

TO THE MEMBERS OF THE SCIENTIFIC JURY OF
Faculty of Chemistry and Pharmacy, Sofia University appointed
by order № RD 38-615 / 22.12.2020 for defense of Doctoral
Thesis of ZAHARI PENKOV VINAROV - PhD student of
independent training at the Department of Pharmaceutical and
Applied Organic Chemistry

OPINION

by Prof. Dr. Ognyan I. Petrov

Sofia University "St. Kl. Ohridski",
Faculty of Chemistry and Pharmacy

Regarding the dissertation for awarding the educational and scientific degree "Doctor", professional field 7.3 Pharmacy, specialty "Technology of dosage forms and biopharmacy", on "Improving the solubility of hydrophobic drugs by solubilization in surfactant micelles"

I. General presentation of the procedure and the doctoral student

The presented set of materials on electronic media are in accordance with the requirements of the Law and all regulations attached to it, related to the procedure for awarding the educational and scientific degree "Doctor".

The doctoral student has attached a certificate of compliance with the national minimum requirements for the degree "Doctor" and a declaration of originality and authenticity under Art. 27, para 2 of the Law.

Zahari Vinarov presents a list of a total of 18 publications, of which 16 are in specialized scientific journals with impact factor and 2 are in popular science journals. The doctoral student is a participant in 7 research projects funded by public organizations and 3 projects funded by industry. Vinarov is the manager of two of the projects.

Brief biographical data: In 2009 Zahari Vinarov graduated from the Faculty of Pharmacy of the Medical University - Sofia, obtaining the qualification "Master of Pharmacy". During the period 2008 until now the candidate has worked in the Department of Chemical Engineering and Pharmaceutical Engineering, Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski", successively holding the positions of researcher, assistant and chief assistant. In 2014 he obtained a doctorate in chemistry at Sofia University "St. Kliment Ohridski" with a scientific dissertation on the topic of "In vitro studies of triglyceride lipolysis in the gastrointestinal tract".

Zahari Vinarov is a member of several international scientific organizations (AAPS, EUFEPS) and editorial boards (MDPI, Wiley).

II. Appropriateness of the topic, familiarity with the scientific problem and expediency of the set goals and tasks

The dissertation presented for doctoral defense is dedicated to current scientific and practical issues dealing with oral delivery of drugs with low solubility. The main emphasis is on the technology of dosage forms of substances with low solubility and high membrane permeability. Through the development of technologies and approaches, possible solutions for increasing the solubility of such drugs are proposed.

The aim of the presented dissertation is to clarify how the molecular structure of surfactants and drugs determine the solubilization capacity of micelles and to give a physicochemical interpretation of the observed effects. The dissertation includes 4 chapters: introduction, materials and methods, solubilization of progesterone and solubilization of fenofibrate and danazol. It is written on 77 pages and contains 33 figures and illustrations and 4 tables. The cited literature includes 110 sources.

In Chapter 1 "Introduction" an attempt is made to give an idea of the state of the art of the studied problem in the literature. However, the lack of a separate chapter, such as Review of the Literature, is detrimental to the reader and does not provide a full opportunity for a comparative analysis of the state of the art achievements in this field with the undisputed achievements of the doctoral student.

The chapter "Materials and methods", presented on 11 pages, describes the studied surfactants and drugs with their chemical structure, water solubility and purity. Experimental methods for determining drug solubilization, micelle size, and critical micelle formation concentration are accurately and clearly described. The applied instrumental methods (HPLC, GC, UV spectroscopy and light scattering) in the research are of great importance for the results obtained by the doctoral student.

III. Characteristics and evaluation of the dissertation

I highly appreciate the results achieved by Zahari Vinarov, described in the dissertation. It was found that the solubilization of hydrophobic drugs increases with increasing length of the hydrophobic tail of the surfactant, regardless of the charge and the type of hydrophilic head. The role of ion-dipole interactions in the solubilization of steroidal drugs in micelles of ionic surfactants has been proven. Ethoxylation of sodium dodecyl sulfate has been shown to reduce solubilization of drugs due to the difficult arrangement of molecules in micelles. Using UV spectroscopy, it has been shown that solubilized fenofibrate is localized in the hydrophobic nucleus of nonionic micelles and in the palisade layer of ionic micelles.

Some of the results of the PhD thesis are published in 2 publications with impact factor and are presented at 9 scientific forums. The total number of points according to the Minimum National Requirements for indicator group D is 32 points with a required 30 points. The SCOPUS citations (excluding self-citations) on these two publications are 39.

IV. Conclusion

The presented by Chief Assistant Zahari Vinarov dissertation and related publications fully meet the requirements of the Law and "The Rules for the development of the academic staff of Sofia University "St. Kl. Ohridski", in terms of volume, quality and original scientific contributions (both fundamental and applied) in the field of dosage form technology.

This gives me reason to convincingly give my positive assessment and to recommend to the respected members of the Scientific Jury to vote for the award of the educational and scientific degree "Doctor" to Chief Assistant. Zahari Penkov Vinarov in the scientific specialty "Technology of Dosage Forms and Biopharmacy".

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Prof. Ognyan Petrov, Ph.D