insects genome size range nearly 170-fold, from 0.1 pg in strepsipteran *Caenocholax feneyesi texansis* to 16.9 pg in the mountain grasshoppers, *Podisma pedestris*. In Crustaceans C-values range about 240-fold, from 0.16 pg in the water flea *Scapholeberis kingii* to 38 pg in the deep-sea shrimp *Hymenodora* sp. In Arachnids (mites, ticks, scorpions and harvestmen) C-values range about 70-fold, from 0.08pg in spider *Tetranychus urticae* to 5.7pg in the jumping spiders of the genus *Habronattus*. The Molluscs represent the most speciose aquatic animal phylum and the second largest group of animal overall.In Molluscs the genome size range about 15-fold with the entire range found among gastropods-from about 0.4pg in the owl limpet

POSSIBLE CONNECTION BETWEEN THE NASAL CYCLE AND CONSCIOUSNESS

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ABSTRACT. It is shown that there is a connection between the dynamics of the nasal cycle and the consciousness states of the brain. Accordingly to hypothesis, the switch of dominated airflow between left and right nostrils in time becomes only in consciousness states of the brain (in awake state, in REM dream and in dream of stages 1-2 of the non-REM sleep). This finding gives possibility to use nasal cycle as 'marker' for consciousness.
Key words: nasal cycle, sleep cycle, consciousness, brain.

INTRODUCTION. The nasal cycle defined as switch of dominate nostril airflow from left to right side and reverse is good studied during diurnal period of day over healthy and sick persons in wake consciousness state [1, 2]. During diurnal period of day the periods of the nasal cycle may have duration between 1.0 and 5.0 hours with random pattern under the influence of various factors [3, 4, 5]. During night sleep the switch of the nostrils occurred nearly in same interval with periodicity multiplied by duration of the sleep cycle [3].The investigations of Atanasov et al. [6, 7] and Kimura et al. [8] have shown the nasal cycle during night sleep is mutually connected to REM stage of the sleep. The experimental results of investigators have shown the change of dominate nostril airflow occurs during one of the stages of REM sleep and never occurred during slow-wave sleep stages. Recently, the awaking (waking) consciousness regard as 'primary consciousness state', wireless the REM stage of the sleep regard as form of 'secondary consciousness state' or 'proto-consciousness' [9, 10]. The consciousness is ambiguous concept, which is focused on multi-disciplinant debates. However, up to now, there is no universal definition for consciousness covering all its essential characters. A clinically defined consciousness has two main components-awareness and arousal [11]. The presence of one or both of the components of the consciousness gives reason to believe that the given person is in a state of consciousness or is near a consciousness state. During diurnal phase of the day the healthy person normally is in awaking consciousness. In this state of consciousness the sensation and perception are vivid and externally generated. The thought is logical and progressive. The movement is continuous and voluntary. The characteristics of consciousness during night sleep are poorly studied. The sleep is divided to non-REM and REM stages, which alternate in a certain sequence forming about 1.5 hours periods [12]. It is established that in REM stage of the sleep there is reason to consider that there is 'minimum threshold' of consciousness [9, 10]. In 'REM proto-consciousness' the sensation and perceptions are vivid and internally generated, and the thought is illogical and bizarre. The movement is command but inhibited. However, just in some of REM stages of the sleep become about 70% nasal cycle reversal between two nostrils [6, 7, 8]. During the non-REM stage of the sleep the sensation and perception are absent. If the sleeper is awakened from REM sleep, dream recall rates are very high, about 80 to 90 percent of the awakenings yield some kind of dream report [13]. Even after non-rapid eye movement (NREM) awakenings (in stage 2), some mental content has been reported quite often [14]. Some researchers advocate the hypothesis that the mind never sleeps, that is, dreaming of some kind is present during the entire sleep process. Accordingly to other authors [15] sleep that contains dream is considered as conscious state while dreamless sleep is unconscious. Lucid dreams are reported far more often in REM sleep too [16, 17]. In fact the lucid dreams could be considered a hybrid state combining essential elements of REM sleep

СПЕЦИАЛИЗИРАН НАУЧЕН СЪВЕТ ПО ФАРМАЦИЯ ПРИ В А К

Атанас Тодоров Атанасов

ВОДНИ ИЗВЛЕЦИ И ФРАКЦИЯ ИЗОЛИРАНА ОТ *GALEGA OFFICINALIS* L., ИНХИБИРАЩИ ТРОМБОЦИТНАТА АГРЕГАЦИЯ

А В Т О Р Е Ф Е Р А Т

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Стара Загора
2005 г.

д-р Атанас Тодоров Атанасов

ТРОМБОЦИТНА АГРЕГАЦИЯ

ДЕЙСТВИЕ НА ЛЕКАРСТВЕНИ И ПРИРОДНИ БИОЛОГИЧНО-АКТИВНИ ВЕЩЕСТВА ВЪРХУ ТРОМБОЦИТНАТА АГРЕГАЦИЯ

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СЪДЪРЖАНИЕ

Инж-физик Атанас Тодоров Атанасов, дх

РЪКОВОДСТВО

ЗА ЛАБОРАТОРНИ УПРАЖНЕНИЯ ПО

БИОФИЗИКА

ЗА ВИСШИТЕ МЕДИЦИНСКИ ИНСТИТУТИ

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N 103

APPLICATION OF NITROXYL RADICALS AS MEDICAMENTOUS FORMS

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EC Classification	
Equivalents	

Abstract

The pharmacological effect of nitroxyls, the comparison of their physical, chemical and biological properties and the applied methods and model implementation indicate that the nitroxyls show common properties with the nitrogen oxide (NO), but unlike it are stable, practically non-toxic and can be administered by precise dosing in vivo. The nitroxyls seize the toxic oxygen radicals O2 and inhibit the aggregation of thrombocytes in vitro. The application is based ion the fact that, by the addition of free stable nitroxyl radicals and other radical-capturing agents and antioxidants, the thrombotic aggregation is suppressed and the toxicity of a number of anti-tumor substances is reduced. The radical capturing agents in the molecules of the medicamentous preparations (spin-labelled substances), introduced in succession or separately, reduce the general toxicity of the preparations. 1 claim

N 104

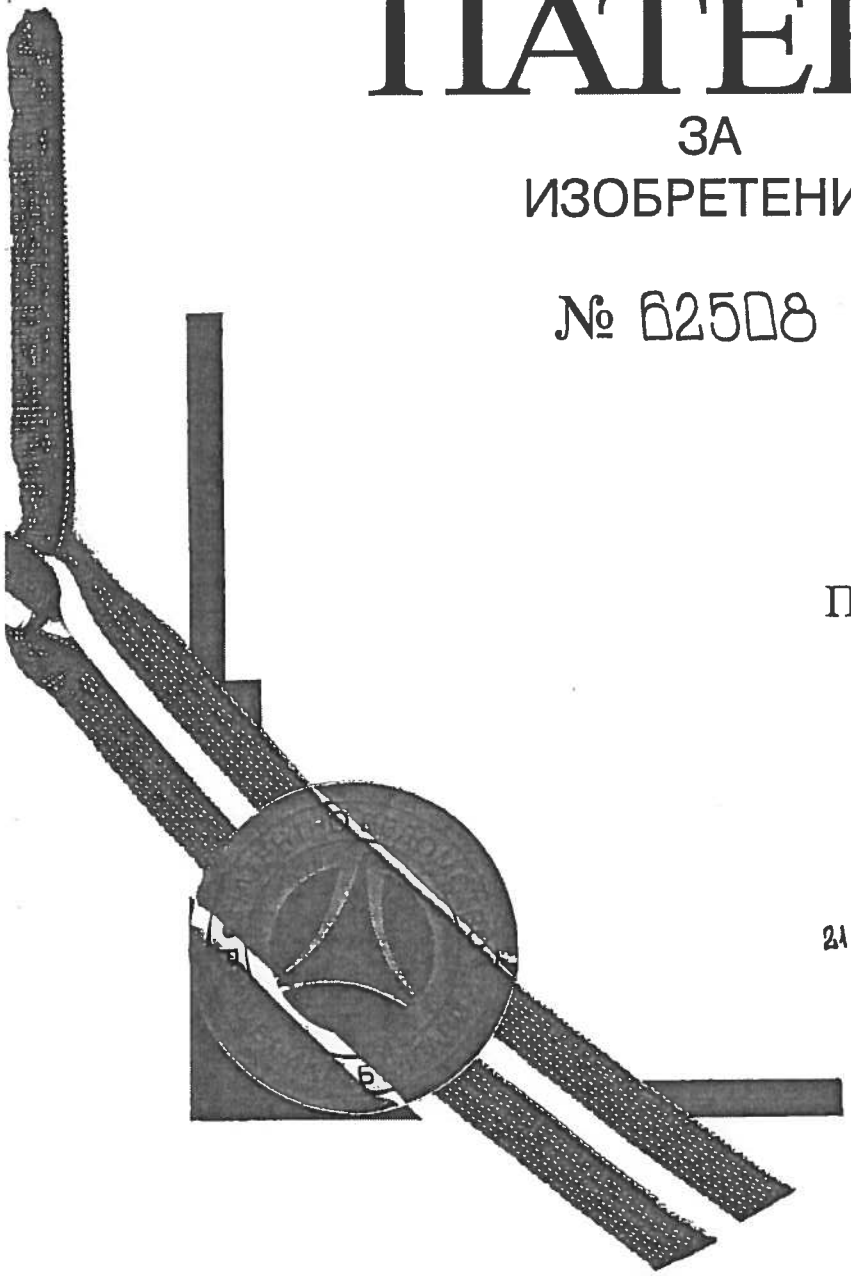
РЕПУБЛИКА БЪЛГАРИЯ

ПАТЕНТНО ВЕДОМСТВО

ПАТЕНТ

ЗА
ИЗОБРЕТЕНИЕ

№ 62508



Председател:

София

21.02.2000г.

N 105

РЕПУБЛИКА БЪЛГАРИЯ

ПАТЕНТНО ВЕДОМСТВО

ПАТЕНТ

ЗА

ПОЛЕЗЕН МОДЕЛ

№ 481

Председател:

София

106

РЕПУБЛИКА БЪЛГАРИЯ

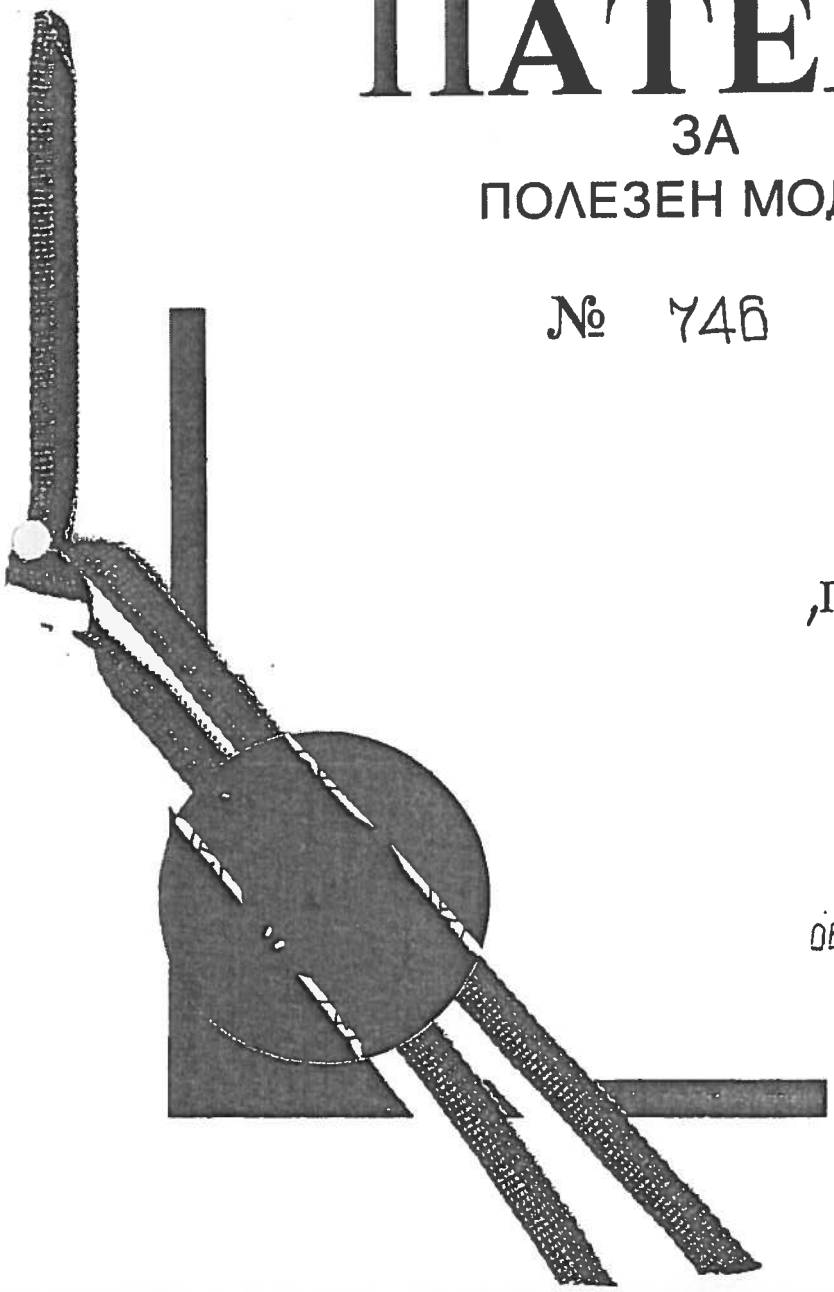
ПАТЕНТНО ВЕДОМСТВО

ПАТЕНТ

ЗА

ПОЛЕЗЕН МОДЕЛ

№ 746

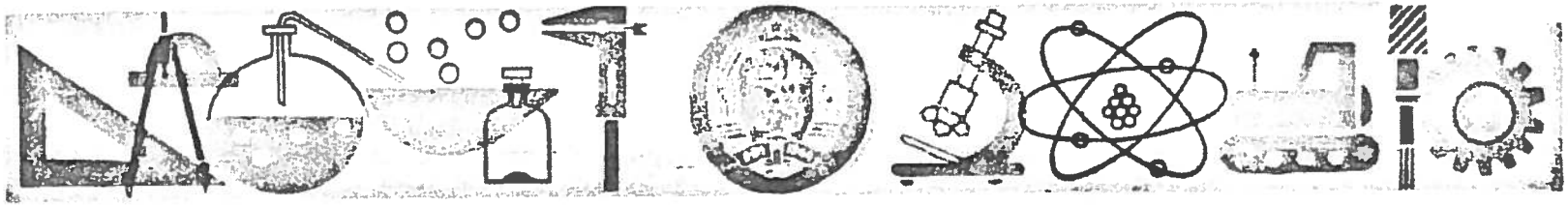


„Председател:

София

06.06.2005г.

№ 107



УДОСТОВЕРЕНИЕ

ИНСТИТУТЪТ ПО ФИЗИОЛОГИЯ ПРИ БЪЛГАРСКАТА АКАДЕМИЯ НА НАУКИТЕ

на основание чл. 57 от Закона за изобретенията и рационализациите дава настоящото удостоверение на АТАНАС АТАНАСОВ

автор на внедрена рационализация относно "Пневматичен микроинжектор"

подадена на 14.12. 1982 г., внедрена на 1.02. 1983 г

Въз основа на горното и на основание чл. 72 от Закона за изобретенията и рационализациите др. АТАНАС АТАНАСОВ

(личен паспорт — серия Ж № 128905) получава званието рационализатор и се ползува с правата и облагите съгласно Закона за изобретенията и рационализациите и Правилника за приложението му.

№ 14 / 2.04. 1984 г.

Гр. София

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ ИНСТИТУТ ПО ФИЗИОЛОГИЯ СОФИЯ

ПРЕДСЕДАТЕЛ: