Appendix 12c

REVIEW

to occupy the academic position:

"Professor"	**X**
"Associate Professor"	
	one of the academic positions indicated shall be marked with the sign "X"

Candidates to occupy the position:

1	**Assoc.Prof.**	**Dr.**	**Petar**	**Todorov**	**Todorov**	**UCTM**
№	academic position	scientific degree	name	middle name	last name	workplace

Scientific area:

4	**Natural sciences, mathematics and informatics Chemical sciences**
code	Name

Professional area:

4.2	**Chemical sciences**
code	Name

Scientific specialty:

Organic Chemisrty

The competition has been announced:

67	**13.08.2021**	**Organic Chemisrty**	**Faculty of Chemical Technologies, UCTM**
in SG issue	Date	for the needs of the Department	Faculty

The review was written by:

Prof.	**DSc**	**Ivanka**	**Borisova**	**Stoineva**	**IOCCP-BAC**
academic position	scientific degree	name	middle name	last name	workplace

1. **Review for the candidate:**

1	**Assoc.Prof.**	**Dr.**	**Petar**	**Todorov**	**Todorov**	**UCTM**
№	academic position	scientific degree	name	middle name	last name	workplace

1.1. Completion of the provided documents:

A) The competition documents are in full compliance with the Regulations	3 points	**X**
B) The documents are complete but do not fully comply with the requirements of the Regulations	2 points	
C) The documents are not completed in accordance with the requirements of the Regulations	0 points	
		one of the answers given is marked with the sign "X"

Missing documents and violated requirements must be described if response C is marked.
In the competition for the academic position "Professor" the only candidate associate professor Petar Todorov presented **26** publications of total **53** and h-factor **7.** The publications in peer-reviewed journals in the databases *Scopus* and *Web of Science* with impact factor are **20**, with impact rank **6**. The obtained results are presented at **41** national and international scientific forums (reports / posters). Participations in research projects for the period 2013-2021, funded by: Research Fund (NSF) **4**, NIS-UCTM **8**, others **7** are also reflected. More than **240** citations of the obtained results are indicated.

1.2. Meeting the minimum requirements under the Regulations:

A) The candidate meets the minimum requirements	20 points	**X**
B) The candidate doesn't meet the minimum requirements	0 points	
		one of the answers given is marked with the sign "X"

It must be filled in if answer B is marked. The publication activity of the candidate is analyzed. The response of the results achieved (quoted) is analyzed.
The documents for the competition for the academic position "Professor" fully comply with the Regulations for acquiring scientific degrees and holding academic positions at UCTM, as well as ZRASRB and PPZRASRB. • Indicator **A1**: Dissertation for the award of educational and scientific degree "Doctor". The candidate Assoc. Prof. Dr. Petar T. Todorov has successfully defended a dissertation on the title "Synthesis, characterization and biological activity of new derivatives of N-phosphonomethylglycine", developed in the Department of Organic Chemistry of UCTM. (**50** points). • According to indicator **B4** Habilitation work in the form of 10 publications in refereed and indexed editions, minimum requirements - **100** points, the candidate presents **193** points. • According to indicator **G5**-11 publications in refereed and indexed journals - total for the indicator - **238** items with a required minimum of **200** items. • According to indicator **D12**-15 citations or reviews in scientific journals at a minimum of **100** points, Assoc. Prof. Todorov presented data for **496** points. • According to indicator **E16-28** management of successfully defended doctoral students - 1 and participation in projects, textbooks and teaching aids, with a minimum required of **150** points, Assoc. Prof. Todorov presents **180. 66** points.

According to all necessary indicators, Assoc. Prof. Dr. Eng. P. Todorov exceeds the minimum requirements for holding the position of "Professor".

1.3. Relevance of scientific and / or applied research:

A) The research is relevant. Part of the research is pioneering (no results are known on the topic by other authors)	7 points	
B) Research is relevant. Results from other authors are known for each of the topics and / or applications studied.	5 points	**X**
C) Most of the research is relevant, but also some results are presented that have no scientific and / or applied value	3 points	
D) The smaller part of the research is relevant	2 points	
E) Research is not relevant	0 points	
		one of the answers given is marked with the sign "X"

The evaluation of the relevance of the research must be substantiated.
The research interests of Associate Professor Petar Todorov are in the field of organic and bioorganic chemistry and are focused on the design, synthesis and characterization of biologically active peptides as potential candidates in creating new drugs for socially significant diseases. The research is especially relevant and promising as the protection of the health of the population is a priority of every country.

1.4. Knowledge of the problems subject of research:

A) The candidate knows in detail the achievements of other authors on the researched topics and/or applications	6 points	**X**
B) The candidate is partially familiar with the achieved results on the researched topics and / or applications	4 points	
C) The candidate has no prior knowledge of the status of the researched problems	0 points	
		one of the answers given is marked with the sign "X"

The evaluation must be substantiated if answer C is marked.
Associate Professor P. Todorov knows in detail the research of other authors on the target problems. This is very clearly reflected in his scientific publications, which cite and analyze the results published in recent years.

1.5. Type of research:

A) Theoretical	4 points	

B) Applied	4 points	
C) Theoretical with application elements	4 points	**X**
D) It does not correspond to the level specified in the Act for the Development of the Academic Staff in the Republic of Bulgaria and the Regulations	0 points	
		one of the answers given is marked with the sign "X"

The level of research must be substantiated if answer D is marked.
The presented results of the candidate's research are of fundamental and applied orientation. Biologically active peptides and their synthetic analogues are used in medical practice and diagnosis.

1.6. Objectives of the research:

A) Realistic and of scientific and / or applied interest	8 points	
B) Realistic, but not of scientific and / or applied interest	4 points	
C) Unattainable (unrealistic)	0 points	
		one of the answers given is marked with the sign "X"

Objectives must be specified. The type of the set objectives must be justified.
The main goal is focused on obtaining new peptide structures with opioid and analgesic action. The research of associate professor Petar Todorov is focused on the design, synthesis and characterization of biologically active substances that participate in the control of various physiological processes. They are expected to have low toxicity, no side effects and potential application in biomedicine. Research focuses on endogenous opioid peptides and hydantoin derivatives

1.7. Methods of research:

A) Adequate to research and set scientific objectives and /or applications	8 points	**X**
B) Partially appropriate, enabling part of the scientific objectives and / or applications to be achieved	4 points	
C) Inappropriate methods	0 points	
		one of the answers given is marked with the sign "X"

Methods must be specified. The type of methods used is justified.

Various modern methods have been used for synthesis and analysis of the obtained products, which shows that the candidate is an established researcher in the field of organic and peptide chemistry. Diffrent chromatographic, spectral (UV, FT-IR), and electrochemical methods have been successfully applied, as well as mass spectral and X-ray diffraction analysis for some of the newly synthesized compounds. Pharmacological studies of the most promising representatives of each series of synthesized compounds were also performed to establish their biological activity and to derive a dependence on the structure / activity of the synthesized peptide mimetics.

1.8. Candidate research contributions:

A) With lasting scientific and / or applied response, they form the basis for new research and applications	20 points	
B) They are of significant scientific and / or applied interest, complete and / or summarize previous research	16 points	**X**
C) They are of scientific and / or applied interest	12 points	
D) Lack of significant contributions	8 points	
E) Lack of contributions	0 points	
		one of the answers given is marked with the sign "X"

Contributions must be specified. The type of results achieved must be justified.

The presented results of the research contain original scientific contributions, which can be characterized as an extension of existing knowledge. All of them are related to the design, synthesis and biological research of new bioactive structures and in particular of endogenous peptides and hydantoin derivatives.

With the approaches of solid-phase peptide synthesis (Fmoc-strategy) new N- and C-modified analogues of peptides from the group of hemoglobin-active peptides were synthesized - hemorphins with affinity for opioid receptors (μ-, δ- and k-) and morphinomimetic properties.

- 5 new analogs of hemorphin-4 (H-Tyr$_1$-Pro$_2$-Trp$_3$-Thr$_4$-NH$_2$) were synthesized and studied. Biological studies indicate that: the most active peptide analogue P4 5 contains an adamantane residue at the N end and a cyclohexane ring at position 2. It suggests that a probable cause of these properties is appropriate conformational binding of the peptide to the IRAP receptor, as well as high lipophilicity and hydrophobicity . Compounds from this group did not show neurotoxicity in the rotarorotarod test to assess minimal motor impairment.
- The study of the structure-biological activity (SAR) relationship leads to the conclusion that the replacement of Pro at position 2 with conformational inhibited amino acids, as well as the introduction of the adamantane residue at the end into the hemorphin 4 molecule may provoke an anticonvulsant effect.
- Synthesis of 5 new N-modified analogs of VV-hemorphin-5 containing aminophosphonic residue was performed, and for the first time α-aminophosphonic acids were introduced into peptides of this type. The resulting peptide mimetics were tested for anticonvulsant activity. From the docking *in silico* study, it can be assumed that binding to the kappa-opioid receptor is the most likely mechanism of action. Modification of the two N-terminal Vals with an aminophosphonate residue was found to result in significant changes in peptide activity and affinity.

- The newly synthesized compounds were also evaluated in vivo for potential antinociceptive activity in acute and inflammatory pain response using a formalin test.
- Contribution is the developed a simple and fast electrochemical method for selective determination of copper in aqueous samples using non-toxic and easily degradable peptide molecules, such as the analogs of VV-hemorphin-5.
- 8 new analogs of VV-hemorphin-7, (H-Val_1-Val_2-Tyr_3-Pro_4-Trp5-Thr_6-Gln_7-Arg_8-Phe_9-NH_2) modified in position 4 and 7 with unnatural amino acids - Ac5c (1-aminocyclopentanecarboxylic acid) or Ac6c (1-aminocyclohexanecarboxylic acid), Dap (diaminopropanoic acid) or Dab (diaminobutanoic acid). In vivo anticonvulsant activity studies showed that a peptide analog in which the Gln molecule at position 7 was replaced by the aliphatic diamino acid Dab showed the most pronounced activity in the 6-Hz test and none of the test compounds showed neurotoxicity in the rotarod test.
- Contribution is the synthesis of new nociceptin analogues in order to study the sympathetic-vagal balance related to blood pressure. Two new N / OFQ (1-13) NH_2 analogs were synthesized, purified, and characterized in which the N-terminal amino acid (phenylalanine) was replaced with 1 - [(methoxyphosphono) methylamino] cycloalkanecarboxylic acid containing seven AFC7-N / OF 1-13) NH_2, (NC7) or an eight membered cycloalkane ring AFC8-N / OFQ (1-13) NH2 (NC8). The results show that NC7 causes a shift in sympathetic-vagal balance as a result of the decrease in the power of sympathetically mediated oscillations, while NC8 involves mechanisms responsible for long-term regulation of heart rate.
- **A series of Schiff bases containing a hydantoin ring was obtained by a condensation reaction between 3-amino-5,5'-dimethylhydantoin / -diphenylhydantoin and various aromatic aldehydes.** All compounds were characterized by various spectral and electrochemical methods, as well as by X-ray diffraction analysis. It has been shown that compounds containing the azomethine -CH = N- groups in Schiff bases can be used as photochromic switches. By varying the polarity of the solvent, direct control of the bidirectional switching behavior from one type to another, i.e. in both trans- / cis-states, can be achieved.

1.9. Participation of the candidate in the achievement of the presented results:

A) The candidate has at least an equal participation in the submitted papers	8 points	**X**
B) The candidate has at least an equal participation in most of the submitted papers	7 points	
C) The candidate has a secondary participation in most of the submitted papers	4 points	
D) The candidate participation is unnoticeable	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the items C or D is marked.
Precise analysis of the submitted materials for participation in the competition unequivocally proves the active and contribution of the candidate associate professor P. Todorov. The scientific publications published in the last 3 years represent 70% of the ones submitted for participation in the competition and in 9 of them he is either the first author and / or the author for correspondence.

1.10. Pedagogical activity:

A) The candidate has effective and sufficient pedagogical activity at the university. The textbooks issued are modern and useful (they	8 points	**X**

meet the requirements of the Regulations). The work with undergraduate and doctoral students is at a high professional level.		
B) The candidate has sufficient pedagogical activity at the university. The textbooks issued satisfy the requirements of the Regulations.	6 points	
C) The pedagogical activity and / or textbooks issued are insufficient (do not meet the requirements of the Regulations)	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the items B or C is marked.

1.11. Critical notes:

A) Lack of critical notes	8 points	
B) Critical notes of a technical nature	7 points	**X**
C) Critical notes that would partially improve the results achieved in a small part of the research	5 points	
D) Critical notes that would partially improve the results achieved in most of the research	3 points	
E) Significant critical notes	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the answers C, D or E is marked.
The candidate did not correctly present the number of points for some scientific publications. For publication in journals with SJR without IF, the points are 6 points, not 15 points as reflected in the various applications. This does not reduce from the overall good impression of the candidate's performance.There are no prospects for future work.

1.12. Conclusion

A) The evaluation of the candidate's activity is **POSITIVE**	This evaluation is assigned to a total number of at least 65 points	**X** **(93)**
B) The evaluation of the candidate's activity is **NEGATIVE**	This evaluation is assigned to a total number below 65 points	
		one of the answers given is marked with the sign "X"

To be filled in if requested by the reviewer
The candidate in the competition, Associate Professor Dr. Eng. P. Todorov is an established scientist and has presented many quality scientific publications with high impact factor, which have not been used in previous procedures. The main contributions have an original scientific and applied nature. The candidate's research and teaching qualifications leave no doubt. The research metric indicators of Associate Professor Dr. Eng. P. Todorov cover and exceed the requirements for holding the position "Professor". The facts listed above are the basis for my positive assessment. I recommend to the esteemed members of the scientific jury to support the proposal for election of Assoc. Prof. Dr. Eng. Petar Todorov for the academic position "Professor" in the professional field 4.2. Chemical sciences, scientific specialty "Organic chemistry".

24.11.2021	The review was written by:	
date	**Prof, DSc Ivanka Stoineva**	Signature