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ЕКСПЕРИМЕНТАЛНИ ПРОУЧВАНИЯ ВЪРХУ НЯКОИ ОТ СТРАНИЧНИТЕ ДЕЙСТВИЯ НА СИМЕТИДИН

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Проучено е влиянието на симетидин в условията на хронично приложение (100 дни) върху 50 мъжки бели мишки. Симетидинът е въвеждан перорално чрез храната и водата. Средната дневна доза на симетидина е от 2,8 до 4,5 g/kg. Теглото на третираните със симетидин мишки не се различава съществено от контролните. На всеки 20 дни са убивани 5 животни от контролната и 5 животни от опитната група за макроскопско и патохистологично изследване.

Продължителността на хексеналовия сън у животните, приемали симетидин, в края на експеримента е 50 % от тази на контролната група.

След 100-дневно третиране със симетидин, приеман чрез храната и водата, не са наблюдавани нито макроскопски, нито хистологично патологични изменения в стомахчетата на опитните животни.

Ключови думи: симетидин, антагонист на H_2-хистаминергични рецептори, рак на стомаха, тегло, храна, вода, патохистологично изследване, индуктори и инхибитори на чернодробните лекарстваметаболизиращи ензими.

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ТРОМБОХЕМОРАГИЧНИ НАРУШЕНИЯ ПРИ ТОКСИКО - СЕПТИЧНИ СЪСТОЯНИЯ

TROMBOHAEMORRHAGIC DISORDES IN TOXICO - SEPTIC CONDITIONS

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РЕЗЮМЕ: *Проучени са клиничното протичане и нарушението в хемостазата при 21 болни деца от токсикосептично протичаща Gram(-) E.Coli инфекция. Болните са на възраст от 3 до 12 месеца. Клиничното наблюдение и лабораторните изследвания разкриват множествени коагулационни нарушения и патологични отклонения, характерни за синдрома на дисеминирана интраваскуларна коагулация.*

Обсъждат се патогенетичните механизми на хемостазните нарушения, като се изтъква значението на съдовата стена за поддържането на реологията на кръвта, както и за участието на ендотоксина на Gram(-) E.Coli и на редица медиатори/ цитокини, TNF-α, PAF и други/ в развитието на тежкото токсико - септично състояние с полиорганно увреждане и развитието на D.I.C.

Разглежда се и терапевтичното поведение при тези случаи.

КЛЮЧОВИ ДУМИ: *тромбохеморагични, токсикосептични, хемостаза, ендотоксин, ентерална токсикоза.*

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SUMMARY: *Investigations of clinical course and the haemostasis disorders in 21 patiens aged between 3 and 12 months with Gram (- VE) E.Coli toxicosepsis infection.*

Clinical observtion and laboratory studies reveal a great deal of coagulopathy and pathological changes characteristic of D.I.C. syndrome.

The pathogenic mechanisms of the haemostasis disorders are discused, and the importance of blood vessel in maintaining the blood reology is emphasized, as well as the participation of the endotoxin of Gram(- VE) E.Coli and other mediators cytokines, TNF-α, PAF and others in the development of severe toxicosepsis with multiple organ involvment and D.I.C.

The therapeutic conduct in these cases is also taken into consideration.

KEY WORDS: *trombohemorrhagic, toxicoseptic, hemostasis, endotoxin, enteral toxicosis.*

Клиничните наблюдения и експерименталните изследвания показват, че ендотоксинът на Gram (-) бактерии може да предизвика редица коагулационни нарушения и патологични отклонения, характерни за синдрома на дисеминираната интраваскуларна коагулация /1,2,3,4,5/.

Цел на настоящото проучване са някои нарушения в хемостазата при болни с Gram(-) коли инфекция, която протича токсико - септично.

МАТЕРИАЛ И МЕТОДИ

Изследвани са 21 кърмачета на възраст от 3 до 12 месеца, от които 12 момчета и 9 момичета с клинико - лабораторни данни за консумативни, тромбохеморагични нарушения, развили се на фона на ентерална токсикоза.

Хемостазното изследване включва определяне на протромбиновото време, тромбиновото време, фибриногена, фибриновите мономери, фибрин - разпадните продукти /ФРП/, камерно изброяване на тромбоцитите и времето на кървене. Освен това са проведени и рутинните хематологични изследвания. Диагнозата се изгради въз основа на клиничната картина и на резултатите от лабораторните и микробиологичните изследвания. При всички болни деца се изолират ентеропатогенни коли бактерии.

Заедно с антиинфекциозната, кардиотонична и рехидратираща терапия, при 16 от болните се проведе и антикоагулантно лечение с хепарин, в доза от 100 до 300 E/kg/m.м./24 h и субституционно с прясна кръв и плазма. Антикоагулантната и субституционна терапия продължи от 3 до 5 дни, в

ГОДИШНИК НА ВИСШИЯ МЕДИЦИНСКИ ИНСТИТУТ - СТАРА ЗАГОРА
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ПОЛУЧАВАНЕ, АНТИБАКТЕРИАЛНА АКТИВНОСТ И НЯКОИ ФАРМАКОЛОГИЧНИ ИЗСЛЕДВАНИЯ НА N-(5-НИТРО-ФУРФУРИЛИДЕНИЛ)-N-(4'-СУЛФОНАМИД)-2-(4,6-ДИМЕТИЛ) ПИРИМИДИН

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Summary. *Georgiev N M (Department of Pharmacology, Higher Medical Institute, 11 Armeiska str., Stara Zagora 6000 Bulgaria), Atanassov P G, Ganeva M G, Sokolova K T, Radev S V and Chemishev B Vl. Synthesis, antibacterial activity and pharmacological studies of N-(5-nitrofurfurilideniyl)-N-(4'-sulfonamide)-2-(4,6-dimethyl) pyrimidine.* ***Annual of the Higher Medical Institute of Stara Zagora [Bulgaria] 1996; 6: 31-32.*** *N-(5-nitrofurfurilideniyl)-N-(4'-sulfonamide)-2-(4,6-dimethyl) pyrimidine {fornitol} containing chemical structures characteristic for bactericidal agents is a new chemical compound (License No. 82586). Antimicrobial activity and minimal inhibitory concentrations for the most common pathogens as well as LD_{50} on mice were determined. From these results, the compound was compared to some therapeutics of common use. Spasmolytic activity on rat intestinal smooth muscle pre-treated with physostigmine, histamine, serotonin or barium chloride was established. The spasmolytic effect was dose-related in barium chloride-induced peristalsis suggesting a nonspecific mechanism of action.*

Key words: *N-(5-nitrofurfurilideniyl)-N-(4'-sulfonamide)-2-(4,6-dimethyl) pyrimidine, antibacterial activity, spasmolytic effect, physostigmine, histamine, serotonin, barium chloride.*

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МОРФОЛОГИЯ НА КЛЕТКИТЕ НА ITO ПРИ ЕКСПЕРИМЕНТАЛНА ИНТОКСИКАЦИЯ НА ПЛЪХОВЕ С CCL4 И СЛЕД ЛЕЧЕНИЕ С ХЕПАТОПРОТЕКТОРИ

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MORPHOLOGY OF ITO CELLS IN EXPERIMENTAL RAT CCL_4 INTOXICATION AND AFTER HEPATOPROTECTIVE THERAPY

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Summary

Ito cells are a main source of extracellular matrix in liver sinusoids in the process of fibrogenesis. This study is aimed to represent morphological shifts of these cells after treatment by flavonoids derived from *Corylus Columa* (F4), compared to those after Crasyl treatment in a model of acute hepatic damage by CCl_4

Thirty six white male Wistar strain rats have been used in this study. Protective effect of F4 is compared to the effect of Crasyl. After 2 days F4 or Crasyl treatment and CCl_4 application in the 3rd and 4th days the Ito cells are „calm". We are discussing the mechanism of the effect of F4 on Ito cells and the depression of their transformation into transitory cells. F4 is a reliable inhibitor of liver fibrogenesis.

Key words: Ito cellss, F4, Hepatoprotectors.

Клетките на Ito са основните

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ВЪРХУ АНТАГОНИЗИРАНЕ ПОТИСКАЩОТО ДЕЙСТВИЕ НА АЛКОХОЛА С АЛИЛНОРМОРФИН В УСЛОВИЯТА НА ОСТЪР И ХРОНИЧЕН ОПИТ

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ON ANTAGONIZING ALCOHOL DEPRESSIVE ACTION BY ALLYLNORMORPHINE IN CONDITIONS OF ACUTE AND CHRONIC EXPERIMENT

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РЕЗЮМЕ: *Проучена е възможността за антагонизиране на аналгетичните ефекти на алкохола при еднократно и многократно (5 дни) приложение с помощта на конкурентния морфинов антагонист алилнорморфин, както и ефективността на алилнорморфина при комбинирано въвеждане на алкохола с дроперидол. Опитите се извършиха върху 60 мъжки бели мишки с тегло от 20 до 25 грама. Алкохолът се въвеждаше пер сондам в доза 5ml/kg. Алилнорморфинът се инжектираше интраперитонеално в доза 1mg/kg, а дроперидолът също интраперитонеално, в доза 0.75 mg/kg. Всички животни бяха тестирани за аналгетична активност по метода "Hot plate". Установено бе, че алилнорморфинът антагонизира аналгетичното действие на алкохола при еднократно и многократно въвеждане, както и при комбинираното му приложение с дроперидол.*

КЛЮЧОВИ ДУМИ: *аналгезия, алкохол, алилнорморфин, дроперидол.*

SUMMARY: *It has been studied the possibility of antagonizing alcohol analgesic effects after a single and repeated (for 5 days) application of the competitive morphine antagonist allylnormorphine as well as the allylnormorphine effectiveness when alcohol is administersd in combination with droperidol.*

The experiment was carried out on 60 male white mices weighing 20 - 25 g. Alcohol was administered orally per sondam in a dose of 5 ml/kg. Allylnormorphine was injected intraperitoneally in a dose of 1 ml/kg, so was droperidol in a dose of 0.75 mg/kg. All the animals were tested for analgesic activity by the "Hot plate" method. It was established that allylnormorphine antagonizes alcohol analgesic action in a single and repeated administration, as well as in its combined application with droperidol.

KEY WORDS: *analgesia, alcohol, allylnormorphine, droperidol.*

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ВЛИЯНИЕ НА 5-НИТРОФУРФУРАЛ-2-ХИДРАЗОН (ЧАР-VI) ВЪРХУ ГЛАДКА МУСКУЛАТУРА ОТ ИЛЕУМ НА ПЛЪХ

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INFLUENCE OF 5-NITROFURFURAL-2-HYDRAZON ON THE SMOOTH MUSCLE OF RAT ILEUM

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РЕЗЮМЕ: *Проучено е влиянието на синтезирания по нов път 5-нитрофурфурал-2-хидразол (ЧАР-VI) върху изолирани препарати от илеум на 78 мъжки бели плъха, линия Wistar с апарат за изследване на изолирани органи "Ugo Basile". Изследван е ефектът на ЧАР-VI върху предварително стимулираната с бариев двухлорид, неостигмин, хистамин и серотонин гладка чревна мускулатура.*

Установено е, че проучваната субстанция, прилагана в крайни концентрации от 1.10^{-3} до 1.10^{-9} g потиска по доза (концентрация)-зависим начин активността на стимулираната с бариев двухлорид, неостигмин и хистамин тънкочревна гладка мускулатура. Потискащият ефект на ЧАР-VI се проявява в различна степен при отделните стимуланти на тънкочревната гладка мускулатура. В концентрация 1.10^{-3} и 1.10^{-4} g ЧАР-VI потиска значимо стимулираната с бариев двухлорид гладка мускулатура, а в концентрация 1.10^{-4} и 1.10^{-6} g - стимулираната с неостигмин тънкочревна гладка мускулатура на плъх. Изследваното вещество потиска слабо, но в много ниски крайни концентрации индуцираната с хистамин и серотонин тънкочревна перисталтика. ЧАР-VI упражнява спазмолитично действие по комплексни механизми.

КЛЮЧОВИ ДУМИ: *5-нитрофурфурал-2-хидразон, илеум на плъх, бариев двухлорид, неостигмин, хистамин.*

SUMMARY: *The influence of 5-nitrofurfural-2-hydrazon (CHAR-VI) synthesized according to a new reaction scheme is studied on isolated smooth muscle preparations from ileum of 78 male Wistar rats using Ugo Basile isolated organ research apparatus. The effect of CHAR-VI on intestinal smooth muscle strips pretreated with barium chloride, neostigmine and histamine was evaluated. The examined substance at final concentrations ranging from 1.10^{-3} to 1.10^{-9} g inhibits dose (concentration)-dependently the activity of rat intestinal smooth muscle strips induced by barium chloride, neostigmine, histamine and serotonin. The inhibitory effect of CHAR-VI varies with the different activators of intestinal smooth muscle contractility. CHAR-VI at final concentrations 1.10^{-3} and 1.10^{-4} g significantly inhibits barium chloride-induced smooth muscle contractions and at final concentrations 1.10^{-4} and 1.10^{-6} g - neostigmine-induced smooth muscle contractions. CHAR-VI slightly inhibits at very low final concentrations histamine and serotonin-induced intestinal smooth muscle peristalsis. CHAR-VI displays spasmolytic activity due to complex mechanisms.*

KEY WORD: *5-nitrofurfural-2-hydrazon, rat ileum, barium chloride, neostigmine, histamine.*

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ХЕПАТОПРОТЕКТИВЕН ЕФЕКТ НА ФЛАВОНОИДИ ИЗОЛИРАНИ ОТ CORYLUS COLURNA

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THE HEPATOPROTECTIVE EFFECTS OF FLAVONOIDS ISOLATED FROM CORYLUS COLURNA

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РЕЗЮМЕ: *Протективният ефект на флавоноиди /F_4/, изолирани от Corylus colurna при експериментален хепатит с тетрахлорметан в сравнителен аспект с Carsyl /Silymarin/ е проучван върху тридесет мъжки бели плъхове. Плъховете с тегло 160 - 180 грама бяха разделени в пет групи по шест животни:*

I - контролна група - третирана 2 дни с 10% 2 ml/kg тетрахлорметан чрез сонда;

II - група - третирани 2 дни с F4 100 mg/kg i.p. и с тетрахлорметан като плъховете от контролната група през третия и четвъртия ден;

III - група - инжектирани 4 дни с F_4 в същата доза, като през третия и четвъртия ден получаваха тетрахлорметан.

Животните от IV и V група бяха третирани като тези от II и III група, но вместо F_4 те получаваха известния с хепатопротективното си действие български препарат Carsyl.

По патохистологичните промени бе установено, че изследваната фракция F_4 упражнява хепатопротективен ефект близък или идентичен с Carsyl при използвания от нас модел на хепатит. Този ефект се дължи най-вероятно на мощното антиоксидантно действие на изследваните флавоноиди, съдържащи се в F_4 (3).

КЛЮЧОВИ ДУМИ: *флавоноиди, тетрахлорметан, Carsyl, хепатопротектор.*

SUMMARY: *The protective effect of flavonoids (F_4) isolated from Corylus colurna was studied on 30 male albino rats with tetrachlormetan - induced hepatitis. The rats weighing between 160 - 180 g were divided into 5 groups (6 animals per group):*

I Control group - treated 2 days with 10% 2 ml/kg tetrachlormethan per sondam;

II Group - treated for 2 days wIth 100 mg/kg F_4 i.p. and with tetrachlormethan on the third and the fourth day at the same dose as that used for the controls;

III Group - injected for 4 days with F_4 in the same dose and on the third and the fourth day with tetrachlormethan.

As a standard hepatoprotector we used the Bulgarian drug Carsyl. That is why the animals of Groups IV and V were treated like those of Groups II and III, but instead of F_4 we applied Carsyl in the same dose.

The results obtained from the pahtohistological study revealed that the pathological changes were similar or even identical in the animals of Groups II and IV, as well as in the rats of Groups III and V. Thus we suggest that the flavonoids, components of F_4 have a hepatoprotective effect similar or identical to that of Carsyl. This efect is most probably due to the decreased cell- membrane permeability and the high antioxidant activity inherent in these compounds (3).

KEY WORDS: *flavonoids, tetrachlormethan, Carsyl, hepatoprotector.*

ВЛИЯНИЕТО НА H_2-ХИСТАМИНЕРГИЧНАТА РЕЦЕПТОРНА БЛОКАДА ВЪРХУ НЯКОИ ЕФЕКТИ НА ФЕНОТИАЗИНОВИТЕ НЕВРОЛЕПТИЦИ

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Резюме: Проучено е влиянието на H_2-хистаминергичната рецепторна блокада по отношение протективното действие на хлорпромазина към груповата фенаминова токсичност. Опитите са извършени върху 40 мъжки бели мишки, с тегло между 20 и 25 грама. Животните са третирани с фенамин в доза 15 mg/kg, хлорпромазин - 10 mg/kg, симетидин - 100 mg/kg, въведени интраперитонеално. Смъртността на мишките се отчита до 24-я час. Установи се, че блокирането на H_2-хистаминергичните рецептори със симетидин антагонизира протективния ефект на хлорпромазина по отношение на груповата фенаминова токсичност у мишки.

Ключови думи: фенамин, хлорпромазин, симетидин, групова фенаминова токсичност

Едно от основните фармакологични свойства на фенамина е неговата значително по-висока токсичност при групирани, отколкото при индивидуално поставени животни /1/. Невролептиците, включително и фенотиазиновите се отличават с антагонизирането на груповата фенаминова токсичност. Тези отношения между невролептиците и фенамина са причина груповата фенаминова токсичност да се използува като популярен и удобен тест при изследване на различни вещества с психотропно действие /1,3/. H_2-хистаминергичната рецепторна блокада със симетидин успешно антагонизира каталептогенното действие на хлорпромазина и халоперидола /2/. Изхождайки от тези литературни данни си поставихме за задача да проучим съществува ли антагонизъм между H_2-хистаминергичната рецепторна блокада със симетидин и намаляващото груповата фенаминова токсичност действие на хлорпромазина.

МАТЕРИАЛ И МЕТОДИ

Опитите са извършени върху 40 мъжки бели мишки с тегло между 20 и 25 грама съгласно методиката /1/. Животните са групирани по 10 и след инжектирането им се поставят в еднакви стъклени вани с размер 23/19/13 сантиметра, покрити с капак от мрежа. Първата /контролна/ група мишки се третира с фенамин-сулфат в доза 15 mg/kg, въведен интраперитонеално /i.p./. Втората група животни се инжектира 30 минути преди фенамина с хлорпромазин - 10 mg/kg i.p., известен със своето антагонистично действие по отношение на груповата фенаминова токсичност. Третата група мишки е третирана с H_2-хистаминергичния блокер симетидин 100 mg/kg i.p. и след 30 минути с фенамин в доза, както предишните групи.

Четвъртата група е третирана по едно и също време със симетидин - 100 mg/kg i.p. и хлорпромазин по 10 mg/kg i.p. и след 30 минути с фенамин в доза - 15 mg/kg.

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НЕЖЕЛАНИ ЛЕКАРСТВЕНИ РЕАКЦИИ ПРИ ТЕРАПИЯ С ПРОТИВОТУБЕРКУЛОЗНИ СРЕДСТВА

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ADVERSE DRUG REACTIONS IN THERAPY WITH ANTI - TUBERCULOSIS DRUGS

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SUMMARY: *The study reports on adverse drug reactions during therapy for tuberculosis in patients with different forms of the disease. The patients were treated in the Clinic for Prevention of Pulmonary Diseases in Stara Zagora.The standard therapeutic scheme and drug dosage were applied. Isoniazid, Rifampicin, Ethambutol, Streptomycin and Pyrazinamid were used. The concomitant diseases were taken into consideration. Before and during the therapy laboratory tests including AsAT, AlAT and creatinine were analysed. At the end of the first, the third, the sixth and the ninth months of the therapy and in cases when spontaneous complaints of patients occurred, the goal of the search was to establish adverse drug reactions like hepato-cellular damages, nephropathia, neuropathia, vestibulopathia, etc. The frequency and the severity of the adverse drug reaction as well as the conditions of their emergence were established. The different methods for reducing and eliminated of adverse drug reactions were applied. The observed frequency of adverse drug reactions was compared with the data from other authors from Bulgaria and abroad.*

KEY WORDS: *tuberculosis, antituberculose drugs, adverse reactions.*

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ПРОФИЛАКТИКА НА ПОСТОПЕРАТИВНОТО ГАДЕНЕ И ПОВРЪЩАНЕ ПРИ ДЕЦА, ПОДЛОЖЕНИ НА ТОНЗИЛЕКТОМИЯ

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PONV PREVENTION IN CHILDREN UNDERGOING TONSILLECTOMY

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SUMMURY: *Children undergoing tonsillectomy are with high ratio of postoperative nausea and vomiting (PONV). In this study compare the effect of Ondansetron and Metoclopramide for prevention of this complication. Sixty pediatric patients, 2 to 11 years old, entered for tonsillectomy with or without adenomectomy in ORL department, were involve in this prospective, double blind, placebo controlled study, for choice of one of this therapeutic regimes - Ondansetron 0,15 mg/kg; Metoclopramide 0,3 mg/kg; and Placebo 0,9% NaCl. Premedication with Midazolam 0,4 mg/kg peroral, for induction and maintenance of anesthesia, Halotan and N_2O, Myorelaxin 1 mg/kg. At the end of anesthesia we apply Doloreduct supp.125 mg for postoperative pain relief. Nurse staff in Department of otorhinolaryngology by the sixth hour recorded all episodes of nausea and vomiting after intervention. Ondansetron occur to be effective in preventing of PONV in this age population. Metoclopramide is without significant effect.*

KEY WORDS: *PONV, Ondansetron, Metoclopramide, tonsillectomy.*

There are compared all of the outpatients' costs for these two drugs- Morphine slow-tard and Fentanyl TTS. The calculation included the price of the drug for 15 days therapeutic course, costs for staff, transport, storage and assignment of the drug. For assessment of the costs for prophylactics and treatment of the adverse drug reactions /ADR/ after the use of the drugs we use the "Decision tree" methodology.

The costs for gain of Fentanyl TTS are exceeded with 28% these for Morphine slow-tard and these reflect on total direct costs for outpatient practice. The costs of treatment of the ADRs are higher with 68% for Morphine slow-tard due to high probability of appearance of the reactions, their seriousness and duration.

The results come to a conclusion that the justifications of the use of Fentanyl TTS are in availability of equal total costs with Morphine slow-tard, but low frequence of ADRs and better quality of life of the patients.

67. SYNTHESIS AND STRUCTURAL ANALYSIS OF ONE MONOTERPENICDERIVATIVE OF 7-THEOPHYLLINEACETIC ACID

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Theophylline and its derivatives, such as 7-theophyllineacetic acid and theophyllinyl-7-acetates, are widely used therapeutically, particularly as bronchodilators and have been important drugs in the treatment of asthma.

In the present study we describe the preparation of [5-methyl-2-(1-methylethyl)-cyclohexyl] 2-[7-(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurinyl]-acetate by using two synthetic approaches. The progress of the reaction was investigated under various conditions.

Structural analysis was carried out by means of spectral and computational methods.

68.. СЪЗДАВАНЕ НА ЛЕКАРСТВЕНИ ФОРМИ ЗА ОЧИ С УДЪЛЖЕНО ДЕЙСТВИЕ

Димитрова Е., Св. Богданова, М. Касърева, Е. Минков

69. HYPOPERFUSION COMPLICATIONS OF THE LOW EXTREMITIES IN PATIENT WITH SEPTIC SHOCK ASSOCIATED WITH HIGH DOSE REGIME OF NORADRENALIN INFUSION

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We are presenting a clinical case of 25-year-old female patient with septic shock and manifesting hypotension. Impossibility of correcting hemodynamic by using dopamine support calls the necessity of using dobutamin and noradrenalin. In this case we have not got enought influence upon arterial blood levels by using dopamine, for that reason it is imperative for us to use dobutamine and noradrenalin in maximal infuse dosage (0.66μg/kg/min), for saving the patient's life. Ischemic complication of the low limbs, which led to amputation of the toes, can be neglected compare to high mortality rate of 30% - 90% from septic shock.

Key words: Noradrenalin, Septic shock.

70. INFORMATIVE VALUE OF THE POOLED PLASMA ANALYSIS (PLA) IN BIOEQUIVALENCE STUDIES

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The trials were performed in healthy voluteers. Ciprofloxacin (C) study was carried out according to a cross-over design in 24voluteers, who received 500 mg C orally, o.i.d. as a film-tablet. C Plasma-concentrations were followed till 24 h after dosing. Phenprocoumon (P) study was performed according to a parallel group design (2 groupsx30 voluteers). The volunteers received 3 mg P, orally, o.i.d. as a film-tablet. Plasma concentrations of P were measured 240 h after dosing. Drug assay in both studies was performed using HPLC methods. The results are shown in Table 1.:

Drug	AUC (μg.h/ml)		Cmax (μg/ml)	
	PPA	IPA*	PPA	IPA
C	1.11	1.02 (0.97-91.06)	1.07	1.02 (0.95-1.09)
P	0.97	0.98 (0.96-1.06)	0.96	1.00 (0.91-1.08)

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ФАРМАКОЛОГИЯТА НА ГРАНИЦАТА МЕЖДУ ДВЕ СТОЛЕТИЯ

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ABSTRACT

Pharmacology plays an important role in the process of the development of new drugs and their introduction into clinical practice. The long history of pharmacology is marked by substantial achievements which led to a therapeutic revolution in the treatment of many diseases.

During the 20th century a lot of new drugs were introduced which greatly improved healthcare (insulin, penicillin, phenothiazines, beta-blockers, angiotensin converting enzyme inhibitors). Progress has been made in the field of cancer chemotherapy and the management of infectious diseases. Considerable advances have been made in the treatment of chronic disease states like diabetes, hypertension, depression and chronic pain. However as AIDS pandemic in the new millenium showed important challenges remain, for example in neuropharmacology, cardiovascular pharmacology, chemotherapy, therapy of autoimmune diseases, pharmacogenetics, molecular pharmacology. These new horizons in pharmacology will be reached with the help of new technologies and through the progress of fundamental sciences in unravelling important biological and pathogenetic mechanisms of normal and pathological processes in humans.

Key words: pharmacology, development, new drugs

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Mini-review

PHARMACOECONOMICS IN EVALUATING HEALTH CARE DECISIONS

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ABSTRACT

There is no public health system in the world that has enough resources required for satisfying its full potential. The continuously increasing costs in public health and the limited financial resources for its various implementations demand a judicious allocation of the available resources and their optimal use to achieve effectiveness in health services. Pharmacoeconomics, like a multi-discipline action field, unites the efforts of clinical pharmacologists, pharmacists, health economists, epidemiologists and others in search of a balance between the costs for health services and their results.
Pharmacoeconomic analyses offer information to the people working in the public health sphere and helps in making reasonable decisions in the most rational allocation of the limited financial resources.

Key words: opportunity cost, incremental cost, benefit, QALY, viewpoint.

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Original Contribution

ФАРМАКОЕПИДЕМИОЛОГИЧНО ПРОУЧВАНЕ НА ФАКТОРИТЕ, ПОВЛИЯВАЩИ ИЗБОРА И ПРЕДПИСВАНЕТО НА ЛЕКАРСТВА

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A PHARMACOEPIDEMIOLOGIC STUDY OF FACTORS INFLUENCING THE CHOICE AND PRESCRIPTION OF DRUGS

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ABSTRACT

The purpose of the study is to assess the influence of different factors on the drug choice and prescription in the ambulatory practice. Methods: This is a pharmacoepidemiologic study using an inquiry form. 153 general practitioners and specialists from the region of Stara Zagora were involved. The results give assistance to decision makers in optimizing drug policy. The study is under the aegis of Bulgarian Ministry of Health and was accomplished by Department of pharmacology and clinical pharmacology of Medical Faculty, Stara Zagora in collaboration with RHIF- Stara Zagora.

Key words: drug prescription, motivation, factors

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Original Contribution

АЛГОМЕТРИЯТА ЧРЕЗ НАТИСК КАТО МЕТОД ЗА ОПТИМИЗИРАНЕ НА ПРОТИВОБОЛКОВАТА ТЕРАПИЯ

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THE ALGOMETRY BY PRESSURE AS A METHOD TO OPTIMIZE PAINRELIEF THERAPY

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ABSTRACT

The algometry by pressure is a way of determine the pain threshold with very high level of accuracy.
The aim of the survey is to determine the pain threshold in a healthy males and females. The target zones are skin areas corresponding with joints and muscles, where the pain presents more often due to inflammatory and degenerative diseases of the musculoskeletal system.
The results from the healthy individuals could be compared with those ones in patients with problems before or during the painrelief therapy. This is a way to prove the effectiveness of the current treatment and if it is necessary to change the medications.

Key words: pressure, algometry, pain, threshold

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TRANSDERMAL DELIVERY OF ANTI INFALMMATORY DRUGS IN THE CASE OF LATERAL EPICONDYLITIS

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ABSTRACT

Lateral epicondylitis (tennis elbow) is a common condition characterized by pain and impaired function of the affected forearm. Analgesia and pain management are two very important aspects in the therapeutic process

A mixture of Diclofenac and Dexamethasone was given locally via dermoelectroporation in the area of the damaged lateral humeral epicondyl. The pain threshold was recorded with Pressure Algometry and used as a criterion for the drug efficacy.

Using this method of application of nonsteroidal and steroidal anti-inflammatory drugs has significant benefits like: quick pain relief, lower traumatic effect for the patient and minimum side effects. Based on these advantages it is thought that dermoelectroporation could be a preferable way of administering anti inflammatory drugs in inflammatory - degenerative conditions related to the musculoskeletal system, such as myotendinosis.

Key words: epicondylitis, dermoelectroporation, pressure algometry.

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TOPICAL DELIVERY OF ANTI INFLAMMATORY DRUGS IN THE CASE OF TENDINOPATHY

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ABSTRACT

Tendinopathy is a common condition characterized by pain and impaired function of the affected tendon and muscle. Analgesia, inflammation and pain management are very important aspects in the therapeutic process. A mixture of Diclofenac and Dexamethasone was given locally via dermoelectropuration in the area of the damaged tendon and muscle. The pain threshold was recorded with Pressure Algometry, 10 cm VAS and used as a criterion for the drugs efficacy.

Using this method of application of nonsteroidal and steroidal anti inflammatory drugs has significant benefits like: quick pain relief, lower traumatic effect for the patient and minimum side effects. Based on these advantages it is thought that dermoelectropuration could be a preferable way of administering anti inflammatory drugs in inflammatory – degenerative conditions related to the musculoskeletal system, such as tendinopaties.

Key words: shoulder pain, pressure algometry, dermoelectroporatio

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HABERLEA RHODOPENSIS: A PLANT WITH MULTIPLE PHARMACOLOGICAL ACTIVITIES

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ABSTARCT

The total leaf extract from the resurrection plant Haberlea rhodopensis was screened for some pharmacological properties. Antioxidant activity was assessed by determining the total (Mg-Zn and Mn) superoxide dismutase (SOD) activity according to the method of Sun et al. Antibacterial tests were performed by the disk-diffusion method. The tests for explicit memory we conducted using the Ugo Basile (Italy) equipment: Shuttle box, Step trough, Step down and Open field. The results showed that the extract demonstrated higher SOD activity compared to the referent compound Troxol, an antibacterial activity against tested pathogenic strains markedly directed towards Gram positive microorganisms, and improved to a greater extent short memory compared to long memory. These facts can be explained by the existence of some phytochemicals such as phenol compounds. The present study has preliminary character and further ones will be developed to confirm our results and identify the compounds responsible for this bioactivity.

Key words: resurrection plant, antioxidant activity, antibacterial activity, memory changes

NEW POSSIBILITIES IN THE PHARMACOLOGICAL TREATMENT OF ABNORMAL CONVULSIVE ACTIVITY IN ACUTE ORGANOPHOSPHATE NERVE AGENTS INTOXICATION

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ABSTRACT

Organophosphates, used as chemical warfare nerve agents and pesticides are the most toxic chemicals known to date. Despite the number of studies done on the subject matter, intoxication caused by such agents is among the most complicated problems in medicine because of the induced increase in abnormal electrical activity in the brain and the subsequent brain damage. The anticonvulsant and neuro-protective effects of conventional benzodiazepines are limited by their side effects, including sedation, amnesia, withdrawal, and anticonvulsant tolerance. Imidazenil is a proposed drug in the treatment of convulsions in acute cases of poisoning with organophosphate nerve agents and an alternative to the currently used benzodiazepines with an improved safety profile.

***Key words**: imidazenil, neuroprotective effect, organophosphates*

ЕФЕКТИВНОСТ НА НЯКОИ ПРОТИВОВЪЗПАЛИТЕЛНИ СРЕДСТВА, ПРИЛАГАНИ ТРАСДЕРМАЛНО, ПРИ ЛЕЧЕНИЕ НА ТЕНДИНОПАТИИ

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EFFICACY OF TOPICAL DELIVERY OF ANTI INFLAMMATORY DRUGS IN THE CASE OF TENDINOPATHY

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ABSTRACT

Tendinopathy is an inflammatory-degenerative painful condition, occurring in tendons and muscle in response to overuse. Except pain, tendinopathy characterized by impaired function of affected joint. Diclofenac and Dexamethasone was given locally via electroporation in the area of wrist tendinitis. The pain threshold was recorded with Pressure Algometer and with 10 cm VAS and used as a criterion for the drug efficacy. Using electroporation of applications of anti-inflammatory drugs has significant benefit like: quick pain relief, non - traumatic approach and lack of adverse effects.

Key words: *electroporation, pressure algometry, tendinopathy.*

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IS INFLAMMATION PRESENT IN EARLY HUMAN TENDINOPATHY?

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ABSTRACT

Tendinopathy is a general term, describes any painful condition, that occurs in or around tendon.The role of inflammatory cells and their products in tendinopathy is not completely understood. Tendinopathy is clinical syndrome, often implying overuse tendon injuries. Characterized by pain, sometimes localized swelling and impaired performance. The pathogenetic mechanisms underlying tendinopathy remain unclear, with much debate whether inflammatory or degenerative hypothesis has the prominent role. Increasing evidence points towards an early inflammatory infiltrate and associated inflammatory cytokine production in human and animals models of tendon disease. IL-21R is present in early human tendinopathy mainly expressed by tenocytes and macrophages. These data suggest that early human tendon injury has an inflammatory, which may provide novel targets in the treatment of tendinopathyes.

Key words: tendinopathy, inflammation, degeneration, treatment

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EARLY DIAGNOSIS AND PREVENTION FROM SPINAL DEFORMITIES IN KINDERGARTEN

(Preliminary communication)

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Abstract

The modern lifestyle, improper diet and reduced physical activity of children are factors that cause the poor posture and different deformations of the spine and chest. The aim of this paper is to perform an early diagnosis and prevention of spinal deformities in kindergartens in the city of Stara Zagora and compiling a kinesitherapeutic program to improve physical activity in children. We studied 242 children aged 6 to 7 years from 22 kindergartens in the city of Stara Zagora during pre-graduate internship of students of specialty „Rehabilitation therapist". An analysis of the results of children diagnostic was made, results were grouped according to the type of spinal deformities. A kinesitherapeutic program was composed including exercise, active games and sports to increase the physical activity of children.

Keywords: *kinesitherapeutic program, rehabilitation programs for prevention, physical development, physical activity exercise, gymnastic exercises, active games, sports, computer diagnosis of foot, kyphosis, lordosis, scoliosis*

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WHAT TREATMENT OF TENDINOPATHY: INFLAMMATION OR DEGENERATION?

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ABSTRACT

Tendinopathy is a common clinical problem in many occupational settings, including athletes. It is characterized by pain in the tendon and impaired performance. Chronic tendon pathology is difficult to treat. The intrinsic pathogenetic mechanisms underlying tendinopathy remain unclear, with much debate whether inflammatory or degenerative hypothesis has the prominent role. Overuse and microruptures of tendon fibres may be considered as the initial disease factors. Several molecules are expressed, some of which promote the healing process, while others, including inflammatory cytokines act as disease mediators.

In this systematic review we present information relating to the effectiveness and safety of the following treatments of tendinopathy: corticosteroid injections, non-steroidal anti-inflammatory drugs (oral and topical), autologous whole blood injections, physiotherapy, eccentric exercise therapy, extracorporeal shock wave therapy, iontophoresis, dermoelectroporation, low-level laser therapy, manipulation, orthoses (bracing), platelet-rich plasma injections, pulsed electromagnetic field treatment, surgery, ultrasound, cryotherapy, heat treatment, sclerosant injection, acupuncture.

Key words: tendinopathy, inflammation, degeneration, treatment.

КОЖНА ПРОПУСКЛИВОСТ И ТРАНСДЕРМАЛНО ВЪВЕЖДАНЕ НА ЛЕКАРСТВА

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SKIN PERMEABILIZATION FOR TRANSDERMAL DRUG DELIVERY

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ABSTRACT. The skin is an attractive area for drug delivery due to its prevalence and easy of access. The efficient delivery of drugs into and across the skin has been a goal of researchers for decades. Transdermal drug delivery offers several advantages, including absence of gastric irritation, painlessness, noninvasiveness, better patient compliance and avoidance of the first –pass metabolism. However, outermost layer of the skin, the stratum corneum limits passive diffusion to drugs molecules. Several techniques have been developed and used for transdermal drug delivery enhancement. These include chemical/lipid penetration enhancers, sonophoresis, iontophoresis, microneedles, electroporation, microdermabrasion, dermoelectroporation (pulse current iontophoresis). Although the principles and mechanisms of these approaches are different, these methods share the same aim of enhancing the movement of the drug through the stratum corneum, either through pore formation or improved diffusive interaction. In this rewiev, microdermabrasion and dermoelectroporation wich refers to the temporary skin perturbation is discussed and the use these techniques for percutaneous transport of some anti-inflammatory drugs.

KEY WORDS: dermoelectroporatio, pulse current iontophoresis, microdermabrasion

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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

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Endocrine cells in pig's gallbladder, ductus cysticus and ductus choledochus with special reference to ghrelin

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In human biliary pathways and gallbladder there have been several reports describing endocrine cells (ECs) mainly in chronic inflammation. In pigs' biliary structures we couldn't find data about ECs. Ghrelin is peptide hormone participating in the growth-hormone-release and in modulation of food intake. It has also pro-inflammatory functions. Ghrelin-positive ECs are the main source of Ghrelin. The present study reveals the presence of ghrelin+ ECs in pigs' gallbladder cystic and choledochal duct – by immunohistochemistry. In pigs gallbladder ECs are very rare. Single Chromogranin A^+, Somatostatin$^+$ and Serotinin$^+$ ECs were observed. In choledochal duct there are Chromogranin A^+, Somatostatin$^+$, Gastrin$^+$ and Ghrelin+ECs more in number as compared to gallbladder. Most ECs were located in d.cysticus. They were also Chromogranin A^+, Somatostatin$^+$, Gastrin$^+$ and Ghrelin$^+$ ECs. In conclusion we support that various ECs including Ghrelin exert action on physiology and pathology conditions in biliary tree in pigs.

Key words: endocrine cells, ghrelin, pigs' biliary system

N 94

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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

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

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

Abstract:	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.

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SKIN PERMEABILITY COEFFICIENT CALCULATION IN THE CASE OF SODIUM DICLOFENAC ADMINISTRATION BY PULSED CURRENT IONTOPHPRESIS

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ABSTRACT. The *in vitro* permeability of diclofenac sodium with donor concentration of 1.25mg/ml -25mg/ml through human skin was evaluated using Franz diffusion cell and pulsed current iontophoresis technics with donor volume 1-3 ml. The skin permeability coefficient was calculated to be in diapason of 1.0×10^{-6} – 4.0×10^{-6} cm/s for the diffusion cell, and in diapason of 5.0×10^{-6} –14×10^{-6} cm/s for pulsed current iontophoresis. The mean values of the Enhanced ratio varied between 2 and 4 folds for optimal donor concentrations of 1.5-25 mg/ml and 3 ml donor drug solution. Therefore, the transdermal injection of diclofenac by pulsed current iontophoresis increases at least skin permeability coefficient 2-4 folds in comparison to passive diffuse of diclofenac trough skin. The result suggests that the water-soluble drugs like diclofenac might be good candidates for transdermal delivery by pulsed current iontophoresis.

Key words: human skin, permeability coefficient, diclofenac sodium, pulsed current iontophoresis.