Politehnica University of Bucharest

Faculty of Applied Chemistry and Materials Science

PhD THESIS

Nano(composite) hydrogels with poly(methacrylic acid) network

- Summary -

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SUMMARY

__Keywords:__ ***hydrogels, poly(methacrylic acid), nano(composite) hydrogels, montmorillonite, Laponite, silica nanoparticles, viscoelastic properties, absorption properties, methylene blue, crystal violet, depollutant properties***

GENERAL OBJECTIVES

Hydrogels are hydrophilic polymeric networks made of natural and/or synthetic polymers capable of absorbing and retaining a large amount of water or aqueous fluids without dissolving due to the crosslinked structure. The first hydrogel was made by Wichterle and Lim in 1960, but since 2010 these materials are more and more studied due to their potential applications in a wide range of fields such as medicine and pharmacy (drug delivery, tissue engineering, wound dressings), agriculture (controlled release of fertilizers, water retention in soil), electronic equipment industry, cosmetics industry, etc.

The most important properties of hydrogels, which must be taken into account in any application, are the water content and the mechanical/viscoelastic properties, to which, depending on the use, others are added, such as biocompatibility in the case of the medical ones.

A special category of hydrogels is represented by hydrogels sensitive to various physical or chemical stimuli. One such stimulus is the pH of the aqueous medium with which the hydrogel comes in contact, and depending on the desired application, the hydrogels can be designed to be pH sensitive. The sensitivity of hydrogels to pH is related to the ionizable groups in the hydrogel network, which can accept or donate protons depending on the pH of the environment in which they are located. One type of such hydrogels studied are acrylic acid-based hydrogels that contain acidic groups in their structure. Acrylic acid hydrogels are used in many fields of medicine, for example drug delivery, intraocular lenses, contact lenses, bone cement for orthopedics, bandages and implants for regenerative medicine. Another possible application for these types of materials is their use for the removal of pollutants from wastewater through possible interactions between the functional groups of polymers and the pollutant.

Among the hydrogels based on acrylic acids, those based on methacrylic acid have an important share due to the characteristic properties of the monomer used in their synthesis, namely: hydrophilicity, high reactivity, water solubility, high reactivity in polymerization processes, but also due to the characteristic properties of the obtained hydrogel such as pH-sensitive character, ability to donate or accept protons at pH changes, mucoadhesive characteristics, good absorption properties, non-toxicity, etc. As a result, poly(methacrylic acid) hydrogels have found applications in fields such as medicine and pharmacy (controlled release of drugs), but also for the treatment of water polluted with various contaminants (heavy metals, dyes).

A major disadvantage of hydrogels is their generally low mechanical properties. The simplest methods of improving the mechanical properties of the usual hydrogels are based on adjusting the crosslinking degree by changing the concentration of monomer introduced in the synthesis process, the crosslinking agent-monomer ratio or by introducing a reinforcing agent. However, these are methods that simultaneously affect the water absorption of the hydrogels.

In this context, the general objective of this thesis was to study the (nano) composite hydrogels with poly (methacrylic acid) network following three research directions:

1. Comparative study of the parameters that influence the water absorption and viscoelastic properties of poly(methacrylic acid) hydrogels;
2. Synthesis and characterization of new (nano)composite hydrogels based on poly (methacrylic acid);
3. Study of the influence of the nature of the reinforcing agent on the properties of (nano)composite hydrogels with poly(methacrylic acid) network.

In the first research direction, the objectives pursued were:

- Study of the influence of monomer concentration on viscoelastic and swelling properties in aqueous media of poly(methacrylic acid) based hydrogels.
- Study of the influence of crosslinking agent concentration on viscoelastic and swelling properties in aqueous media of poly(methacrylic acid) hydrogels.
- Study of the influence of the concentration of a reinforcing agent in the category of natural clays (montmorillonite-MMT) on the viscoelastic and swelling properties in aqueous media of poly(methacrylic acid) based hydrogels.

The second direction of research had the following objectives:

- The obtaining and characterizing of new composite hydrogels based on poly(methacrylic acid) and Cloisite 93A (organo-modified montmorillonite with methyl-di acid sulfate (hydrogenated tallow) ammonium, commercial product) used both as such and hydrophobically modified;
- The obtaining and characterization of new nanocomposite hydrogels based on poly(methacrylic acid) and Laponite XLG (a commercial and synthetic clay from the hectorite class).

The main objectives of the last research direction were:

- Investigation of the influence of the nature of the reinforcing agent on the structure of poly(methacrylic acid) hydrogels..
- Study of the influence of the nature of the reinforcing agent on the swelling properties in aqueous environments of the (nano)composite hydrogels based on poly (methacrylic acid).
- Investigation of the influence of the nature of the reinforcing agent on the viscoelastic properties of the (nano)composite hydrogels based on poly(methacrylic acid).
- Analysis of the influence of the nature of the reinforcing agent on the depollutant properties of poly(methacrylic acid) (nano)composite hydrogels.

CHAPTER 1. Literature review

Hydrogels are a class of materials that have been studied extensively over time. These have been reported since 1960 by Wichterle and Lim who developed a hydrogel based on 2-hydroxyethyl methacrylate (HEMA), and in 2010 hydrogels began to become one of the most important categories of materials studied. Today, hydrogels still fascinate scientists and researchers in all fields, making great steps in the types of systems used to make them and their applications. An important category of hydrogels is composite hydrogels. In order to prove the importance of these materials, a query of the articles of PubMed platform was performed using the keywords: "hydrogels" and "composite hydrogels". Figure 1.1 shows a clear upward trend in the number of items for these materials.

A special class of these materials is composite hydrogels, which can generally be defined as hydrophilic polymeric networks capable of retaining a quantity of aqueous solutions in the presence of small particles as reinforcing agents. Composite hydrogels are an improved alternative to conventional hydrogels because, by introducing a reinforcing agent into their structure, properties such as thermo-mechanical, optical, electrical and friction properties can be improved.

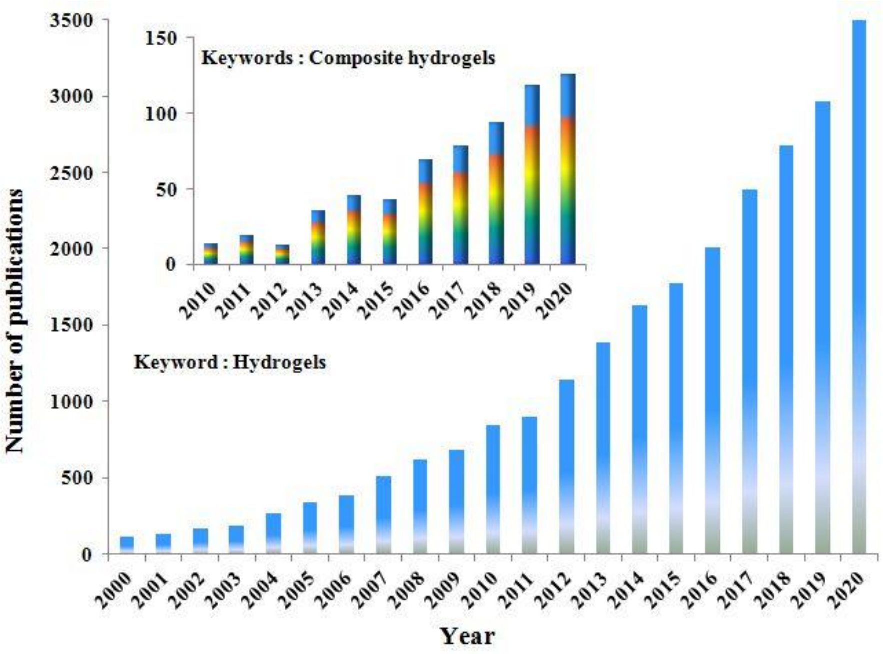

Figure 1.1 Histograms based on the number of articles published in the last 20 years

ORIGINAL CONTRIBUTIONS

CHAPTER 2. Comparative study of the monomer, crosslinking agent and reinforcing agent concentration influence on the viscoelastic and swelling properties of poly(methacrylic acid) hydrogels

The present chapter aimed to compare the effects of the monomer methacrylic acid (MAA) and reinforcing agent montmorillonite (MMT) concentrations and crosslinking agent N,N methylenebisacrylamide (BIS)/monomer (MAA) ratio on the viscoelastic properties and water absorption at various pH values of the crosslinked PMAA hydrogels. To the best of our knowledge, this is the first report of such a study. For a better comparison of the effect of the various components, the viscoelastic properties of hydrogels were investigated immediately after synthesis (“as-prepared hydrogels”), when their composition was identical to that of the precursor solution, while the water absorption/swelling degree was calculated in relation to the amount of polymer in the hydrogel only.

The studied hydrogels were obtained by the radical copolymerization of MAA with BIS in aqueous solution, in the presence of APS as the initiator, by using different concentrations of monomer, crosslinking agent and MMT, within the usual concentration range employed for the synthesis of hydrogels.

2.3.1 Influence of monomer concentration

The effect of the monomer concentration was studied for three different values, namely, 10, 20, 30 wt% based on the whole reaction mass by keeping constant the crosslinking agent (BIS, 2 mol% to MAA) and the initiator (APS, 1 mol% to MAA) concentrations.

The viscoelastic properties of hydrogels depend on their swelling degree and therefore, to study the intrinsic effect of monomer concentration, measurements were made immediately after the synthesis of hydrogels, when the swelling degree was practically the same in all cases, dictated by the intial composition of the hydrogel. The amplitude sweep measurements (Figure 2.1a) showed that the linear viscoelasticity region (LVER) was wider at lower monomer concentrations, indicating a higher elasticity of the hydrogel at lower monomer concentrations, while the frequency sweep measurements (Figure 1b) demonstrated the crosslinked character of the hydrogels as indicated by the storage modulus (G’) being larger than the loss modulus (G”) over the entire frequency range investigated.

The progressively more rigid hydrogels with a denser network, formed with increasing monomer concentration, displayed a 10 times increase in the G’ value at 1 Hz when doubling the monomer concentration, and a 30 times increase in G’ when the monomer concentration was tripled (Table 2.2)

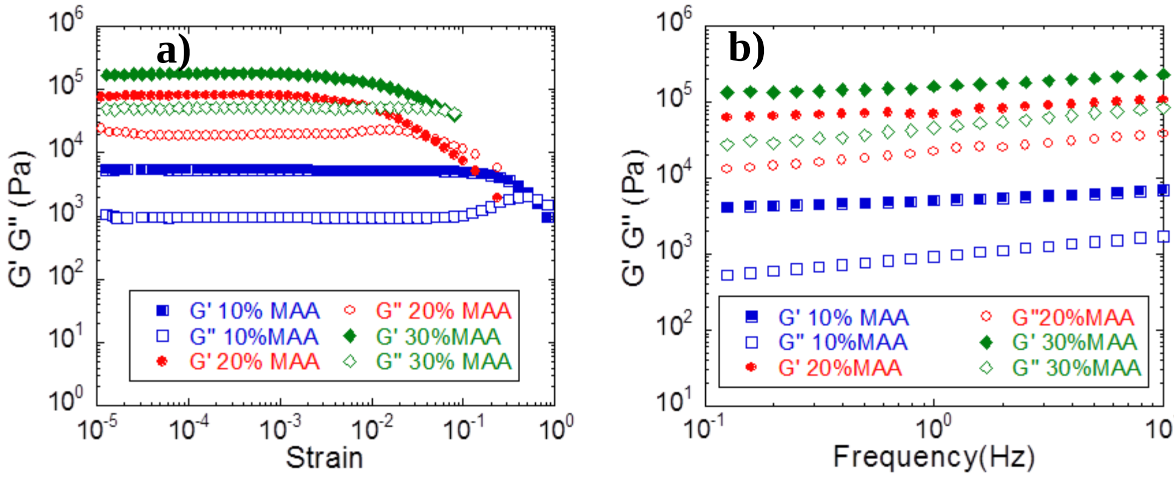

Figure 2.1 The influence of monomer concentration on the viscoelastic properties of PMAA hydrogels (a) Amplitude sweep measurements (b) Frequency sweep measurements. Hidrogel composition: MAA, 2 mol% BIS based on MAA, 0% MMT.

Table 2.2. Dependence of the viscoelastic moduli (frequency sweep measurements) and some structural network parameters on monomer concentration [a]

Sample	**G'×10^3 (Pa)** [b]	**G''×10^3 (Pa)** [b]	**$\bar{M}_c$ (Da)** [c]	**$\rho_c \times 10^{-4}$ (mol/cm^3)** [d]
SH[e]	5.05	0.92	874.9	14.7
H20% MAA	53.8	13.3	368.7	35.0
H30% MAA	160	46	193.8	66.6

[a] Hydrogel composition: MAA, 2 mol% BIS based on MAA, 0% MMT;
[b] G' and G" at 1 Hz obtained during the frequency sweep analyses;
[c] Average molecular weight between crosslinks at pH 1.2;
[d] Crosslinking density at pH1.2;
[e] SH: 10%MAA, 2 mol%BIS based on MAA, 0%MMT.

The equilibrium swelling degree (ESD) under various pH conditions (1,2; 5,4; 7,4) of hydrogels with different PMAA content was determined by measurements of the swelling degree as a function of time at 37 °C.

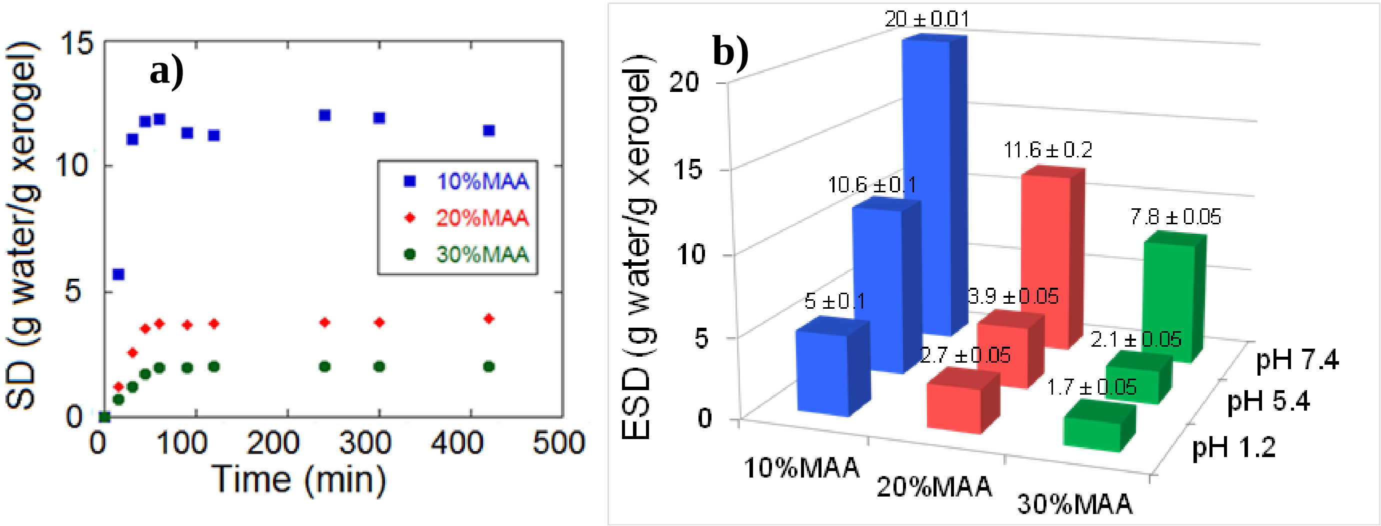

Figure 2.3 The influence of monomer concentration on the swelling properties of hydrogels (a) Swelling curves at pH 5.4; (b) The effect of monomer concentration on the swelling degree (72 h) at different pH values (1.2; 5.4; 7.4). Hidrogel composition: MAA, 2 mol% BIS based on MAA, 0% MMT.

As we expected based on the pH-sensitive character of the hydrogels, no matter the monomer concentration in the synthesis step was, ESD increased with increasing pH, the highest swelling degree being obtained at pH 7.4 (Figure 2.3b).

Regardless of the pH value of the medium, the swelling degree increased with the decrease of the monomer concentration in agreement with previous reports. This can be explained by the decrease of the crosslinking density, as a consequence of both a lower proportion of chain entanglements at smaller monomer concentrations (Figure 2.3b) and the covalent crosslinking bridges being partially replaced by loops resulting through intramolecular cyclization.

2.3.2 Influence of crosslinking agent concentration

The concentration of the crosslinking agent in the hydrogel network is an important parameter to investigate because it directly affects the swelling degree and therefore the viscoelastic properties of the hydrogel. In this study, the effect of 3 different concentrations of crosslinking agent was investigated, namely 1, 2 and 3 mole% to monomer, the concentration of monomer being 10 wt% based on the whole hydrogel composition.

The use of a higher concentration of crosslinking agent in the synthesis process leads to hydrogels with a higher density of crosslinking bridges, and therefore, more crosslinked structures are obtained that have higher mechanical properties. Indeed, the amplitude sweep and frequency sweep rheological measurements (Figure 2.4) showed that the hydrogels synthesized at a higher concentration of BIS were more rigid, displaying higher G' values, in agreement with the expected formation of a more crosslinked network. Also, the frequency sweep measurements (Figure 2.4b) highlighted G' > G" over the entire frequency range studied, thus confirming the crosslinked character of the hydrogels. The difference between G' and G" increased with decreasing frequency indicating the presence of a wide-mesh network , in agreement with the BIS concentration used.

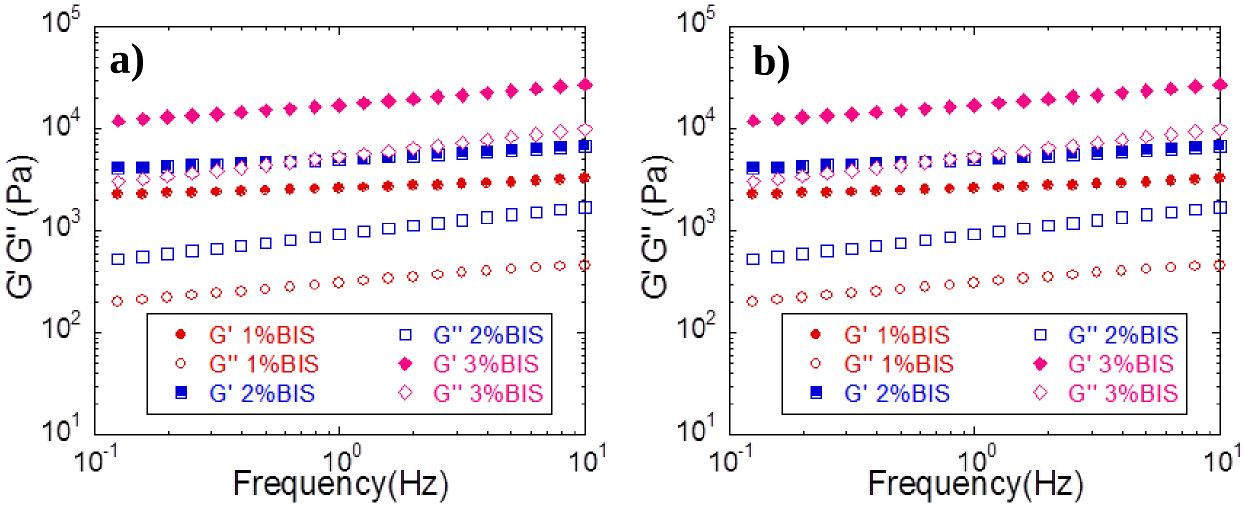

Figure 2.4 The influence of crosslinking agent concentration on the viscoelastic properties of PMAA hydrogels (a) Amplitude sweep measurements (b) Frequency sweep measurements. Hidrogel composition: BIS, 10% MAA based on the whole hydrogel composition, 0% MMT.

The adjustment of the crosslinking agent concentration is one of the most important methods of controlling the crosslinking density of a hydrogel and, as a consequence, of the ability to swell in water. Indeed, our experiments showed that by raising the concentration of BIS, the swelling degree of the hydrogel decreased, regardless of the pH of the medium (Figure 2.5), due to a higher crosslinking density .

Tripling the BIS concentration resulted in a reduction of ESD of only 1.2 times at pH 1.2, as compared to approximately 3.3 times and 2.5 times at pH 5.4 and 7.4, respectively. In comparison with the hydrogels synthesized at various monomer concentrations, the effect of increasing BIS concentration on ESD had a relatively similar amplitude at pH 5.4 and 7.4, but the behavior was very different at acidic pH, when tripling the BIS concentration led to an insignificant decrease of ESD, as compared to a decrease of almost 3 times in the previous case. This dissimilarity at pH 1.2 is the consequence of the large difference between the influence of the two parameters upon the crosslinking density: a 3 times increase of monomer concentration led to a 4.5 raise of ρ_c as compared with only 1.5 increase for the same increase of the crosslinking agent concentration. Regarding the effect of the pH of the medium, in this case as well, the pH increase led to an increase of ESD as expected, the reason of this effect being explained above. It is worth noting, however, that the two series of hydrogels behaved differently from this of point view as well. Namely, while in the case of hydrogels obtained at different monomer concentrations the ratio R = (ESD at pH 7.4) / (ESD at pH 1.2) practically did not depend on the monomer concentration at synthesis ($R \approx 4$), in the case of the crosslinking agent concentration modification, R decreased with the increase of the amount of BIS from about 6 for the hydrogel with 1 mole% BIS to monomer, to 4 and about 3 in the case of hydrogels with 2 mole% BIS and 3 mole% BIS, respectively.

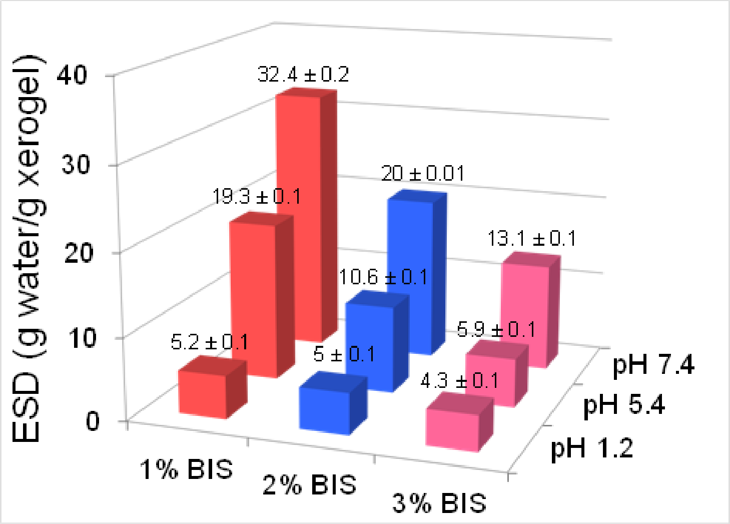

Figure 2.5 The influence of crosslinking agent concentration on swelling degree (72h) at different pH values. The results express average values ± standard errors. Hidrogel composition: BIS, 10% MAA based on based the whole hydrogel composition, 0% MMT.

2.3.3 Influence of reinforcing agent concentration

This chapter describes the influence of the reinforcing agent concentration, which can affect the viscoelastic and swelling behavior of the hydrogel together with monomer and crosslinking agent concentrations. Hydrogels with 10 wt% monomer in the precursor solution were analyzed, the concentration of the crosslinking agent being 2 mole% to monomer. The concentrations of the investigated reinforcing agent were 1, 2, 3 wt% based on the whole mass of hydrogel, respectively 9.65, 19.3, 28.95 wt% in comparison to the amount of monomers. The composite hydrogels obtained were structurally characterized by FT-IR, TGA and XRD analyses to highlight the presence of the reinforcing agent, and the rheological properties and water absorption in solutions with various pH values were determined. Also for a representative sample (H2%MMT) we performed SEM analyses.

The FT-IR spectra of nanocomposite xerogels contained the peaks characteristic of the stretching vibrations of the Si-O-Si and Si-O-Al groups in MMT, thus confirming its presence in the material (Figure 2.6). It was also observed that the peak intensity characteristic of MMT increased in accordance with the amount of reinforcing agent introduced in the step synthesis.

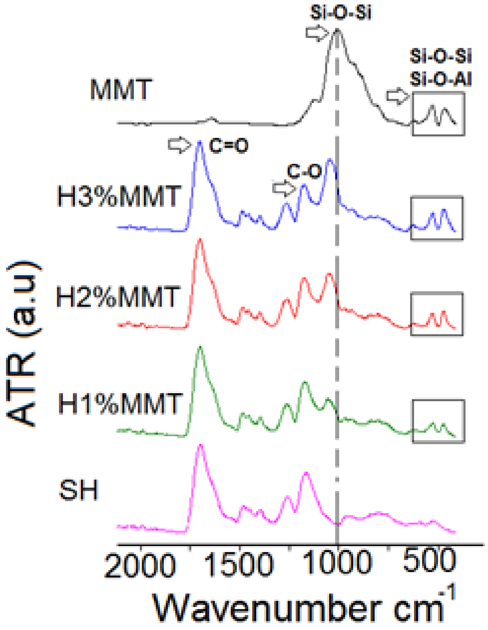

Figure 2.6 FT-IR spectra of the composite xerogels investigated and MMT. SH: mol%BIS based on MAA, 0%MMT

The X-ray diffractograms (XRD) obtained for the studied composites and the pure MMT are presented in Figure 2.7. XRD analysis demonstrated the obtaining of intercalated nanocomposites hydrogels.

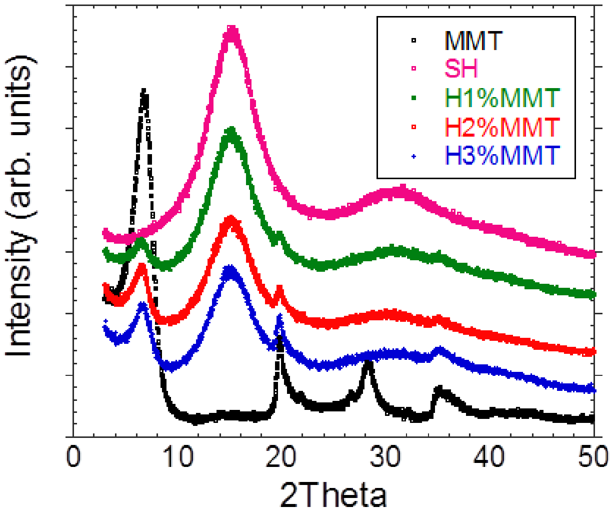

Figure 2.7. The diffractograms of MMT and the xerogels investigated. SH: 10%MAA, based on MAA, 0%MMT

As in the case of the unreinforced hydrogels, the viscoelastic properties were investigated immediately after synthesis. Amplitude sweep measurements (Figure 2.9a) showed that even in the case of composite hydrogels the viscoelastic properties were kept constant over a wide range of deformation (10^{-5}-10^{-1}), and therefore no appreciable decrease in elasticity (narrowing of LVER) with increasing amount of MMT was noticed. The frequency sweep measurements (Figure 2.9b) showed that G' was higher than G" over the whole frequency range investigated, thus demonstrating the crosslinked character of the hydrogels.

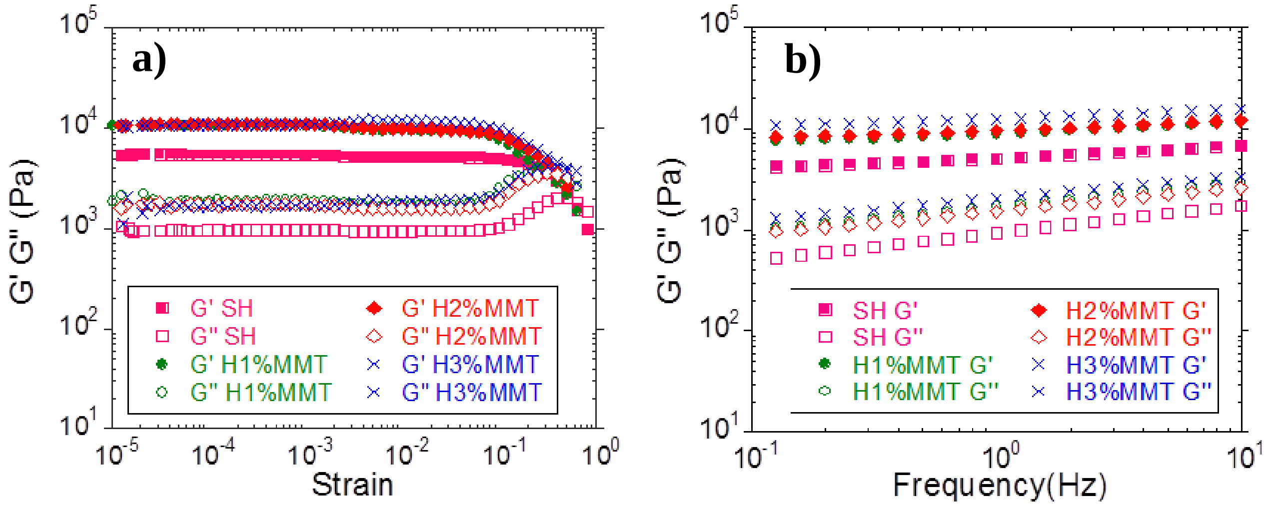

Figure 2.9 The influence of MMT concentration on the viscoelastic properties of PMAA hydrogels (a) Amplitude sweep measurements (b) Frequency sweep measurements. SH: 10%MAA, 2 mol%BIS based on MAA, 0%MMT

The introduction of MMT into hydrogels led to an improvement of their mechanical properties, a fact demonstrated by the increase of the values of the viscoelastic modules with increasing clay concentration. For a 10 wt% initial monomer concentration, G' was approximately 2 times higher when 3 wt% MMT was used as compared to the non-reinforced hydrogel (Figure 2.9). However, tripling the amount of the reinforcing agent in the hydrogel (from 1 wt% to 3 wt%) led to a relatively small increase of G' of about 1.5 times (from $8.8\cdot10^3$ Pa to $12.4\cdot10^3$ Pa), much lower in comparison to the increase of G' when the monomer concentration (≈ 30 times) or crosslinking agent (≈ 6 times) tripled, which seems to indicate that the existing interaction between the clay and the network was weak in the presence of water.

The influence of the amount of MMT on the swelling degree of the composite hydrogels was studied at pH 1.2; 5.4 and 7.4 (Figure 2.10). The results showed that the swelling degree increased with increasing pH, as expected, in agreement with the pH sensitive character of these PMAA hydrogels. Raising the concentration of MMT at pH 5.4 and 7.4 determined enhanced water absorption. This can be explained by the fact that MMT had very little influence upon the crosslinking degree of the hydrogel (Table 7), but instead, because of its basic character (a 2 wt% MMT aqueous dispersion displayed a pH of 8.9), MMT led to the formation of carboxylate groups in the hydrogel during the synthesis stage, the proportion of which was higher for larger MMT concentrations.

The results showed that, at strongly acidic pH, the increase of MMT concentration led to a slight decrease of ESD (1.1 times for a 3-fold increase of MMT concentration – Figure 2.10), as a consequence of the enhanced crosslinking density.

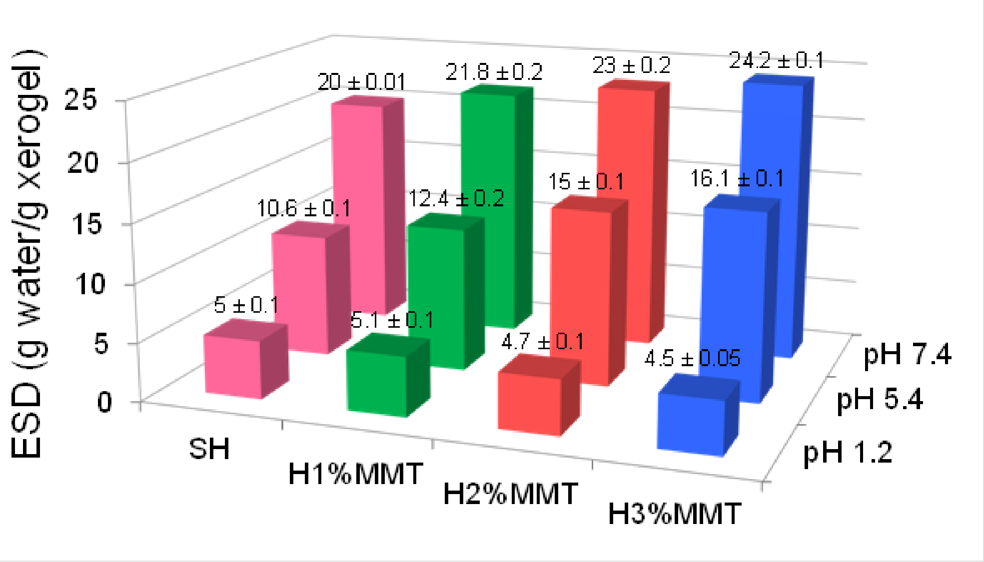

Figure 2.10 The influence of reinforcing agent on the swelling degree (72h) at different pH values. Results express average values ± standard errors. SH: 10%MAA, 2 mol%BIS based on MAA, 0%MMT.

The results showed that the most important effect on the viscoelastic properties was displayed by monomer concentration, the tripling of which led to an about 30-fold increase of G' as compared to an increase of only 5 times in the case of BIS and 1.5 times when MMT concentration was raised from 1 wt% to 3 wt% (Figure 10). (Figure 2.13).

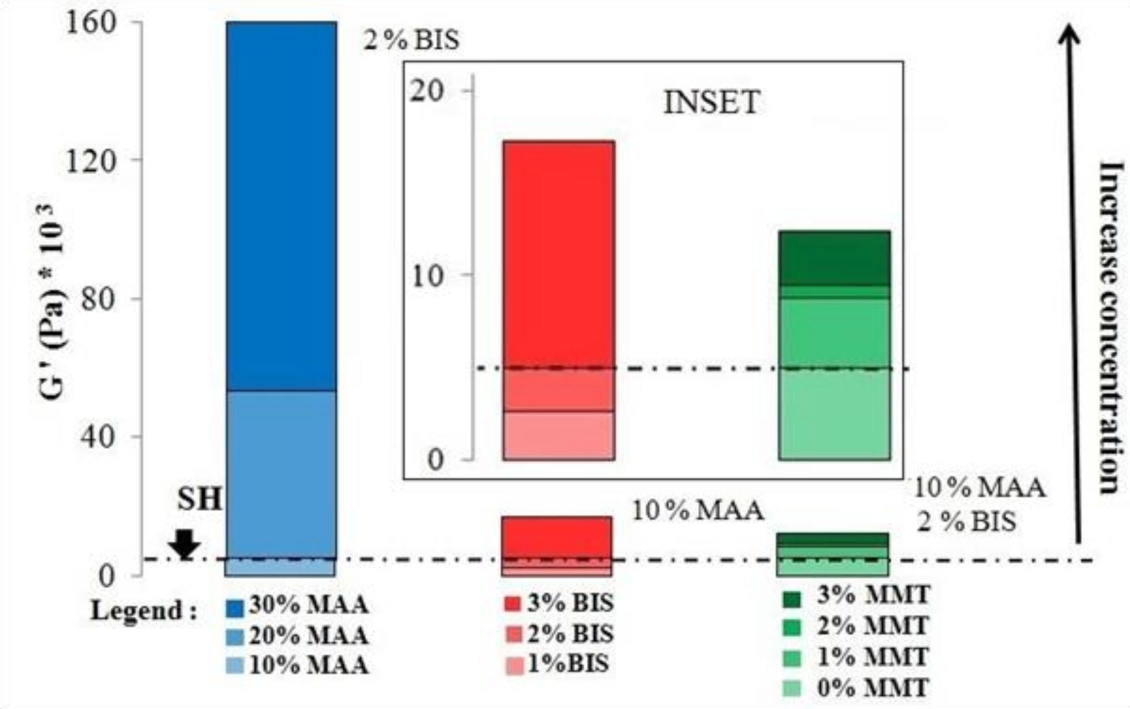

Figure 2.13 Comparative influence of the monomer, crosslinking agent and reinforcing agent concentrations upon the viscoelastic properties of PMAA hydrogels.

CHAPTER 3. Synthesis and characterization of new (nano)composite hydrogels with poly(methacrylic acid) network

3.1 Hydrogels based on poly(methacrylic acid) and modified montmorillonite

The aim of this study was to synthesize new materials based on poly(methacrylic acid) and commercial Cloisite 93A clay hydrophobized and to evaluate the influence of modified clay on the physico-chemical properties of the new hydrogels. The biocompatibility of these new nanocomposites has also been investigated in vitro.

The desired materials to be obtained are foreseen to become novel bio agent carriers with enhanced mechanical properties. Moreover, by introducing advanced hydrophobic modified clays into PMAA matrix, we created the premises to obtain novel nanocomposite hydrogel structures with combined hydrophilic-hydrophobic behavior necessary for sustained release of co-entrapped polar/non-polar substances.

Time dependant swelling profiles of the hydrogels in de-ionized water were summarized in Figura 3.1 where it was observed that the reinforced hydrogels showed a higher swelling degree compared to the control.

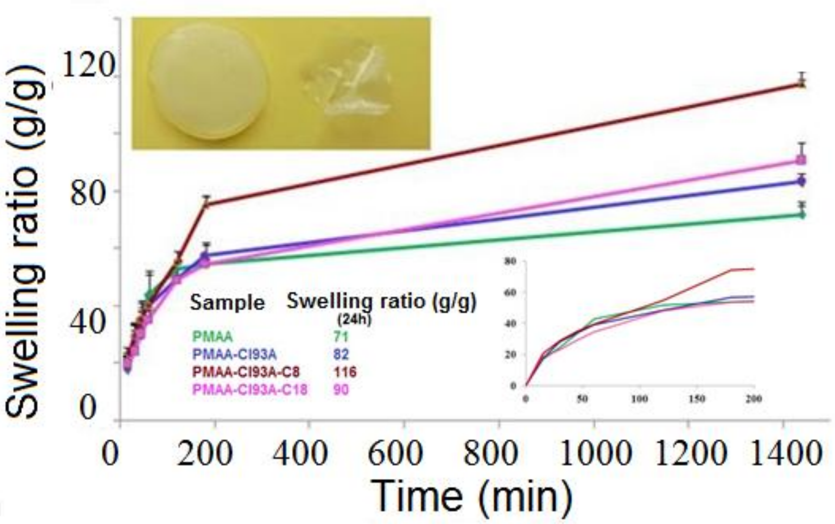

Figure 3.1 Time dependent swelling profiles of the hydrogels and appearance of the dried and swollen hydrogels,

The deswelling behavior of the equilibrium swollen hydrogel samples was followed by TGA/DTG analyses. The obtained data points to the water restricting capacity due the presence of clay layers which behaved as a barrier in the water outflow from the hydrogel networks (Figure 3.2).

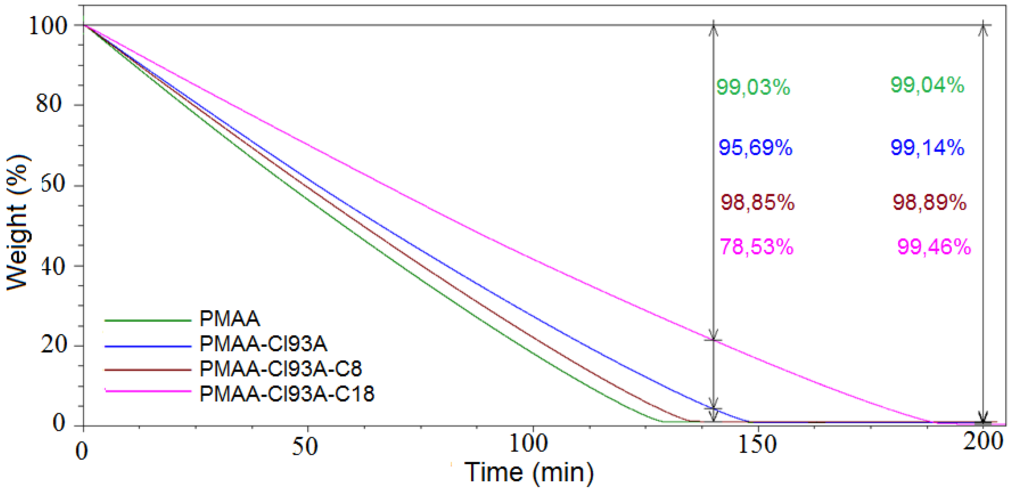

Figura 3.2 Mass loss of equilibrium swelled hydrogels as a function of time measured at constant temperature (37 ^{o}C)

FTIR analysis of the investigated nanocomposite hydrogels demonstrated the inclusion of clays in the hydrogel network by identifying the peaks characteristic of the reinforcing agents, but also that the clay layers interacted with the PMAA network..

The storage and loss moduli of the crosslinked hydrogels were represented as a function of frequency in Figure 3.6. It was observed that the addition of inorganic filler led to an increase in the storage modulus of the composite hydrogels PMAA-Cl93A-C8 and PMAA-Cl93A-C18. The values of the storage module obtained showed that of the nanocomposite hydrogels investigated, the PMAA-Cl 93A-C18 sample had the highest value.

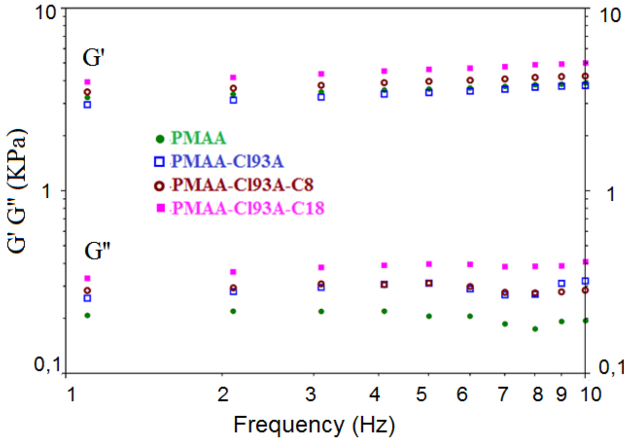

Figure 3.6 DMA results obtained for the investigated hydrogels

XRD analysis demonstrated the obtaining of predominantly intercalated composite hydrogels. This was also confirmed by TEM analysis where Cl93A-C18 clay could be visualized in TEM images in the form of layers of clay interleaved inside the polymer. Moreover, even if the intercalated state predominated, some layers of exfoliated clay could be observed in the polymer matrix (Figure 3.7).

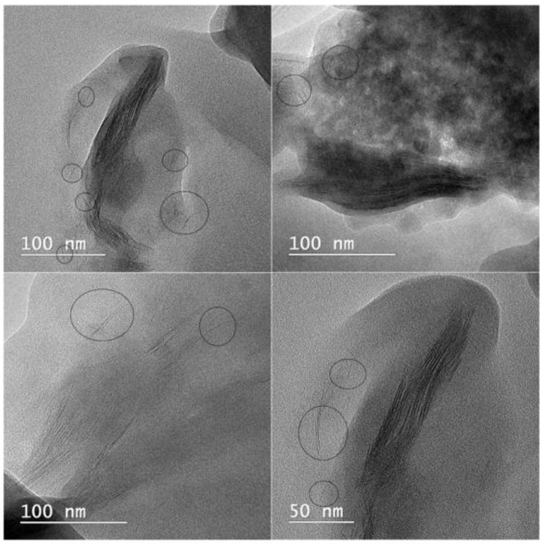

Figure 3.7 TEM images for the PMAA-Cloisite 93A-C18 sample

The cytotoxic effect of hydrogels on the viability of normal MDBK and tumor cells HT-29 was also analyzed. The metabolic activity of normal and tumor cells was not affected by the direct treatment with nanocomposite hydrogels, the proliferation of MDBK cells being intensified as compared to the control, especially for the hydrogels reinforced with Cl93A-C18 clay. The microscopic investigation confirmed the results obtained by the MTS method, namely that the tested PMAA-clay systems did not affect the viability and proliferation of the two cell lines after 24 and 48 hours of direct treatment and that the hydrogels obtained present biocompatibility.

3.2 Nanocomposite hydrogels based on poly(methacrylic acid) and Laponite XLG

The novelty of this chapter is the investigation for the first time of new hydrogels based on poly (methacrylic acid) and different concentrations of Laponite XLG.

FT-IR spectroscopy was employed to demonstrate the presence of clay in the hydrogel matrix and to observe if interactions between components occurred. All xerogel spectra displayed the characteristic peaks of the carboxylic group (1692 cm^{-1} C=O, 1160 cm^{-1} C-O, Figure 3.11a) of the PMAA matrix. In the case of the nanocomposite hydrogels, the characteristic peaks of Laponite were also identified at 970 cm^{-1} (stretching vibrations of the Si-O and Si-O-Si bonds) and 442 cm-1 (Mg-O bond stretching vibration), their intensity increasing with the amount of Laponite in the hydrogel.

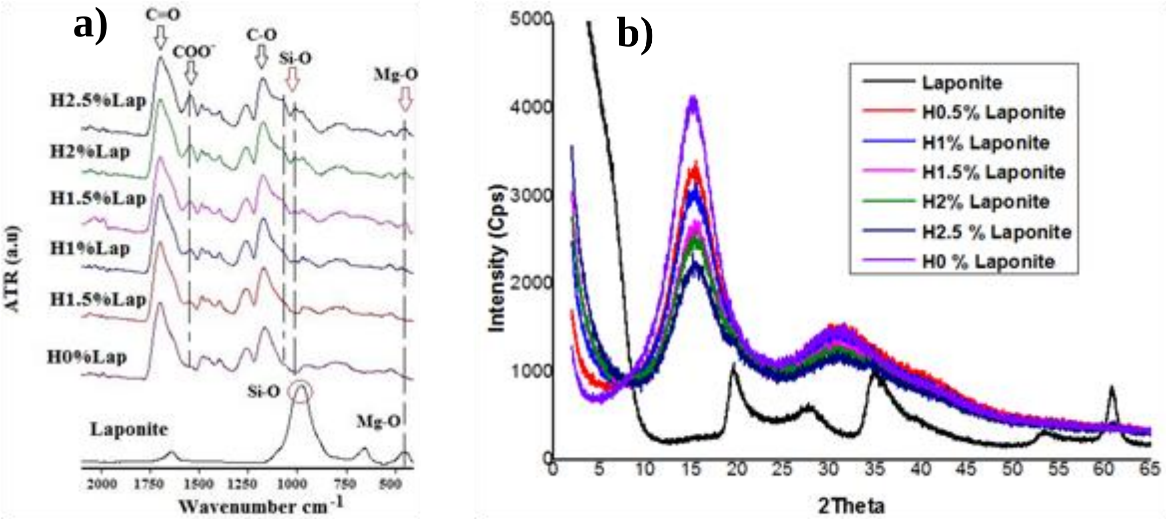

Figure 3.11 FT-IR (a) and XRD (b) spectra of hydrogels reinforced with different concentrations of Laponite XLG

Figure 3.11b, which shows the spectra obtained by XRD analysis, suggests that predominantly exfoliated nanocomposite hydrogels were obtained. This assumption was supported by the TEM analysis which showed that Laponite was substantially exfoliated and evenly dispersed in the polymer matrix. (Figure 3.12).

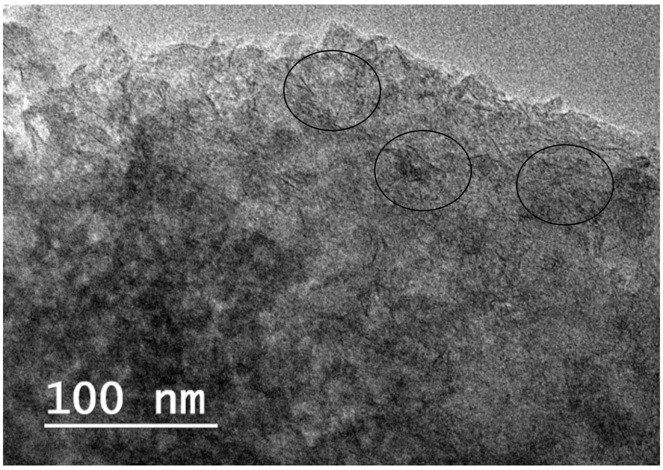

Figure 3.12 TEM image of the H2%Lap xerogel

The viscoelastic properties of hydrogels were investigated immediately after synthesis, when the swelling degree of hydrogels was practically identical in all cases, in order to be able to make a more accurate assessment of the influence of the Laponite amount. So, it was observed that G' increased with increasing Laponite concentration, while, despite G" increase (Figure 3.15a), the loss angle decreased (Figure 3.15b), indicating that the reinforcing agent determined an improvement of the hydrogel elastic character. Also, the increase of the complex modulus G* (Figure 3.15b) and simultaneously of G' (Figure 3.15a), about 4 times with the increase of the reinforcing agent concentration from about 5% to 24% (relative to the polymer) indicated a clear stiffening/improving effect of the mechanical properties of the hydrogel under the action of the clay.

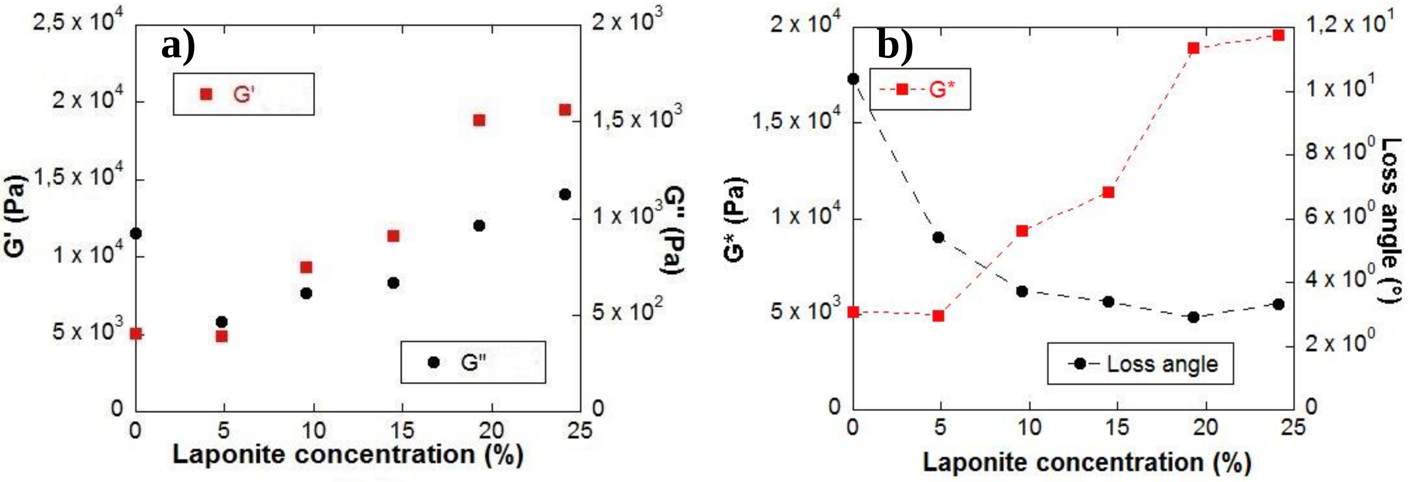

Figure 3.15 The dependence of a) G' and G'' and b) G and loss angle at 1 Hz on Laponite concentration (Frequency sweep measurements)*

The ability of hydrogels to absorb water is decisive for their use as biomaterials, including as supports for controlled drug release. In this study, the influence of Laponite concentration on the swelling degree of hydrogels at three different pH values (1.2;5.4;7.4) was investigated. The swelling degree for all hydrogels synthesized varied with the pH value, in agreement with the pH-responsive character of the PMAA hydrogels, but also in function of the concentration of reinforcing agent. The swelling degree increased with the pH value of the medium because at a pH larger than 5 the carboxyl groups in the hydrogel ionized and the polymer chains became negatively charged (Figure 3.16).

At pH = 1.2, the increase in Laponite concentration affected the swelling degree very little. At pH 5.4 and 7.4 the swelling degree increased with the concentration of Laponite in the hydrogel, the increase being steeper at pH 5.4. The phenomenon is explained by the presence in the structure of Laponite of the basic groups which in reaction with the acidic groups in the polymer led to the formation of additional carboxylate anionic groups, which led to an increase in the swelling degree.

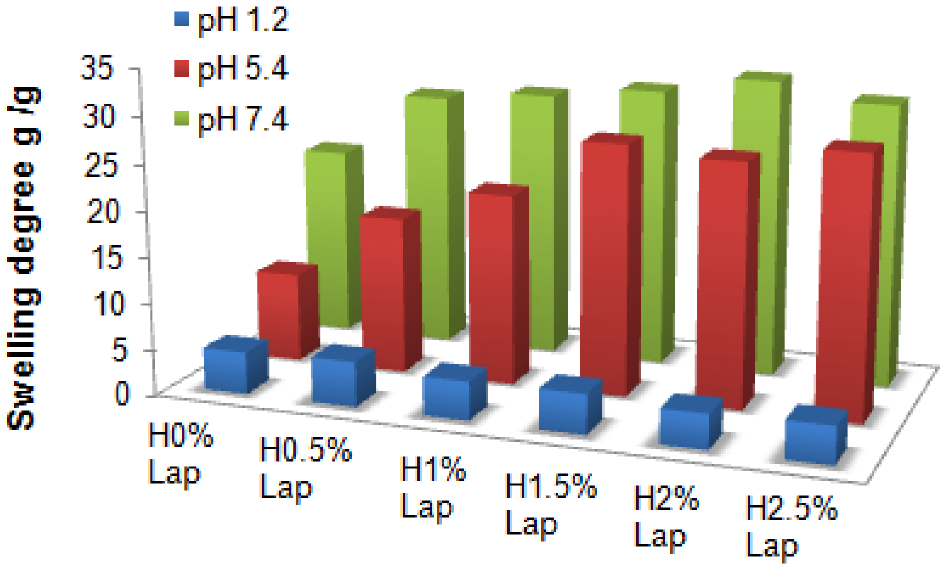

Figure 3.16 Dependence of the swelling degree of the nanocomposite hydrogels on Laponite concentration and pH of the medium. Swelling time 24 h; temperature 37 °C.

The release properties of hydrogels were tested by means of a model drug, namely caffeine. The presence of caffeine in xerogels has been demonstrated by FTIR and EDAX analysis. It can be seen that the caffeine release took place quickly in both environments.

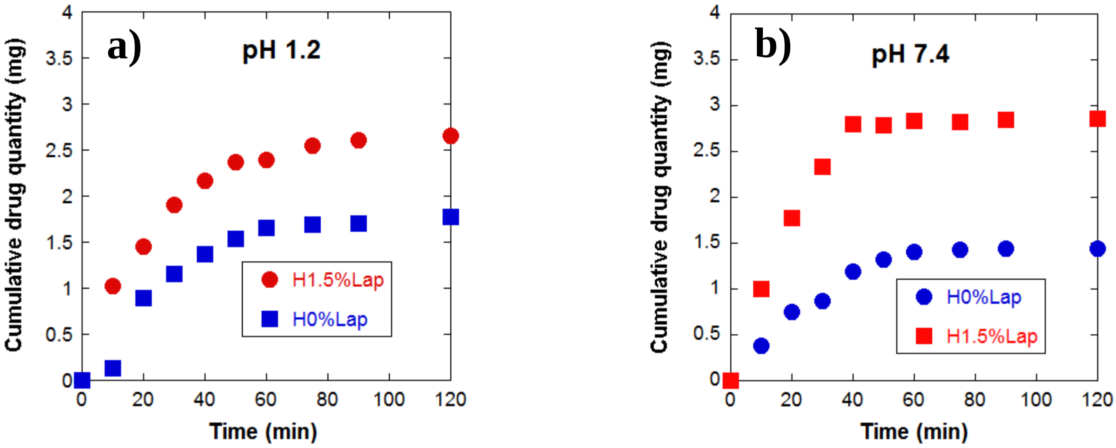

Figure 3.20 Caffeine release a) pH 1.2; b) pH 7.4

Therefore, the results showed that Laponite had practically no influence on the release properties of the nanocomposite hydrogels under the experimental conditions used. By contrast, the addition of Laponite influenced the amount of drug absorbed by the hydrogel including a larger amount of drug compared to the control sample.

CHAPTER 4. Comparative study of the effect of several reinforcing agents on the properties of (nano)composite hydrogels based on poly(methacrylic acid)

The present work aims to show how the main properties of the PMAA hydrogels can be engineered by means of several silicon-based fillers, namely Laponite XLS (XLS), Laponite XLG (XLG), montmorillonite (MMT), and two commercial brands of pyrogenic silica differing mainly by the particle size and zeta potential of their 1.5% aqueous dispersion. On this purpose, the effect of these fillers on the structure and swelling, viscoelastic and depolluting properties of the (nano)composite hydrogels was comparatively studied in correlation with the filler characteristics. To the best of our knowledge, this is the first report of such a comparative study of the influence of various reinforcing nanoagents, in particular clays and pyrogenic silica, in correlation with their characteristics, on the properties of some hydrogels, particularly pH-sensitive PMAA-crosslinked hydrogels. This chapter also comparatively show for the first time how the cationic dye absorption ability of a composite hydrogel depends on the reinforcing agent used. It should be mentioned as well that, although nanocomposite PMAA hydrogels reinforced with pyrogenic silica have already been reported in a paper which analyzes only the physical interactions occurring in the nanocomposite hydrogel, the present work provides for the first time the extended characterization of these hydrogels, both structurally and in terms of rheological and swelling properties. The results presented in this paper may be useful in selecting an appropriate filler so that to adjust the properties of a PMAA hydrogel in agreement with the intended application.

The studied hydrogels were obtained by the radical copolymerization of MAA with N, N'-methylenebisacrylamide (BIS) in aqueous solution, in the presence of ammonium persulfate (APS) as initiator, by using different reinforcing agents (XLG, XLS and MMT clays and two types of pyrogenic silica nanoparticles - HDK and FS).

Due to the pH-sensitive nature of PMAA hydrogels, their contact with aqueous solutions with different pHs causes changes of the contained functional groups leading to different swelling behavior. To observe these changes, the hydrogels were analyzed by FT-IR after swelling at pH 1.2, 5.4 and 7.4, drying, and grinding (Figura 4.2).

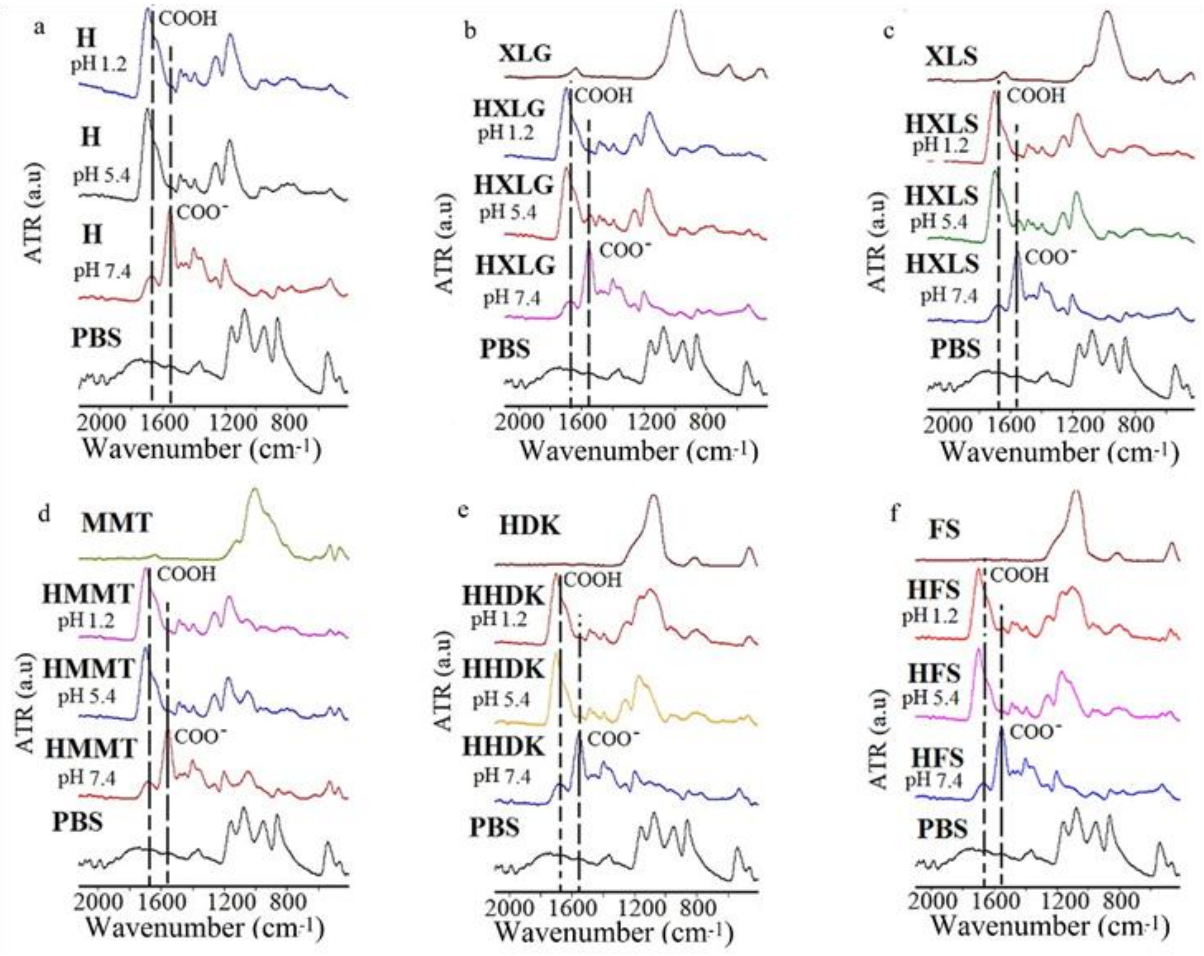

Figure 4.2 FT-IR spectra of (nano)composite hydrogels swelled at different pH values

The FTIR spectra of the hydrogels swelled at pH 7.4 displayed a peak characteristic to the carboxylate group at 1537 cm^{-1}, simultaneously with the decrease of the COOH maximum from 1650 cm^{-1}, which can be explained by the basic character of the swelling medium, whose pH was appreciably higher than the pKa value of the MAA units in the hydrogel. The decrease of pH to 1.2 led to the conversion of all hydrogel groups to COOH, and therefore, to the dissappearance of the COO^- peak in all spectra.

At pH 5.4 only the spectra corresponding to the hydrogels reinforced with the two types of Laponite showed the peak characteristic of the COO^- group, this being due to the basic groups contained by Laponite in its structure. Also, in all cases, the presence of the reinforcing agent in the polymer matrix was highlighted through the peaks characteristic of the Si-O bonds in its composition.

XRD analysis demonstrated the production of exfoliated nanocomposite hydrogels in the case of hydrogels reinforced with the two types of Laponite clay (Figure 4.3a and b), intercalated composite hydrogels in the case of those reinforced with MMT (Figure 4.3c).

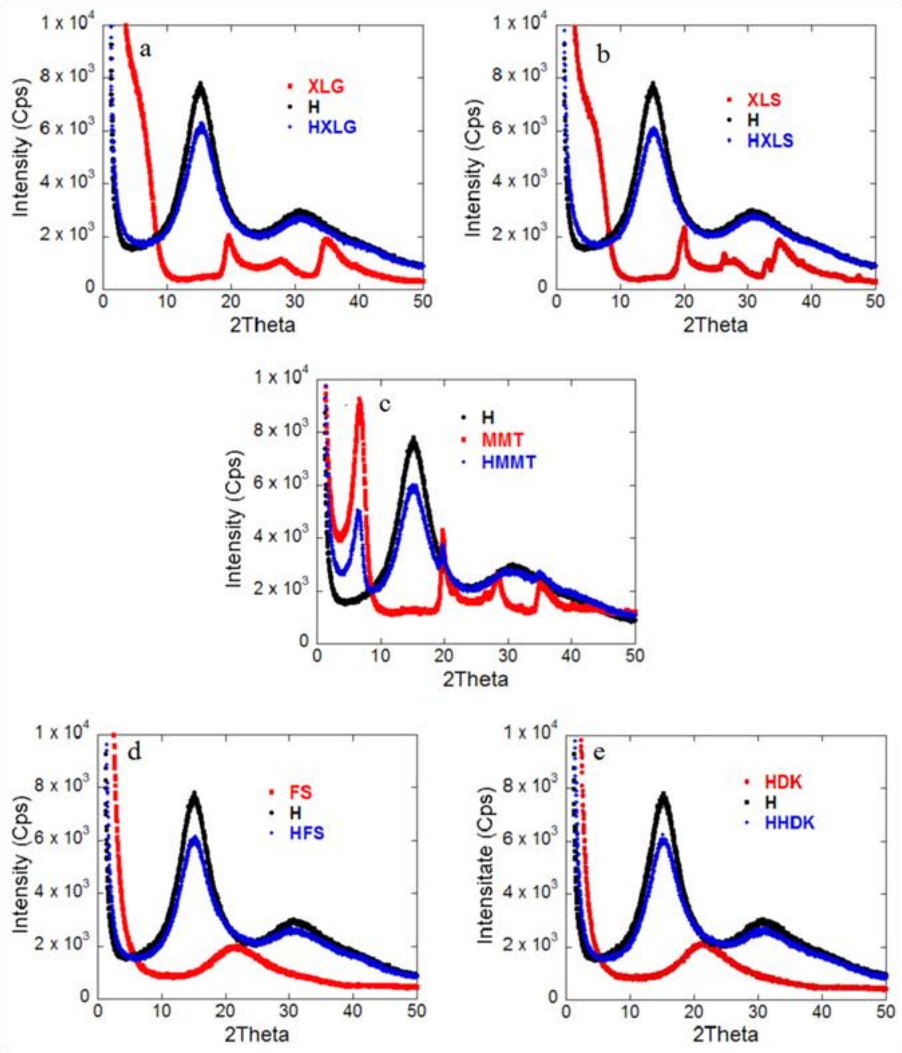

Figure 4.3 XRD spectra of the hydrogels investigated and of the reinforcing agents used

In the case of hydrogels reinforced with silica nanoparticles, it was highlighted that there was a strong interaction between the polymeric component and the inorganic component

(Figure 4.3d and e). XRD analysis was confirmed by TEM analysis.

Swelling studies have shown that at acidic pH the swelling equilibrium was reached in less than 200 minutes, and at low basic pH in about 500-1000 minutes. Also, as the pH of the swelling medium increases, the equilibrium degree swelling has increased due to the formation of an increased number of ionized groups in the hydrogel. Regarding the effect of reinforcing agents on SDe, it depended on both the nature of the reinforcing agent and the pH of the swelling medium. Thus, at strongly acidic pH (pH 1.2), the reinforced hydrogels showed a lower SDe compared to the control due to the slightly crosslinking effect of the reinforcing agents on the polymeric matrix. At pH 5.4 SDe there was a significant increase for all samples the most pronounced increase occurred in the case of hydrogels synthesized in the presence of Laponite XLS and XLG. At this pH, the swelling degree of the pyrogenic silica-containing composite hydrogels was lower than that of the control hydrogel due to the crosslinking effect of the particles. At pH 7.4, surprisingly, the SDe of hydrogels reinforced with pyrogenic silica exceeded the equilibrium swelling degree of the others samples due to the Si-OH functional groups in their structure that ionized at this pH (Figure 4.9).

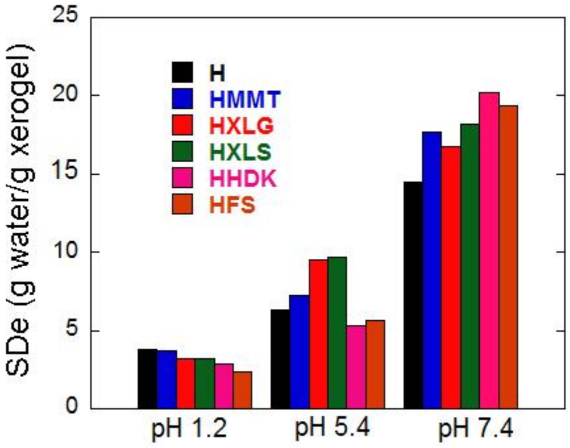

Figure 4.9 Equilibrium swelling degree in three different pH media

The frequency sweep measurements showed in all cases G' higher than G" over the whole investigated range, thus confirming the crosslinked character of the hydrogels. Also, rheological measurements showed that the introduction of reinforcing agents resulted in an improvement in mechanical properties (increased G') compared to the control hydrogel, at an approximately constant swelling degree (initial hydrogels). Rheological measurements of swelled hydrogels at equilibrium in deionized water (pH 5.4) showed, as expected, a decrease in G' due to the increased swelling degree. Another conclusion was that in the swollen state the hydrogels reinforced with pyrogenic silica showed the best mechanical properties (Figure 4.14).

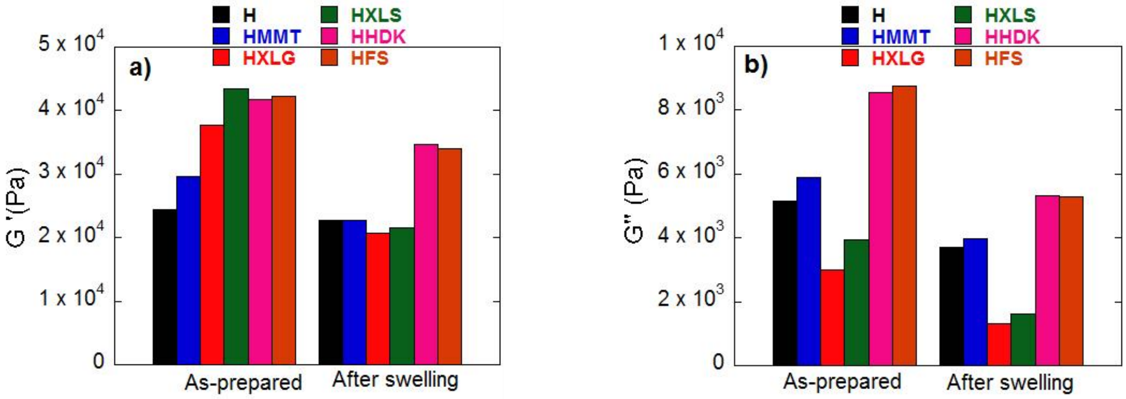

Figure 4.14 Frequency sweep rheological measurements on both as-prepared and equilibrium-swelled (pH = 5.4) hydrogels: a) storage modulus; b) loss modulus

Strong hydrogels were only obtained for XLG and XLS as fillers, when the tan δ values were less than 0.1 in both as prepared and equilibrium-swollen states (Figure 4.15).

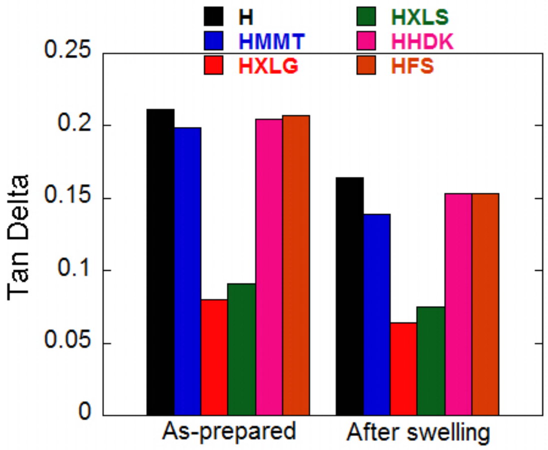

Figure 4.15 1Hz loss factor values of the hydrogels investigated, both in the initial state and swelled to pH 5.4

The absorption properties of synthesized composite hydrogels for methylene blue and crystal violet, used as basic (cationic) dye models, were also investigated.

The study of dye absorption by the (nano)composite hydrogels showed similar results in the case of both dyes, but the behavior of the hydrogels was different. Thus, HXLS showed the highest rate of dye absorption among all hydrogels, practically the entire amount of dye being absorbed from solution in less than 30 min, a performance that was not achieved by the other hydrogels even after 30 h (Figure 4.17)..

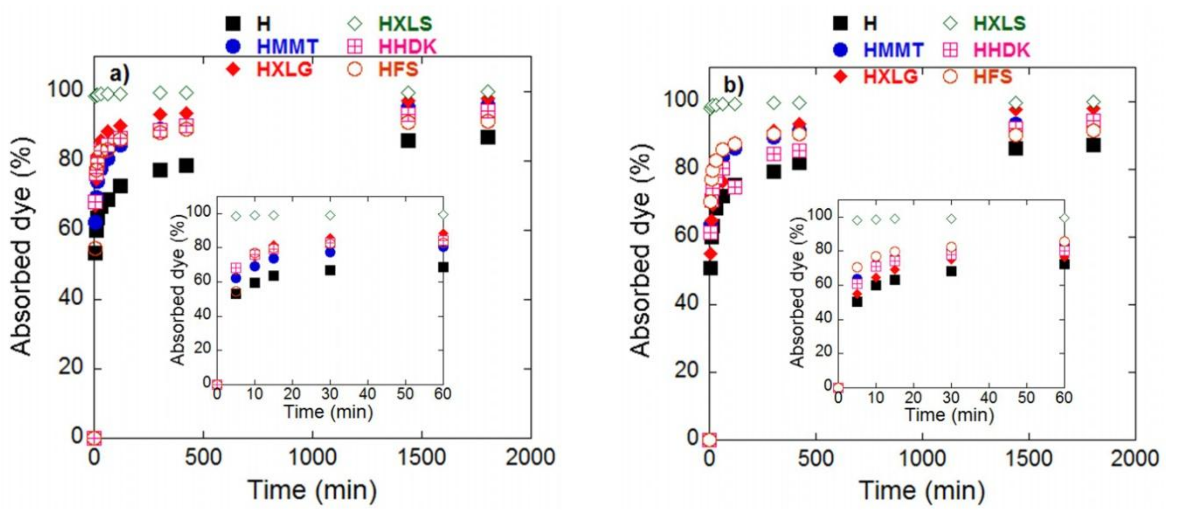

Figure 4.16 Time dependence of the percentage of dye absorbed by the (nano)composite hydrogels: a) methylene blue; b) crystal violet.

General conclusions and original contributions

General conclusions

The PhD thesis aimed to comparatively investigate some parameters (concentration of monomer/crosslinking agent/reinforcing agent, nature of reinforcing agent) on the properties of poly(methacrylic acid) hydrogels and also to develop and characterize new pH-sensitive (nano)composite hydrogels of this type, which have improved physico-chemical and mechanical properties with potential applications in medicine (drug-controlled release) and treatment of water contaminated with dyes. For this purpose, three main research directions were pursued:

1. *Comparative study of the parameters which influence the water absorption and viscoelastic properties of poly(methacrylic acid)-based hydrogels.*

The studies carried out in this direction of research have led to the following conclusions:

- ✓ Increasing of monomer/crosslinking agent/reinforcing agent concentration improved viscoelastic properties;
- ✓ The most important effect on the viscoelastic properties was the monomer concentration, by tripling it an increase of G' of about 30 times was obtained, compared to an increase of only 5 times obtained in the case of BIS concentration and 1.5 times at increasing the concentration of MMT;
- ✓ Increasing the concentration of monomer from 10% to 30% of the total mass or crosslinking agent from 1% to 3 mole% to monomer led to a decrease in water

absorption of hydrogels due to the the crosslinking degree increase;

- ✓ The presence of MMT in the hydrogel matrix led to a different swelling behavior depending on the pH of the environment, so that at pH 1.2 the hydrogels reinforced with MMT had a slightly lower swelling degree than the control, while at pH 5.4 and 7.4 the swelling degree of the hydrogels filled with MMT increased with the increase of the MMT concentration;
- ✓ The synthesis of the hydrogel in the presence of MMT led to the obtaining of intercalated composite hydrogels.

2. *Synthesis and characterization of new (nano)composite hydrogels with poly(methacrylic acid) network*

Within this research direction composite hydrogels based on poly(methacrylic acid) reinforced with commercial clay Cl93A (montmorillonite organomodified with methyl-di acid sulfate (hydrogenated tallow) ammonium) as such, and modified with octyl dimethylmethoxysilane (Cl93A-C8) or octadecyl dimethylmethoxysilane (Cl93A-C18) (subchapter 3.1) and poly(methacrylic acid) composite hydrogels, respectively, reinforced with different concentrations of Laponite XLG synthetic clay (subchapter 3.2) were studied.

The studies carried out in this direction of research have led to the following conclusions:

- ✓ Hydrophobized commercial Cl93A clay slowed down the process of water release from the hydrogel network;
- ✓ Mechanical properties have been improved by introducing clays into the polymer matrix;
- ✓ Nanocomposite hydrogels obtained based on PMAA and Cl93A showed good biocompatibility;
- ✓ Exfoliated or intercalated nanocomposite hydrogels were obtained depending on the type of clay used in the synthesis, Laponit XLG generating exfoliated structures, and Cl93A commercial clay leading to intercaleted structures;
- ✓ The viscoelastic properties of PMAA-based hydrogels with Laponite XLG added increased proportionally to the increase in the concentration of the reinforcing agent;
- ✓ At pH 1.2 the increase of Laponite concentration affected the swelling degree very little, while at pH 5.4 and 7.4 the swelling degree increased with the concentration of Laponite in the hydrogel due to the basic groups present in the structure of Laponite that have led to the formation of carboxylate groups in

the hydrogel matrix;

- ✓ The introduction of Laponite into the PMAA matrix led to the retention of a larger amount of drug compared to the control hydrogel due to the higher swelling of the nanocomposite hydrogel, however without having a slowing effect on the release process.

3. *Study of the influence of the nature of the reinforcing agent on the properties of (nano)composite hydrogels with poly(methacrylic acid) network*

Within this research direction, (nano)composite hydrogels based on poly(methacrylic acid) and various silicon-based reinforcing agents (Laponite XLG / XLS, montmorillonite, pyrogenic silica HDK / FS) and their effect on the properties of the synthesized hydrogels were studied.

The studies conducted led to the following conclusions:

- ✓ The structure of the synthesized hydrogels was influenced by the pH of the aqueous dispersions of the reinforcing agents used and by the pH of the swelling medium used;
- ✓ Exfoliated or intercalated nanocomposite hydrogels were obtained depending on the type of clay used in the synthesis: Laponit XLS and XLG clays generated exfoliated structures, and MMT clay led to intercalated structures;
- ✓ The swelling degree was influenced by the pH of the aqueous dispersion of the reinforcing agent used and by the accentuated or less accentuated exfoliation of the reinforcing agent in water;
- ✓ At a strongly acidic pH, the synthesized hydrogels showed a lower swelling degree compared to the control due to the interaction of the reinforcing agents with the polymeric matrix;
- ✓ At pH 5.4 the swelling degree increased in the order of HHDK≈HFS <H<HMMT<HXLS≈HXLG being influenced by the basic pH of the aqueous dispersions of Laponit XLG, Laponit XLS and MMT and by the better dispersion in water of XLG and XLS as compared to MMT;
- ✓ At pH 7.4 the swelling degree increased massively for all synthesized hydrogels due to the formation of an increased number of ionized groups in the hydrogel regardless of the reinforcing agent used;
- ✓ At pH 7.4 the swelling degree increased in the order of H <HXLG

<HMMT≈HXLS <HFS <HHDK, the highest degree of swelling being obtained in the case of hydrogels reinforced with pyrogenic silica due to ionization of Si-OH functional groups in the silica structure;

- ✓ The swelling equilibrium was reached much faster in a strong acidic and slightly acidic environment (> 200 min) as compared to a weak basic medium (500-1000 min);
- ✓ The viscoelastic properties of PMAA-based hydrogels and various reinforcing agents increased in the initial state compared to the control regardless of the reinforcing agent used as follows: G'(H) <G' (HMMT) <G '(HXLG) <G' (HXLS) ≈G '(HHDK) ≈G' (HFS), while in the swelled state the order was: G' (HXLG) ≈ G' (HXLS) <G'(H) ≈ G' (HMMT) <G' (HFS) ≈ G '(HHDK);
- ✓ In the case of hydrogels reinforced with Laponite XLS and XLG, strong nanocomposite hydrogels were obtained;
- ✓ The depolluting activity of the studied hydrogels occurred through an absorption process of the investigated dyes and not through an adsorption one;
- ✓ All synthesized (nano)composite hydrogels showed a higher absorption capacity compared to the control
- ✓ The hydrogel reinforced with Laponit XLS showed the highest dye absorption rate, most likely due to the fact that Laponite XLS is modified with tetrasodium pyrophosphate;
- ✓ This study demonstrated the importance of choosing the reinforcing agent to obtain hydrogels with adequate properties (swelling, absorbent/depolluting, viscoelastic) depending on the intended application.

Original contributions

The general objective of this PhD thesis was the study of (nano)composite hydrogels with poly(methacrylic acid) network in the presence of various reinforcing agents, with the potential use for controlled release of drugs or for absorption of dyes. Below are a series of elements of originality in this doctoral thesis:

1. Comparative investigation of the effect of the concentration of monomer, crosslinking agent and reinforcing agent on water absorption and viscoelastic properties of poly(methacrylic acid) hydrogels;

2. Highlighting the fact that, among the studied parameters, the one that most influences the viscoelastic properties of hydrogels is the monomer concentration;
3. Obtaining and characterizing of new hydrogels based on PMAA and hydrophobic modified Cl93A/Cl93A clay
4. Demonstration of the ability of Cl93A clay hydrophobically modified to slow down the water release process from the hydrogel network;
5. Highlighting the biocompatibility of PMAA and Cl93A based hydrogels;
6. Study of the structure, viscoelastic and swelling properties of new PMAA-Laponite XLG nanocomposite hydrogels;
7. Demonstration of obtaining exfoliated nanocomposite hydrogels based on Laponite XLG with improved viscoelastic properties;
8. Comparative study of the effect of various silicon-based reinforcing nanoagents on the properties of (nano)composite hydrogels with poly(methacrylic acid) network;
9. Demonstrating that both the viscoelastic properties and the swelling degree of the hydrogels and the absorption of the dyes have been influenced by the type of reinforcing agent used by means of its characteristics;
10. Premiere presentation of the structural, rheological and swelling properties of hydrogels based on PMAA and pyrogenic silica nanoparticles;
11. Highlighting that the most pronounced effect on the viscoelastic properties and crosslinking density of hydrogels among all reinforcing agents used was pyrogenic silica nanoparticles;
12. Comparison of cation dye absorption properties of a polymeric matrix according to the reinforcing agent used;
13. Demonstrating that the nature of the reinforcing agent significantly influences the absorption properties of hydrogels with PMAA network.

Dissemination of results

The results of the PhD thesis were disseminated by presenting at 7 international conferences and symposia and by publishing/submitting for publication 4 articles in ISI-listed journals. The list of publications and participation in conferences is presented in Annex 1.

Articles

1. R. Ianchis; **C.M. Ninciuleanu***; C. Gifu; E. Alexandrescu; R. Somoghi; A. Gabor; S. Preda; C.L. Nistor; S, Nitu; C. Petcu; M. Icriverzi; P. Florian; A. Roseanu. Novel Hydrogel-Advanced Modified Clay Nanocomposites as Possible Vehicles for Drug Delivery and Controlled Release. *Nanomaterials* **2017**, *7*, 443.(FI$_{2021}$= 5,076)
2. **C.M. Ninciuleanu**; R. Ianchis; E. Alexandrescu.; C. Mihaescu; B. Trica; C. Scomoroscenco; C.L. Nistor; C. Petcu; S. Preda; M. Teodorescu. Nanocomposite hydrogels based on poly(methacrylic acid) and Laponit XLG, *UPB Scientific Bulletin, Series B: Chemistry and Materials Science,* **2021**, 83 (1), 43-57 (FI$_{2021}$=0)
3. **C.M. Ninciuleanu**; R. Ianchiş; E. Alexandrescu; C. Mihăescu; C. Scomoroşcenco; C.L. Nistor; S. Preda; C. Petcu; M. Teodorescu. The Effects of Monomer, Crosslinking Agent, and Filler Concentrations on the Viscoelastic and Swelling Properties of Poly(Methacrylic Acid) Hydrogels: A Comparison. *Materials* **2021**, 18 (FI$_{2021}$=3,623)
4. **C. M. Ninciuleanu**; R. Ianchiș; E. Alexandrescu; C. I. Mihăescu; S. Burlacu; B. Trică; C. L. Nistor; S. Preda; C. Scomoroscenco; C. Gîfu; C. Petcu; M. Teodorescu. Adjusting the properties of poly(methacrylic acid) (nano)composite hydrogels by means of the filler. – under evaluation for publication

Communications

1. **C.M. Ninciuleanu**, R. Ianchis, C. Gifu, E. Alexandrescu, R. Gabor, C. Nistor, S. Nitu, C. Petcu., B. Trica, S. Preda, ,,A new nanocomposite hydrogel vehicle for the treatment of gastrointestinal cancer”, Priorities of Chemistry for a Sustainable Development - PRIOCHEM XIV ed., Bucharest, Romania, 10-12 October (2018)
2. **C.M. Ninciuleanu**, R. Ianchis, C. Gifu, E. Alexandrescu, S. Preda, C. Scomoroscenco, C.L Nistor, C. Mihaescu, C. Petcu, M. Teodorescu, "Poly(methacrylic acid) nanocomposite hydrogels", 9th International Conference of the Chemical Societies of the South-East European Countries, Târgoviște, Romania, 8-11 May (2019)
3. **C.M. Ninciuleanu,** R. Ianchis, E. Alexandrescu, B. Trica, S. Preda, C. Scomoroscenco, C. Mihaescu, C.L. Nistor, C. Petcu, M. Teodorescu, "Composite Hydrogels Based on Poly(methacrylic Acid) Reinforced with Laponite Inorganic Filler", Priorities of Chemistry for a Sustainable Development - PRIOCHEM XV ed., Bucharest, Romania, 30 October - 1 November (2019)
4. **C.M. Ninciuleanu**, R. Ianchis, C.L. Nistor, C. Scomoroscenco, C. Mihaescu, E. Alexandrescu, C. Petcu, M. Teodorescu, Preliminary Studies for Obtaining a New Nanocomposite Hydrogel Platform as an Anti-Exercise Induced Fatigue Dietary Supplement, Early Career Scientists - NATO's STO Bucharest (2019)
5. **C.M. Ninciuleanu**, R. Ianchis, C.L. Nistor, C. Scomoroscenco, C. Mihaescu, E. Alexandrescu, B. Trica, C. Petcu, S. Preda, M. Teodorescu, "Composite Materials Based on Poly(methacrylic) Acid and Three Different Fillers", 3rd International Conference on Emerging Technologies in Materials Engineering-EmergeMAT, Bucharest, Romania, 29-30 October (2020).
6. **C.M. Ninciuleanu**, R. Ianchis, E. Alexandrescu, C. Mihaescu, S. Preda, C. Scomoroscenco, S. Burlacu, C.L. Nistor, C. Petcu, M. Teodorescu, ,,Poly(methacrylic acid) Composite Hydrogels With Potential Uses as Devices in Medical and Environmental Protection Fields” Nanotechnology and Nanoscience, Malvern, USA 25-26 January 2021.

7. **C.M. Ninciuleanu,** R. Ianchis, E. Alexandrescu, C. Mihaescu, B. Trica, C. Scomosroscenco, C. Nistor, S. Burlacu, C. Gîfu, C. Petcu, Silviu Preda, M. Teodorescu, „Composite hydrogels with potential use in dyes removal", Applications of Chemistry in Nanosciences and Biomaterials Engineering – NanoBioMat, Bucharest, Romania 25-27 November (2021)-**best paper award**