O P I N I O N

submitted by Prof. Silviya Zhivova Todorova, PhD

Institute of Catalysis - Bulgarian Academy of Sciences

(member of the scientific jury)

on the dissertation of Prof. Dr. Margarita Dimitrova Popova

Full Professor at the Institute of Organic Chemistry with Centre of Phytochemistryof the Bulgarian Academy of Sciences,

Entitled "NOVEL APPROACHES IN THE PREPARATION OF NANOPOROUS MATERIALS WITH APPLICATION AS CATALYSTS OR DRUG CARRIERS"

1. General overview of the procedure and candidate

The documents presented by Prof. Dr. Margarita Dimitrova Popova is in accordance with the Regulations for the development of the academic staff of IOCCP-BAS and meets the criteria of IOCCP-BAS for obtaining the scientific degree "Doctor of Science".

The dissertation is written on 215 pages and contains 173 figures, 53 tables and 18 diagrams. I find it especially positive that the dissertation is written in English. In this way, the results presented in the dissertation could be used by a significantly wider audience.

The scientific career of Prof. Popova is relates to IOCCP-BAS. In the period 1991-1998 she was a PhD student, after that she obtain the academic positions of assistant, assistant professor, associate professor and professor. She successfully combines scientific and administrative work. She has been the Scientific Secretary of the IOCCP-BAS for two consecutive terms, and at the moment She is the Scientific Secretary of the Nanosciences, New Materials and Technologies Division of the Bulgarian Academy of Sciences. The publishing activity of Prof. Popova - 110 for the whole period of scientific activity is impressive, as the main part are in international journals with high impact factor. Prof. Popova publishes an average of 4 articles per year, which is an indicator of her extremely high scientific activity and efficiency.

2. Relevance of the topic

Prof. Popova's research interests are focused on one of the fastest growing and modern scientific fields, namely the application of new nanomaterials as catalysts and development of new drug delivery systems.

Control of air pollution is one of the main problems of the European Union's (EC) environmental policy (http://ec.europa.eu/environment/index_en.htm). In 2013, the EU proposed the Clean Air Policy Package, which sets out measures to reduce harmful emissions by 2030. In December 2019, the European Commission presented the so-called Green Deal, also known as the Green Pact, which is a set of policies aimed at making Europe climate neutral by 2050.

One of the most efficient and cost-effective technologies for VOC elimination is complete catalytic oxidation. Most of the industrial catalysts for the combustion of VOCs are based on precious metals. Their high cost, limited availability and deactivation both at high temperatures and in the presence of catalytic poisons is a motive for looking for new catalysts. Metal oxides of transition elements are an alternative to precious metals. One of the main scientific fields in which Prof. Popova works is catalysts based on transition metals. Mesoporous carriers with different structure were used for their development. Another part of the dissertation is in the field of nanomedicine and focuses on one of the most current, serious, and rapidly developing topics of modern times, namely the design of new drug delivery systems, allowing to solve problems related to the short half-life of drugs, their unwanted side effects and low solubility.

2. Understanding the problem

The introduction gives a brief but important picture of the problems related to the different applications of nanomaterials, their preparation and functionalization. The relevance of the conducted research is shown, and the directions of the research are clearly verified. Since the discovery of ordered mesoporous silica materials in the 1990s, synthesis and applications of mesoporous solids have been studied extensively. Mesoporous silica materials have attracted much attention because of their large surface area, uniform pore-size distribution, large pore size, and wide potential applications in the fields of separation, adsorption, and catalysis. The mesoporous support would give rise to well-dispersed and stable metal particles, supplying abundant pores and large surface area, thus possessing a great potential in further improvement of the catalytic performance. The review of the literature data provides a detailed analysis of the state of research in terms of preparation, functionalization, characterization of mesoporous silicates and their advantages as catalysts and drug delivery systems (DDS). The advantages and disadvantages of the various existing drug delivery systems are outlined.

4. Research methodology

Based on the in-depth analysis of the literature, the aim of the thesis is formulated, namely the novel approaches in the development of new nanosized materials with tailored properties benefitting their application in two main directions: as catalysts for processes related to the protection of clean air and as drug carriers ensuring the controlled delivery of drugs in oral, dermal or parenteral systems. Following this goal, catalysts based on one or more oxides supported on mesoporous silicates and zeolites have been developed. Various synthetic and post-synthetic approaches have been applied. Catalytic materials have been tested in the oxidation reactions of several contaminants, such as toluene *n*-hexane, acetone, and the method of preparation-structure-properties relationship has been outlined.

Nanoporous materials have been developed for the preparation of drug delivery systems, including modified mesoporous silicates and zeolites, hybrid mesoporous silicate-polymer carriers, nanosized magnetic composites. All materials are characterized comprehensively by modern physicochemical methods and the results obtained are interpreted correctly and professionally.

5. Characteristics and evaluation of the dissertation and contributions

The results are formed in logically connected chapters, following the tasks of the thesis. The interpretation of the experimental data has been compared with data for similar systems in the literature, and a critical evaluation has always been made. The reliability of the obtained results is also guaranteed by comparing the results of clarifying the same problem, obtained through different research methods. The dissertation has contributions of theoretical and scientific-practical nature. The dissertation is easy to read. The presented figures and tables are formed strictly and precisely and allow very fast reading of the information. The topic of the dissertation fully corresponds to the scientific specialty. The contributions of the dissertation are precisely defined and substantiated, they have a fundamental and scientifically applied character. I would mention only some of them, as they are well summarized in the attached reference:

1. The role of the modification method, the type of the carrier and the procedure of pre-treatment of monocomponent and two-component oxide catalysts supported on mesoporous silica and coal ash zeolites, on catalytic activity, selectivity, and stability in the process of complete oxidation of VOC is clarified. The optimal ratio between the oxide phases in multicomponent systems has been established.

2. A dual adsorption/catalytic system for VOC oxidation and CO_2 adsorption was developed based on cheap fly ash zeolites for maximum environmental effect.

Prof. Popova is the first in Bulgaria to start developing new drug delivery systems based on mesoporous silicates. Hers is also the first publication with a Bulgarian author on this subject. In this area, some of the main achievements are:

3. A novel route to modify the mesoporous MCM-41 and SBA-15 materials with carboxylic groups was developed, applying mild conditions combined with less toxic reagents. An advantage of the developed method is that it allows work with non-toxic chemicals, involving modification with cyanosilane.

4. For the first time, a reaction with ninhydrin has been proposed for the quantitative determination of primary amines in a heterogeneous phase, which allows to optimize the degree of modification of mesoporous silicates with amino groups.

5. For the first time, it has been shown that sulfadiazine-loaded Ag-MCM-41, Ag-SBA-15 and AgY materials can successfully replace Ag sulfadiazine and its water solubility and antimicrobial properties are significantly improved.

6. A two-component system with the anticancer drug mitoxantrone and the anti-inflammatory drug prednisolone based on spherical mesoporous magnetic iron oxide/silica nanoparticles with a core/shell structure has been developed. The particle size is about 100 nm and has a high specific surface area (> 800 m^2/g). The cytotoxicity of the loaded mitoxantrone in the developed system is preserved.

6. Evaluation of the publications and the personal contribution of the candidate

The thesis is developed based on 28 publications, all belonging to category Q1, one of which is in a journal leading the category. Prof. Popova is the author of correspondence in 18 publications, which shows her leading role in research. The points in criterion **Г** exceed 4.7 times required, and in the points in criterion **D** -6.8 times the requirements of IOCCP-BAS. All of Prof. Popova's scientific papers have been published in some of the most leading international journals in the field of catalysis and materials science: Applied Catalysis A (IF-3.82), Catalysis Communications (IF=2.80), ChemCatChem (IF =5.37), Catalysis Letters (IF=2.31), Applied Catalysis B (IF=16.68), Journal of Solid State Chemistry (IF=2.24), Microporous and Mesoporous Materials (IF=4.55), Catalysis Letters (IF=2.294), Journal of Colloid and Interface Science (4.04), European Journal of Pharmaceutical Sciences (4.60). The total number of citations is 1400 according to SCOPUS and the h-index of Prof. Popova is 22.

Professor Popova has participated in 67 prestigious international scientific conferences with poster and oral presentations. Throughout her scientific career, Margarita Popova has been a member of the research team of 20 projects funded by the Research Fund, and she is the head of 5. Prof. Popova is a representative of Bulgaria in the Management Board of 3 COST projects. Within the framework of the bilateral agreements of BAS (EBR), Prof. Popova manages 4 projects with the Research Canter for Chemistry, Hungarian Academy of Sciences, Budapest, 2 of which are on the topic of the dissertation. The leading of 9 different projects, including international ones, clearly shows the leading ability of Margarita Popova and her possibility to perform important scientific tasks.

I am impressed by the volume of research, which is an indication of diligence and dedication to scientific research. My opinion of the author's personal participation in the dissertation research is based on the content of the dissertation and my personal impressions. The introduction and the literary review of the dissertation shows that Prof. Popova is very well familiar with the available literature, which helped her to plan clearly and precisely the scientific research

and to choose methods and approaches to achieve the goals of the thesis. I am convinced of the in-depth knowledge of the developed problems.

7. Abstract

The presented abstract objectively presents the structure and content of the dissertation.

8. Recommendations for future use of dissertation contributions and results

I have no critical notes and recommendations concerning the dissertation.

CONCLUSION

The thesis contains scientific and scientific-applied results, which represent an original contribution to science and meet all the requirements of the Law for Development of the Academic Staff in the Republic of Bulgaria (LDASRB). The presented materials and dissertation results fully comply with the specific requirements of the Regulations of IOHCF-BAS for application of LDASRB.

The thesis contains scientific and applied results, which represent an original contribution to science and meet all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the application of LDASRB of the Ministry of Education and the respective Regulations of BAS, as well as the specific requirements of the IOCCP-BAS. The dissertation shows that Prof. Dr. Margarita Dimitrova Popova has in-depth theoretical knowledge and professional skills in the scientific specialty "Organic chemistry".

Due to the above, I confidently give my positive assessment of the research presented in the dissertation, the results, and contributions, and I propose to the esteemed scientific jury to award the degree of "Doctor of Science" to Prof. Dr. Margarita Popova in Scientific Field 4. "Natural Sciences, Mathematics and Informatics", professional field 4.2 "Chemical Sciences", scientific specialty "Organic Chemistry".

All facts represented above giving me justification to give my positive estimate and to recommend convincingly to the members of the Scientific Jury to award the degree of "Doctor of Science" to Prof. Dr. Margarita Dimitrova Popova in scientific field 4. "Natural Sciences, Mathematics and Informatics", professional field 4.2 "Chemical Sciences", scientific research specialty "Organic Chemistry".

Sofia, 18. 09.2021 Prof. Silviya Todorova, PhD