

R E V I E W

of the materials submitted for participation in the competition for holding the academic position "**Associate Professor in Microbiology**", announced in the Government newspaper no. 13/15.02.2022 for the needs of the **Medical College, Thracian University, Stara Zagora** a field of higher education 4. Natural sciences, mathematics and computer science; professional field 4.3. Biological sciences

Candidate: Chief Assist. Dr. Nedelina Stoyanova Kostadinova

The review is prepared by Prof. **Margarita Kambourova**, DSc, Stephan Angeloff Institute of Microbiology, BAS

According to an order № 1031 / 12.04.2022 of the Rector of the Thracian University, Stara Zagora, I am included in the Scientific Jury for the selection of the academic position "Associate Professor" for the needs of the Medical College of the Thracian University. In the announced competition (Government newspaper No. 13 / 15.02.2022) the only candidate is Dr. Nedelina Stoyanova Kostadinova, Chief Assistant at the Institute of Microbiology (IMicB), BAS. As a member of the Scientific Jury, I declare that we have no common papers with the candidate.

1. Brief information about the candidate's career development

Dr. Kostadinova graduated in 2004 as a Bachelor of Biology at Plovdiv University "Paisii Hilendarski", and in 2006 as a Master in Microbial and Plant Biotechnology at the same university with excellent marks. In the period 2008-2012 she was a full-time doctoral student in the Laboratory of Mycology, IMicB, BAS. In 2013 she successfully defended her dissertation "Cellular response to low-temperature stress in Antarctic fungi" and received the scientific and educational degree "Doctor"; up to now her scientific career passes in IMicB as a Specialist, Assistant and Ch. Assist. Her interest in a scientific career is evidenced by the two three-month specializations in France (2010) and Spain (2015), her participation in training courses organized by Zeiss and Thomson-Reuters in Sofia, a German language course and its early admission (2009) to the Union of Scientists in Bulgaria, Microbiology Section. During her employment in the Institute she readily joined the administrative and organizational activities such as organizing Balkan Congresses in Microbiology, jubilee celebrations of IMicB, seminars, editing

proceedings from scientific forums, Secretary of the Scientific Council of IMicB, BAS. Her pursuit in a scientific development and her good communication skills are the basis for many productive collaborations with colleagues from IMicB and other institutes of BAS (IOCCP, IEMPAM, INB, IBIR), Medical Faculty, Sofia University, Medical University, Rose Institute and essential oils in Kazanlak, UCTM, Department of Plant Physiology and Soil Biology in Krivoy Rog, Ukraine, Faculty of Natural Sciences at the University of Zagazig, Egypt, University of Pavia, Italy, University of Liege, Belgium, Max Planck Institute, Germany. As can be seen from the submitted information (Doc 9), the number of habilitated co-authors alone is 30.

2. Description of the presented scientific papers and scientometric indicators

2.1. Requirements of the Law for the Development of the Academic Staff of the Republic of Bulgaria (RASRB)

The materials provided in the competition include all documents according to the Regulations of the Thrakia University for admission to the competition (Doc.1-17). The candidate participates in the competition for "Associate Professor" with 28 papers, different from those for a "Doctor" degree. The monograph is not a subject to this review, as it matches the dissertation book. It is worth to note that 2/3 of papers (18) are in journals with SJR / JCR, two are in journals without IF but referenced in WoS / Scopus, three are in other journals, four book chapters and one in a Proceedings from a national conference. Her works have found a place in a number of prestigious international journals such as Fungal Biology, Amino Acids, Polar Biology, Journal of Basic Microbiology, Geomicrobiology Journal, Metabolic Brain Disease, Engineering in Life Sciences and others. The IF of the publications included in the competition for Assoc. Prof. is 29,114 (The total IF of all publications is 31,61), and the h-index is 7. An evaluation of the quality of her publications is the Diplom "Best microbiologist" awarded by the Foundation "Acad. Prof. Dr. Stephan Angeloff" in 2013.

As can be seen from the results reflected in Table 1, the indexes of the candidate in all criteria exceed those required by RASRB. The list of the index "B" includes six publications, one of which with Q1, three with Q2 and two with Q3. Among the 12 papers with Impact Factor / SJR included in List D, three are in journals with Q1, seven with Q2, one with Q3 and one with Q4. She is a co-author of four chapters in collective monographs. The reference prepared by the TrU Library contains 113 citations (without auto-citations) in SCOPUS and Web of Sciences of

Dr. Kostadinova's scientific publications. Although according to RASRB there are no requirements for "Associate Professor" on indicator E, the number of points collected by Dr. Kostadinova is impressive and comes from a participation in 5 international and 14 national research projects, in one of which she is a leader with attracted funding of BGN 8,000. Additionally, she is a member of teams, implemented four projects with private companies and one with the Ministry of Culture. Her wide scientific interest is demonstrated by her participation in 80 conferences (Application 2), 27 of which are international.

Table 1. Minimum national criteria for the scientific degree "Associate Professor"

Group of criteria	Content	Required points for Assoc. Prof.	Ch. Assistant Nedelina Kostadinova (points)
A	Index 1	50	50
Б	Index 2	-	
B	Indexes 3 or 4	100	115
Г	Sum of the indexes from 5 to 10	200	302
Д	Index 11	50	226
E	Sum of the indexes from 12 to 18	-	251.6
Total sum		-	944.6

2.2. Additional requirements for "Associate professor" of TrU

The candidate also meets the specific requirements reflected in the Rules of Procedure of TrU (Table 2). She has an educational and scientific degree "Doctor", she held the position of "Ch. Assist." for 9 years. The official note presented by Sofia University on the educational activity of Dr. Kostadinova reflects her annual classroom exercises in the BF of Sofia University "Kliment Ohridski" in the disciplines of Cytology and Cellular Biology for the last six years. An expression of her interest in teaching is the supervising of MS student in 2017.

Table 2. Additional criteria of TrU for the position “Assoc. Prof.”

Academic degree	<i>Associate Professor</i>	<i>Chief Assist. Nedelina Kostadinova</i>
Educational and scientific degree "Doctor"	yes	yes
Duration of the occupied position "Ch. Assist. ”	2	9
Teaching activities, including part-time (years)	2	6

3. Main directions in the research work and the most important contributions

The main object of research in the scientific activity of Ch. Assist. Kostadinova is the metabolic response of filamentous fungi at the conditions of the cellular stress such as antioxidant protection and the synthesis of specific enzymes, some of them of biotechnological importance. In her scientific work there are three main directions, in which she formulates a number of important scientific and scientific-applied contributions, some of which are original and others - confirmatory. In my opinion, the most significant among them are the following:

Thematic area I: Adaptation of fungi to low temperatures. Oxidative stress and antioxidant protection of cells due to low temperature and other types of stress. A total of 140 strains are isolated and identified from soil samples from Livingston Island, Antarctica. The effect of low temperature stress on a number of physiological parameters such as growth, glucose consumption, accumulation of reserve carbohydrates, activity of main antioxidant enzymes superoxide dismutase (SOD) and catalase (KAT) is studied. The mechanism of elimination of the toxic superoxide radicals by purified enzyme SOD is established. The received results are reflected in scientific publications №№ 1, 2, 3, 4, 6, 7, 8, 9, 12, 13, 20, 21, 24, 25, 26, 32, 33.

Scientific contributions:

1. Oxidative stress in Antarctic fungi at low temperatures depends in the species affiliation.
2. Examination of the effect of short-term stress of 4 and 10 ° C on Antarctic fungi reveals accumulation of SOR (superoxide radicals) in model strains, followed by a change in the activity of enzymes from the Tricarboxylic Acid Cycle, an increase in the amount of damaged proteins, accumulation of reserve carbohydrates and increased activity of the antioxidant protection.
3. Under an oxidative stress a mesophilic strain of *Aspergillus glaucus* 363 is isolated as a good producer of SOD active at low-temperature. The increased SOD activity is maintained after returning to optimal temperature conditions.

4. For the first time, a gene coding low-temperature active Cu / Zn-SOD in fungi is sequenced.
5. After purification of *Aspergillus glaucus* 363 culture liquid, two isoenzymes Cu / Zn-SOD I and Cu / Zn-SOD II are identified.

Scientific-applied contributions:

1. Laboratory technology for efficient synthesis of low-temperature active SOD from *A. glaucus* 363 is developed.
2. An effective purification scheme is established by which the specific activity of Cu / Zn-CODII was higher than that of the commercially available mesophilic enzyme.

Thematic area II: Tolerance to heavy metals and its relationship with antioxidant enzyme protection in fungi. The relationship between tolerance to extremely high concentrations of Cu- and Zn-ions and the different cellular response in fungi isolated from metal-contaminated soils from the mine tailing ponds in Vlaykov Vrah, Bulgaria has been studied. Representatives of the phyla Ascomycota, Basidiomycota and Zycomycota have been isolated. The fungal response to the combined toxicity of heavy metal mixtures (Cu, Cd, Ni and Zn) and the oxidative stress occurred in two model strains, *A. fumigatus* 3-2, isolated from the tailings pond near Vlaykov Vrah mine, Bulgaria and *A. fumigatus* G, isolated from the industrial zone of Krivoy Rog, Ukraine was investigated. The results of the research are reflected in scientific publications №№ 11, 14, 28, 31.

Scientific contributions:

1. Strain *A. fumigatus* 3-2, shows remarkably high tolerance to Cu and Zn.
2. The heavy metal toxicity was found to induce an oxidative stress and changes in the activity of antioxidant enzymes in the cells as well as in the amounts of the reserve carbohydrates glycogen and trehalose.
3. Different tolerances to the combined toxicity of heavy metal mixtures have been observed in model strains. Lower oxidative stress was found in *A. fumigatus* G cells.

Scientific-applied contributions:

1. The sharp increase in the activity of SOD and CAT in the presence of Cu and Zn ions in comparison to the control identifies *A. fumigatus* strain 3-2 as a promising producer for future biotechnological developments.
2. The high tolerance of the two model strains of filamentous fungi to a combination of heavy metals determines their potential in bioremediation processes.

Thematic area III: Antioxidant and antifungal activity of plant extracts and other natural products. The chemical composition of six essential oils synthesized by representatives of the genus *Rosa*, growing in Bulgaria, Moldova and China was determined, and their antioxidant and antifungal activity against *Aspergillus flavus* and *Aspergillus niger* were compared. The antimicrobial and radical-capturing activities of extracts and fractions from the above-ground and underground parts of *G. urbanum* (urban enchantress) in bacteria and yeast have been studied. The total phenolic content is determined. The results of the research are reflected in scientific publications №№ 10,15,19,22,23.

Scientific contributions:

1. The essential oil from Bulgarian *R. damascena* IX-4 demonstrates the best superoxide-capturing activity, followed by the oil of *R. rugosa* Thunb. from China.
2. The highest resistance to rose oils is shown by the model strain of *A. niger*.
3. Among the pure compounds obtained from rose oils, the antifungal activity of geraniol is the highest, followed by nerol, citronellol, methyl eugenol and eugenol.
4. For the first time, two compounds new for the genus *Geum* have been identified, as well as two new for the species *G. urbanum*.
5. The mucus and fractions of snail *C. aspersum* as a natural product have a good ability to counteract the formation of COP.

Scientific-applied contributions

1. The antibacterial effect of geranium extracts depends on the type of the extracting solvent as well as the bacterial affiliation. The ethyl acetate and butanol fractions showed the highest content of polyphenols, the strongest antibacterial potential and the most significant superoxide-capturing activity.
2. The pure seven compounds isolated from the geranium extracts have different effects on different microorganisms - catechin has bactericidal activity against *S. aureus* and *P. aeruginosa*, and tormentic acid has a bacteriostatic effect on *S. aureus* and shows antifungal activity against the yeast *C. albicans*.

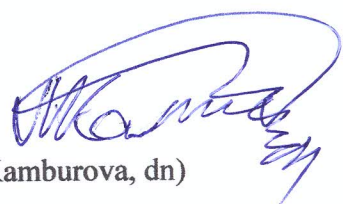
Along with these three main directions, Ch. Assist. Kostadinova works on a number of other s such as:

- Isolation of lignolytic fungi capable of degrading three types of lignocellulosic wastes (№ 17,18, 29).
- The ability of fungi to decompose organic wastes accumulated during scientific space expedition (№ 27, 30).
- Study of fungi as contaminants of various monuments (№ 16)
- Synthesis of the biotechnologically important enzyme sialidase from a non-pathogenic microbial strain *P. griseofulvum* P29 (№ 5).
- Study of the neuroprotective activity of endogenous kyotorphin on Alzheimer's disease, which showed increased motor activity, reduced anxiety, impaired spatial and working memory in rats (№ 6).
- Study of the effect of the losartan receptor antagonist on type 2 diabetes mellitus in hypertensive rats (№ 13).

CONCLUSION

Based on the materials presented in the competition and the analysis of their significance, I believe that the scientific and metric indicators of Ch. Assist. Kostadinova exceed the quantitative criteria for holding the academic position of "Associate Professor", laid down in RASRB, as well as the Additional Requirements of TrU. She is an established scientist in the field of physiological response to filamentous fungi, under normal and stressful conditions. Publishing mainly in reputable international journals is an evidence for her international recognition. She is a desirable and productive partner in Bulgarian and international teams. Her scientific activity is accompanied by active teaching. Based on the above, I confidently support her candidacy and recommend to the scientific jury to propose to the Faculty Council at the Medical College, TrU to elect Ch. Assist. Kostadinova for "Associate Professor of Microbiology" in professional field 4.3. Biological sciences.

May 16, 2022.
Sofia

Reviewer: 
(Prof. M. Kamburova, dn)