UNIVERSITY **POLITEHNICA** OF BUCHAREST
Faculty of Applied Chemistry and Materials Science
Department of Bioresources and Polymer Science

Phd THESIS SUMMARY

HYBRID MATERIALS BASED ON POLYMERS AND POROUS CLAY HETEROSTRUCTURES

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Introduction

The development of new types of hybrid materials is one of the most innovative scientific discoveries that has led to significant developments in the field of nanotechnology. Hybrid materials are materials with unique properties, which include components characterized by different properties, which by contact lead to a synergistic effect [1-4].

Controlled release systems (DDS) of active substances are an important branch of the biomedical field. Thus, depending on the site of action of the active substance, the dose to be administered, the concentration of the active substance and the rate of release of the medicinal product, a release system must be designed to meet all of these requirements. Depending on the desired application, DDS can be modified to adjust the release profiles of the active substance, maintain a controlled release of the active substances, minimize the adverse effects of the active substance and improve the bioavailability of medicines. An "ideal" system used in the release of active substances must have the following properties (be biocompatible, be inert, reduce the toxicity of active substances, increase the encapsulation efficiency of various active substances, adjust the release profiles of active substances) [71, 72, 73, 74]. Hybrid materials based on polymers and inorganic components such as clays, used in DDS have important properties such as: biocompatibility, high ability to encapsulate various active substances, the ability to regulate the release profiles of active substances, improve the rheological properties of the organic component. These hybrid organic-inorganic systems are much more versatile than traditional materials used in DDS and have the ability to regulate the release profiles of active substances [81-86].

In conclusion, the development of new hybrid materials (organic-inorganic type) used as DDS, is a field of research with a significant impact on biomedical applications. The synthesis of materials with different functionalities and biological activities makes DDS have an improved encapsulation capacity, adjust the release profiles of active substances, reduce the toxicity of active substances and minimize the adverse effects of drugs on the body.

ORIGINALITY AND OBJECTIVES OF THE Phd. THESIS

The Phd. thesis, Hybrid materials based on polymers and porous clays heterostructures, aims to make an important original contribution to the development of hybrid materials. The aim of this Phd. thesis is to synthesize new inorganic materials such as porous clays heterostructures (PCHs), to investigate PCHs as hosts for encapsulating active substances and to obtain hybrid systems based on PCHs and polymers, with properties that direct these materials to the biomedical field. To this end, the Phd. thesis, through the research studies carried out, brings an original contribution in the field of systems with controlled release of antitumor active substances.

The objectives that were the basis of the originality of the experimental study of this Phd. thesis are the following:

- Advanced synthesis and characterization of new types of porous inorganic materials such as porous clays heterostructures (PCHs).
- Study of the influence of the reaction parameters (the amount of surfactant, the degree of hydration of the modified montmorillonite, the reaction time, the pH value of the reaction medium, the type of co-surfactant) on the synthesis and properties of PCHs
- Synthesis and characterization of new materials such as PCHs obtained using new types of co-surfactant, two polyetheramines (surfonamine B100 and surfonamine B200)

●Functionalization of PCHs with various organic coupling agents (3-aminopropyltriethoxysilane (APTES) and 3-glycidoxypropyl-trimethoxysilane (GPTMS)) in order to demonstrate the properties of PCHs that can be modified.

● Investigated PCHs as hosts for encapsulating antitumor active substances (5-Fluorouracil-5-FU and Methotrexate-MTX).

● Establishing the optimal parameters for encapsulation of active substances in PCHs by studying the influence of the parameters of the 5-FU encapsulation process in PCHs (influence of the pH of the encapsulation medium, influence of the encapsulation time, influence of the temperature of the encapsulation medium).

● Tested the encapsulation capacity of Methotrexate (MTX) in PCHs and studied the influence of the molar ratio between reactants on the properties of porous clays heterostructures used as encapsulating agent for MTX.

● Synthesis and characterization of new types of hybrid materials such as films based on natural / synthetic polymer and PCHs. Obtaining hybrid materials such as sodium alginate-PCHs and obtaining hybrid materials such as polyvinyl alcohol and PCHs.

● Synthesis and characterization of hybrid materials such as sodium alginate beads and PCHs with applications in DDS, intended for encapsulation of 5-Fluorouracil. Study of the influence of PCH concentration on the encapsulation capacity of the hybrid system and on the release profiles of 5-FU in the hybrid system

♦ The first objective of this experimental study is the synthesis of new types of PCHs varying the different reaction parameters (the amount of surfactant, the degree of hydration of the modified MMT, the reaction time, the pH value of the reaction medium and the type of co- surfactant).

The originality of this experimental study was highlighted by the development of a protocol for the synthesis of PCHs aimed at modifying the reaction parameters in order to obtain PCHs with tunable textural properties aimed at obtaining new systems with controlled release of active substances. The main novelty of this study is the introduction of new types of co-surfactants in the synthesis of PCHs. For the first time in the literature, the influence of two polyetheramines used as co-surfactant (polyetheramine B100 and polyetheramine B200) on the properties of PCHs compared to a classical amine (eg. dodecylamine) used in the synthesis of PCHs has been studied. Various modern methods of characterization have been used to demonstrate all the changes in the synthesis of new types of PCHs and to study the influence of reaction parameters. By studying the textural parameters of the porous clay heterostructures obtained under different reaction conditions, it can be confirmed that the introduction of new types of co-surfactants has a significant influence on the textural properties of the final materials. The introduction of new types of co-surfactants (polyetheramines: B100 and B200) has shown that the type of co-surfactant plays a key role in the synthesis of PCHs. Thus, PCHs with different structures, tunable textural properties and pores of different shapes and sizes were obtained.

In the case of PCHs synthesized with a classical co-surfactant (DDA), a material with a partially exfoliated structure was obtained in contrast to PCHs synthesized with polyetheramines B100 and B200 where PCHs with a predominantly exfoliated structure were obtained. These results were confirmed by XRD and TEM analyzes. BET analysis first confirmed the conversion of MMT to PCHs and also demonstrated the influence of co-surfactant type on the textural properties of PCHs obtained. After removal of the organic fractions from the precursors of PCHs, porous materials with tunable textural properties were obtained. The use of B100 in the synthesis of PCHs favors the formation of a PCHs characterized by a high porosity (Vt = 1.01 cm3 / g)

compared to PCH-DDA (Vt = 0.85 cm3 / g) and PCH-B200 (Vt = 0.59cm3 / g). Also, PCHs using different co-surfactants have different specific surfaces (SBET-PCH-DDA = 655m2 / g, SBET-PCH-B100 = 420m2 / g, SBET-PCH-B200 = 512m2 / g)). In conclusion, the study of the textural parameters of PCHs demonstrated the importance of the type of co-surfactant used in the synthesis of PCHs. Thus, PCHs with different porous structures and pores of different shapes and sizes are obtained. This objective of the Phd. thesis brings valuable original contributions to the field of porous inorganic materials by establishing each optimal reaction parameter.

♦ The second important objective of the experimental study of the Phd. thesis is the functionalization of PCHs with organic compounds in order to modify the properties of PCHs

The second important objective of the Phd. thesis research study demonstrates the ability of PCHs to be functionalized with amino and epoxy groups (aminopropyltriethoxysilane (APTES), 3-glycidoxypropyl-trimethoxysilane (GPTMS)). The modification of PCHs has been highlighted by various modern analysis techniques and the results obtained have indicated that the properties of PCHs are influenced by the type of coupling agent used.

♦ The third important objective of the experimental study of the Phd. thesis is to investigate PCHs as hosts for encapsulating antitumor drugs.

In this experimental study, the originality of the Phd. thesis consists in the investigation of PCHs as hosts for encapsulation of antitumor active substances (5-Fluorouracil-5-FU and Methotrexate-MTX). For the first time in the literature, PCHs have been studied for their ability to encapsulate active substances. This research proposes to establish the optimal parameters for encapsulation of the active substances (5-FU and MTX) in PCHs. In case of 5-FU encapsulation in PCHs, the optimal reaction parameters were investigated (the influence of soaking parameters(time, temperature and pH) on drug encapsulation). All the results of the research study showed that the optimal parameters for encapsulating 5-FU in PCHs are: 20 0C, 30 minutes, using a reaction medium with a pH value = 11. PCHs have also been proposed as systems for encapsulating MTX. Two types of PCHs (different molar ratios) were synthesized and proposed as hosts for MTX encapsulation. The results of the textural parameters showed that MTX completely occupies micro-pores and part of the meso-pores and also confirms the presence of MTX on the surface of PCHs, a fact confirmed by the decrease of the specific surface of the clay loaded with MTX. The results of the UV-VIS analysis demonstrate that PCHs loaded with MTX (EE = 97% - 98%) have a significantly higher encapsulation efficiency than MMT loaded with MTX (EE = 45%). All the results obtained in this chapter suggested that PCHs can be successfully used as hosts for the encapsulation of antitumor active substances, thus making valuable original contributions to the field of controlled release systems.

♦ The fourth important objective of this Phd. thesis is the synthesis of hybrid materials of the organic-inorganic type (polymer-clay).

Within this objective, the element of originality is the introduction of PCHs in the synthesis of new hybrid materials based on natural polymer (sodium alginate) and synthetic polymer (polyvinyl alcohol) and PCHs - film type. For the first time in the literature, PCHs-type clay has been used as an inorganic component in a hybrid polymer-clay system. The influence of PCHs on the properties of hybrid films has been investigated using advanced characterization techniques. The experimental study has shown that the introduction of PCHs into a polymer matrix has a strong influence on the properties of hybrid materials. The results of thermogravimetric analysis (TGA) demonstrate that the presence of PCHs in the polymer matrix improves the thermal

stability of the hybrid film. Also, the results of the mechanical analysis in dynamic regime (DMA) indicate that the presence of PCHs in the system leads to an increase in the storage modulus.

Hybrid materials based on sodium alginate and pearl-like PCHs were also synthesized in this experimental study. The originality of this hybrid material is given by the proposed hybrid system (AS-PCHs) as a host for 5-Fluorouracil encapsulation. For the first time in the literature, a hybrid system based on sodium alginate and PCHs has been proposed as a host for 5-FU encapsulation. The results obtained demonstrated the high encapsulation capacity of 5-FU in hybrid materials (sodium alginate-PCHs) compared to simple sodium alginate. Also, within this objective, the influence of the concentration of PCHs in the system was studied. The results of the UV-VIS analysis showed that the encapsulation efficiency of 5-FU in the hybrid material is strongly influenced by the presence of PCHs in the system. Thus, samples containing PCHs show a much higher encapsulation efficiency than neat alginate. Also, the release profiles of the hybrid materials based on sodium alginate and PCHs are influenced by the presence of PCHs in the polymer matrix. Dependence of the amount of drug released on the concentration of PCHs used in the hybrid system has been demonstrated. Also, the presence of clay in the polymer matrix has the role of ajusting the release profiles of 5-FU by reducing the "burst release" effect present in the case of neat sodium alginate.

Using the modern investigative techniques, valuable information is obtained regarding the chemical structure of the material, the textural parameters, the morphology of the materials, the thermal stability, the capacity of the materials to encapsulate active substances and to control the release of active substances.

To demonstrate the objectives of this Phd. thesis we used the following analysis techniques: Fourier Transform Infrared Spectrometry (FT-IR), Thermogravimetric Analysis (TGA), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Diffraction X-ray (XRD), X-ray Photoelectron Spectrometry (XPS), Dynamic Mechanical Analysis (DMA), Textural Properties Analysis - BET Analysis, Ultraviolet-Visible Spectrophotometry (UV-VIS), Zeta Potential, Elemental Analysis

The Phd. thesis, Hybrid materials based on polymers and porous clay heterostructures, is structured in two main parts: **PART I. THE CURRENT STATE OF RESEARCH IN THE FIELD** and **PART II. ORIGINAL CONTRIBUTIONS**

The first part of the Phd. thesis (Chapter 1. Hybrid Materials) presents theoretical information about hybrid materials (polymer-clay type). Studies of data from the specialty literature on the synthesis of hybrid materials, their properties and applications in the field of controlled release of active substances have been performed. The individual components of the polymer-clay hybrid material were also studied, highlighting the importance of the properties of the individual components but also the properties of the hybrid material intended for encapsulation and release of active substances. Also in the critical study of the literature data, extensive research was carried out in the field of porous clay heterostructures (PCHs) in which the ways of obtaining these types of inorganic materials and the properties of these clays are concretely presented. At the same time, the factors that influence the synthesis, properties and applications of porous clay heterostructures are pointed out.

The second part of the Phd. thesis, dedicated to the original contribution, is structured in several main chapters: **Chapter 2.** Originality and objectives of the Phd. thesis, **Chapter 3.** Characterization techniques, **Chapter 4.** Synthesis of porous clay heterostructures (PCHs),

Chapter 5. Functionalization of PCHs with silanizing agents, **Chapter 6.** Investigation of PCHs as hosts for encapsulation of active substances, **Chapter 7.** Obtaining hybrid polymer-PCHs, **Chapter 8.** Obtaining hybrid polymer-based materials and PCHs with applications in field of controlled release systems of active substances, **Chapter 9.** General conclusions

Keywords: hybrid materials, polymer, clay, porous clay heterostructures, active substances

Chapter 4.
SYNTHESIS OF POROUS CLAY HETEROSTRUCTURES (PCHs)

4.1. Objectives of the research study

The objective of this chapter is the synthesis of porous inorganic materials such as porous clay heterostructures (PCHs) starting from a layered silicate such as montmorillonite (MMT). This main objective aims at the synthesis of PCHs with tunable textural properties (specific surface area, pore distribution and size), with applications in the field of controlled drug delivery systems. In order to demonstrate the importance of this objective of the research study, the most important reaction parameters that can influence the synthesis of these materials (PCHs) were studied: the amount of surfactant, the degree of hydration of the modified MMT, the reaction time, the pH value reaction medium and type of co-surfactant.

4.3. Synthesis protocol of PCHs

♦ HDTMA intercalation between montmorillonite layers

Organophilization of MMT was performed by a cation exchange reaction. The presence of HDTMA-Br leads to a cation exchange reaction between Na cations in clay galleries and organic cations.

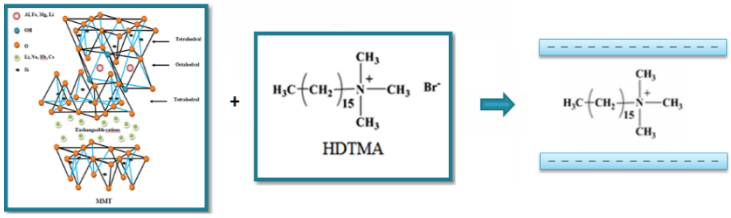


Fig.4.2. MMT organophilization

♦ Precursor silica (TEOS) polymerization between montmorillonite layers, in the presence of HDTMA as surfactant and DDA as cosurfactant

The second step was focused on the synthesis of PCHs precursors using organically modified MMT that was treated with a precise amount of neutral amine (DDA) and silica precursor (TEOS) in the presence of water. The molar ratio used in the PCHs synthesis was 1:20:120 (modified MMT:DDA:TEOS)

♦ Thermal treatment of PCH to remove the organic templates. The thermal treatment of PCHs precursors involves calcination at 650 ◦C for 6 h in air in order to remove the organic templates.

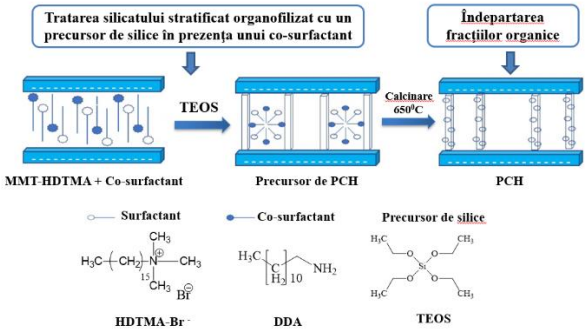


Fig.4.4. Synthesis of PCHs

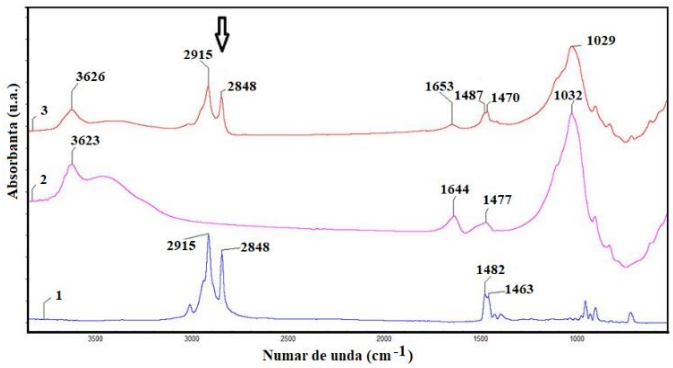
Using this synthesis strategy, new types of PCHs were obtained and the following parameters that can influence the properties of PCHs were also studied: the amount of surfactant, the degree of hydration of the modified MMT, the reaction time, the pH value of the reaction medium and the type of co-surfactant.

4.4. Results and discussion

4.4.1. Organophilization of MMT

4.4.1.1. Fourier Transform Infrared Spectrometry (FT-IR

The organophilization of MMT was first confirmed by FT-IR analysis which is a technique used to study the interactions between layered silicates with different modifying agents (surfactants) or to evaluate the molecular conformation of the modifying agent in the clay gallery.

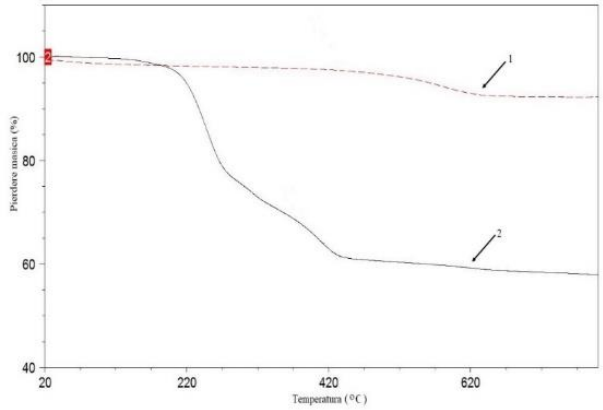


The organophilization process of MMT with HDTMA was confirmed by the appearance of new peaks at 2915 and 2848 cm^{-1} (attributed to antisymmetric and symmetric C-H stretching vibrations from methylene groups and a new peak at 1487 cm^{-1} assigned to C-H bending vibrations). These peaks are also identified in the spectrum of the surfactant (HDTMA) (Fig.4.5)

Fig.4.5. FT-IR spectra**:** 1-HDTMA, 2-MMT, 3-MMT-HDTMA

4.4.1.2. TGA tests

The second analysis technique used to demonstrate the organophilization of montmorillonite was thermogravimetric analysis. As can be seen in Fig. 4.6, the TG profiles of the MMT show two main mass losses: he desorption of physico-sorbed water on the clay external surface and a second step at higher temperature (>500 ^{0}C) that corresponds to the thermal dehydroxylation process of internal surface silanol groups.



Compared to simple MMT, organophilized MMT (MMT-HDTMA) has a different TG profile. It is observed that the TG curve profile of MMT-HDTMA shows an additional weight loss in the temperature range (200-500 0C), attributed to the degradation of the organic compound intercalated between the MMT layers. Increased weight loss from 7% (for MMT) to 42% (for MMT-HDTMA) confirms the presence of organic fraction within MMT.

Fig.4.6. TGA curves: 1-MMT si 2-MMT-HDTMA

4.4.1.3. Difracţia de raze X (XRD)

The third method of analysis used to study the modification of montmorillonite is the XRD technique, which provides valuable information about the intercalation of HDTMA into MMT and the possible arrangements of organic compounds (surfactant, co-surfactants) in the clay gallery. The starting clay (MMT-Na) involved in the synthesis of PCHs exhibits a crystalline structure characterized by a basal distance (d001) of 12.5 Å (Figs. 6-a). Small amounts of feldspar and quartz were detected. After HDTMA intercalation, the basal distance is increased to 3.98 nm (Fig.4.7).

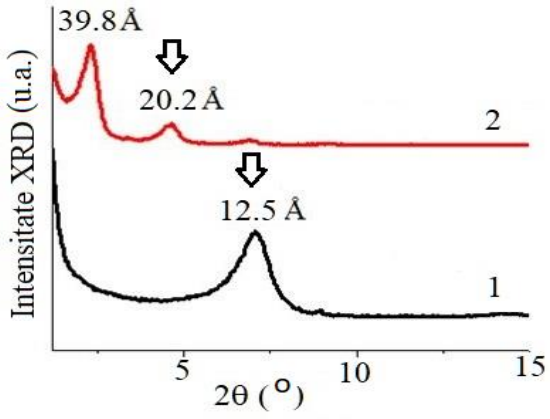


Fig.4.7. X-ray difractograms: 1-MMT-Na şi 2-MMT-HDTMA

4.4.1.4. Microscopie electronică de transmisie (TEM)

TEM analysis was also used to demonstrate the modification of MMT with HDTMA. As can be seen from the TEM micrographs, the MMT has a crystalline structure with parallel oriented layers characterized by a low basal distance (Fig.4.8-a)

The treatment of MMT with HDTMA led to an increase of basal distance with a maintaining of the layered structure (Fig.4.8 b). The TEM results are in agreement with the XRD results.

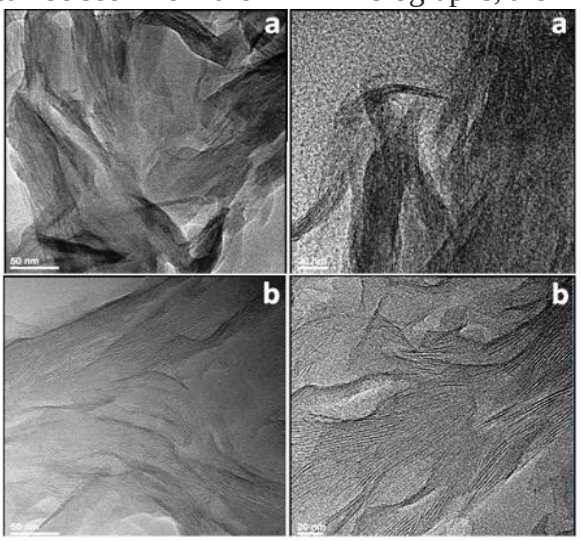


Fig.4.8. HRTEM images: a-MMT-Na, b-MMT-HDTMA

4.4.2. Confirmation of obtaining PCHs (After calcination)

4.4.2.1. Fourier Transform Infrared Spectrometry (FT-IR)

The first characterization technique that confirmed the structure of PCHs was FT-IR analysis, a method that confirmed the formation of the structure of PCHs by the presence of peaks characteristic of amorphous silica.

Table 4.1. Assignment of the characteristic peaks of PCHs

Wavenumber (cm^{-1})	Assignment of the characteristic peaks
3738	Stretching vibration of the OH group from Si–OH
3441	Stretching vibration of the OH group of water molecules adsorbed on PCH
1631	Bending vibration of adsorbed water molecules
1083	Stretching vibrations of three dimensional silica network
807	Symmetric stretching vibrations of Si–O–Si or Si–O–Al
575	Bending vibration of Al-O
458	Bending vibration of Si-O

4.4.2.2. XRD characterization

XRD analysis was also used to demonstrate the structure of the obtained PCHs. As can be seen, Fig.4.10 shows the diffractograms recorded for MMT and PCHs. It is observed that the starting clay (Nanofil 116) consists mainly of MMT and small amounts of feldspar and quartz. For PCHs, the diffraction peak (001) attributed to the ordering of the clay layers was detected at lower values of the angle 2θ (6.90), this indicates an increase in interbasal distance (d001) by 1.9 nm from MMT. This increase has been attributed to the pillaring process. In addition, the intensity of this basal reflection was low, and we can therefore conclude that the structure of this material is mainly exfoliated. The diffraction peaks, characteristic (0 2 0, 110, 2 0 0, 0 6 0) of the stratified clay were detected in the PCHs diffractogram, also a significant decrease of these intensities was registered, which is due to the formation of pillars in the interlayer space of the MMT. The broadband in the range 15-23^0 is attributed to the amorphous silica that constitues pore walls. This type of stratified structure was confirmed by TEM analysis

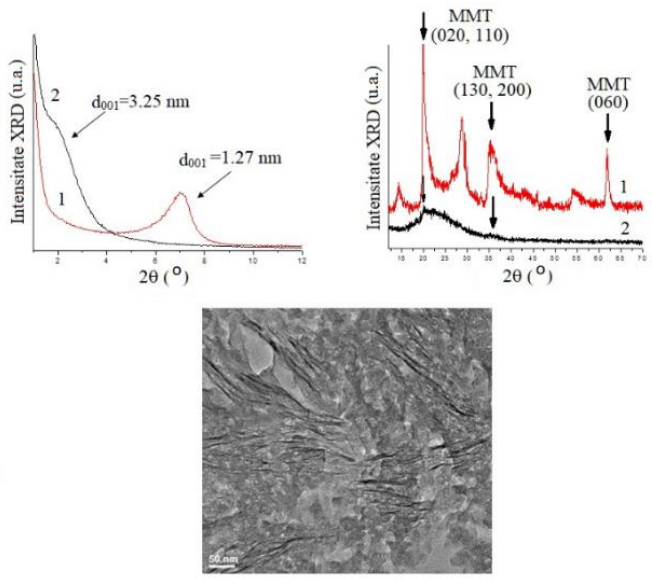


Fig.4.10. X-ray diffractograms and TEM image of PCHs

4.4.3. Factors that influence the synthesis of PCHs

4.4.3.1. The influence of the amount of surfactant used for MMT organophilization

According to synthesis procedure described in subchapter 4.3. Different amounts of HDTMA-Br (0.25g; 0.5g; 1g, 2g, 3g, 5g, 6g) were used in order to identify the optimal amount of modifying agent.

♦ **Fourier Transform Infrared Spectrometry (FT-IR)**

Modified clay (MMT-HDTMA) with different amounts of HDTMA was primarily characterized by FT-IR analysis to identify possible interactions between the inorganic component (MMT) and the organic component (HDTMA) during the cation exchange reaction.

The FT-IR, MMT-HDTMA spectra show the following characteristic peaks: 3017 cm-1, 2917 cm-1, 2849 cm-1 and 721 cm-1. These peaks were assigned as follows: 3017 cm-1 corresponding to C-H stretching vibrations involved in CH3 -N; 2917 cm-1 and 2849 cm-1 correspond to C-H asymmetric and symmetric vibrations and 721 cm-1 was assigned to C-H bending vibration. The appearance of peaks at 3017 and 721 cm-1 in the FTIR spectra of modified MMT was found to be dependent on the HDTMA concentration used. These two peaks were detected only for the montmorillonites treated with higher HDTMA amounts (1-6 g). The FTIR analysis results highlighted an increase of peak intensity corresponding to the C-H bending vibrations for modified montmorillonite with high HDTMA amounts. The changing of this peak position (from 1482 to1470 cm-1) indicates the presence of additional interactions (like hydrophobic interactions) in case of montmorillonites modified with different HDTMA concentration.

♦ **X-ray diffraction (XRD)**

The influence of the amount of HDTMA was also highlighted by XRD analysis (Table 3). As can be seen from Table 4.2, the amount of HDTMA used in the organophilization of MMT has a significant influence on the basal distance of MMT. In the case of MMT modified with a small amount of HDTMA (0.25g and 0.5g), the basal distance of the clay increases by 1 Å.

Table.4.2. Results of XRD analysis for modified montmorillonite with different amounts of HDTMA

Samples	**Basal distance d_{001}(Å)**
MMT-Na	12.5
MMT-HDTMA-0.25g	13.3
MMT-HDTMA-0.5g	13.6
MMT-HDTMA-1g	**38.1; 19.1**; 12.7
MMT-HDTMA-2g	**38.1; 19.1**; 12.6
MMT-HDTMA-3g	**37.9; 19.1**; 12.6
MMT-HDTMA-4g	**38.0**; 18.9; 12.8
MMT-HDTMA-5g	**38.15; 19.1**; 12.8
MMT-HDTMA-6g	**39.8; 20.2**; 12.9

These results are consistent with the findings of the FT-IR analysis. The presence of a large amount of HDTMA causes a significant increase of basal distance. After evaluating the results of the FT-IR and XRD analyzes, it can be concluded that the modified MMT with a large amount of HDTMA (6 g) can be used successfully in the PCHs synthesis.

4.4.3.2. The influence of MMT-HDTMA hydration degree

In this study we started with a quantity of 0.5 g of MMT modified with 6 g HDTMA which was hydrated with different amounts of water (200µl, 400 µl, 1 ml, 2 ml, 5 ml).

♦ **Fourier Transform Infrared Spectrometry (FT-IR)**

Significant changes were identified in the FT-IR spectra for both PCHs precursors (before calcination) and PCHs (after calcination). The formation of the three-dimensional network

was highlighted by FT-IR analysis by changing the position of the peak from 1067 to 1079 cm -1 for the precursors of PCHs and the peak from 1067 to 1084 cm -1 for PCHs (after calcination).

♦ **X-ray diffraction (XRD)**

The results of the XRD analysis also indicate that the synthesis of PCHs is influenced by the volume of water in the system.

Table 4.3. XRD results of precursors of PCHs (before calcination) and PCHs (after calcination)

Influence of hydration degree		**Influence of reaction time**		**Influence of pH value**	
Sample	**Basal distance (Å)**	**Sample**	**Basal distance (Å)**	**Sample**	**Basal distance (Å)**
PCH-1a-n	27.6	PCH-1h-n	34	PCH-pH1-n	38.0
PCH-1a-c	30.3	PCH-1h-c	35	PCH-pH1-c	35.3
PCH-2a-n	28.8	PCH-3h-n	**36**	PCH-pH2-n	38.3
PCH-2a-c	31.6	PCH-3h-c	**37**	PCH-pH2-c	35.2
PCH-3a-n	29.9	PCH-5h-n	36	PCH-pH3-n	37.5
PCH-3a-c	31.6	PCH-5h-c	35	PCH-pH3-c	34.7
PCH-4a-n	32.5	PCH-22h-n	35	PCH-pH7-n	36.5
PCH-4a-c	33.1	PCH-22h-c	36	PCH-pH7-c	34.5
PCH-5a-n	32.6	PCH-67h-n	36	PCH-pH8-n	**38.4**
PCH-5a-c	**34.8**	PCH-67h-c	36	PCH-pH8-c	36.6
-	-	-	-	PCH-pH 9-n	35.9
-	-	-	-	PCH-pH9-c	35.6

This analysis was performed for PCH precursors and for PCHs after calcination. The results of the XRD analysis are presented in Table 4.3. From the XRD results presented in Table 4.3 it can be seen that the basal distance of the modified MMT with HDTMA (MMT-HDTMA) is influenced by the degree of hydration. A larger volume of water in the system favors the hydrolysis of TEOS (silica precursor) and also leads to the formation of the three-dimensional network between the silicate layers. Using this synthesis strategy, a PCHs with a basal distance of 34.8 Å was obtained. From the results of the XRD analysis it can be concluded that the ratio between water and TEOS significantly influences the basal distance of PCHs precursors. An optimal volume of water used in the synthesis of PCHs is of significant importance in the complete hydrolysis of TEOS.

4.4.3.3. The influence of reaction times

The synthesis of PCHs was performed according to the synthesis procedure described in subchapter 4.3. where we varied the reaction time (1h, 3h, 5h, 22h, 67h).

♦ Fourier Transform Infrared Spectrometry (FT-IR)

The results of the FT-IR analysis showed that the reaction time did not have a significant influence on the synthesis of PCHs. The FT-IR spectra of the PCH precursors showed the same peaks at similar wavelengths regardless of the reaction time. Similar results were obtained for PCHs (after calcination).

♦ X-ray diffraction (XRD)

The results of the XRD analysis showed that silica formation between the modified MMT layers occurred in the first 3 hours. PCHs precursors synthesized at the 3-hour reaction time showed high basal distance values (36 Å) (Table 4.3). After this reaction time the basal distance of the PCHs remained constant.

4.4.3.4. The influence of the pH value of the reaction medium

The synthesis steps of PCHs were described in subchapter 4.3. with the mention that different pH values of the reaction medium were used (pH = 1, 2, 3, 4, 7, 8, 9).

♦ X-ray diffraction (XRD)

As seen in table 4.3, the synthesis of PCHs was also influenced by the pH of the reaction medium. The results of the XRD analysis showed that the highest basal distance was recorded for the synthesized samples at pH = 8 (precursor of PCHs (38.4 Å and calcined PCH 36.6 Å)). These results lead to the conclusion that the interactions between surfactant / co-surfactant and silica precursor, hydrolysis of TEOS and the rate of polycondensation reaction are influenced by the pH value of the reaction medium.

4.4.3.5. The influence of co-surfactant type

In this study the same synthesis protocol mentioned in subchapter 4.3 was used, with the mention that in addition to the classic co-surfactant (DDA), two new types of co-surfactant were used, two polyether monoamines (different structures and different values of hydrophilic-lipophilic balance (HLB): surfonamine B100 and surfonamine B200. The molar ratio between the reactants was 1:20:20 (MMT-HDTMA: Amine: TEOS). In the final stage, a heat treatment (650 0C with a heating rate of 10C / min) was performed in order to remove the organic phase.

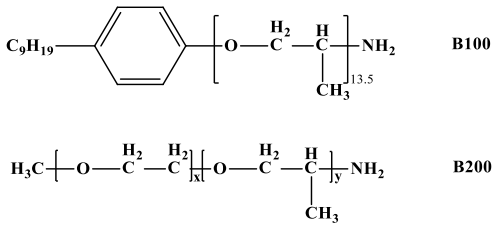


Fig.4.16. Chemical structures of surfonamine B100 and surfonamine B200

Highlighting the influence of co-surfactant type on the properties of PCHs

♦ FT-IR spectrometry

First, FT-IR spectrometry was used to investigate changes that may occur with the use of different co-surfactants. In the FTIR spectra of PCH precursors, several peaks assigned to the antisymmetric and symmetric C-H stretching vibrations from methylene groups (2930-2856 cm^{-1}), C-H bending vibrations (1458-1470 cm^{-1}) and Si-O stretching vibrations (1072 cm^{-1} for DDA, 1110 cm^{-1} for B200 and 1100 cm^{-1} for B100) were detected. In the case of PCH precursors synthesized using polyeteramines as co-surfactants, some additional peaks were detected. Thus,

the new peak appeared at 2971/2973 cm^{-1} was attributed to C-H stretching vibrations from methyl groups and the aromatic ring vibrations of PCH-B100 were confirmed by the presence of peak at 1510 cm^{-1}. In the case of calcined samples (PCH-DDA, PCH-B100 and PCH-B200), FT-IR results confirm that the calcination process was complete. Therefore, all the peaks attributed to the vibrations of the organic fractions have disappeared, indicating that the calcination process was complete and the organic fractions were removed. FT-IR analyzes also confirmed the presence of isolated terminal silanol groups.

♦ **X-ray diffraction (XRD)**

The XRD results confirm the influence of the co-surfactant type on the precursor structures of PCHs (PCH-DDA-n, PCH-B100-n and PCH-B200-n) and PCHs (PCH-DDA, PCH-B100 and PCH-B200) (Fig. 18- a, b). Compared to the structure of MMT modified with HDTMA, the XRD diffractograms of the precursors (PCH-DDA-n, PCH-B100-n) show a wide diffraction peak attributed to the basal distance. In the case of PCH-DDA-n the basal distance recorded a value of 41.4 Å, while PCH-B100-n exhibits a lower value 34.9 Å. For the PCH-B200-n precursor, XRD analysis indicates the formation of an exfoliated structure due to the absence of the peak attributed to the basal distance. For PCH-B200 and PCH-B100, the peak assigned to the basal distance was not detected and therefore these materials can be included in the class of materials with exfoliated structure. XRD results were also confirmed by TEM analysis.

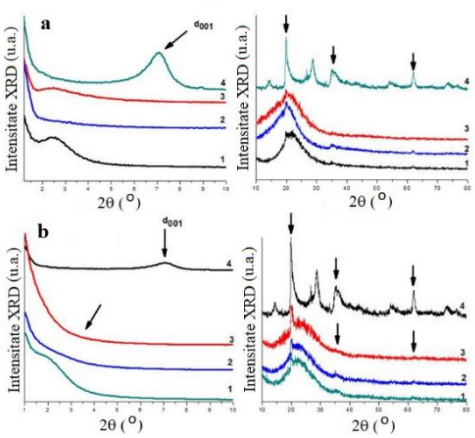


Fig.4.18. X-ray diffractograms of: **a)** PCHs precursors: 1- PCH-DDA-n, 2- PCH-B200-n, 3-PCH-B100-n şi **b)** PCHs: 1-PCH-DDA, 2-PCH-B200, 3-PCH-B100 and 4-MMT

♦ **TEM Analysis**

TEM analysis was also used to investigate the influence of co-surfactant type on the PCHs structure. In the case of the PCH-DDA sample, TEM images indicated the presence of some few stacked layers tactoids with parallel orientation that could be responsible for the small peak shoulder that appeared in XRD analysis.

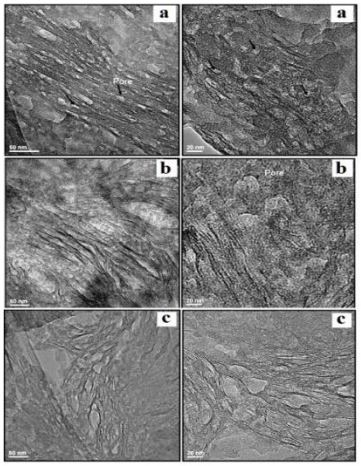


Fig.4.19. HRTEM images: a-PCH-DDA, b-PCH-B100, c-PCH-B200.

For samples PCH-B100 and PCH-B200, the TEM analysis points out that the samples show a predominantly exfoliated structure (Fig. 4.19-c,d). In addition, TEM analysis was used to highlight the presence of pore structure PCHs. PCH samples are characterized by porous structures with pores of different shapes and sizes. PCHs synthesized using surfonamines B100 (PCH-B100) and B200 (PCH-B200) are characterized by porous structures with pores of different sizes and irregular shapes.

♦ **Textural parameters**

The textural properties of MMT and PCHs (PCH-DDA, PCH-B100, PCH-B200) were determined primarily to demonstrate the conversion of MMT to PCHs and also to demonstrate the importance of the type of co-surfactant on the textural properties of PCHs.

Tabel 4.4. Textural parameters

Sample	$S_{BET}(m^2/g)$	$V_t\,(cm^3/g)$
MMT	50	0.07
PCH-DDA	655	0.85
PCH-B100	420	1.01
PCH-B200	512	0.59

Compared to MMT, all PCHs samples exhibit a high specific surface area value (S_{BET} between 420 and 655 m2 / g) and a high increase of Vt (> 0.59 cm3 / g). These changes have been attributed to the formation of PCHs. The results of the analysis of the textural parameters suggest that the type of co-surfactant influences the textural parameters of the PCHs.

The use of surfonamine B100 in the synthesis of PCHs favors the formation of PCHs characterized by a high porosity (Vt = 1.01 cm3 / g) compared to PCH-DDA (Vt = 0.85 cm3 / g) and PCH-B200 (Vt = 0.59 cm3 / g). The synthesis of PCHs using polyetheramine B200 as co-surfactant was characterized by a lower surface area value (S_{BET} = 512 m^2 / g) lower than PCH-DDA (S_{BET} = 655 m^2 / g) and higher compared to PCH-B100 (S_{BET} = 420 m^2 / g). PCH-B200 has a lower porosity than the other two types of PCHs. The nitrogen adsorption-desorption isotherms proved that the type of amine used as co-template strongly affects the PCH porosity, indicating that the co-surfactants were involved in micelle formation and therefore the pore size was influenced by micellar size and volume

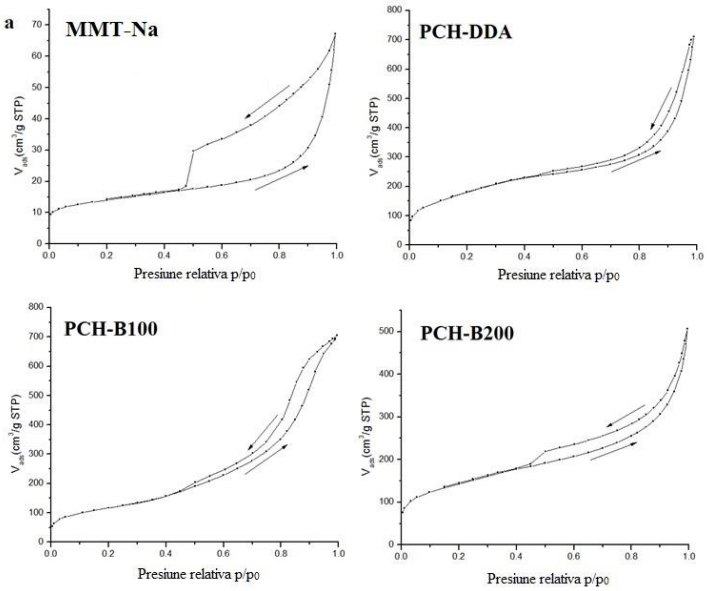


Fig.4.20 Nitrogen adsorption-desorption isotherms

Chapter 5.
FUNCTIONALIZATION OF POROUS CLAY HETEROSTRUCTURES WITH SILANE COUPLING AGENTS

5.1. Objectives of the experimental study

The main objective of this chapter is to treat inorganic materials such as PCHs with various organic coupling agents. This method is an attractive strategy to improve the physical and chemical properties of inorganic materials. In this chapter PCHs were modified with two coupling agents 3-aminopropyltriethoxysilane (APTES) and 3-glycidoxypropyl-trimethoxysilane (GPTMS).

5.3. Functionalization of PCHs with APTES and GPTMS

Functionalization of PCHs with amino and epoxy groups was accomplished by modifying the inorganic material with two coupling agents: APTES and GPTMS. The functionalization method used to modify the PCHs was of the post-synthesis type.

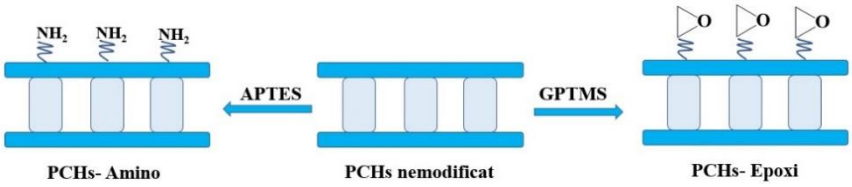


Fig.5.3. Functionalization of PCHs with APTES and GPTMS

5.4. Results and discussion

5.4.1. Characterization of modified PCHs

5.4.1.1. Fourier Transform Infrared Spectrometry (FT-IR)

The presence of coupling agents in PCHs was highlighted by the appearance of new peaks at 2927 cm -1 (APTES) and 2951 cm-1 (GPTMS), peaks attributed to the streaching vibrations of C-H from CH2 groups of the coupling agents.

5.4.1.2. Thermogravimetric analysis (TGA)

Thermogravimetrical analysis also confirmed the modification of PCHs. The TG curves of modified PCHs (Epoxy-PCH, Amine- PCH) samples show a different profile that included three degradation steps: (1) dehydration, due to the physically adsorbed water (20-200^0 C), (2) degradation of organic coupling agents (200-500 ^{0} C) and (3) dehydroxylation process of hydroxyl groups located between the tetrahedral sheets of MMT (500-800 ^{0} C).

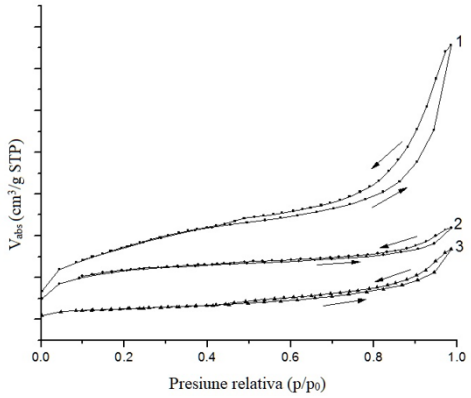
5.4.1.3. X-ray diffraction (XRD)

The results of the XRD analysis indicate that the structure of modified PCHs (PCH-epoxy, PCH-amino) is influenced by the functionalization reaction with different coupling agents. GPTMS-modified PCHs (PCH-epoxy) exhibit an intercalated structure demonstrated by the presence of the characteristic peak d001 shoulder that exists in the MMT structure compared to PCH-epoxy. In the case of clay modified with APTES (PCH-amino), the XRD diffractogram indicates an exfoliated structure, a structure confirmed by the absence of the d001 peak, a peak attributed to the basal distance.

5.4.1.4. Study of textural parameters

Textural properties of unmodified PCH and modified PCHs (Epoxy-PCH, Amine-PCH) were determined in order to point out the modification of PCHs with silane coupling agents (APTES and GPTMS). Figure 5 shows the nitrogen adsorption-desorption isotherms for

unmodified and modified PCHs. The BET results indicated that the modified samples are charaterized by lower values of specific surface area (S_{BET}=381- 91 m^2 /g) and total pore volume (Vt =0.2- 0.3 cm^3 /g) than unmodified PCH (S_{BET}= 628 m2 /g and V_t= 0.8 cm3 /g). According to these results it can be concluded that silane coupling agents are located inside the pores and also on the surface of PCHs.



Tabel 5.1. Proprietățile texturale ale PCH nemodificat si ale PCHs modificate (PCH-epoxi si PCHs-amino)

Proba	S_{BET} (m^2/g)	V_p (cm^3/g)
PCH nemodificat	628	0.8
PCH-epoxi	381	0.2
PCH-amino	91	0.3

Fig. 5.7. Nitrogen adsorption-desorption isotherms of: 1- PCH, 2-PCH-epoxi, 3-PCH-amino

Chapter 6.

INVESTIGATION OF PCHs AS HOSTS FOR ENCAPSULATION OF ACTIVE SUBSTANCES

6.1. Objectives of the experimental study

The main objective of this chapter is to investigate PCHs as hosts for encapsulation of antitumor active substances (5-Fluorouracil-5-FU and Methotrexate-MTX) and to establish the optimal parameters for encapsulation of antitumor active substances in PCHs.

6.2. The investigation of PCHs as Hosts for 5-Fluorouracil (5-FU) encapsulation

The purpose of this subchapter is to study PCHs as hosts for the encapsulation of 5-Fluorouracil (5-FU) and also to establish the optimal parameters for encapsulating 5-FU in PCHs. Thus, the following encapsulation parameters were studied: The influence of soaking parameters (time, temperature and pH value) on drug encapsulation

6.2.2. Synthesis protocol

To study the optimal 5-FU encapsulation parameters in PCHs was used the following synthesis protocol.

The influence of pH value on 5-fluorouracil encapsulation in PCHs was studied by solubilizing 10 mg of 5-FU in 10 ml of encapsulation medium (pH with different values (2, 3, 4, 5, 6, 7, 8 , 9, 10, 11)) and then 50 mg of PCHs were dispersed.

The influence of soaking time was studied by solubilizing 10 mg of 5-FU in 10 ml of encapsulation medium (pH 9 and pH 11) and then 50 mg of PCHs were dispersed. The mixture was maintained for 5, 10, 30, 60, 120, 180, 240, 360 minutes.

The same amounts of drug and PCHs were used to study the influence of temperature on the 5-FU encapsulation. In this case, the mixtures based PCH and drug dissolved in 10 ml of medium solution were stirred for 1 h at different temperature (20 ^{0}C, 40 ^{0}C and 60 ^{0}C).

All the samples were centrifuged and freeze dried at -50 ^{0}C.

6.2.3. The influence encapsulation parameters of 5-FU in PCHs

6.2.3.1. Influence of the pH value on 5-FU encapsulation within PCHs

♦ Zeta potential

The zeta potential of PCH was shifted from +3 mV (at pH 2) to -44 mV at a basic pH > 9. A significant variation of PCH zeta potential was observed in the 2–6 pH range, followed by a stabilization registered at pH value above 8. The value of negative zeta potential (-44 mV), in the basic pH value, implies that the PCH is well dispersed and stable against aggregation in the aqueous solution. The Zeta potential has shown that PCHs particles are stable in aqueous solutions by adjusting the pH value to a high value (> 10). The pH value of the contact medium can influence both the surface charge of PCHs, the stability of these clays and the solubility of the drug. Taking into account these aspects we can conclude that the optimal pH value for the contact medium is pH = 11.

♦ Fourier Transform Infrared Spectrometry (FT-IR)

The presence of 5-FU in PCHs was highlighted in the first stage using FT-IR spectrometry. The appearance of two peaks at 1689-1701 cm^{-1} (attributed to C = C stretching vibration) represents a confirmation of the presence of the drug in PCHs. In addition, the FTIR analysis highlighted a dependence of encapsulated drug concentration on the pH value of incubation solution. The peak assigned to C=C stretching vibrations showed a higher intensity in case of PCH-5- FU systems synthesized at high pH value (pH > 8). The peaks assigned to C-H asymmetric and symmetric stretching vibrations (2970, 2921 cm^{-1}) were detected for host–guest system synthesized at pH of 11. The results of the FT-IR analysis is in agreement with the results of the Zeta potential measurements - regarding the effect of high pH value on drug entrapment within PCH, due to the PCH surface activation and enhancement of drug solubility.

♦ Ultraviolet-Visible Spectrophotometry (UV-VIS)

UV-VIS analysis confirmed the results of the FT-IR analysis regarding to the influence of the pH value of the contact medium on the encapsulation of 5-FU in PCHs.

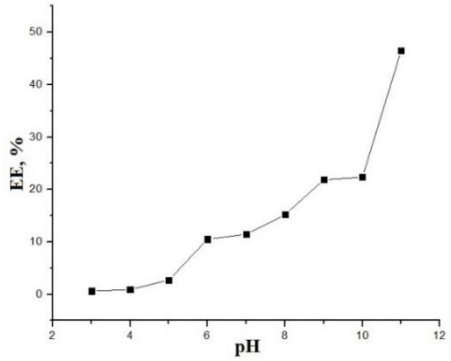


Fig.6.3. The encapsulation efficiency of 5-FU in PCHs at different pH values of the contact medium

The highest encapsulation efficiency (44%) was recorded for the PCH-5-FU-pH 11 sample. This behavior can be attributed to the synergistic effect of PCHs surface activation and higher 5-FU solubility in the base medium.

♦ Textural properties of PCHs

The results of the BET analysis confirmed the conversion of MMT to PCHs. Compared to MMT, PCHs show a high value of specific surface area (SBET = 734 m2 / g) and a substantial increase of Vt (0.71 cm^3 /g). These changes prove the formation of PCHs.

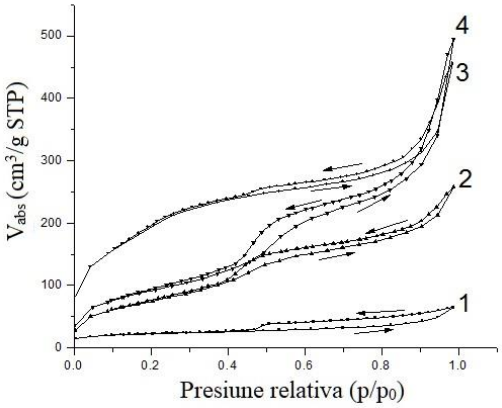


Fig.6.5. N_2 adsorption-desorption: 1-MMT, 2-PCH-5-FU-pH 9, 3-PCH-5-FU-pH 11, 4-PCH

Tabel 6.2. Textural parameters

Sample	S_{BET} (m^2/g)	V_t (cm^3/g)
MMT	80	0.10
PCH	734	0.71
PCH-5-FU-pH 9	334	0.54
PCH-5-FU-pH 11	279	0.40

S_{BET}: specific surface area, **V_t:** Total pore volume

After encapsulation of the drug in PCHs, a significant decrease in the values of the textural parameters (Vt and SBET) was recorded. This change in textural parameters confirmed that 5-FU was adsorbed on the surface of PCHs (grafted on the surface of PCHs) but also identified within the pores of PCHs (encapsulated in the pores of PCHs). The textural properties of 5-FU-loaded PCHs are according with the results of previous analyzes. The PCH-5-FU-pH-11 sample shows a significant decrease in textural parameters (specific surface area and total pore volume) which demonstrates that the drug is found in the pores of PCHs and also on the surface of PCHs. A high pH value of the contact medium influences the encapsulation capacity of PCHs. The results of the BET analysis demonstrate that PCHs can be used as hosts for 5-FU encapsulation.

6.2.3.2. The influence of soaking temperature on the 5-FU encapsulation in PCHs

♦ Fourier Transform Infrared Spectrometry (FT-IR)

FT-IR spectra proved that the temperature of the contact medium does not have a significant influence on the encapsulation of 5-FU in PCHs. Regardless of temperature value, in all cases, the peak assigned to C=C stretching vibrations (1691/1693/1695 cm^{-1}), from drug structure, was detected. The intensity of this peak was maintained constant in all cases, this result

being a qualitative proof that drug encapsulation efficiency does not depend on temperature of incubation solution.

♦ TGA tests

The results of the thermogravimetric analysis are accordance with the conclusions of the FT-IR analysis. TG profiles suggest that PCHs used as hosts show similar weight losses (7.3%), showing that an equal amount of drug was retained by PCH samples.

♦ Ultraviolet-Visible Spectrophotometry (UV-VIS)

The results of the UV-VIS analysis confirm the conclusions of the FT-IR and TGA analysis regarding the influence of temperature on the encapsulation efficiency of 5-FU in PCHs. Also, the results of the UV-VIS analysis indicate a dependence of the encapsulation efficiency of 5-FU in PCHs depending on the pH value (maximum encapsulation efficiency is recorded at a pH value of the contact medium pH = 11).

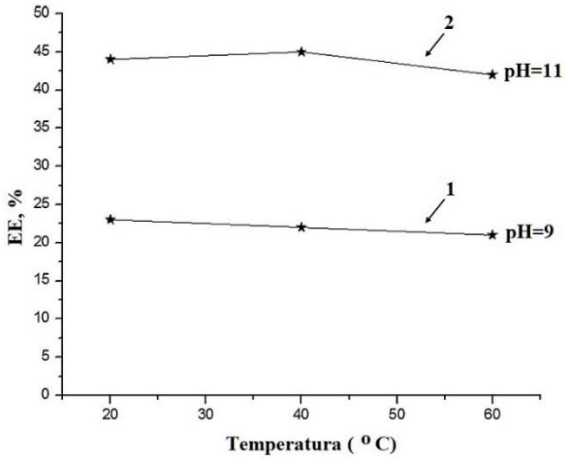


Fig.6.8. Dependence of drug EE against temperature for different host–guest systems synthesized at various pH value.

6.2.3.3. Influence of soaking time on the 5-FU encapsulation in PCHs

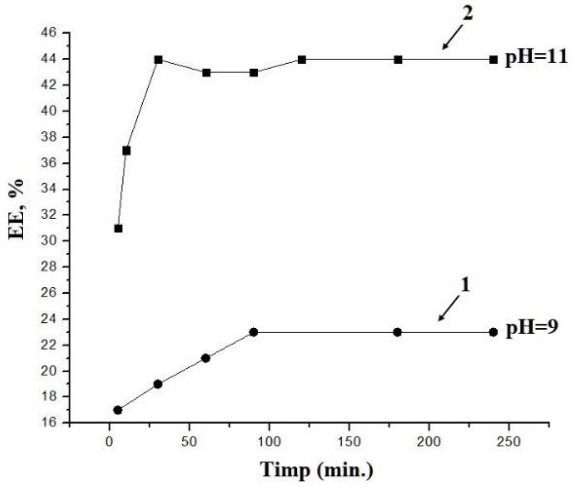
♦ Fourier Transform Infrared Spectrometry (FT-IR)

FT-IR spectra of PCHs loaded with 5-FU at different times were recorded to confirm the presence of the drug in PCHs. FT-IR spectra show that 5-FU loaded into PCHs reached equilibrium after 180 minutes. From this point on, the drug concentration gradient is equal both inside and outside of the PCHs. The intensity of the peak attributed to C = C stretching vibrations from 5-FU structure remained constant after 180 minutes. FT-IR analyzes provide only qualitative information on the dependence of 5-FU encapsulation at different times, a quantitative evaluation being obtained by UV-VIS analysis.

♦ Ultraviolet-Visible Spectrophotometry (UV-VIS)

The encapsulation efficiency of 5-FU in PCHs was calculated using the results provided by UV-VIS spectra. The maximum encapsulation efficiency of 5-FU in PCHs (EE% = 44%) was reached after 30 minutes at the pH value equal to 11. After this time, the encapsulation of 5-FU in

PCHs recorded a small decrease (for 60 minutes and 90 minutes), the equilibrium starting after 180 minutes. After this time, the EE% was kept constant



A decrease of incubation solution pH value leads to lower drug EE. For example, at pH = 9 the encapsulation efficiency of 5-FU in PCHs reached a maximum value of EE = 23% after 90 minutes. This variation of the encapsulation efficiency of 5-FU in PCHs by changing the pH value may be attributed to different PCHs surface charging or the solubility of 5-FU. Zeta potential measurements indicated that the value at pH = 9 is equal to that at pH = 11 (44mV) therefore, the solubility of 5-FU remains the main factor that influence the encapsulation efficiency of 5-FU in PCHs.

Fig.6.11. Drug encapsulation efficiency (EE) of PCH against soaking time at different pH value.

6.3. Investigation of PCHs as Hosts for Methotrexate (MTX) Encapsulation

The aim of this experimental study was to investigate PCHs as hosts for MTX encapsulation. PCHs were synthesized using two molar ratio between reactants and were proposed as hosts for MTX encapsulation.

6.3.2. The protocol for the synthesis of PCHs for encapsulation of MTX

PCHs were synthesized according to a modified method described in Chapter 4.3. noting that in this sub-chapter we varied the ratio between the reactants, so we obtained two types of PCHs using different molar ratios between the reactants (modified clay: amine: silica precursor→ 1: 20: 120; 1: 1: 7.5). The samples were abbreviated PCH-1-1: 20: 120 and PCH-2-1: 1: 7.5.

♦ ***Synthesis of PCHs-MTX host-guest systems***

The protocol synthesis of PCHs-MTX systems was performed according to the following procedure: 0.05g PCHs were soaked in an aqueous solution containing 10 mg MTX solubilized in 5 ml of demineralized water in the presence of 40 µL 37%. The obtained suspensions were stirred for 24 hours in the absence of light. Samples (PCHs-MTX) were centrifuged at 6000 rpm for 10 min. The final samples were abbreviated: PCH-1-MTX; PCH-2-MTX. The supernatant was collected and analyzed by UV-VIS technique in order to determine the encapsulation efficiency of MTX in PCHs.

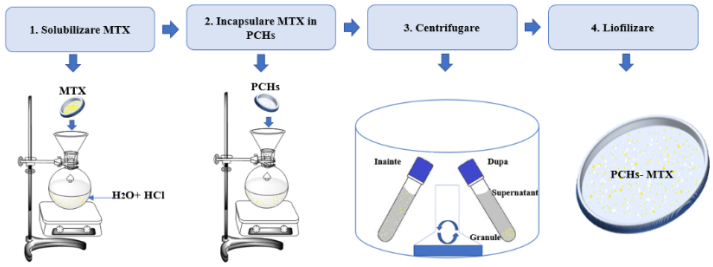


Fig.6.13. Synthesis of PCHs-MTX host-guest systems.

6.3.3. Results and discussion

6.3.3.1. Study of textural parameters

The results of the BET analysis showed that the new inorganic hosts (PCH-1 and PCH-2) proposed for MTX encapsulation had significantly higher values of textural parameters compared to the MMT used as starting layered clay in the synthesis of PCHs (Table 6.3). PCHs samples exhibit a broad pore distribution, with both micropores and mesopores pore volume and a shift to larger mesopores can be noticed with increasing MMT content in the PCHs samples, from sample PCH-1 to PCH-2

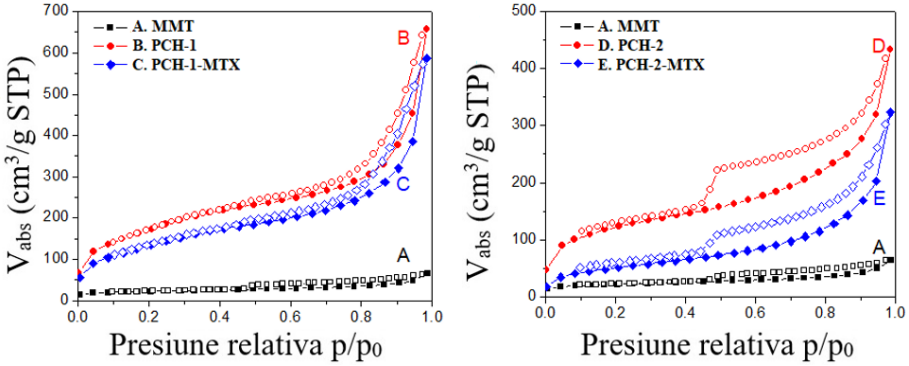


Fig.6.14. Nitrogen adsorption-desorption isotherms of: A) MMT, B) PCH-1, C) PCH-1-MTX, D) PCH-2 si E) PCH-2-MTX

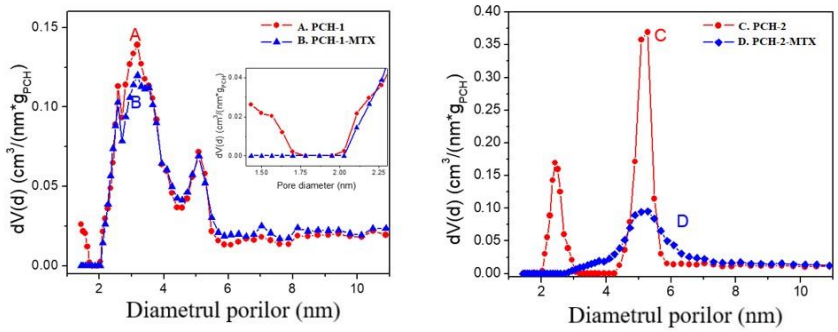


Fig.6.15. Pore size distributions of: A) PCH-1, B) PCH-1-MTX, C) PCH-2 si D) PCH-2-MTX

The presence of the porous structure and large specific surface area of PCHs can provide two possible mechanisms for adsorption of MTX within PCHs (1-MTX adsorbed on the surface of PCHs and 2-MTX encapsulated in the pores of PCHs).

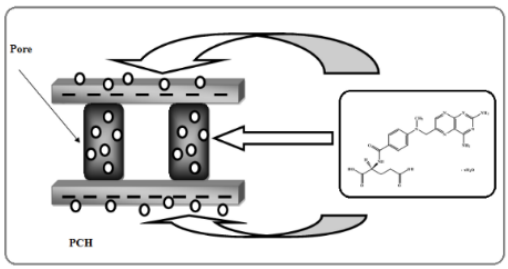


Fig.6.16. mechanisms for adsorption of MTX within PCHs

Tabel 6.3. Textural parameters of : PCHs şi PCHs-MTX

SAmples	S_{BET} (m^2g^{-1})	$V_{micropore}$ (cm^3g^{-1})	V_t (cm^3g^{-1})
MMT	78	0.0123	0.09
PCH-1	628	0.0201	0.85
PCH-1-MTX	497	0.0000	0.73
PCH-2	442	0.0004	0.44
PCH-2-MTX	191	0.0000	0.27

Pore size distribution corresponding to PCHs-MTX drug samples demonstrates that drug molecules are predominantly encapsulated in micropores and smaller mesopores (Table 6.3.). This has been highlighted by all PCHs-MTX system. This technique confirms the presence of MTX in the PCHs samples.

6.3.3.2. Fourier Transform Infrared Spectrometry (FT-IR)

FT-IR analyzes confirmed the structure of inorganic hosts (PCH-1 and PCH-2) and in the case of the samples entrapped with MTX (PCHs-MTX), the presence of drug molecules is demonstrated by the appearance of characteristic peaks of MTX detected at 1734 cm -1 (stretching vibrations of carbonyl groups from free carboxyl groups), 1645 cm -1, (assigned to vibrations of CO–NH bond), 1605 cm -1 (stretching vibrations of C=C bond from MTX structure).

6.3.3.3. X-ray photoelectron spectrometry (XPS)

The presence of drug molecules on the surface of inorganic clay PCHs was also demonstrated using XPS analysis (Table 6.4.)

Table 6.4. XPS analysis : PCHs and PCHs-MTX

Sample	O1s	Si2p	N1s	C1s	Mg1s
PCH-1	62.5	37.5	0	0	0
PCH-2	67.4	29.6	0	2.5	0.5
MTX	15.2	0	20.8	64	0
PCH-1-MTX	57.1	29.1	3.8	10	0
PCH-2-MTX	55.6	26.9	4.5	13	0

The XPS results indicated the presence of a low amount of C (2.5%) for PCH-2 sample assigning to the residual carbon formed after the calcination [64]. This signal was detected for PCH-2 because this material was synthesized by using a higher content of starting clay modified with organic template/co-template. The presence of signals assigned to C1s and N1s in the XPS spectra of samples containing MTX (PCH-1-MTX, PCH-2-MTX), confirms the adsorption of MTX on the surface of PCHs. As can be seen from Table 6.4, the presence of MTX in PCH-2 shows a higher atomic percentage for the elements N1s and C1s compared to PCH-1. The results confirm that PCH-2 is much more involved in the surface interactions between PCHs and MTX due to the reactivity attributed to silanol groups which are in a higher concentration in this type of material (higher MMT-modified content).

6.3.3.4. Zeta potential

This type of analysis has been useful in characterizing the particle surface charge. Zeta potential values were substantially influenced by the type of PCHs (different molar ratios). The Zeta potential value decreased from -10 mV (PCH-1) to -24mV (PCH-2). The presence of MTX in PCHs was also confirmed by Zeta potential measurements (Table 6.5).

Tabel 6.5. Zeta Potential

Sample	Zeta Potential (mV)
MMT	-31
PCH-1	-10
PCH-1-MTX	-15
PCH-2	-24
PCH-2-MTX	-26

This variation of potential zeta values was attributed to a different concentration of silanol groups that characterizes the PCHs samples. PCH-2 samples includes the highest content of starting clay (MMT) and therefore it was characterized by the highest concentration of silanol groups. After the MTX loaded within inorganic porous samples, the values of zeta potential were lowered, this change being assigned to the presence of carboxyl groups from the MTX structure. These results confirmed that MTX was sucessfully loaded (grafted and embedded) into the inorganic hosts [64]. This decrease of potential zeta value was recorded for all inorganic hosts.

6.3.3.5. CHN elemental analysis

Elemental analysis was useful to confirm the presence of the drug (MTX) in inorganic hosts, PCHs. In case of inorganic hosts, low percentages of carbon as contaminant (between 0.9 and 1.2%) was detected. In addition, the PCH-2 sample exhibits the highest drug encapsulation efficiency confirmed by higher value of carbon (13 %) and nitrogen (4.5%) percentages.

6.3.3.6. X-ray diffraction

The results of the XRD analysis confirm the formation of the structure of PCHs by significantly increasing the basal distance (d001) from 12.5 Å (characteristic peak for MMT) to 34 Å for PCH-1, respectively 38 Å for PCH-2 (Fig 6.19). This increase is attributed to the process of polymerizing of silica precursor between the MMT layers. The presence of the broad peak suggests that PCHs still contain layers of MMT. In the case of samples containing MTX (PCH-1-MTX, PCH-2-MTX), the results of the XRD analysis suggest that the materials are characterized by a combination of interlaced-exfoliated structures and, in addition, the low variation (from 3.3 nm to 3.4 nm for PCH-MTX) or constant values of d_{001} (3.8 nm for PCH-2-MTX) indicate that the drug was encapsulated in the pores of the clay and also grafted on PCHs surface. These results show that the encapsulation of MTX in PCHs is in acordance with the results of the BET analysis which demonstrates the significant variation of the textural parameters after the encapsulation of MTX in PCHs.

6.3.3.6. Transmission Electron Microscopy (TEM)

TEM results confirm the results of XRD analysis regarding the structure of PCHs before and after drug encapsulation (Fig. 6.20.). TEM images of the inorganic host (PCH 1 and PCH-2) indicated a similar morphology. TEM images also show the presence of pores with different shapes and sizes .

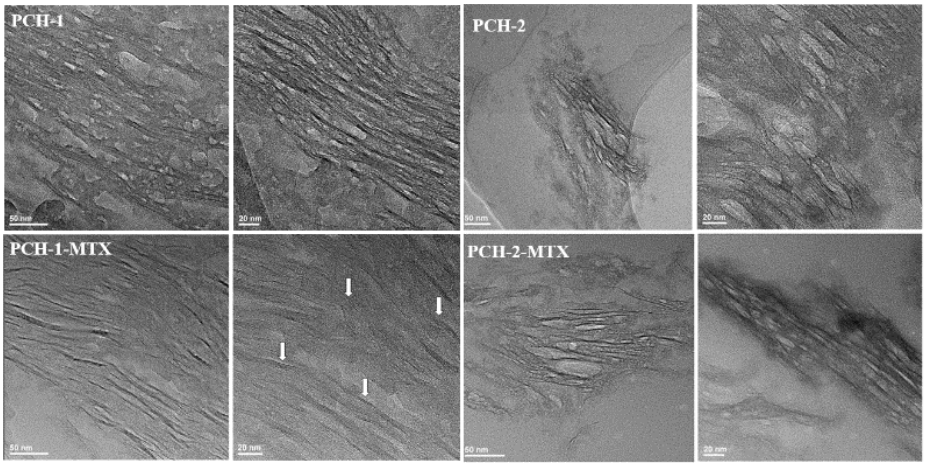


Fig.6.20. TEM images of: PCH1, PCH-1-MTX, PCH-2, PCH-2-MTX

6.3.3.6. UV-VIS spectrophotometry

The results of the UV-VIS analysis provide information on the encapsulation efficiency of MTX in PCHs and the influence of the type of PCHs on the release profiles of MTX in PCHs. he new inorganic hosts exhibits a higher drug encapsulation efficiency than classical layered silicates (e.g. MMT) due to the superior textural parameters (S_{BET} and Vt)

Tabel.6.7. Encapsulation efficiency of MTX in different inorganic hosts (PCHs and MMT)

Probe	EE, %
PCH-1- MTX	97
PCH-2 – MTX	98
MMT-MTX	45

The release of MTX from MMT and PCHs into SGF is dependent on the type of clay. For example, the percentage of MTX released from MMT is much lower (9.7%) than the MTX released from PCHs - 73%, 89%. The highest amount of drug (MTX) released from PCHs was recorded for the PCH-1-MTX sample which can be attributed to better textural properties.

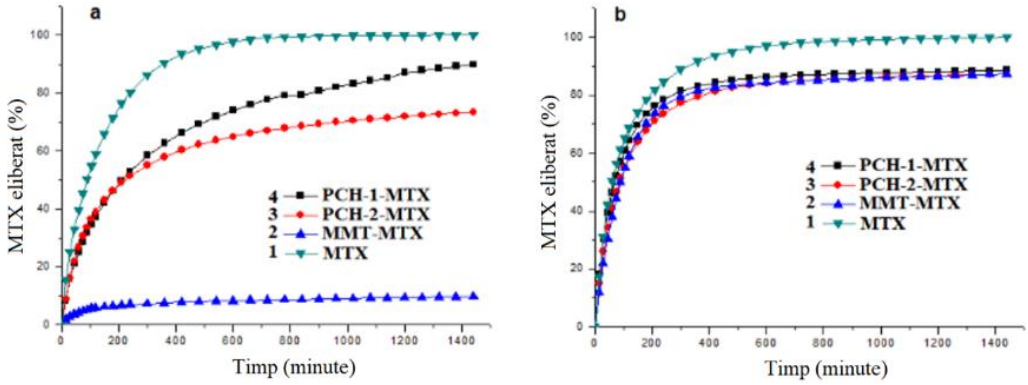


Fig.6.21. Drug release curves at different pH: a-SGF (pH = 1.2) and b-SIF (pH – 7.4)

Chapter 7.
OBTAINING HYBRID MATERIALS BASED ON POLYMER AND PCHs

7.1. Objectives of the experimental study

The objective of this chapter is the synthesis of new types of hybrid materials based on a natural / synthetic polymer and PCHs. At this stage of the experimental study, the synthesis of hybrid materials based on sodium alginate (AS) as well as polyvinyl alcohol (VPA) and film-type

7.2.3. Synthesis of hybrid materials based on AS and PCHs

The synthesis of hybrid films based on AS and PCHs involves the following steps: (1) Preparation of AS solutions of different concentrations (1, 2, 3%) - solubilization of AS in demineralized water under magnetic stirring at room temperature; (2) Dispersion of PCHs (different concentrations: 1, 3, 7, 10%) in AS solutions by sonication; (3) Solvent pouring and evaporation (mixtures of AS-PCHs were poured into Petri dishes and left at room temperature for solvent evaporation for 5 days.)

7.2.4. Results and discussion

7.2.4.1. Fourier Transform Infrared Spectrometry (FT-IR)

The presence of PCHs in the AS film is demonstrated by increasing the peak intensity from 1088 cm^{-1} which depends on the concentration of PCHs, the highest peak intensity was recorded for the sample with the highest content of PCHs (10%). The same changes were recorded for hybrid films with concentrations other than AS 2% and 3%. In addition, the peak attributed to the stretching vibration of the OH group is shifted to higher values for all hybrid films compared to AS films that do not contain PCHs. This may explain the formation of hydrogen bonds between AS and PCHs

7.2.4.2. Thermogravimetric Analysis (TGA)

Compared to 1% AS neat films, AS-PCH-1% hybrid films showed a slight increase in thermal stability (Tonset 15% increase by 2-6 0C and Tonset 40% increase by 2-12 0C). This improvement in the thermal stability of hybrid materials has been attributed to the barrier effect induced by the presence of PCHs in the system. The variation of thermal stability depends on both the concentration of AS and the concentration of PCHs

7.2.4.3. Dynamic Mechanical Analysis (DMA)

The results of the DMA analysis indicated a small decrease in Tg of approximately 5-6 ^{0}C for films with a PCH content of 7 and 10%, and hybrid films based on 3% AS and a concentration of PCHs of 1 and 3% showed a slight increase by 2 ° C. The viscous polymer solution is an important factor that can influence the dispersion of PCHs in the polymer matrix (AS). Therefore, Tg values were also determined for 1 and 2% AS-based hybrid materials. The presence of PCHs in 1% AS films favors the increase of storage modulus even for high PCH concentration (7 wt. %) which may be attributed to PCH acting in this case as a reinforcing agent. The low concentration of SA solution allowed a good dispersion of PCH and therefore the agglomeration tendency was minimized. At higher PCH concentrations (10 wt. %) a decrease of storage modulus was recorded probably due to the PCH agglomeration which diminished its reinforcing effect. The DMA results highlighted also a significant influence of SA solution concentration on dynamic mechanical properties (especially for storage modulus). The increase of SA solution concentration ensures higher viscosity which hinders PCH dispersion. The high viscosity of SA solution does not favor uniform dispersion of PCH and an agglomeration tendency

occurred. We concluded that in this case PCH acts as a plasticizing agent. Also for hybrid films based on SA 2 wt. % an increase of storage modulus was recorded only for lower PCH concentrations (1 wt. %)

7.3. Synthesis of hybrid materials based on polyvinyl alcohol (PVA) and PCHs

7.3.1. Objectives of the experimental study

The objective of this subchapter is the synthesis of new types of hybrid materials based on a synthetic polymer (PVA) and PCHs. In this subchapter, new hybrid materials based on PVA and PCHs were synthesized and the influence of the concentration of PCHs on the properties of hybrid materials (thermal stability, degree of swelling) was studied.

7.3.3. Synthesis of hybrid materials based on PVA and PCHs

Hybrid films based on PVA and PCHs were prepared by the solvent casting / evaporation method. This synthesis was performed in three steps. In the first stage the PVA was solubilized in an autoclave for one hour at 120^0 C. In the second stage different concentrations of PCHs (1%, 10%) were dispersed in the APV by sonication (Power = 130 W and Amplitude = 50%) for 30 minutes. In the last step, the hybrid materials were obtained by pouring into Petri dishes and left at room temperature to evaporate the solvent.

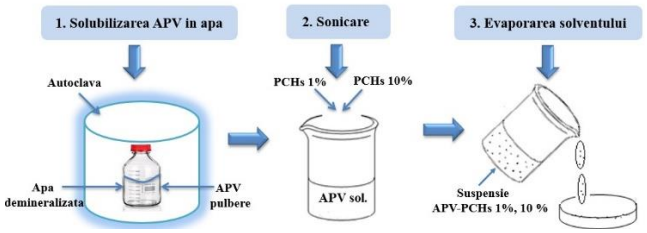


Fig.7.14. Synthesis steps of hybrid films

7.3.4. Results and discussion

7.3.4.1. Fourier Transform Infrared Spectrometry (FT-IR)

The presence of PCHs in the hybrid materials based on PVA-PCHs was highlighted by the following two peaks: one at 3731 cm-1 assigned to the terminal silanol groups vibrations and the other one at 3617 cm-1 attributed to the geminal and associated terminal silanol groups

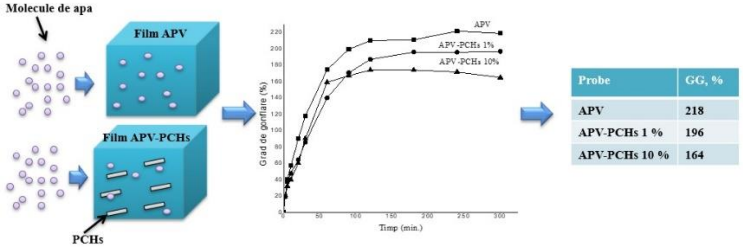
7.3.4.2. Thermogravimetric Analysis (TGA)

The results of TGA tests also highlight an increase of thermal stability for the samples which contain PCHs compared with neat PVA film. The sample with the lower concentration of PCHs (PVA-PCHs 1 wt.%) shows an increase of T_{onset} 15% with 5^oC and the sample with 10 wt.% PCHs (PVA-PCHs 10%) shows an increase of T_{onset} 15% with 12^oC compared to neat PVA film. The improvement of thermal stability of hybrid films was attributed to the barrier effect that was induced by the presence of PCHs

7.3.4.3. Study of the degree of swelling

The evaluation of the degree of swelling was determined following the following experimental protocol: the samples were initially weighted before being immersed in a tube that contains 10 mL of demineralized water and after being removed the excess of water, they were weighed at different swelling times. The barrier effect of PCHs was also confirmed by swelling tests. From the swelling results, it can be observed that the presence of PCHs causes a decrease of the swelling degree, this being assigned to the barrier effect of PCHs (Fig. 7.17). Thus, the sample with the higher

concentration of PCHs (PVA-PCHs 10 wt.%) exhibits a swelling degree of 165% in comparison to neat PVA film that provides 218% swelling degree.
The barrier effect of PCHs prevents the diffusion of water molecules into the PVA films



Probe	GG, %
APV	218
APV-PCHs 1 %	196
APV-PCHs 10 %	164

Fig.7.17. Schematic diagram of water diffusion in PVA film and hybrid materials based on PVA and PCHs. In the middle, the swelling degree curve of: 1-PVA film, 2-PVA-PCHs 1 wt.%, 3-PVA-PCHs 10 wt.%

Chapter 8.
THE SYNTHESIS OF HYBRID MATERIALS BASED ON POLYMER AND PCHS WITH APPLICATIONS IN THE FIELD OF CONTROLLED RELEASE OF ACTIVE SUBSTANCES

8.1. Objectives of the experimental study

The objective of this subchapter is the synthesis of some hybrid materials based on sodium alginate (AS) and PCHs proposed for the first time in the specialty literature as hosts for the encapsulation of an antitumor drug (5-FU). The influence of the concentration of PCHs in the hybrid system on the encapsulation efficiency of 5-FU in AS-PCHs as well as the influence of the concentration of PCHs on the release profiles of 5-FU in the hybrid system (AS-PCHs-5-FU) were also studied.

8.3. Synthesis Hybrid Materials based on Sodium Alginate (AS) and PCHs for 5-Fluorouracil Encapsulation

These hybrid materials were synthesized in the form of pearls and were obtained by the method of ionotropic gelation. The preparation of hybrid beads based on AS and PCHs was performed using the following protocol : In the first step, 10 mg of 5-FU were dissolved in 10 mL of deionized water at room temperature (RT) under magnetic stirring. In the second step, different PCHs concentrations (1, 3, and 10 wt%) were dispersed in 5-FU solution under magnetic stirring for 1 h at RT. Into the obtained suspensions a certain amount of AS was added to achieve 2% AS solution, and then the hybrid systems (AS-PCHs-5-FU) were stirred for 24 h in the absence of light at RT. In the final step, each suspension was dropped into calcium chloride solution (1 wt%) in order to obtain the hybrid beads by inotropic gelation. The hybrid beads were maintained in CaCl2 solution for 30 min and then were collected by filtration. After filtration, the supernatant was used to determine the encapsulation efficiency of 5-FU from hybrid beads. The amount of 5-FU entrapped in the AS-PCHs system was determined using UV-Vis spectrophotometer at $\lambda = 265$ nm. The beads were air dried for further characterization

8.4. Results and discussion

8.4.1. Fourier Transform Infrared Spectrometry (FT-IR)

FT-IR analysis was used to demonstrate the presence of PCHs and 5-FU in the polymer matrix (AS), as well as to identify possible interactions between the components involved in the structure of the hybrid material.

The presence of PCHs and 5-FU in the AS matrix was demonstrated by shifting the following peaks to higher values: (1) the 3343 cm-1 peak and (2) the 1408 cm-1 peak . Also, the results of the FT-IR analysis indicate that the displacement of this peak is dependent on the concentration of PCHs in the system. In the case of hybrid materials that include a high concentration of PCH (10%), the highest displacement of the peak attributed to the stretching vibration of the hydroxyl group is recorded.

The presence of the inorganic component (PCHs) in the polymer matrix (AS) induces a peak shift from 3343 cm-1 to higher values (3361/3371/3382 cm-1), which can be attributed to physical interactions such as bonds hydrogen set between AS and PCHs.

The presence of 5-FU in the hybrid material was highlighted by shifting the peak from 1408 cm-1 in AS to higher values in the case of hybrid materials (eg 1425 cm-1 for AS-PCHs 10%).

8.4.2. Thermogravimetric analysis

Thermogravimetric tests were performed to identify PCHs in the hybrid system (AS-PCHs). As can be seen in Table 8.2 the presence of PCHs in the system was confirmed by increasing the thermal stability of the hybrid beads. All hybrid materials (AS-PCHs) have thermogravimetric profiles similar to those of neat AS, but the presence of PCHs in the system induces the barrier effect, so the degradation temperature of samples containing PCHs was shifted to higher values ($T_{d15\%}$ and $T_{d40\%}$). . For example, the sample containing 10% PCHs has an improved thermal behavior compared to other hybrid AS-PCHs.

Tabel 8.2. Thermal properties

Sample	**$T_{d15\%}$ (°C)***	**$T_{d\ 40\%}$ (°C)****
NaAlg-5-FU	194	284
AS-5-FU-PCHs 1 %	194	285
AS -5-FU-PCHs 3 %	196	287
AS-5-FU-PCHs 10 %	201	303

8.4.3. Scanning Electron Microscopy (SEM)

SEM images confirm the presence of the inorganic component in the structure of AS-PCHs hybrid materials. Thus, unlike simple pearls (containing only AS) characterized by a smooth surface that suggests the existence of a uniform structure, in the case of all hybrid materials (AS-PCHs) a rough surface is identified due to the presence of PCHs. In the case of hybrid materials with a high content of PCHs (10%) a pronouncement of this characteristic is highlighted and therefore it can be concluded that there is a dependence of the surface roughness of the hybrid materials (AS-PCHs) depending on the content of PCHs in the hybrid material.

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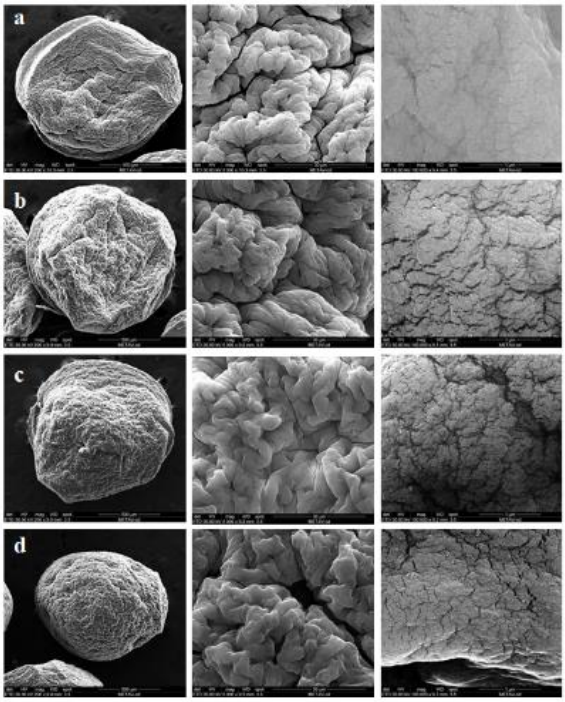

Fig.8.4. SEM images of: a-AS, b-AS-PCH-1 %,

c- AS-PCH-3 %, d- AS-PCH-10 %

The results of the EDAX analysis of AS-PCHs hybrid beads confirmed the presence of clay in the polymer matrix by the appearance of new signals characteristic of Si and Al elements, elements that are also found in the structure of PCHs (Figure 8.5.c).

8.4.4. Ultraviolet-Visible Spectrophotometry (UV-VIS)

♦ Determination of encapsulation efficiency and 5-FU release profiles from AS-PCHs hybrid beads.

UV-VIS results confirmed the influence of the presence of PCHs in the AS polymer matrix. The concentration of PCHs influences both the encapsulation efficiency of 5-FU in AS-PCHs and the release profiles of 5-FU from hybrid beads (AS-PCHs).

The values of the encapsulation efficiency of the hybrid beads (AS-PCH-1,3,10%) are significantly modified compared to the neat AS loaded with 5-FU. The lowest encapsulation efficiency was recorded for AS (EE = 60%), and samples containing PCHs (EE = 70%) had a higher encapsulation efficiency AS-5-FU. This can be attributed to the textural properties of PCHs (large specific surface area, high porosity) which demonstrate the importance of PCHs in the hybrid system. The presence of PCHs in the polymer matrix increases the encapsulation efficiency of 5-FU in AS-PCHs.

The release profiles of 5-FU from hybrid materials in the simulated gastric fluid and in the simulated intestinal fluid are shown in Fig. 8.7. The tests were performed in triplicate

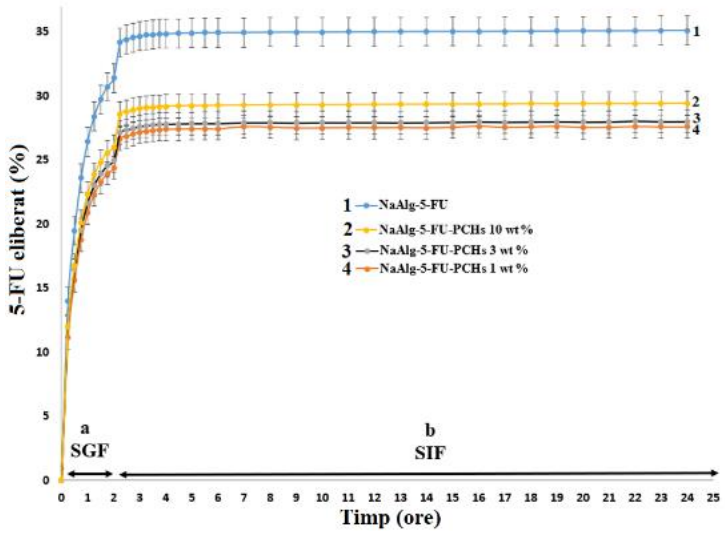

Figure 8.7. Drug release profiles in SGF (a) and SIF (b) for: 1-AS-5-FU, 2-AS-5-FU-PCHs-10%, 2-AS-5-FU-PCHs-3%, 2-AS-5-FU-PCHs-1%

As can be seen from the release profiles of the hybrid materials, they can be adjusted using PCHs in the system. Neat AS beads recorded the highest percentage of 5-FU released (35%) in 24 h in both SGF and SIF. Samples containing PCHs also recorded a lower percentage of drug released in 24 h (AS-5-FU-PCHs 10% - 29% - 5-FU released, AS-5-FU-PCHs 3% - 28% -5 -FU released and AS-5-FU-PCHs 1% - 27% - 5-FU released). Thus, the presence of PCHs and the concentration of PCHs used in the synthesis of hybrid pearls (AS-PCHs) significantly influence the 5-FU release profile of AS-PCHs. In both release media (SGF and SIF), the highest amount of drug released is recorded for the AS-5-FU-PCH-10% system. A dependence of the amount of drug released on the concentration of PCHs used in the hybrid system was also identified. This can be attributed to the fact that PCHs can capture some of the $CaCl_2$ and therefore the final structure of hybrid pearls (AS-PCHs) is affected.

In addition, the presence of PCHs in AS beads induces a structure with a high porosity that allows easier diffusion of drug molecules through the polymer matrix, due to the increase in the number of pores with increasing concentration of PCHs. and the fact that in the SGF, all samples show a progressive increase in the percentage of drug released and a linear 5-FU release profile will be recorded in the SIF. This behavior can be attributed to the sensitivity of AS to pH variations. Also, the presence of PCHs in the AS beads has the ability to reduce the rapid release of the drug (burst release effect) at the time of administration. This phenomenon can be attributed to the barrier effect induced by the presence of PCHs in the polymer matrix (AS).

CHAPTER 9
GENERAL CONCLUSIONS

Following the research studies carried out in order to fulfill the objectives proposed in the Phd. thesis, Hybrid materials based on polymers and porous clay heterostructures, the following general conclusions can be drawn:

The synthesis strategy of the new porous clay heterostructures (PCHs) as well as the study of the optimal reaction parameters led to the obtaining of new inorganic materials with tunable textural properties. The synthesis steps of PCHs were highlighted using modern characterization techniques (Fourier Transform Infrared Spectrometry (FT-IR), X-ray Diffraction (XRD), Thermogravimetric Analysis (TGA), Transmission Electron Microscopy (TEM), Analysis textural properties). All results confirmed the formation of PCHs structure and also the optimal reaction parameters were established (amount of surfactant, degree of hydration of the organophilized MMT, reaction time, pH value of the reaction medium, type of co-surfactant).

The introduction of new types of co-surfactants (polyetheramines: B100 and B200) in the synthesis of PCHs has shown that the type of co-surfactant plays a key role in the synthesis of these clays. Thus PCHs with different structures, different textural properties are obtained and also pores of different shapes and sizes can be identified. In the case of PCHs synthesized with a classical co-surfactant (DDA) a material with partially exfoliated structure was obtained in contrast to PCHs synthesized with polyetheramines B100 and B200 where PCHs with predominantly exfoliated structure were obtained. These results were confirmed by XRD and TEM analyzes. BET analysis first confirmed the conversion of MMT to PCHs and also demonstrated the influence of co-surfactant type on the textural properties of PCHs obtained. The use of polyetheramine (B200) with a high molecular weight and moderate hydrophilicity favors the formation of PCHs with a higher specific surface value as opposed to PCH-B100.

The strategy of synthesis of heterostructured porous materials (PCHs) as well as the study of the optimal reaction parameters led to the obtaining of new inorganic materials with tunable textural properties.

Another objective of the Phd. thesis research study was the functionalization of PCHs with amino and epoxy groups (aminopropyltriethoxysilane (APTES), 3-glycidoxypropyl-trimethoxysilane (GPTMS)). The modification of PCHs was highlighted by various analysis techniques (FT-IR, XRD, TGA, BET) and the results obtained indicated that the properties of PCHs are influenced by the type of coupling agent used in the modification of PCHs. The results of the XRD analysis indicate that the structure of the modified PCHs is influenced by the functionalization reaction with different coupling agents. Thus PCHs-epoxy has an intercalated structure compared to PCH-amino which has an exfoliated structure.

Investigation of PCHs as hosts for encapsulation of active substances (antitumor drugs) recommends these materials in the field of controlled release systems of active substances
The proposal of PCHs as hosts for encapsulating antitumor active substances (5-FU and MTX) has been confirmed using various modern characterization techniques (Textural parameter analysis, FT-IR, TGA, TEM, XRD, UV-VIS). All results suggested that PCHs can be used as hosts for encapsulating active substances.

In case of 5-FU encapsulation in PCHs, the optimal reaction parameters were investigated (the influence of soaking parameters (time, temperature and pH value) on drug encapsulation). Thus, following the research study, the optimal parameters for encapsulation of 5-FU in PCHs were identified. All results confirmed that the optimal parameters for encapsulating 5-FU in PCHs are: 20 ° C, 30 minutes, using a reaction medium with a pH value = 11.

PCHs have also been proposed as systems for encapsulating MTX. Two types of PCHs (different molar ratios) were synthesized and proposed as hosts for MTX encapsulation. These were investigated as hosts using the following analysis techniques: determination of textural parameters, FT-IR spectrometry, X-ray photoelectron spectrometry, (XPS), X-ray diffraction, (XRD), transmission electron microscopy (TEM) and also UV-VIS spectroscopy. The results of the BET analysis revealed that the type of PCHs can influence the encapsulation capacity of MTX. Thus, PCHs containing a higher amount of MMT have lower textural properties than PCHs with a lower MMT content. Another aspect concluded with the help of BET analysis is that MTX can be present both on the surface of PCHs (grafted) and inside the pores of PCHs (encapsulated). The results of the textural parameters showed that MTX completely occupies micropores and part of the mesopores and also confirms the presence of MTX on the PCH surface, which is confirmed by the decrease of the textural parameters of PCHs loaded with MTX. FT-IR spectrometry confirms the presence of MTX in PCHs by the appearance of characteristic peaks of MTX. The results of the XRD analysis suggest that the materials (PCH-1, PCH-2, PCH-1-MTX, PCH-2-MTX) are characterized by a combination of interleaved-exfoliated structures. TEM analyzes confirm the results of XRD analysis on the structure of these materials before and after drug encapsulation. It also highlights the presence of pores of different shapes and sizes in PCHs. The results of the UV-Vis analysis show that PCH-1 (EE = 97%) and PCH-2 (EE = 98%) have a significantly higher MMT encapsulation efficiency than MMT (EE = 45%).

The synthesis of hybrid materials based on natural polymer (AS) and synthetic polymer (PVA) and PCHs was performed in order to study the influence of PCHs in the polymer matrix. In the case of hybrid materials based on AS and PCHs, it has been identified that the concentration of AS and also the concentration of PCHs have an important role in the synthesis of hybrid materials but also on their properties (thermal stability, glass transition temperature and preservation modulus). The use of a low concentration of PCHs in the hybrid AS-PCHs system can have beneficial effects on thermal stability. This improvement in thermal stability is attributed to the barrier effect induced by the presence of PCHs in the system. The synthesis of the hybrid system based on PVA and PCHs brings valuable information in the field of hybrid materials such as polymer-clay. Thus, the introduction of PCHs in PVA has the ability to improve the thermal stability of hybrid films, which is attributed to the barrier effect induced by the presence of PCHs. This barrier effect has also been confirmed by swelling tests. The APV-PCHs hybrid system thus induces a decrease in the degree of inflation.

The proposal of a new hybrid material based on sodium alginate and PCHs as a host for the encapsulation of active substances (5-FU) makes an important original contribution in the field of controlled release systems of active substances. The presence of PCHs in the polymer matrix (AS) leads to improved encapsulation efficiency of the active substance (5-FU) and also has the role of adjusting the release profiles of the active substance. Following the results obtained, the following aspects were concluded: hybrid materials based on AS and PCHs have the ability to encapsulate 5-FU during host synthesis (AS-PCHs), hybrid materials have a high encapsulation efficiency compared to neat AS, encapsulation efficiency of 5-FU and the release profiles of these hybrid hosts are dependent on the concentration of PCHs in the system.

All the properties of PCHs highlighted in each chapter of the Phd. thesis show the importance and originality of this material (PCHs) which brings valuable information in the field of controlled release systems of active substances.

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RESULTS DISSEMINATION

List of ISI papers

1. S.A. Gârea, **A.I. Mihai**, A. Ghebaur, C. Nistor, A. Sârbu Porous clay heterostructures: A new inorganic host for 5-fluorouracil encapsulation, International Journal of Pharmaceutics 491 (2015) 299–309. **IF. 5.875**

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Poster:

- **Anda-Ionelia MIHAI**, Alexandra-Sorina GÂREA, Adi GHEBAUR, Andreea-Mădalina PANDELE, Horia IOVU,A New Property of Porous Clay Heterostructures: Drug Delivery System, YOUNG SCIENTISTS JOINING FORCES FOR EXCELLENCE IN BIOMATERIALS RESEARCH Bucharest, May 28th -29th 2015
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