National University of Science and Technology
POLITEHNICA Bucharest
Doctoral School of Chemical Engineering and Biotechnologies
Department of Science and Engineering of Oxide Materials
and Nanomaterials

# *PhD Thesis*

# *Mesoporous systems loaded with polyphenols and natural extract of Melissa officinalis with antimicrobial activity*

## *-Summary -*

**Scientific coordinator:**

**Prof. PhD Eng. Anton Ficai**

**PhD student:**

**Chem. Eng. Gabriela Alexandru (Petrișor)**

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# *CONTENT*



**Keywords:** mesoporous silica, 3-aminopropyltriethoxysilane, polyphenols, *Melissa officinalis* extract, simulated biological fluids, antimicrobial activity.

## List of Abbreviations

**DDS** – Drug Delivery Systems

**MSNs** – Mesoporous Silica Nanoparticles

**MCM** – Mobil Composition of Matter

**CTAB** – N-cetyl-N,N,N-trimethylammonium bromide

**TEOS** – tetraethyl orthosilicate

**APTES** – (3-aminopropyl)triethoxysilane

**GA** – gallic acid

**FA** – trans-ferulic acid

**CA** – Caffeic acid

**p-CA** – p-Coumaric acid

**CAT** – Catechin

**MO** – *Melissa officinalis*

**MOE** – *Melissa officinalis* extract

**NaCl** – Sodium chloride

**TFA** – trifluoroacetic acid

**NaOH** – sodium hydroxide

**HCl** – hydrochloric acid

**$KH_2PO_4$** – potassium hydrogen phosphate

**SEM** – Scanning electron microscopy

**FTIR** – Fourier transform infrared spectroscopy

**ATR** – Attenuated Total Reflectance

**XRD** – Powder X-ray diffraction

**TEM** – Transmission electron microscopy

**HRTEM** – High-Resolution Transmission Electron Microscope

**TGA** – Thermogravimetric analysis

**DSC** – Differential scanning calorimetry

**HPLC-DAD** – High Performance Liquid Chromatography with Array Diode Detector

**BET** – Brunauer–Emmett–Teller

**EDS** – Energy Dispersive Spectroscopy

# I. CRITICAL STUDY OF THE LITERATURE DATA

## Chapter 1. Research on mesoporous silica and recent advances in biomedical applications

Based on recent research, new systems capable of being loaded with active substances, drugs or natural extracts have been developed. These researches focused on the development of controlled release systems that have the property of ensuring a delivery of the drug directly to the target organ [1-3]. Nanocarriers can be classified according to the nature of the substances from which they can be synthesized (organic or inorganic) and are found in the form of micelles, liposomes, hydrogels, vesicles, solid lipid nanoparticles, dendrimers, carbon nanotubes, metal nanoparticles, mesoporous silica nanoparticles, polymer nanoparticles, etc. [4-8] (Figure 1).

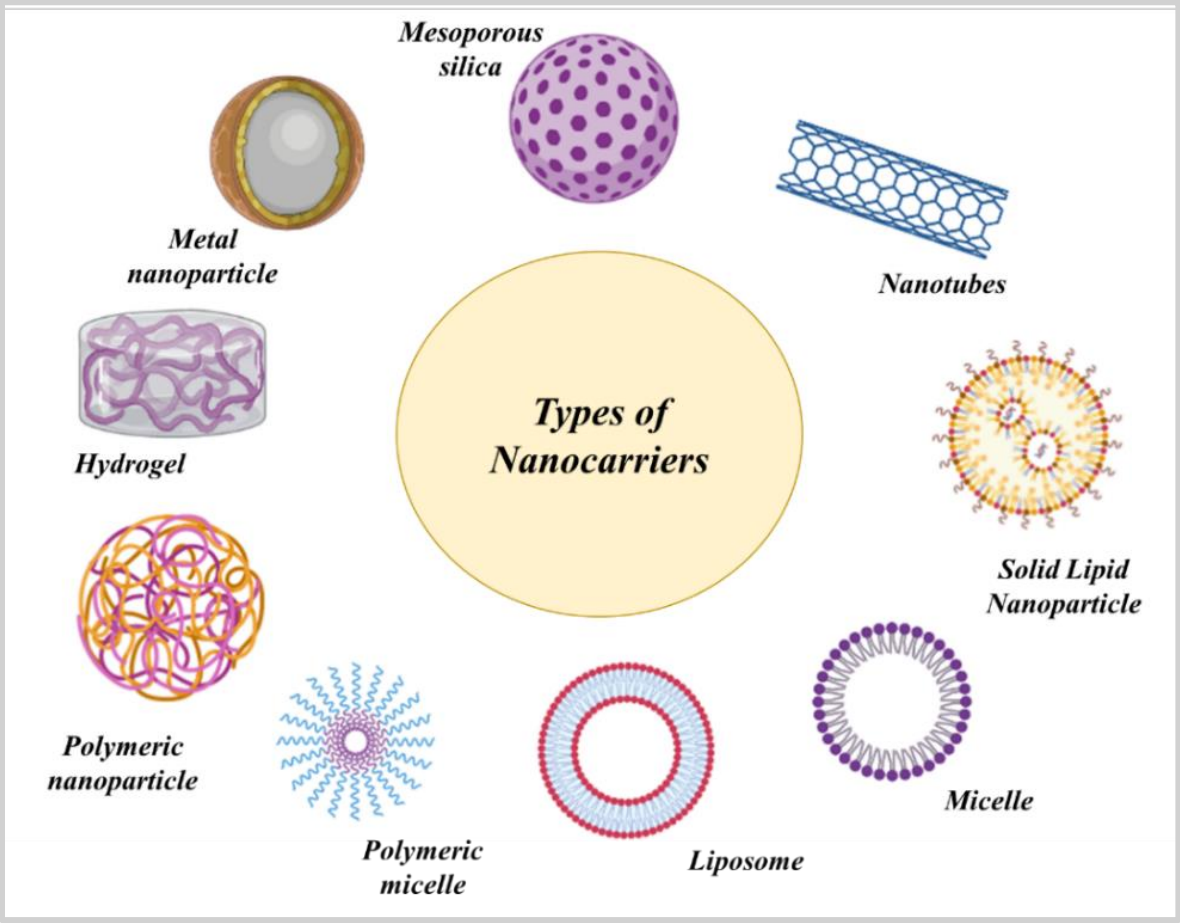



***Figure 1.*** *Types of nanocarriers (realized with BioRender.com)*

Mesoporous silica nanoparticles (MSNs) have attracted the attention of many researchers due to their structure that makes them applicable in many fields. One of the main applications of MSNs is to be used as a carrier material in controlled release systems. By adjusting and controlling the

properties of MSNs, the delivery process can be tailored for efficient delivery and achieving the desired therapeutic effect. According to the well defined structure of MSNs and the active surface containing many silanol groups (Si-OH), they allow the binding of various functional groups of organic nature. Organic functionalization is done by attaching amino ($-NH_2$), thiol (-SH) or carboxy (-COOH) functional groups to obtain certain surface characteristics of MSNs.

A great challenge is the choice of the carrier system and the substance or medicine that can be loaded because there must be compatibility and have the desired biological activity.

Medicinal plants are a rich source of bioactive compounds that can be used for the development of new drugs [9]. Active substances are found in various parts of plants and active compounds can be extracted from most medicinal plants that have direct therapeutic effects or indirect therapeutic effects.

Natural polyphenols are found in many plants and presents a great interest to medicine due to their multiple pharmacological activities such as anticancer, antioxidant, antimicrobial and many others [10-13].The structure of polyphenols (due to the hydroxy groups) is responsible for a good interaction between them and a wide variety of active substances.

Considering the multiple biological properties of natural substances, as well as a good compatibility between them and the materials from which the nanocarriers are made, the development of systems based on biologically active substances represents an important strategy to be studied.

In this thesis, I studied the controlled release systems researched so far based on mesoporous silica as a carrier system, loaded and functionalized with different active substances, drugs or natural extracts. Based on the literature study, I made a review of plant research medicinal *Melissa officinalis.*

Following the study of literature, I synthesized two kinds of mesoporous silica with the main goal of designing new drug release systems. The MSNs were functionalized with (3-aminopropyl)triethoxysilane (APTES) and loaded with polyphenols (gallic acid, caffeic acid, para-coumaric acid, trans-ferulic acid and catechin), and natural extract of *Melissa officinalis*, natural bioactive substances with antimicrobial and antioxidant properties with various applications in the biomedical field.

# II. ORIGINAL CONTRIBUTIONS

## Chapter 2. Materials and Methods

In this chapter, the materials and methods used in the synthesis of mesoporous silica type MCM-41 and MCM-48 are described, as well as in the functionalization synthesis with APTES. Methods of loading mesoporous materials obtained with polyphenols (GA, CA, p-CA, FA and CAT) and hydroalcoholic extract of *Melissa officinalis* were described.

This chapter includes the description of the methods and equipment used in the characterization of the obtained systems and the release tests performed in two types of simulated biological fluids.

## Chapter 3. Goals of the thesis and originality

The novelty of this study consists in the development of systems containing mesoporous silica nanocarriers, MCM-41 and MCM-48, loaded with polyphenols (GA, FA, CA, p-CA and CAT), but also with natural extract of *Melissa officinalis.*

Starting from the main objective of this PhD thesis to obtain mesoporous materials loaded with polyphenols and natural extract, we defined the following general objectives:

The first objective was to synthesize mesoporous silica nanoparticles and load them with polyphenols.

The second objective was to functionalize the two types of mesoporous silica with APTES and load the materials with trans-ferulic acid to observe the differences in the release profiles of trans-ferulic acid in two simulated biological fluids.

Following the literature study on the natural extract of *Melissa officinalis* we set the third objective to develop mesoporous silica materials loaded with natural extract of *Melissa officinalis*.

After obtaining all the materials, I considered the fourth objective to characterize the obtained systems from a morphological and structural point of view.

The last general objective consisted in testing the properties and establishing the possible uses of the obtained materials in biomedical applications.

## Chapter 4. Published research articles

### 4.1. *Melissa officinalis*: Composition, Pharmacological Effects and Derived Release Systems- A Review

This article is a literature review of the medicinal plant *Melissa officinalis* regarding its composition, pharmacological effects and derived delivery systems. Chemical studies on the composition of the *Melissa officinalis* plant have shown that it mainly contains flavonoids, terpenoids, phenolic acids, tannins and essential oil. *Melissa officinalis* is considered a medicinal plant due to the numerous pharmacological effects associated with its chemical composition (Figure 2). Most studies have focused on *Melissa officinalis* leaf extracts obtaining phenolic profiles correlated with the effects: antiproliferative, antiangiogenic, antioxidant, antidepressant, anti-Alzheimer, cardioprotective, antimicrobial, etc.

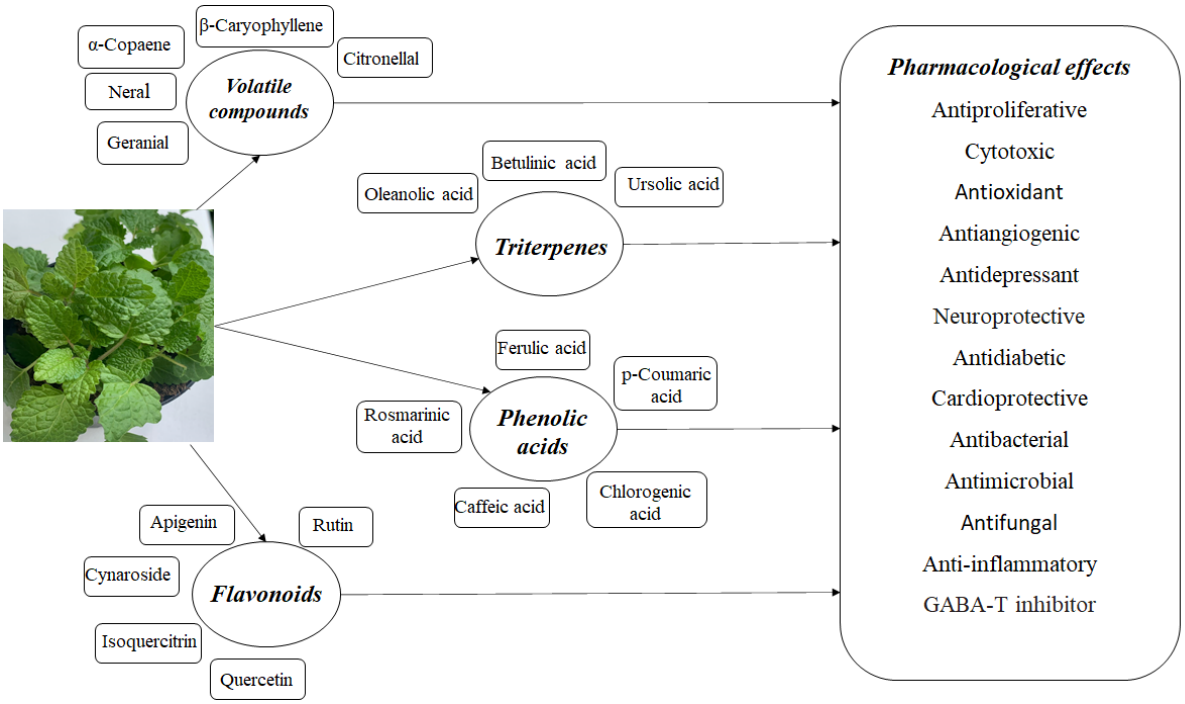



***Figure 2.*** *Composition and pharmacological effects of the plant Melissa officinalis*

The paper represents a detailed study on the pharmacological effects of different types of extracts and essential oils from *Melissa officinalis*. The article presents estimated human equivalent doses related to the doses and concentrations determined in the research articles. In the last part of the article, there is a summary of the controlled release systems that contain both

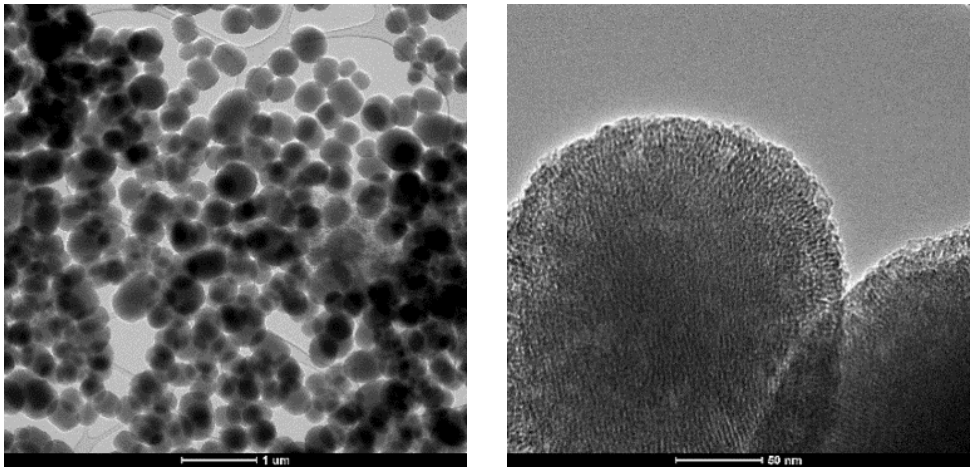
substances found in the composition of *Melissa officinalis*, as well as different types of controlled release systems developed to date that contain *Melissa officinalis* extract.

This review presents a broad perspective on the composition of the medicinal plant *Melissa officinalis*, as well as the pharmacological effects attributed mainly to the presence of a high amount of polyphenolic compounds. Studies on the chemical composition of the essential oil and many types of extracts have been reported and, depending on the area, period and method of harvesting the plant, different concentrations of active substances have been obtained. By investigating the mechanisms of action and the pharmacokinetics of extracts and active compounds, new systems with biologically active activities for the human body and the environment can be obtained. The controlled release systems developed so far represent a future perspective for the development of new systems.

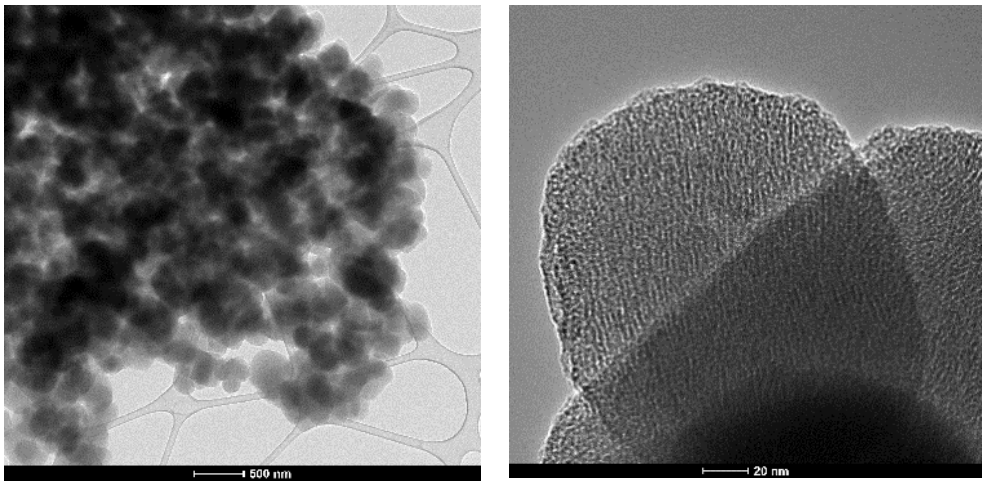
### 4.2. Mesoporous Silica Materials Loaded with Gallic Acid with Antimicrobial Potential

In this research article, we synthesized two types of mesoporous silica, MCM-41 and MCM-48, by the classical template method starting from different amounts of CTAB. The obtained materials were loaded under vacuum with three different amounts of gallic acid (0.41 g, 0.82 g, 1.21 g), finally obtaining 6 types of loaded mesoporous systems.

MCM-41 and MCM-48 were analyzed by TEM, observing the mesoporous structure of the materials and uniform particle size distribution.



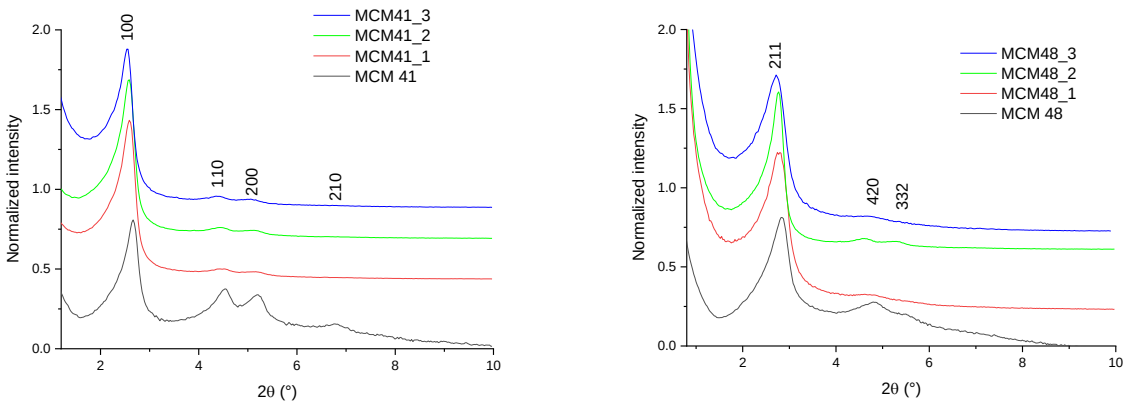

**MCM-41**




**MCM-48**

***Figure 3.*** *TEM images of mesoporous supports*

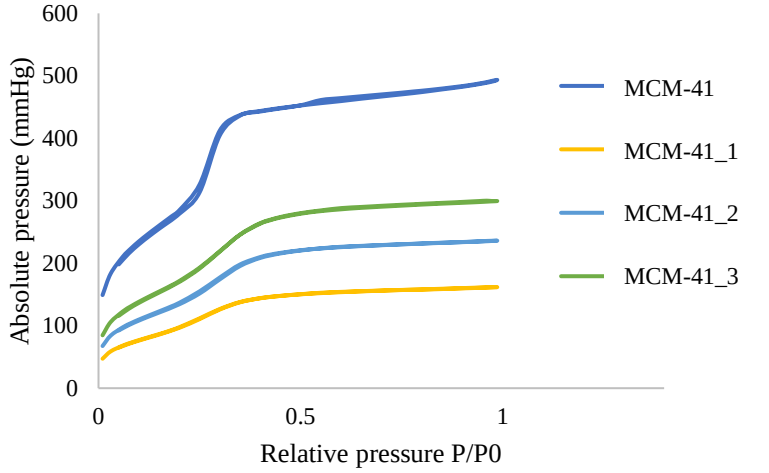
All the materials were analyzed by X-ray Diffraction, noting that all the diffractograms recorded on the mesoporous MCM-41 type materials (Figure 4, a) show four diffraction peaks corresponding to the (100), (110), (200) and (210) crystallization planes characteristic of the ordered hexagonal structure characteristic of the MCM-41 material. The diffractograms recorded on the mesoporous MCM-48 materials show two major peaks corresponding to the (211), (420) crystallization planes and a minor peak, corresponding to the plane (332), in agreement with the literature data (Figure 4, b).



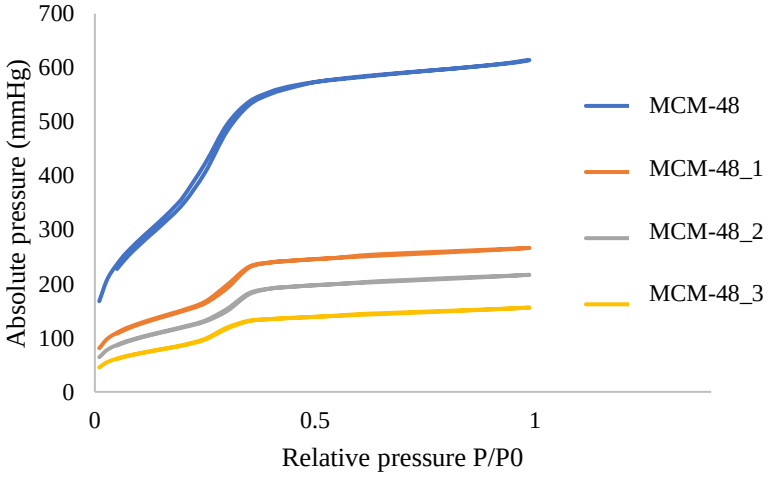

a) b)

***Figure 4.*** *XRD diffractograms of the samples: a) MCM-41, MCM-41_1, MCM-41_2, MCM-41_3; b) MCM-48, MCM-48_1, MCM-48_2, MCM-48_3*

The materials were subjected to BET analysis, obtaining adsorption/desorption curves from which it is observed that all materials exhibit reversible type IV isotherms, indicating that the materials have an ordered pore structure. From the pore characteristic results we observed a significant decrease in the specific BET surface area as well as the pore volume compared to MCM-41 and MCM-48 uncaged which means that the polyphenols were mostly adsorbed in the pores.




a)



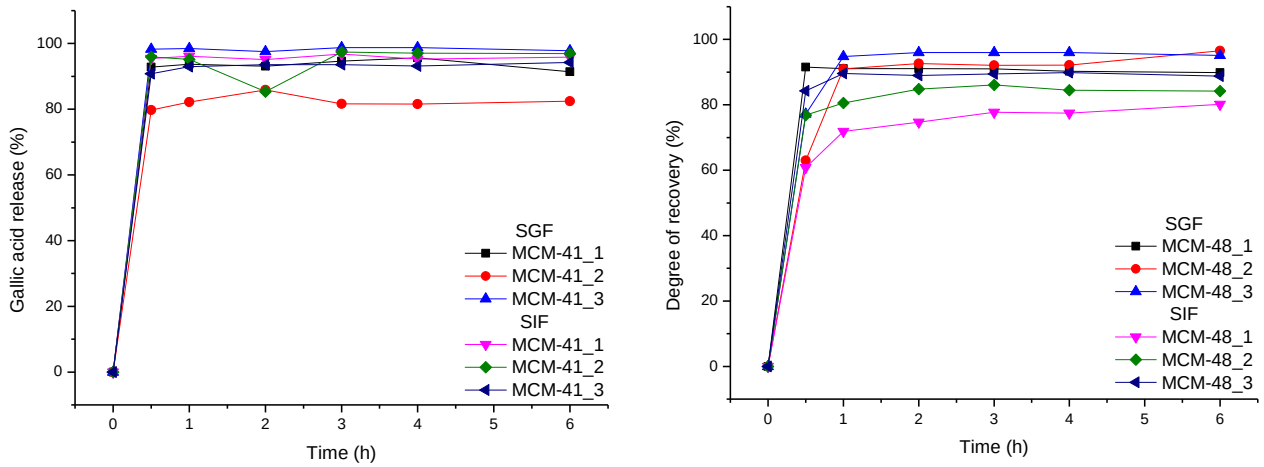

b)

***Figure 5.*** *Adsorption/desorption isotherms recorded on materials: a) MCM-41, MCM-41_1-3 and b) MCM-48, MCM-48_1-3*

In this article, the obtained materials were analyzed by SEM, FT-IR and TG-DSC from which we obtained very good results observing the spherical morphology of silica particles with

dimensions of 200-400 nm and also the loading of nanoparticles with the different amounts of gallic acid.

Materials loaded with gallic acid were subjected to release tests in two simulated biological fluids with different pH (simulated gastric fluid with pH=1.2 and simulated intestinal fluid with pH=6.8) through which the different release profiles of gallic acid were observed. Gallic acid was released differently from the 6 materials because parameters such as the amount of loaded substance, the type of loaded material and the type of simulated biological fluid influenced the release profile (Figure 6).




(a) (b)

***Figure 6**. Gallic acid release from (a) MCM-41, (b) MCM-48 mesoporous supports in SGF and SIF*

After the materials were characterized and we observed that the gallic acid loading was effective, the nanoparticles were subjected to biological tests by which the antibacterial effects of gallic acid, cell viability, inflammasome activation and apoptosis activation were evaluated.

### 4.3. New Mesoporous Silica Materiald Loaded with Polyphenols: Caffeic Acid, Ferulic Acid and p-Coumaric Acid as Dietary Supplements for Oral Administration

In this research article we started from previously synthesized mesoporous materials of type MCM-41 and MCM-48 and loaded them under vacuum with three types of polyphenols: caffeic acid, para-coumaric acid and trans-ferulic acid. From their analysis we noticed that the materials were loaded with polyphenols differently and had different release profiles, although we

used the same amount of polyphenol. These differences between materials may be due to the fact that the structure of the polyphenols is different and their solubilities differ.

From the BET, SEM and TG-DSC analyses, we observed that the mesoporous materials were loaded with polyphenols and that they have an ordered mesoporous structure, with slightly variable particle sizes between 150-400 nm.

Following the FT-IR analysis, the absorption spectra of the systems were obtained, noting that in all the absorption spectra there are absorption bands specific to the stretching vibrations of the asymmetric Si-O-Si units, the deformation vibrations of the Si-O-Si units and silanol groups specific to mesoporous silica.

In the absorption spectra of materials loaded with polyphenols, the specific absorption bands of -OH groups and carbonyl groups appear, which indicates the presence of organic structures of polyphenols (Figure 7 and 8).

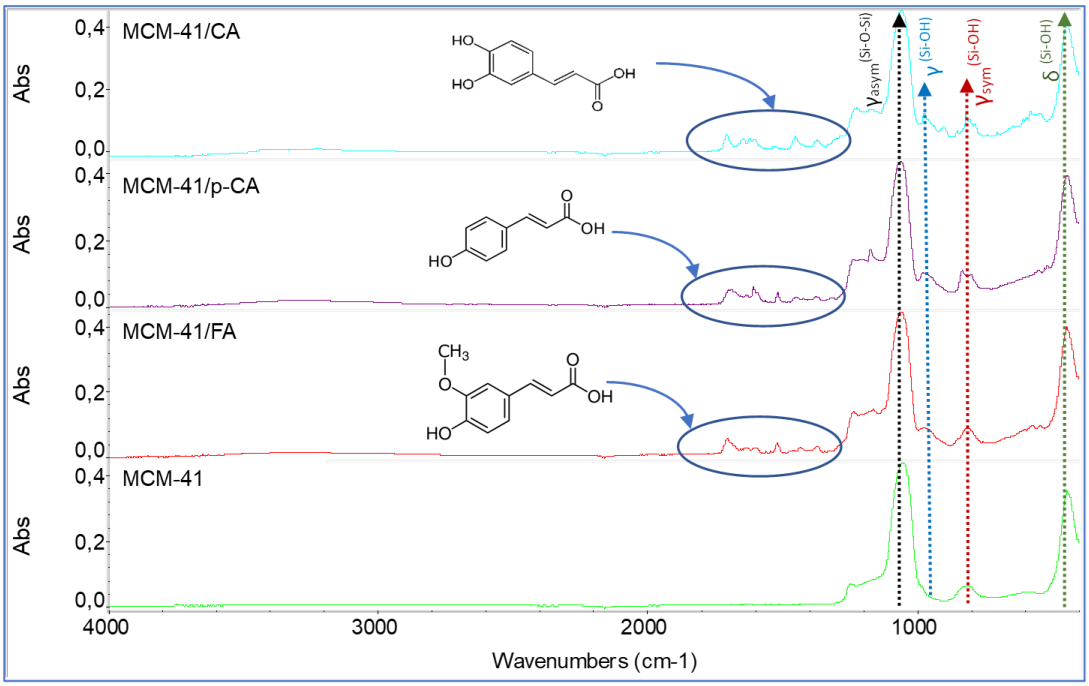



***Figure 7.*** *FTIR spectra of samples MCM-41, MCM-41/CA, MCM-41/p-CA, MCM-41/FA*

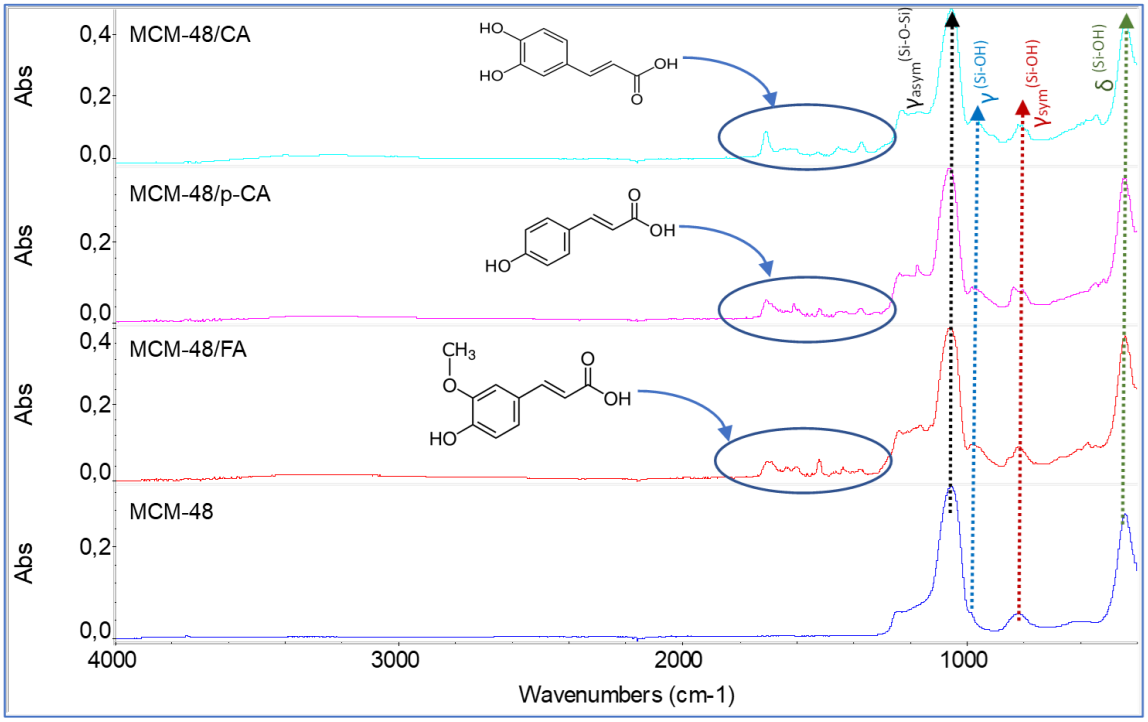



***Figure 8.*** *FTIR spectra of samples MCM-48, MCM-48/CA, MCM-48/p-CA, MCM-48/FA*

In this research study, we performed the release studies of polyphenols from the mesoporous matrix in two simulated biological fluids with different pH (SGF with pH=1.2 and SIF with pH=6.8). Releases were monitored for 2 h in SGF and 6 h in SIF, observing different release profiles of polyphenols (Figure 9).

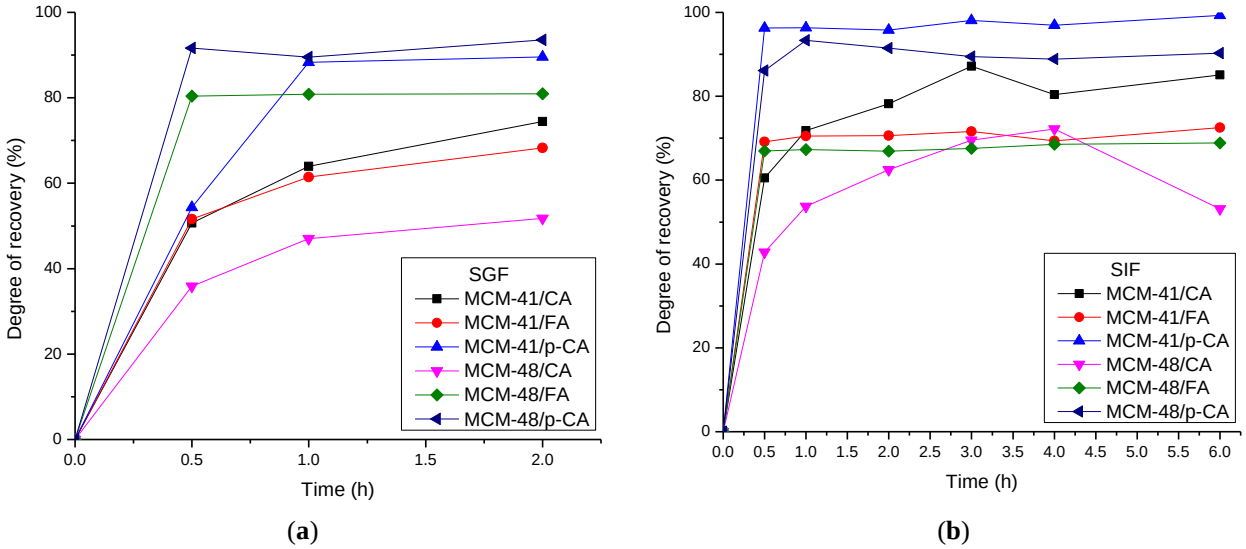



***Figure 9.*** *Release profiles of polyphenols in a) SGF and b) SIF*

## 4.4. Increasing Bioavailability of trans-Ferulic Acid by Encapsulation in Functionalized Mesoporous Silica

In this research article I have considered the results obtained previously and have chosen to functionalize with 3-aminopropyltriethoxysilane (APTES) the mesoporous materials MCM-41 and MCM-48 by the post-grafting method and load the functionalized materials under vacuum with acid trans- ferulic (Figure 10).

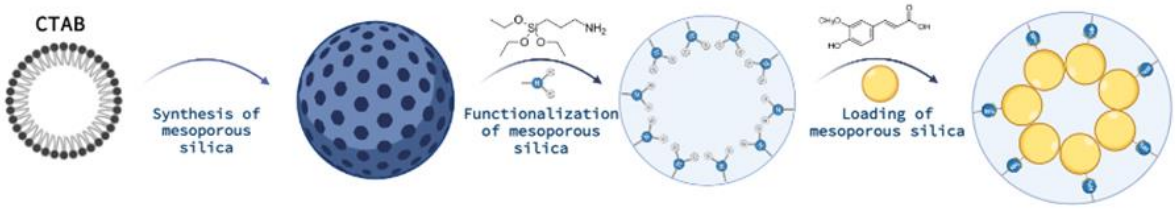
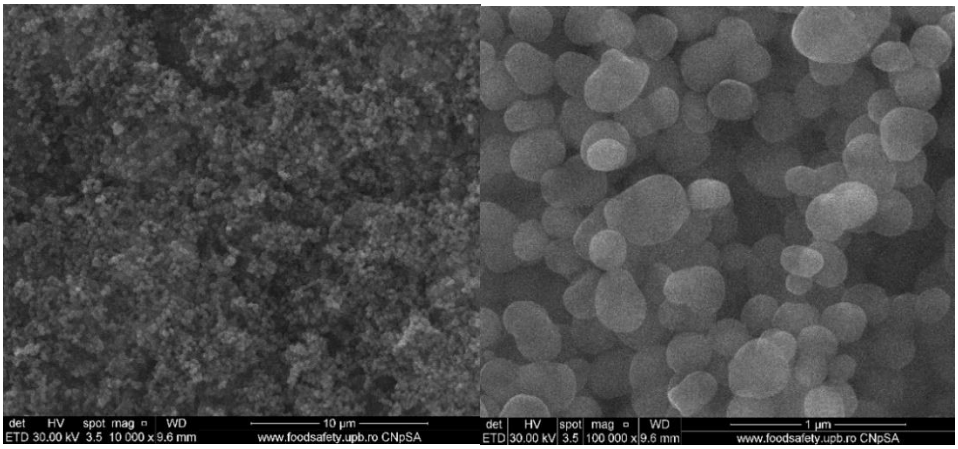
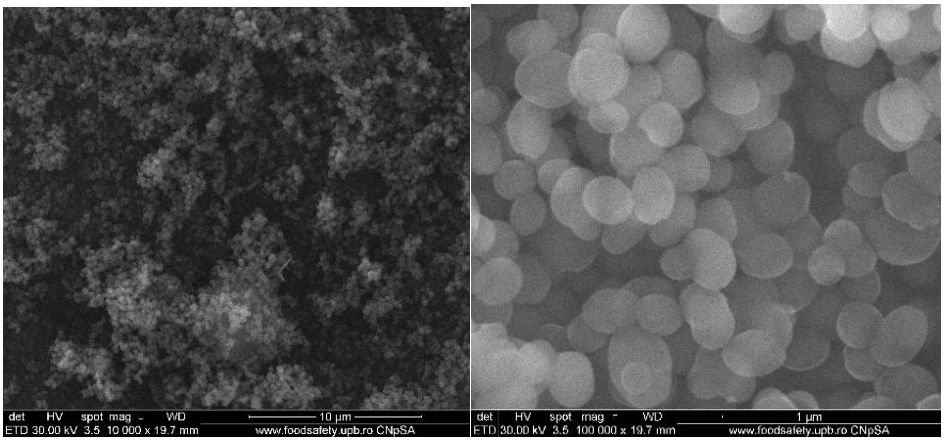



***Figure 10.*** *Synthesis of FA-loaded functionalized mesoporous systems*

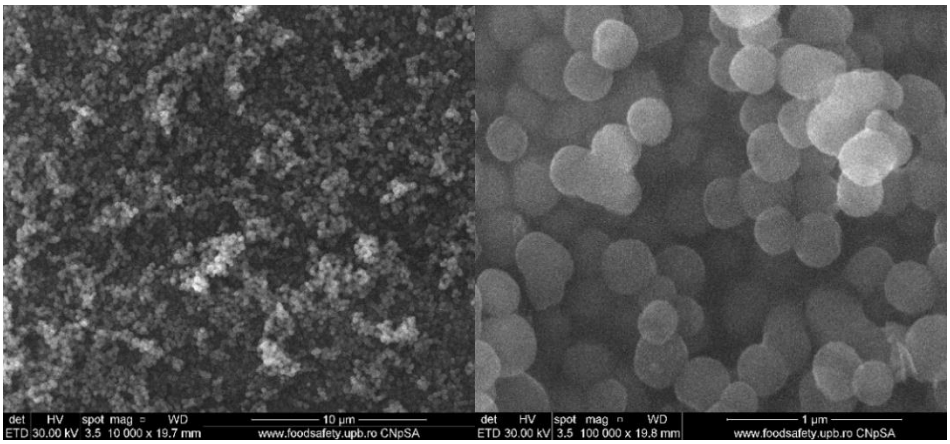
Through SEM analysis we observed that the materials kept their mesoporous structure, with particle sizes between 150-400 nm.




**MCM-41**



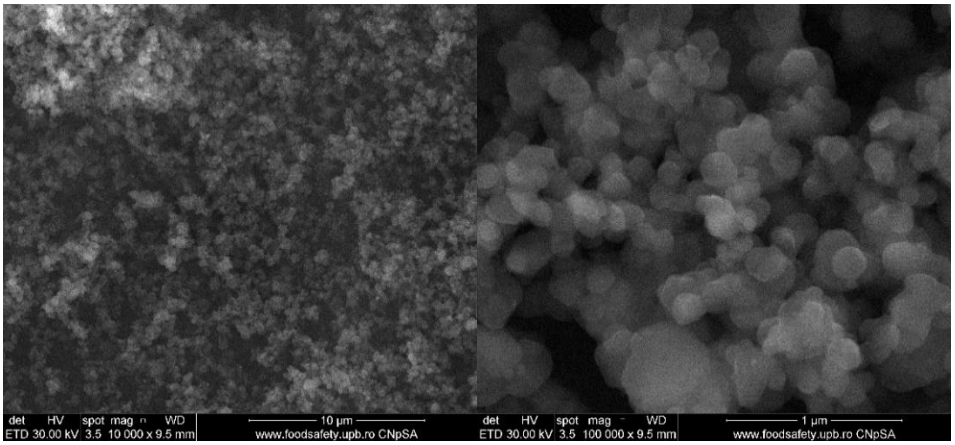

**MCM-41_FA**



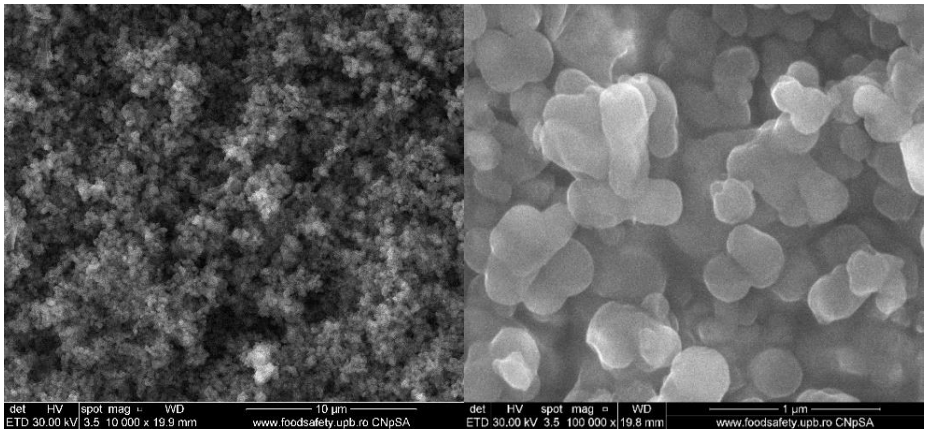

**MCM-41_APTES_FA**

***Figure 11.*** *SEM images of FA loaded in mesoporous materials type MCM-41*

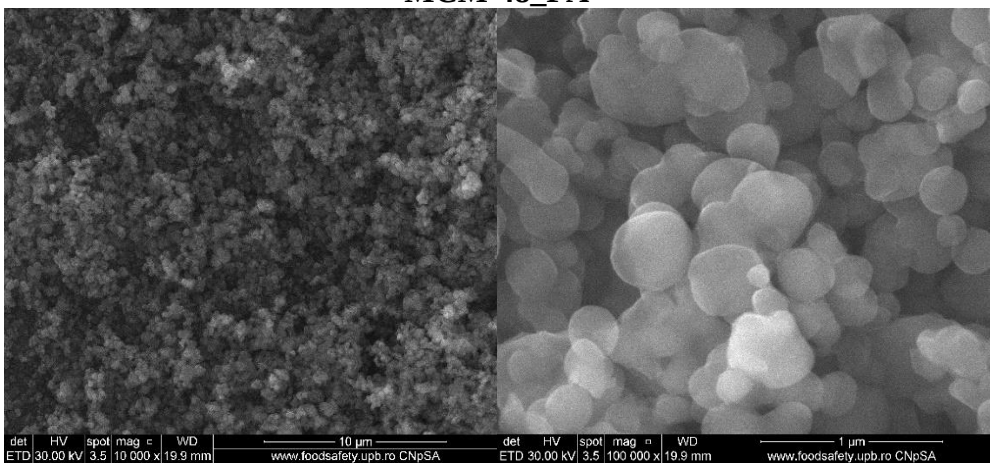
Nanoparticles with mesoporous MCM-41 support retain their spherical shape and uniformity after functionalization with APTES and loading with FA (Figure 11). In the case of nanoparticles with MCM-48 mesoporous support, they have a quasi-spherical shape and have a tendency to agglomerate after loading with FA (Figure 12).




**MCM-48**



**MCM-48_FA**




**MCM-48_APTES_FA**

***Figure 12.*** *SEM images of FA loaded in mesoporous materials type MCM-48*

The results of XRD and BET analyzes showed that the obtained systems retain their mesoporous structure after functionalization and the pore size is significantly reduced after loading with FA, which means that an effective loading has occurred inside the pores. In the FT-IR absorption spectra we observed both absorption bands specific to silica and absorption bands specific to $NH_2$, OH and C=O groups.

The thermogravimetric analysis of the obtained systems indicated a successful functionalization with APTES, observing in the TG-DSC diagrams a strong thermal effect recorded at 300$^o$C (Figure 13 and 14).

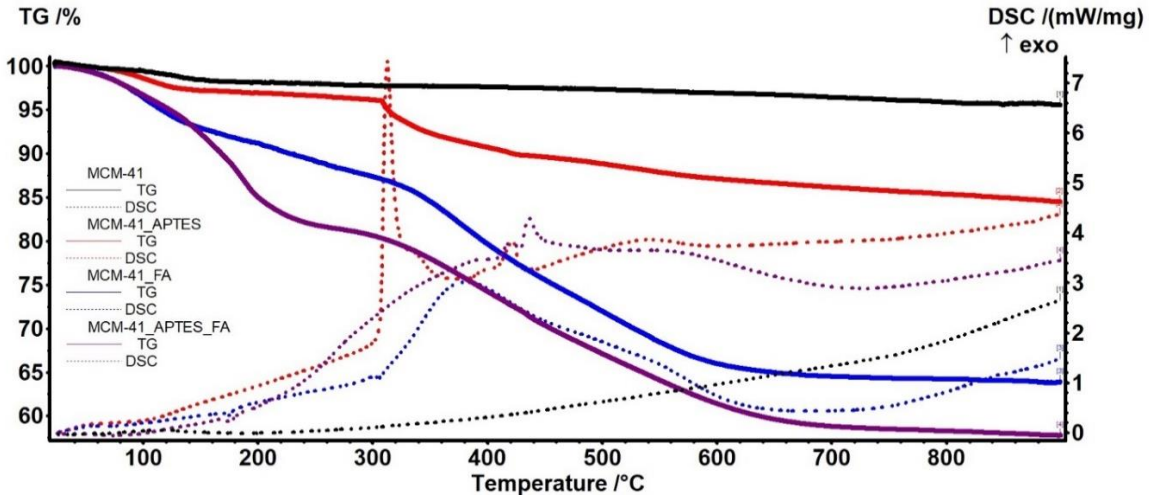



***Figure 13.*** *TG-DSC curves of mesoporous materials type MCM-41*

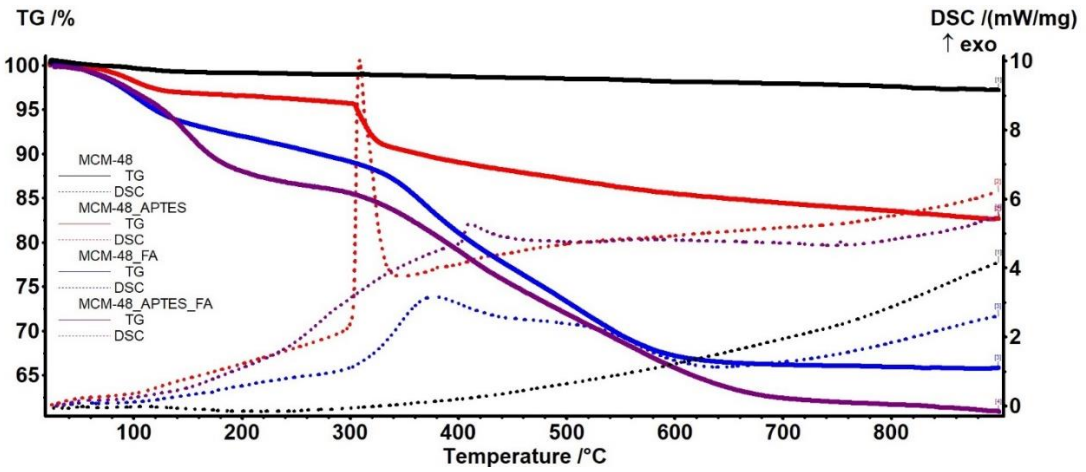



***Figure 14.*** *TG-DSC curves of mesoporous materials type MCM-48*

To observe the behavior of the functionalized systems, I chose to study the release of FA in two simulated biological fluids, SGF and SIF. The non-functionalized materials had a rapid release from the first 30 minutes as opposed to the functionalized materials where we obtained profiles with a slow release of FA and a reduced amount after 20 hours (Figure 15). From these release studies we observed that functionalization with amino groups significantly changes the release profiles of the loaded active substances, which means that the materials may have applicability in controlled release systems depending on the desired action.

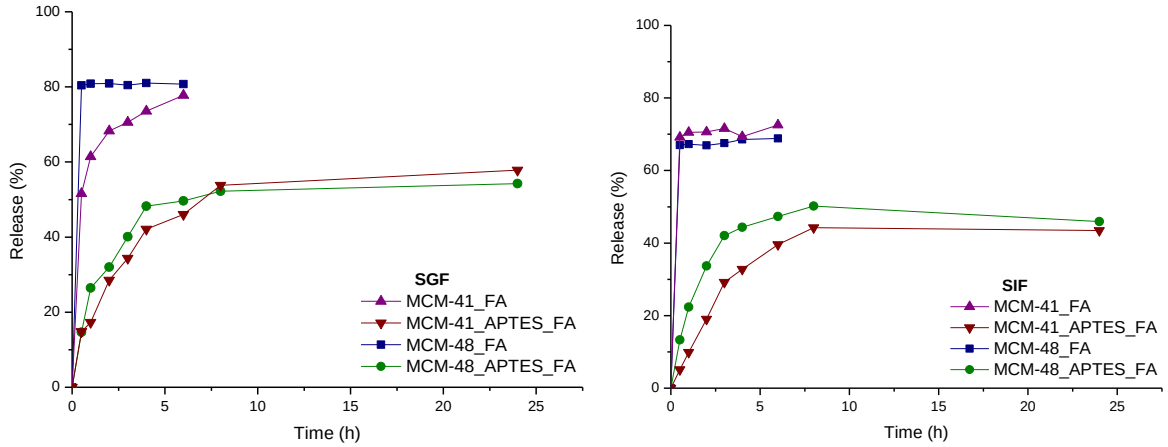



***Figure 15.*** *Release profiles of FA from the systems obtained in SGF and SIF*

The obtained systems were tested to evaluate the antimicrobial activity on four strains of *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Candida albicans* ATCC 1023. Among all the samples studied, MCM-41_APTES_FA prevented the adhesion of pathogenic strains to the inert substrate , respectively, mature and stable biofilm development, and showing the most pronounced inhibitory effect.

### 4.5. The Antimicrobial Potency of Mesoporous Silica Nanoparticles Loaded with *Melissa officinalis* Extract

The originality of this article lies in obtaining MSNs loaded with natural extract of *Melissa officinalis* (MOE). The natural extract of *Melissa officinalis* is a concentrated hydroalcoholic extract so that it has a high concentration of rosmarinic acid and a high amount of polyphenolic compounds. The concentrated extract was loaded into MSNs under vacuum in several steps, obtaining four types of extract-loaded materials: MCM-41@MOE, MCM-41@APTES@MOE, MCM-48@MOE, and MCM-48@APTES@ MOE.

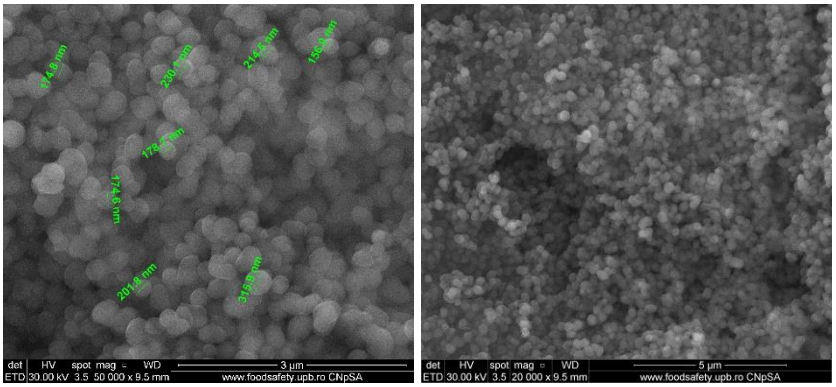
The obtained systems were characterized from a morphological and structural point of view, noting that all materials retain their mesoporous structure. Following the BET analysis, we noticed that the materials reduced their specific BET surface area and pore volume, which means that the active substances from the MOE were loaded into the pores of the materials (Table 1). In the case of the functionalized materials loaded with MOE, we observed a significant decrease in the specific BET surface, which proves that the pores of the mesoporous materials have a high volume that was almost completely occupied.

***Table 1.*** *Textural parameters of materials loaded with MOE*

| Sample | Volume of pores $cm^3/g$ | BET Surface Area $m^2/g$ |
|---|---|---|
| **MCM-41** | **0.783** | **1365** |
| **MCM-41@MOE** | 0.1024 | 143.9 |
| **MCM-41@APTES** | 0.5706 | 1014 |
| **MCM-41@APTES@MOE** | 0.0295 | 22.43 |
| **MCM-48** | **0.9423** | **1582** |
| **MCM-48@MOE** | 0.1074 | 143.8 |
| **MCM-48@APTES** | 0.7371 | 1555 |
| **MCM-48@APTES@MOE** | 0.0835 | 76.14 |

From the SEM images of the systems we observed that the MSNs were efficiently loaded. In the case of the systems with MCM-41 (Figure 16 a,b), the nanoparticles have a spherical shape with dimensions between 150-350 nm, and in the case of the systems with MCM-48 (Figure 16 c,d), the nanoparticles have a quasi-spherical shape with dimensions between 100-300 nm. Particle agglomerations are observed in all SEM images of the materials, which means that a small amount of MOE has deposited on the surface of the nanoparticles.

**a)**

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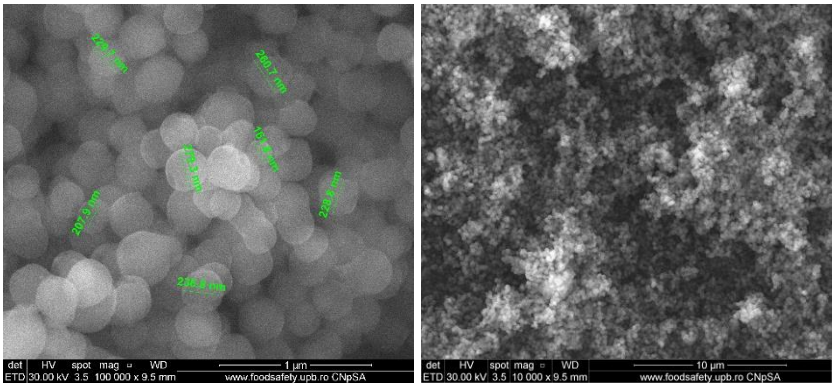


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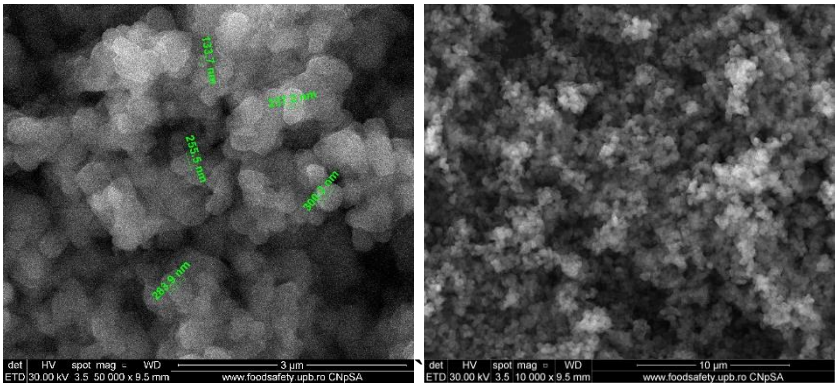


**d)**

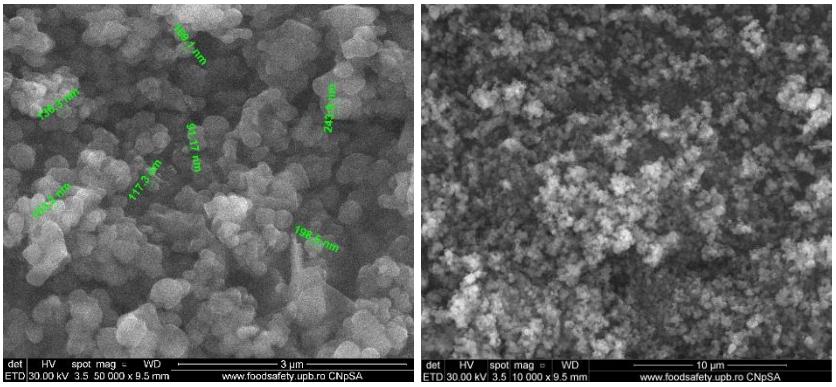
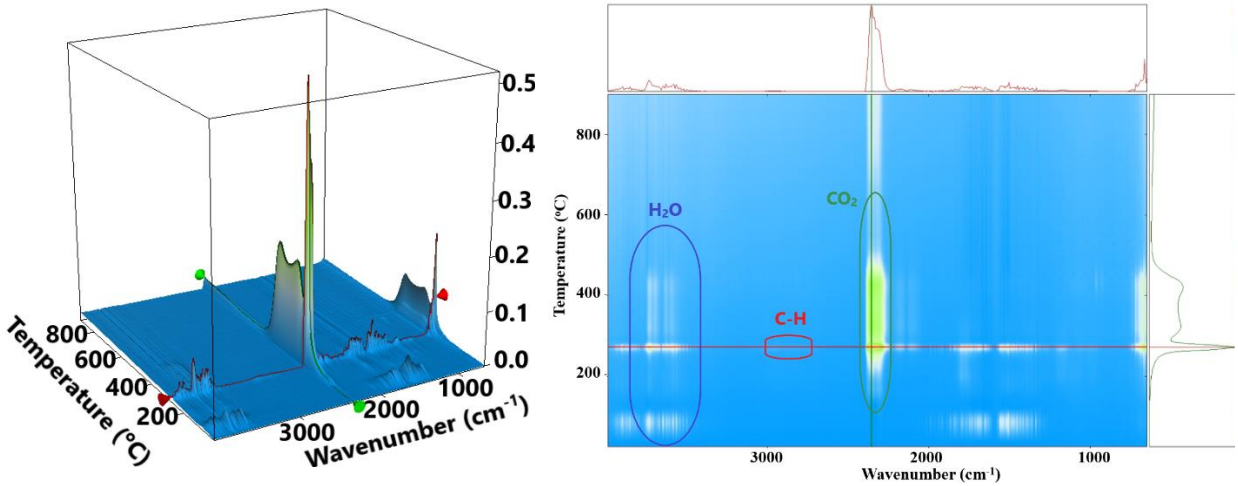



***Figure 16.*** *SEM images of the materials: a) MCM-41@MOE, b) MCM-41@APTES@MOE, c) MCM-48@MOE and d) MCM-48@APTES@MOE*

From the FTIR and TG-DSC analyzes we obtained results regarding the structure of the obtained systems observing that the materials were loaded with a high amount of polyphenolic compounds from MOE. Following the FTIR analysis for the gases released from the thermal analysis of MCM-41@MOE (Figure 17) we noticed that a high amount of CO2 was released, a process that can be attributed to the partial oxidation of the organic substances charged in the mesoporous silica.




**a)** **b)**

***Figure 17.*** *3D FTIR diagram for the gases evolved from thermal analysis of MCM-41@MOE (a) and its 2D projection in temperature/wavenumber space (b)*

The obtained materials were tested against both reference strains and clinical strains belonging to Gram-positive strains previously isolated from intra-hospital infections, against Gram-negative bacteria and yeasts, observing a high sensitivity for S. aureus ATCC 25923 with a mean minimum inhibitory concentration in the range of 0.156-1.25 mg/mL, followed by C. albicans ATCC 10231 (0.078-2.5 mg/mL) and E. faecium ATCC 13048 (0.5 mg/mL).

In the last research article accepted for publication, entitled "New drug delivery system with catechin loaded in mesoporous silica nanoparticles" we obtained two materials of type MCM-41 and MCM-48 loaded with catechin. These materials were characterized to show the structure of the mesoporous silica, but also its loading with catechin. To provide insight into the use of the two materials obtained, we performed the release studies in two simulated biological fluids and showed the difference between the release profiles of catechin from the two mesoporous materials.

Therefore, these studies published in international journals provide an important insight into the use of polyphenols and natural extract of *Melissa officinalis* in controlled release systems with various biological applications.

## Chapter 5. General conclusions

The development of new controlled release systems and their research is an important step for nanomedicine in the future. Both the transport system and the active substance contribute with major importance to the action of controlled release systems to the target organ.

In this thesis I made a detailed study of controlled release systems where mesoporous silica is used as a carrier material. Following the literature study, we observed the diversity of active substances, natural extracts and essential oils loaded in both mesoporous silica and other types of materials and their biological effects.

In the second part of the study, we synthesized the mesoporous materials MCM-41 and MCM-48 and functionalized them with APTES. Following the characterization of the materials, it was found that they have a mesoporous structure with high pore size and volume. We loaded the obtained materials with polyphenols and *Melissa officinalis* extract. The results of the characterization analyzes showed that the obtained systems were loaded with high amounts of polyphenols and *Melissa officinalis* extract and also have very good properties to be researched from a biological point of view.

The systems had different behaviors in the two types of simulated biological fluids and a slow release of active substances was observed in the systems where the mesoporous silica was functionalized with APTES. The differences in the release mode of the active substances may be associated with the different solubilities and interactions of the polyphenols with the mesoporous silica supports. MCM-41 and MCM-48 were tested and very low toxicity was observed, meaning that the materials can be used in controlled release systems.

The results of the research studies represent an important step for nanomedicine, demonstrating that different mesoporous silica supports are able to transport active substances and natural extracts to have the desired biological effect.

## Chapter 6. Perspectives

The use of natural substances and natural extracts in medicine represents a great challenge for *in vivo* biological studies. Although the obtained results promote the obtained materials as useful for biomedical applications, additional biological studies are needed. The synthesis process of MSNs and materials loaded with active substances must be improved using green solvents and substances to reduce toxicity and adverse effects. The materials loaded with concentrated hydro-alcoholic extract of *Melissa officinalis* are of particular interest due to the pharmacological effects that this extract offers, but detailed studies are needed, especially *in vivo* depending on the desired biological application. Additional studies would be necessary such as the behavior of the extract, the release study from the mesoporous silica matrix and their cytotoxic effects.

Therefore, the obtained materials demonstrated an innovative character for the synthesis of materials based on silica with mesoporous structure, functionalized and loaded with active substances and natural extract. The obtained materials proved that they can be used as drug delivery systems with antimicrobial activity. As future perspectives, the mesoporous materials obtained in this research study represent a promising future in the development of controlled release systems following *in vivo* studies.

## Chapter 7. Dissemination

### 7.1 List of publications

7.1.1 **Gabriela Petrisor**, Ludmila Motelica, Luminita Narcisa Craciun, Ovidiu Cristian Oprea, Denisa Ficai, Anton Ficai; ***Melissa officinalis*: Composition, Pharmacological Effects and Derived Release Systems—A Review**; *International Journal of Molecular Sciences*, 2022, 23, 7, 3591; 10.3390/ijms23073591; Q1; IF= 5.6.

7.1.2 **Gabriela Petrisor**, Denisa Ficai, Ludmila Motelica, Roxana Doina Trusca, Alexandra Cătălina Bîrcă, Bogdan Stefan Vasile, Georgeta Voicu, Ovidiu Cristian Oprea, Augustin Semenescu, Anton Ficai, Mircea Ionut Popitiu, Irina Fierascu, Radu Claudiu Fierascu, Elena Lacramioara Radu, Lilia Matei, Laura Denisa Dragu, Ioana Madalina Pitica, Mihaela Economescu, Coralia Bleotu; **Mesoporous Silica Materials Loaded with Gallic Acid with Antimicrobial Potential**, *Nanomaterials*, 2022, 12, 1648; https://doi.org/10.3390/ nano12101648; Q1; IF= 5.3.

7.1.3 **Gabriela Petrisor**, Ludmila Motelica, Denisa Ficai, Roxana Doina Trusca, Vasile-Adrian Surdu, Georgeta Voicu, Ovidiu Cristian Oprea, Anton Ficai, Ecaterina Andronescu; **New Mesoporous Silica Materials Loaded with Polyphenols: Caffeic Acid, Ferulic Acid and p-Coumaric Acid as Dietary Supplements for Oral Administration**, *Materials*, 2022, 15, 7982; https:// doi.org/10.3390/ma15227982; Q2; IF= 3.4.

7.1.4 **Gabriela Petrisor**, Ludmila Motelica, Denisa Ficai, Cornelia-Ioana Ilie, Roxana Doina Trusca, Vasile-Adrian Surdu, Ovidiu-Cristian Oprea, Andreea-Luiza Mîrt, Gabriel Vasilievici, Augustin Semenescu, Anton Ficai, Lia-Mara Ditu; **Increasing Bioavailability of Trans-Ferulic Acid by Encapsulation in Functionalized Mesoporous Silica**, *Pharmaceutics*, 2023, 15, 660; https:// doi.org/10.3390/; Q1; IF= 5.4.

7.1.5 **Gabriela Petrisor**, Ludmila Motelica, Roxana Doina Trușcă, Andreea-Luiza Mîrț, Gabriel Vasilievici, Justinian-Andrei Tomescu, Cristina Manea, Andreea Ștefania Dumbravă, Viorica Maria Corbu, Irina Gheorghe-Barbu, Denisa Ficai, Ovidiu-Cristian Oprea, Bogdan-Ștefan Vasile, Anton Ficai, Anca Daniela Raiciu, **The Antimicrobial Potency of Mesoporous Silica Nanoparticles Loaded with *Melissa officinalis* Extract**, *Pharmaceutics*, 2024, 16 (4), 525; https://doi.org/10.3390/pharmaceutics16040525; Q1; IF= 5.4.

7.1.6 **Gabriela Petrisor**, Ludmila Motelica, Denisa Ficai, Roxana Doina Trusca, Adrian Vasile Surdu, Georgeta Voicu, Ovidiu Cristian Oprea, Anton Ficai, **New drug delivery system with**

**catechin loaded in mesoporous silica nanoparticles**, U.P.B. Sci. Bull., Series B, 2024 (accepted for publication).

7.1.7 **Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Cristian Oprea, Georgeta Voicu, Anton Ficai; Abstract: **"Mesoporous Silica Systems Loaded with Polyphenols"**, *Chemistry Proceedings*, 2022, *7*(1), 15; https://doi.org/10.3390/chemproc2022007015.

7.1.8 Denisa Ficai, Ludmila Motelica, **Gabriela Petrișor**, Irina Fierascu, Radu Claudiu Fierascu, Anton Ficai, Coralia Bleotu; Abstract: **"Porous Materials as Platforms for the Delivery of Polyphenols"**, *Chemistry Proceedings*, 2022, *7*(1), 77; https://doi.org/10.3390/chemproc2022007077.

### 7.2 Conference and workshop participations

7.2.1 **Gabriela Petrișor**, Anton Ficai, **"Controlled release systems based on active substances from *Melissa officinalis*"**, *International Scientific Conference "Applications of Chemistry in Nanosciences and Biomaterials Engineering"* (presentation, on-line), 2020, Bucharest, Romania.

7.2.2 Denisa Ficai, Ludmila Motelica, **Gabriela Petrișor**, Irina Fierescu, Radu Claudiu Fierescu, Anton Ficai, Coralia Bleotu, **"Porous Materials in the Treatment of Microbiota-related Diseases"**, *Workshop "Smart Functional Nanomaterials: From Synthesis To Advanced Applications"* (on-line), 7-8 May, 2021, Rome, Italy.

7.2.3 **Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Oprea, Anton Ficai, **"Mesoporous systems loaded with polyphenols for treatment of dysbiosis"**, *International Scientific Conference "Applications of Chemistry in Nanosciences and Biomaterials Engineering"(presentation, on-line)*; 25-26 June 2021, Bucharest, Romania.

7.2.4 **Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Oprea, Anton Ficai, **"Mesoporous systems loaded with epicatechin and catechin for the treatment of colon cancer",** *International Workshop COST Challenges of tumor profiling in translational research* (presentation), 20-21 September 2021, Bucharest, Romania.

7.2.5 **Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Oprea, Georgeta Voicu, Anton Ficai, **"Mesoporous silica systems loaded with polyphenols"**, *International Symposium "Priorities of chemistry for a sustainable development" PRIOCHEM XVII* (presentation, on-line), 27-29 October 2021, Bucharest, Romania.

7.2.6 Denisa Ficai, Ludmila Motelica, **Gabriela Petrișor**, Irina Fierascu, Radu Claudiu Fierascu, Anton Ficai, Coralia Bleotu, **"Porous Materials as Platforms for the Delivery of Polyphenols"**, *International Symposium "Priorities of chemistry for a sustainable development" PRIOCHEM XVII* (presentation, on-line), 27-29 October 2021, Bucharest, Romania.

7.2.7 **Gabriela Petrișor**, Ludmila Motelica, Roxana Doina Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Cristian Oprea, Georgeta Voicu, Dan Eduard Mihaiescu, Anton Ficai; **"Mesoporous silica systems loaded with epicatechin and catechin for the treatment of colon cancer"**, *International Scientific Conference "Applications of Chemistry in Nanosciences and Biomaterials Engineering"* (presentation, on-line), 25-27 November 2021, Bucharest, Romania.

7.2.8 **Gabriela Petrișor**, Ludmila Motelica, Denisa Ficai, Ovidiu Oprea, Anton Ficai, Ecaterina Andronescu; **„Porous material for biomedical applications"**; *9th Edition International Scientific Practical Conference "Training By Research For a Prosperous Society"* (presentation, on-line), 19-20 march 2022, Chişinău, Moldova.

7.2.9 **Gabriela Petrișor**, Denisa Ficai, Ludmila Motelica, Roxana Doina Trusca, Alexandra Catalina Bîrca, Bogdan Stefan Vasile , Georgeta Voicu, Ovidiu Cristian Oprea, Augustin Semenescu, Anton Ficai , Mircea Ionut Popitiu, Irina Fierascu, Radu Claudiu Fierascu, Elena Lacramioara Radu, Lilia Matei , Laura Denisa Dragu, Ioana Madalina Pitica, Mihaela Economescu and Coralia Bleotu; **"Mesoporous Silica Materials Loaded with Gallic Acid with Antimicrobial Potential"**, *International Scientific Conference „Applications of Chemistry in Nanosciences and Biomaterials Engineering"* (presentation, on-line), 22-24 June 2022, Bucharest, Romania.

7.2.10 **Gabriela Petrișor**, Ludmila Motelica, Denisa Ficai, Cornelia-Ioana Ilie, Roxana Doina Trusca, Adrian Vasile Surdu, Georgeta Voicu , Ovidiu Cristian Oprea, Lia-Mara Ditu, Anton Ficai; **"New Mesoporous Silica Materials Loaded With Ferulic Acid As Food Supplements For Oral Administration"**, *International Symposium "Priorities of chemistry for a sustainable development" PRIOCHEM XVIII* (presentation, on-line), 26-28 October 2022, Bucharest, Romania.

7.2.11 **Gabriela Petrișor**, Ludmila Motelica, Denisa Ficai, Roxana Doina Trusca, Adrian Vasile Surdu, Georgeta Voicu, Ovidiu Cristian Oprea, Anton Ficai; **"Functionalized Mesoporous Silica Materials Loaded with Ferulic Acid",** *International Scientific Conference "Applications of*

*Chemistry in Nanosciences and Biomaterials Engineering"* (presentation, on-line), 24-26 November 2022, Bucharest, Romania.

7.2.12 **Gabriela Petrișor**, Ludmila Motelica, Denisa Ficai, Roxana Doina Trusca, Ovidiu Cristian Oprea, Andreea-Luiza Mirț, Gabriel Vasilievici, Justinian-Andrei Tomescu, Cristina Manea, Anton Ficai, Anca Daniela Raiciu **"Mesoporous materials loaded with *Melissa officinalis* extract",** *International Scientific Conference "Applications of Chemistry in Nanosciences and Biomaterials Engineering"* (presentation, on-line), 28-30 June 2023, Bucharest, Romania.

7.2.13 **Gabriela Petrișor**, Ludmila Motelica, Denisa Ficai, Ovidiu Cristian Oprea, Trușcă Roxana, Ecaterina Andronescu, Alina Holban, Anton Ficai **"Antimicrobial composite packaging films"** (poster), 19-21 June 2024, Bucharest, Romania.

### 7.3 Awards

7.3.1. **Gold metal** granted by Euroinvent European Exhibition of Creativity and Inovation for the work entitled **"Controlled release systems for maintaining the balance of the gastrointestinal microbiota and improving health and method of obtaining them", Gabriela Petrișor**, Ludmila Motelica, Ioana Bardis, Laura-Denisa Dragu, Lilia Matei, Ioana-Madalina Pitica, Denisa Ficai, Irina Fierascu, Radu Claudiu Fierascu, Ovidiu Cristian Oprea, Anton Ficai, Coralia Bleotu; 13 May 2023, Iași , Romania.

7.3.2. **Best paper award** received at International Scientific Conference "Applications of Chemistry in Nanosciences and Biomaterials Engineering", for the work entitled **"Mesoporous systems loaded with polyphenols for treatment of dysbiosis", Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Oprea, Anton Ficai, 25-26 June 2021, Bucharest, Romania.

7.3.3. **Session award** received at International Symposium "Priorities of chemistry for a sustainable development" PRIOCHEM XVII, for the work entitled **"Mesoporous silica systems loaded with polyphenols", Gabriela Petrișor**, Ludmila Motelica, Roxana Trusca, Vladimir Lucian Ene, Denisa Ficai, Ovidiu Oprea, Georgeta Voicu, Anton Ficai, 27-29 October 2021, Bucharest, Romania.

### 7.4 Patent application

**Gabriela Petrișor**, Ludmila Motelica, Ioana Bardis, Laura-Denisa Dragu, Lilia MATEI, Ioana-Madalina Pitica, Denisa Ficai, Irina Fierascu, Radu Claudiu Fierasacu, Ovidiu Cristian Oprea, Anton Ficai, Coralia Bleotu, **"Sisteme cu eliberare controlată pentru menținerea echilibrului microbiotei gastrointestinale și îmbunătățirea sănătății și procedeu de obținere a acestora"**, Nr. OSIM: A/00649/18.10.2022.

### 7.5 Other activities

Participation at the **School of Science Interdisciplinary Summer Course Program** (iSCOPe) organized by the Technical University of Dresden in Dresden, Germany, September 10-18, 2022.

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