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Dedicated to the memory of
Professor Candin Liteanu on his 100th anniversary

AN INVESTIGATION ON MULTI-LAYERED HYDROGELS BASED ON POLY(N, N-DIMETHYLACRYLAMIDE – CO – 3, 9-DIVINYL-2, 4, 8, 10-TETRAOXASPIRO (5.5) UNDECANE)**

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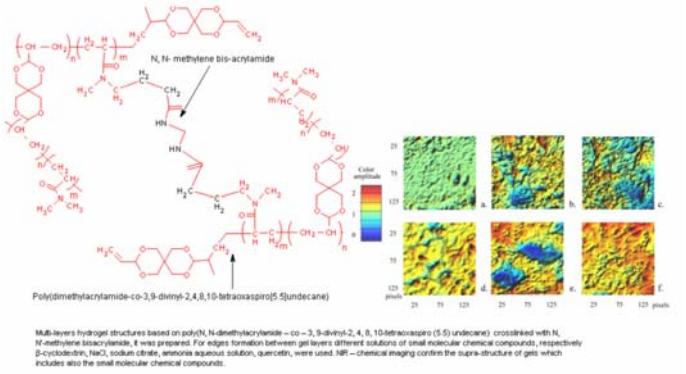
Assembled multi-layered hydrogel structures based on poly(N, N-dimethylacrylamide – co – 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) crosslinked with N, N'-methylene bisacrylamide, were prepared. The chemical composition of gels was confirmed by FTIR and ^{1}H-NMR spectra. The configuration and supra-structure of hydrogel layers were visualized by optical and scanning electron microscopy, while the imprinting effect of the small molecular chemical compounds solutions on the gels surface was emphasized by NIR – chemical imaging. Water sorption / desorption measurements evidenced as well the dependence of swelling capacity of the prepared hydrogels on the solution variant used for inter-layers border formation.



INTRODUCTION

Hydrogels gained increased attention in the latter half of the 20th century owing especially to their essential characteristic, which is the ability to respond to relatively small changes in stimuli with relatively large changes in volume that allows a wide variety of applications.[1-9]

Thus, hydrogels, as macromolecular networks, capable of absorbing, retaining and releasing water solutions in a reversible way and in response to specific environmental stimuli, are widely used in the biomedical field for different applications as for example personal care products, drug delivery and controlled release systems, or in catalysis and biosensing activities.

For these applications, especially for drug delivery controlled release, the presence of hydrophobic domains into hydrophilic matrix adjusts the control of the rate of delivery. The systems properties are controlled by the polymeric structures composition, and are as well dependent on the interactions between the phases and the methods of synthesis.[10] There is a great challenge

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in creating three-dimensional hydrogel structures with precise patterns for specific bioactive compounds, or biomolecules and cell types to be positioned more appropriate into the structural complexity of the polymeric network. This kind of complex supra-structure will able to be exploited in biological processes and to respond to physical and biochemical stimuli. As the requirements for engineering of biomedical hydrogel products grow more complex, the need for fabrication technologies capable of producing gels with micro-architectures and biochemical functionalities tailored in three-dimensional space increases permanently.

In this context Ladet *et al.* reported on the processing of a multi-layer "onion-like" structured material based on a polysaccharide physical hydrogel.[11] The structure allows the formation of a succession of "inter-layer spaces" between hydrogel layers well suited for an easy cell introduction and culture. The same group investigated the bioactivity of new chitosan-based multi-layer hydrogel (MLH) architectures towards chondrocyte-like cells. The microstructure of the hydrogels constituting the layers precludes any living cell penetration, whereas their lower scale architecture allows the protein diffusion. Data suggested the use of MLH structures as complex chondrocytic cell bioreactors, for various biomedical applications like the inter-vertebral disk replacement.[12] The multi-sheets structures offer as well the advantage of better control over the properties. Additional the preparation of biodegradable hydrogels allows a controlled degradation layer by layer providing support for attachment and growth of cell lines.[13] The common technique to assemble a multi-layered hydrogel is starting from a gel-core template and creates polymer sheets around the gel-core template. The reaction parameters, such as crosslinker type and content, reaction temperature, are essential in thickness of the polymer sheets and time of gelation. [14, 15]

The hydrogels sheets were prepared by physical or chemical gelation. Ladet *et al.* used physical gelation of polysaccharides achieved by balancing solvophobic and solvophilic interactions to prepare complex polymeric architectures with free "inter-layer" spaces well suited for cell or drug. The inter-layer space allows the penetration and development for different cell types or drugs which can leads to production of complex, multi-cellular and multilayer tissues with high interest for skin and bone tissue engineering.[11]

The free radiation method was applied to prepare multi-layered hydrogels based on polysaccharides and isocyanate functional prepolymers as crosslinkers.[15] The advantage of tailor-made three-dimensional multi-layer tubular or spherical structures is the controlled properties presented in order to incorporate and release therapeutic agents in tissue engineering or to be used in the food and cosmetic.

In our previous studies it was presented the preparation of a new copolymer based on poly(N,N-dimethylacrylamide – co – 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) - p(DMA-co-U) which have biodegradable and biocompatible character, binding properties, amphilicity, good oxidative and thermal stability, good film forming capacity, and acid pH sensitivity.[16] The copolymer crosslinked with N, N' – methylene-bis-acrylamide (MBAa) possesses the ability to form a hydrogel structure.[17] The new network system presents high hydrophilicity, and sensibility at pH and temperature.

Based on this polymer structure new multi-layered gel systems were prepared using different small molecular chemical compounds, which have double purpose for constructing the edge of interfacial supramolecular assemblies and to improve the coupling capacity of gels.[18, 19] The multi-layer 'onion-like' gel systems were tested as matrix for coupling drugs.

In the present study hydrogels assembled in form of multi-layered structures were prepared by crosslinking of p(DMA-co-U) with MBAa. The inter-layer spaces were created by using different solutions of small molecular chemical compounds (as it is noticed in Table 1). The multi-layer hydrogels were successfully assembled starting with gel-core templates followed by layer-by-layer successive method. The purpose was to prepare multi-layer porous hydrogels with different morphologies and properties. The formation of the hydrogels was evidenced by FTIR and ^{1}H-NMR spectra. The configuration of hydrogel sheets was visualized by optical and scanning electron microscopy, while imprinting effect of the swelling – gelation chemical solutions on the gels surface have been emphasized by chemical imaging. Water sorption/ desorption measurements shows the dependence on type of substrate existing between the polymeric sheets which form the structure.

RESULTS AND DISCUSSION

FT-IR analysis. The characteristic IR bands of multi-layered hydrogels are illustrated in Fig. 1, highlighting the crosslinking reaction by the peak at 3334 cm^{-1} corresponding to -NH stretching of the *N, N'* – methylene bisacrylamide unit.

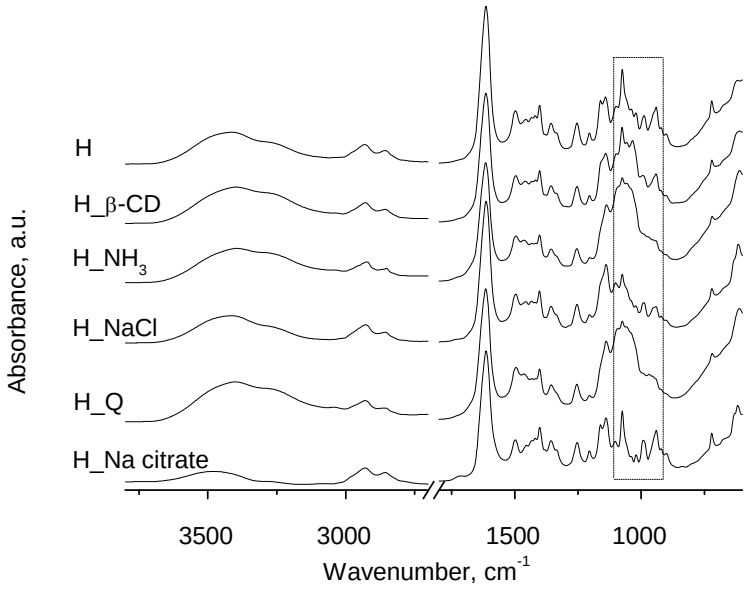


Fig. 1 – FT-IR spectra of the multi-layered hydrogels.

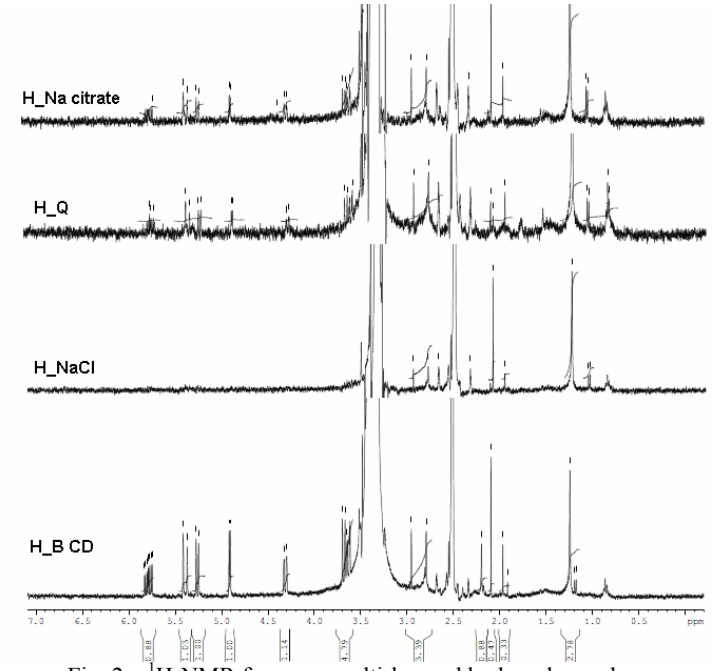


Fig. 2 – ^{1}H-NMR for some multi-layered hydrogel samples.

Particularities on FT-IR spectra appear in two IR regions, respectively from 3673 cm^{-1} to 3061 cm^{-1} and 1099 cm^{-1} to 912 cm^{-1}. The IR broadband from 3673 cm^{-1} to 3061 cm^{-1} includes the overlapped bands corresponding to OH stretch (H-bonded or free form of functional group) and -NH stretching of crosslinked agent. On 1099 ÷ 912 cm^{-1} region common IR bands are evidenced, as it will be discussed below. The IR band from 1099 cm^{-1} is shifted to 1093 cm^{-1} (H_Q) and to 1103 cm^{-1} (H_Na citrat) and is attributed to C-O functional group. The IR band from 1039 cm^{-1} (H) is shifted to 1034 cm^{-1} (H_β-CD), to 1022 cm^{-1} (H_NaCl) and to 1020 cm^{-1} (H_Na citrate) and corresponds to spiroacetal moiety of 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane.

^{1}H-RMN. The crosslinking reaction of poly(N, N- dimethylacrylamide - co - 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) with *N,N'*-methylene bisacrylamide by the proton peaks in ^{1}H-NMR spectra (Fig. 2), is also confirmed: 4.81 ppm (corresponding to –OCHO-acetal), 3.9 ppm (-CH_2-), 3.37ppm (OH), 1.84 ppm (-CH_3), 1.467 ppm (-CH_2) and 0.928 ppm (CH_3).

Optical microscopy analysis. The surface analysis of the polymeric structures and the groove between the hydrogel sheets are presented in Fig. 3. As it can be observed, the use of specific solutions for the creation of thin edges and inter-domain borders between the polymer-gel layers determined modifications of the surface of the hydrogels. Relative continuous and dense morphology presents all the prepared multi-layered gels. The insertion of particles, which correspond to small molecular chemical compounds: quercetin, β–cyclodextrin or NaCl present into solutions used for border gels formation, is also evident. These particles respect the shape and possibilities of physical bonds of the precursor: filaments in case of NaCl, cylindrical sticks for β–CD, or four-arm shaped form in case of Q, which can be ascribed to hydrogen bonds realized through 5, 7, 3', and 4' OH groups.

SEM analysis. Morphological analysis was performed in cross-section of the freeze-dried polymeric multi-layered gels (Fig. 4). More similarities between hydrogels made with coating solution prepared with organic compounds of β-CD, Q and Na citrate can be noticed. These structures have the morphology of the polymer networks with homogeneous porous microstructure like the honeycomb, well defined, dense and interconnected pores. At the same time, H_Q sample presents the same specific morphology but denser, with significant decrease of pore size which suggests the increased interactions inside the network. As it is well known, the morphology aspects of the polymeric matrix are important for the final properties of the compound such as vapor sorption capacity and ability to incorporate, transport and release a therapeutic agent, aspects that interest the potential medical and pharmaceutical applications of the multi-layered hydrogels.

The presence of small molecular compounds from the coating solutions used for edges between hydrogel layers formation is evidenced by the EDAX analysis in Table 1.

The equilibrium of the percentage ratio of the C, H, O, N elements, and the inclusion of Na and Cl in case of H_NaCl and H_Na citrate, attests the presence of small molecular compounds in the composition of the prepared hydrogels.

Near infrared data chemical imaging analysis. The surface of multi-layered hydrogels was analyzed by the identification of principal component analysis (PCA) technique, using as control compound the surface of hydrogel based on poly(N, N- dimethylacrylamide - co - 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) (H) (Fig. 5). The data undergoing for these types of correction, respectively the spectral data were corrected by applying baseline correction and Standard Normal Variate (SNV) correction and the optical data were centered. The SNV correction was realized in respect to baseline shifts and slopes of spectral data, in order to calculate the average and to scale all the observation data.

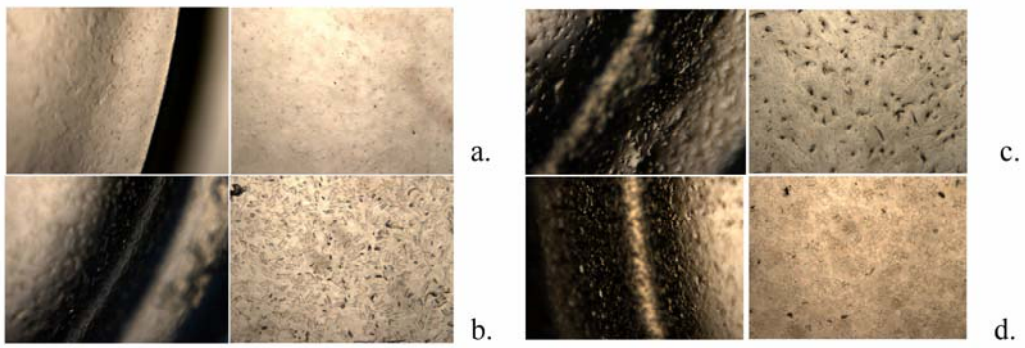


Fig. 3 – Optical microscopy image of the inter-layer space and surface of hydrogels: H (a), H_ β-CD (b), H_NaCl (c) and H_Q (d). Magnification: 40X.

Table 1

The percentage of the elements identified in the composition of hydrogels by EDAX analysis

Sample name	C, %	N, %	O, %	Na, %	Cl, %
H	76.73	10.07	13.20	-	-
H_NaCl	72.03	9.27	15.06	1.97	1.67
H_NH_3	76.77	9.53	13.70	-	-
H_β-CD	69.97	9.26	20.77	-	-
H_Na citrate	74.06	9.48	15.80	0.66	-
H_Q	62.62	11.18	26.2	-	-

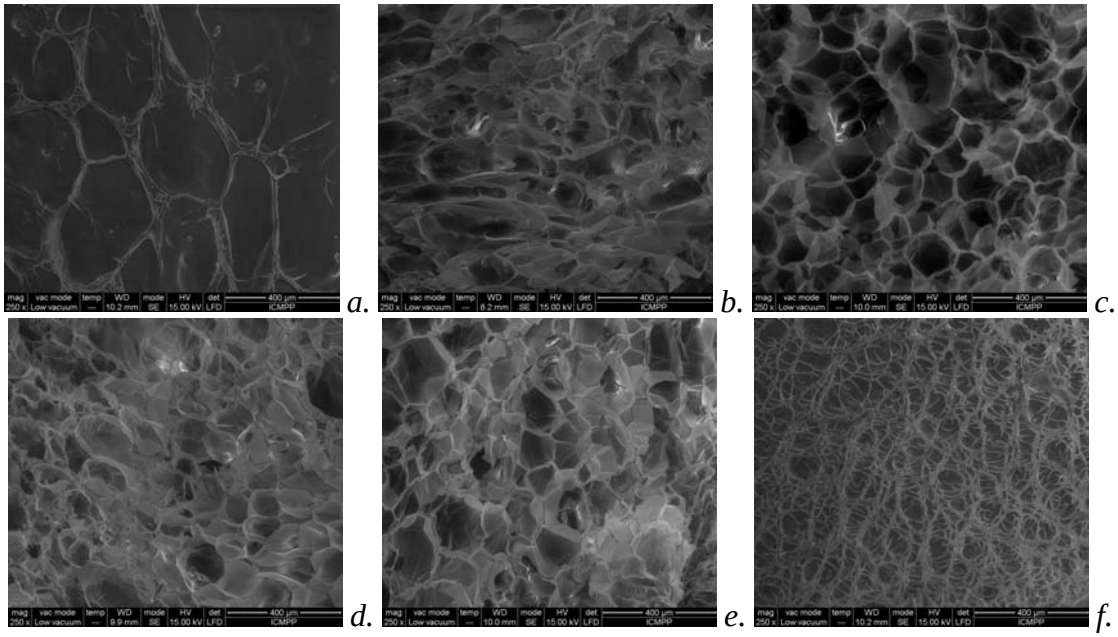


Fig. 4 – SEM images of the cross-section view of freeze-dried hydrogels: H (a), H_ NH_3 (b), H_ NaCl (c), H_ Na citrate (d), H_ β-CD (e), and H_ Q (f). Magnification: 400 μm.

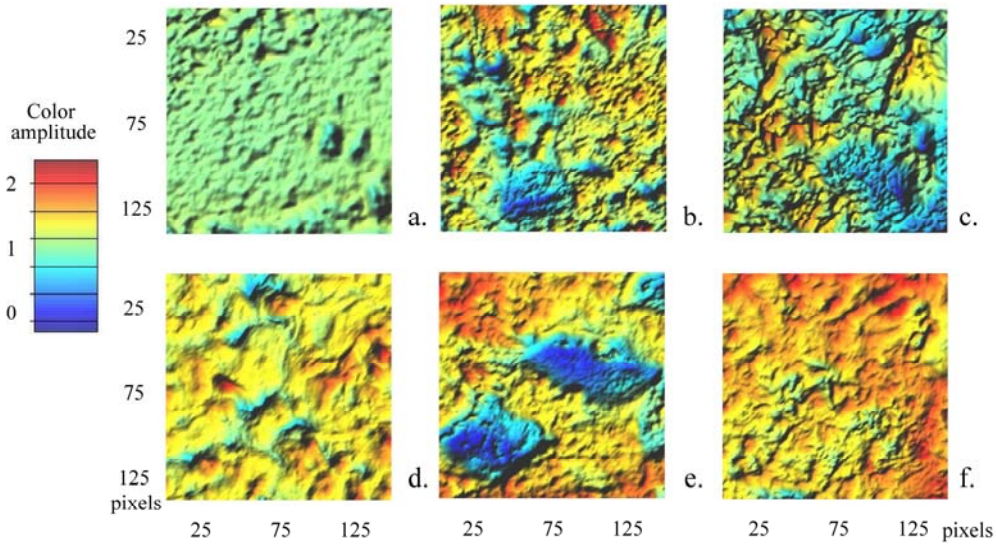


Fig. 5 – PCA model of surface analysis by NIR-CI of multi-layered hydrogels: H – control compound (a), H_ β-CD (b), H_ NaCl (c), H_ Na citrate (d), H_ NH_3 (e) and H_ Q (f).

NIR chemical imaging is extensively used in pharmaceutical applications to analyze the distribution uniformity of the active ingredients in tablets or powder blends and correlate with product performance. But this technique is relatively new in polymer fields.[20] Furukawa *et al.*[21] used this technique to evaluate the homogeneity of binary blends between poly(hydroxybutyrate) and poly(lactic acid). Shinzawa *et al.*[22] has been explored by NIR imaging the effect of the grinding on cellulose excipient at the molecular level. Presently, near-infrared spectroscopy method in combination with chemometrics is widely employed in analysis, because it involves a fast, non-destructive and inexpensive method, as well as easy operation for quantitative determination of many constituents. In these analyses NIR imaging technique is helpful in criticality assessing of ingredients distribution during the development phase of a formulation or process.

In our study NIR imaging confirms the different morphologies of the prepared hydrogels due to the solutions used for border formation between gel-layers, evidenced as well by optic microscopy and SEM analysis. As it can be observed from Fig. 5, more homogenous structures were registered in case of H_Q and H_Na citrate hydrogels. This aspect is justified by the physical bonds better distributed between organic small molecular chemical compound and the polymeric network. It can be also concluded on the responsibilities of the electrostatic interactions and hydrogen bonds between polymer matrix and small molecular compounds for stabilizing the edges of the supramolecular complex gels and inducing as well the conformational and size of the meshes of the border formed between gel layers.

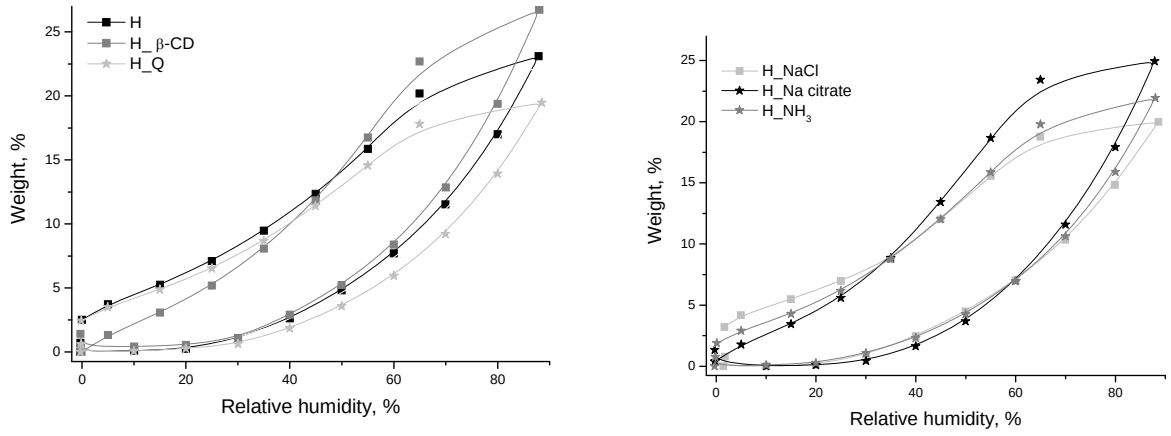
Vapor sorption capacity. As it is well known, the swelling capacity of hydrogels depends on both internal parameters, related to the macromolecular network, and external, related to the environment contacting the material. Fig. 6 a, b present the sorption / desorption isotherms registered for the studied multi-layered hydrogels.

The sorption / desorption isotherms of these systems indicate hysteresis loop, having the particularities of maximum swelling capacity. The small molecular chemical compounds, present on the hydrogels surfaces as well between gel layers, can be regarded as spacers, which can play multiple roles, as for example: increasing the macromolecular network expanding properties, increasing the average distance between two adjacent crosslinking sites and thus reducing the effective crosslinking density of the polymer network, and decreasing the number of crosslinker molecules active for other crosslinking reactions.

Among the studied hydrogels, the highest capacity to adsorb water vapors presents H_β-CD multi-layered hydrogel, which is up to 26.7 % in the controlled humidity medium of 88% RH. This value is higher than the corresponding one to the control compound gel. The behavior is attributed to the hydrophilic character generated by the primary and secondary OH groups of β-CD. The attachment of β-CDs to the preformed hydrogels can bring further new functionalities to the multi-layered hydrogels, as for example complexation or decomplexation of the bioactive compounds.

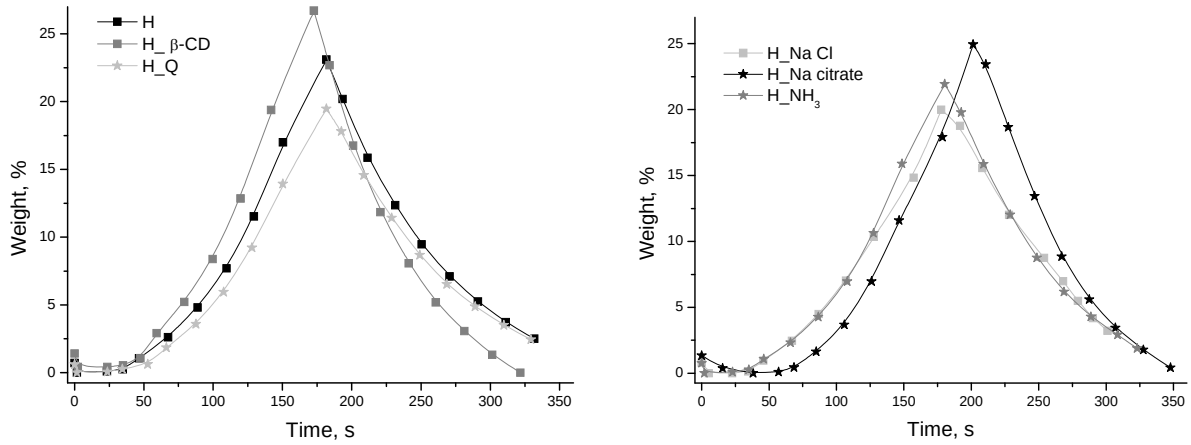
Similar shape of the sorption / desorption isotherms present H_NaCl and H_Q multi-layer hydrogel systems having the lowest values of the adsorption capacity for the water molecules up to 20 % and 19.5 %, respectively. The slow inhibition of water adsorption of the hydrogel with quercetin layer is sustained by its morphological aspect, respectively the pore size of network which is less small than of the other multi-layer hydrogels.

The difference between the sorption capacities is correlated with the differences in their structure and morphology. Increasing the pore size of the polymeric networks from 7 – 15 μm (H_NaCl) or 10 – 25 μm (H_β-CD) to 15 – 25 μm (H_Na citrate) is reflected in the sorption capacity of the polymer gel structures (Fig. 7 a, b). Even it was expected the presence of charge to improve the swelling capacity, it seems that the morphology was the decisive factor in determining the swelling capacity of gels; this fact may be due to the scarcity of small molecular ionizable compounds capable to affect the adsorption capacity of multi-layered structures.



(a) (b)

Fig. 6 – The sorption / desorption isotherms for hydrogels.



(a) (b)

Fig. 7 – The evolution of sorption capacity as weight percentage with time.

BET Analysis of Adsorption Data. Brunauer-Emmett-Teller (BET) isotherm is widely-used method for extracting effective surface areas and adsorption energies from isotherm data. Our study performed on the automated gravimetric analyzer IGAsorp equipment allows for this kind of determination. Data obtained from the adsorption process were fitted on Brunauer-Emmett-Teller (BET) equations 1 and 2, using statistical estimation of adsorption sites occupied during water multilayer formation as a consequence of water adsorption:

$$\frac{P_n}{V(P_0 - P_n)} = \frac{1}{V_m C} + \left[\frac{C-1}{V_m C}\right]^* \frac{P_n}{P_0} \qquad (1)$$

$$\frac{1}{V\left[\left(P_0 / P\right) - 1\right]} = \frac{C-1}{V_m C}\left(\frac{P}{P_0}\right) + \frac{1}{V_m C} \qquad (2)$$

where P_n and P_o are the equilibrium and the saturation pressure, V is the adsorbed water volume, V_m is the monolayer adsorbed water content, and C is the BET constant. The determined values of the specific surface area and water monolayer adsorbed content are summarized in Table 2.

According to the weighing measurements, the influence upon adsorption process of the small molecular compound used for coatings, it is evidenced. Thus, the variation of sorption capacity from 23 % for hydrogel control compound, to 26.7 % for hydrogel with β-CD layer or 19.5 % in case of hydrogel with natrium citrate layer, it was registered.

The increase of the specific surface area as well of the water monolayer adsorbed content in case of H_NaCl and H_β-CD are in agreement with the small molecular compound used for coating. Thus, the presence of fixed charges – H_NaCl case –, typical of polyelectrolyte gels, determines a significant swelling of the polymer in water due to the charge repulsion among polymer chains, and such swelling property is useful in environment-sensitive swelling of hydrogels for controlled drug release.

In case of H_β-CD sample, the increase of the specific surface area and water monolayer adsorbed content is justified by the increase in hydrophilicity owing to the cyclodextrines hydrophilic exterior. Their use is of interest in this context given their hydrophilic exterior, which is useful for maintaining the bulk hydrophilicity and swelling state of the hydrogel, and their hydrophobic interior, which can facilitate the entrapment and controlled release of hydrophobic drugs.

Table 2

The BET data (area and monolayer) evaluated from sorption isotherms in the relative humidity range 0-80%

Sample	Weight (% d. b.)	BET analysis	
		A_{BET} (m^2/g)	Monolayer (g/g)
H	23	232	0.07
H_NaCl	24.9	378	0.11
H_NH_3	19.9	223.5	0.06
H_Na citrate	19.5	187	0.05
H_β-CD	26.7	352	0.1
H_Q	21.9	222	0.06

Abnormal special behavior was registered in case of H_NH_3 and H_Na citrate samples, which necessitates further investigation, as for example pH influence upon swelling. These studies are in course.

MATERIALS AND CHARACTERIZATION METHODS

Preparation of *multi-layered hydrogels*

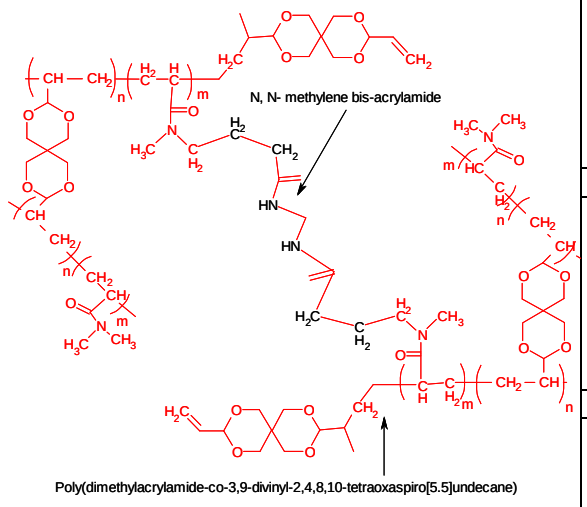
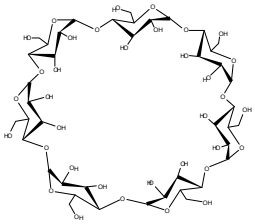
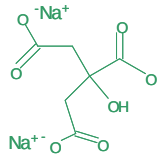
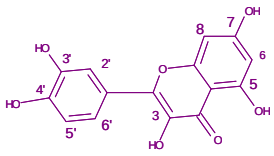
The preparation of poly(*N,N*-dimethylacrylamide-co-3,9-divinyl-2,4,8, 0-tetraoxaspiro (5.5) undecane) (p(DMA-co-U)) copolymer was realized through radical polymerization process in N, N – dimethyl acetamide solution and in the presence of benzoyl peroxide (PBO) as initiator; details concerning the synthesis are already presented.[16]

The gel-strip assemblies are prepared by chemical crosslinking processes. Thus, multi-layered gel preparation implies first the hydrogel core obtainment which was realized by crosslinking p(DMA-co-U) copolymer with *N,N'*-methylene bisacrylamide (MBAa) using ammonium persulfate (APS) (from Sigma) as initiator and N,N,N′,N′-Tetramethylethylenediamine (TEMED) (from Sigma) as reaction accelerator. The gelifying process was previously in detail presented.[17] The percentage ratio between APS and TEMED was about 10 to 1. After thorough stirring for 60s to ensure complete dissolution of the copolymer and homogeneity of the solution, the mixture was dropped into a glass 15 mm in diameter and 30 mm in depth and airtight covered to allow the cross-linking reaction and prevent vaporization of water. The reaction takes place for 30 minutes. The multi-layered structures are created around the polymer-gel middle previously synthesized.

The achievement of thin edges between the polymer-gel layers constitutes the particularity of these "onion-like" structures. Thus, the multi-layered substrate provides an interface with successive hydrogel sheets. For edges formation gel-sheets are firstly immersed and kept 10 min in contact with different solutions of: β-cyclodextrin (β-CD) (1); NaCl aqueous solution 1M (2); sodium citrate aqueous solution 1M (3); ammonia aqueous solution (25%) (4); quercetin (1%) solubilised in ammonia (25%) (5), and just in pure water, sample variant which represents the control compound (H) (6) (Table 3).

Table 3

The multi-layered hydrogels composition

Polymer gel structure	Chemical structure of the small molecular compounds used for edge achievement	Sample notation
Poly(N, N- dimethylacrylamide - co - 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) crosslinked with N, N-methylene bis-acrylamide 	Witness – pure water –	H
	β-cyclodextrin: 	H_β-CD
	Sodium chloride: Na^+Cl^-	H_NaCl
	Sodium citrate: 	H_Na citrate
	Ammonia: $NH_4^+OH^-$	H_NH_3
	Quercetin: 	H_Q

Then, a new gel layer is prepared by adding a new set of 2ml gelifying components, consisting of p(DMA-co-U)/MBAa/APS_TEMED (at a ratio of $2/0.03/5x10^{-4}/5x10^{-5}$), in N, N dimethylacetamide (DMAc)/water (at 4/5 ratio) mixture. After 30 minutes time for gelation the process was repeated in accord with the number of layers that are intended to be achieved.

Characterization

FT-IR spectra of the prepared compounds were recorded on a Vertex Brucker Spectrometer in absorption mode ranging from 400 to 4000 cm^{-1}. The sample was grounded with potassium bromide (KBr) powder and compressed into a disc to analysis. Spectra were acquired at 4 cm^{-1} resolution as an average of 64 scans.

^{1}H-NMR experiments were performed with a Bruker Avance DRX 400 spectrometer equipped with a 5-mm broad band probe. ^{1}H-NMR spectra were recorded at a frequency of 400 MHz in $CDCl_3$.

Optical microscopy images of hydrogels, shortly after synthesis, have been collected with a microscope MIcros Austria (with a halogen lamp) which operates at 220-240 V and 50-60 Hz. The visualization of hydrogel surface has been processed at a magnification of 40X.

SEM micrographs of freeze dried hydrogels were collected in similar conditions regarding the freezing time and method, vacuum pressure, temperature, etc., in order to evidence the morphological differences registered as result of the influence of the solution used for edge and layer formation. The morphology of cross-sectioned samples have been observed using Scanning Electron Microscope, Quanta 200 with EDAX - Elemental Analysis System, in low vacuum atmosphere.

The multi-layered hydrogels were investigated by ***chemical imaging*** on near infrared region (NIR-CI) with statistical analysis methods. Acquisition of optical and spectral data was carried with an integrated Chemical Imaging Workstation, provide by SPECIM Spectral Imaging Ltd (Finland). The optical data have been collected with an ImSpector N17E imaging spectrograph for a resolution of each image of 320 X 640 pixels. The chemical images were taken with a NIR spectral camera, respectively an imaging spectrograph type ImSpector N17E at a rate of 60 – 350 Hz. The original image was recorded at a spatial resolution of 320x640 pixels and they has been collected as a cube of data with two pixels variable (X and Y axis) and the third as absorbance variable (Z axis). The data was processed with EVINCE chemometric software package in order to explore the spectral and spatial information and classified and quantified the image content.

Water vapor sorption capacity of the samples was measured by using the fully automated gravimetric analyzer IGAsorp equipment supplied by Hiden Analytical, Warrington (UK). Water vapor sorption capacity for the samples at 37^{o}C in the 0-90 % relative humidity (RH) range, it was investigated. The vapor pressure was increased in 10% humidity steps, every having a pre-established equilibrium time between 10-20 minutes. The drying of the samples before sorption measurements was carried out at 37^{o}C in flowing nitrogen (250 mL/min) until the weight of the sample was in equilibrium at RH<1 %. An ultrasensitive microbalance measures the weight change as the humidity is modified in the sample chamber at a constant regulated temperature. The measurement system is controlled by the software package which is using Brunauer-Emmett-Teller (BET) theory for multi layer adsorption and extraction of the effective surface areas and adsorption energies from isotherm data. The used *BET equation* is accordingly to

$$\frac{1}{V[(\frac{p_0}{p})-1]} = \frac{C-1}{V_m C}(\frac{p}{p_0}) + \frac{1}{V_m C} \quad (3)$$

where p and p_0 are the equilibrium and the saturation pressure of adsorbates at the temperature of adsorption, V is the adsorbed liquid quantity , and V_m is the monolayer adsorbed liquid quantity, and C is the *BET constant*:

$$C = \exp(\frac{E_1 - E_L}{RT}) \quad (4)$$

with E_1 the heat of adsorption for the first layer, and E_L is that for the second and higher layers. The equation (3), which is BET adsorption isotherm, was plotted as straight line with $V[(\frac{P_0}{P}) - 1]$ on the y-axis and $\emptyset = \frac{P}{P_0}$ on the x-axis according to experimental results. The linear relationship of the equation was maintained in the range of $0.05 < P/P_0 < 0.35$. The value of the slope A and the y-intercept I of the line were used to calculate the monolayer adsorbed liquid quantity V_m and the BET constant C, for which the following equations were used:

$$V_m = \frac{1}{A + I} \text{ and } C = 1 + \frac{A}{I}$$

CONCLUSIONS

The study is devoted to investigations made on poly(*N,N*-dimethylacrylamide-co-3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) copolymer system which can be included into the "smart" polymer class owing to the gel formation capacity, binding properties, amphilicity, good oxidative and thermal stability, biocompatibility, good film formability, pH sensitive response. The stereochemistry of the copolymer network ensures as well intramolecular strategies for further coupling processes of various molecular compounds as the polymer matrix to become for example a multi-sensitive structure or a drug delivery system.

In the present study multi-layers hydrogels based on poly(N, N-dimethylacrylamide – co – 3, 9-divinyl-2, 4, 8, 10-tetraoxaspiro (5.5) undecane) crosslinked with N,N'-methylene bisacrylamide were synthesized and characterized. The achievement of edges and borders between layers, after constructing the gel core, was realized by using the following solutions of small molecular chemical compounds: β-cyclodextrine, NaCl, sodium citrate, ammonia aqueous solution and *q*uercetin. The achievement of the new structures was confirmed by FTIR and ^{1}H-NMR spectra.

The morphology of the supra-structure systems was investigated by optical and SEM microscopy, and near-infrared chemical imagining technique. It was underlined a relatively homogeneous porous structure based on the 3D polymeric network which includes as well the small molecular compounds, and also it was evidenced the different dimensions, shapes and morphologies as function of the substrate chosen for edges and borders preparation. The morphology was a decisive factor in determining the swelling capacity of gels. Thus, increasing the pore size of the polymeric network was reflected in growth sorption capacity of the polymer gel structure.

The sorption / desorption investigations confirmed the dependence of the swelling behavior of the multi-layered gels on the type of small molecular compounds present in the systems. The difference between the sorption capacities was correlated by the diversity in the structure and morphology of gel systems. Among the studied hydrogels, the highest capacity to adsorb water vapors was presented by H_β-CD multi-layered hydrogel, being followed by H_Na citrate system.

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