

## **BRIEF REVIEW**

**by Assoc. Prof. Dr. Emiliya Demireva Cherneva-Ivanova,  
Faculty of Pharmacy, Medical University of Sofia**

With respect to the Doctoral Thesis presented for awarding the degree  
“**Doctor of sciences**” in the Professional Field 4.2. “Chemical sciences “  
Scientific specialty “Bioorganic Chemistry, Chemistry of nature and physiologically active  
compounds “

**Author:** *Assoc. Prof. Dr. Vania Nikolova Mantareva, Institute of Organic Chemistry with Centre  
for Photochemistry, BAS*

**Topic:** Phthalocyanine photosensitizers for photodynamic method towards drug resistance

### **1. General description of the presented materials**

The presented to me set of documents and materials by Assoc. Prof. Dr. Vania Mantareva with respect to defense of Doctoral Thesis meets all the requirements of The Law of the Development of Academic Staff in the Republic of Bulgaria and The Regulations on the terms and conditions for awarding scientific and academic degrees in IOCCP-BAS.

### **2. Relevance of the topic**

The topic of the PhD thesis is of great importance and it is regarding to one of the major priorities of public health worldwide, particular dealing with drug resistance exhibited by pathogenic microorganisms and tumors. That is why it is important to search for new, more effective ways and therapeutic methods to deal with infections caused by multidrug resistance.

### **3. Knowledge of the problem**

In the PhD thesis, a broad number of literature references (372), published in quality journals, are presented and analyzed. The literature review is very well structured, detailed and includes historical data for phtalocyanines and application of the phototherapy through the years. Attention is paid to the requirements for the photosensitizers, mechanism of photodynamic action, as well as the role of action of different oxygen forms. Part of the references from the literature review is dedicated to the resistance of pathogenic microorganisms and some pathways to deal with it. General methods for synthesis of phtalocyanines are also presented. All of the above reveal the importance of this problem and excellent knowledge about it of Assoc. Prof. Dr. Mantareva.

#### **4. Research methodology**

The research methodology includes the conduction of a considerable number of reactions in inert environment, as well as isolation of the synthesized compounds in pure form with column chromatography, which is of importance for their subsequent investigations as photosensitizers.

To prove the structure of the synthesized phthalocyanine complexes and derivatives, various analytical methods such as elemental analyses, IR-, NMR- and Mass (MALDI-TOF) spectroscopies were used. The crystal structure of two Si(IV) complexes was determined.

The photochemical properties related to singlet oxygen generation, the photophysical properties and the photostability of the synthesized compounds were studied by spectrophotometry.

The photobiological studies on accumulation and cellular localization of the new phthalocyanine complexes are conducted according to the methodology, which includes chemical extraction and quantity determination of bonded molecules in pathogenic cells by analysis of the fluorescence spectrum. The photodynamic activity of the compounds was studied *in vitro* and additional light irradiation step was included in the work protocol.

#### **5. Characteristic and evaluation of dissertation thesis and contributions**

The topic of the dissertation corresponds to the scientific specialty. The dissertation thesis is related to the synthesis of new complexes with phthalocyanine fragment using metallic diamagnetic and non-metallic ions by modified or new synthetic procedures.

An important part of the dissertation is the study of the photochemical properties of the complexes by determining the lifetime, the quantum yield of the singlet oxygen and photostability. *In vitro* photocytotoxicity studies show high levels of cell accumulation in *Candida Albicans*, Gram(+) and Gram(-) bacterial pathogens and high selectivity of the photocytotoxicity.

The contributions of the dissertation are precisely defined and substantiated. Of particular interest are the methodological contributions, namely the development of a method for pharmacokinetic studies based on chemical extraction, and the development of protocols for photobiological studies with light irradiation.

#### **6. Assessment of the dissertation's publications and personal contribution**

The scientific results in the thesis of Assoc. Prof. Dr. Mantareva are presented in 21 scientific reports. The articles are of high quality and have found a good reflection in the

international scientific literature, which is evident from the number of the journals with quartiles in the relevant scientific field (Q1)-7, (Q2)-4, (Q3)-5, as well as the number of the noticed citations: 128. The results were reported in 12 scientific events and were funded by 5 projects.

### **7. Abstract**

The Abstract adequately reveals the main results and contributions of the dissertation thesis.

### **8. Critical remarks and recommendations**

After critical reading of the thesis, I do not have any significant remarks or recommendations. My only comment is that English text appears in some tables and figures.

## **CONCLUSION**

The dissertation thesis of Assoc. Prof. Dr. Mantareva consists of significant scientific results bringing significant contribution in the field of “Bioorganic Chemistry, Chemistry of nature and physiologically active compounds”, and it has found a good reflection in the international scientific literature. The volume and quality of the research correspond to all of the requirements of The Law of the Academic Staff Development in the Republic of Bulgaria and the Regulations on the terms and conditions for awarding scientific and academic degrees in IOCCP-BAS.

The submitted dissertation thesis describes Dr. Mantareva as an excellently prepared, highly qualified and erudite researcher.

Based on the above, I give my **positive assessment** of the conducted research, achieved results and scientific contributions and suggest the esteemed academic board to award the degree “Doctor of Sciences” to Assoc. Prof. Dr. Vania Mantareva in the Professional Field 4.2. “Chemical Sciences “, scientific specialty “Bioorganic Chemistry, Chemistry of nature and physiologically active compounds “

21.07 2021 г.

**Reviewer:**

(Assoc. Prof. Dr. Emiliya Cherneva)