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Synthesis and Properties of Thermo-Sensitive Hydrogels Based on PVA/Chitosan/PNIPAAm

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ABSTRACT

Thermo-sensitive hydrogels were prepared by graft copolymerization of Polyvenylalcohol and chitosan with N-Isopropylacrylamide via gamma radiation. Characterization of hydrogels such as DSC analysis and swelling and solubility tests in different ratios were investigated. DSC and solubility analysis showed chitosan and PVA and NIPAAm monomer were grafted via gamma radiation successfully. Results show swelling of samples increased with to PVA increasing. Swelling ratio and curves results administrated hydrophilicity / hydrophobicity of hydrogel that this property is due to presence of PNIPAAm in different temperatures. These unique properties of the hydrogel would make it a promising support for drug delivery systems and tissue regeneration.

Key words: Thermo-sensitive hydrogel, Polyvenylalcohol, Chitosan, N-Isopropylacrylamide, Gamma radiation.

INTRODUCTION

During recent decades several materials and medical devices have been produced for medical purposes. For tissue engineering, it is desirable to recover the monolayer cells in a cell sheet structure at the end of the culture stage without using a biochemical or chemical reagent. Such a cell sheet constructed in vitro could be useful in various clinical situations to regenerate tissues (especially epithelial tissues) such as artificial skin and artificial cornea .Cell sheet engineering has been developed to avoid tissue reconstruction limitations using biodegradable scaffolds or single cell suspension injection[1-4]. Cell sheets are developed by thermo responsive culture dishes. Thermo responsive polymers are grafted to dishes covalently, which allow different cell types to attach and proliferate in 37 °C. Cells detach spontaneously when temperature decreases below 32 °C, without using enzymes, and this is due to the natural specification of the intelligent polymers also due to the detachment of the cell metabolic changes made by the polymer resulting from decreasing temperature[5-9]. Environmental sensitive systems or intelligent polymers are those that react to environmental small changes. In fact, those functional polymers that react to their readjustment or physical and chemical changes in the environment are generally known as stimuli

responsive or intelligent polymers. Thermo responsive polymers show a balanced and proper hydrophilic-hydrophobic in their structures. They were able to switch on–off the receptor using the transition between extended and coiled form of the molecule[10-12]. PNIPAAm and its copolymers are among those materials which have LCST. PNIPAAm shows LCST in 32 °C. While the temperature is over 32 °C, polymer is solid and also hydrophobic and when it is below 32 °C, it is completely hydrated and shows hydrophilic properties[13].Chitosan (CS) is a natural cationic polymer obtained from N-deacetylation of chitin [(1–4)-2-acetamiodo-2-deoxy-d-glucose], which is the second most abundant natural polymer on earth after cellulose. This polysaccharide is considered to be nontoxic, biodegradable, It has been used as an anticoagulant, a wound-healing accelerator, and drug delivery material [14-16] . Graft copolymerization of vinyl monomers onto CS can introduce desirable properties and enlarge the field of the potential applications by choosing various types of side chains [17-20]. In recent years, a number of initiator systems have been developed to initiate grafting copolymerization. Radiation graft copolymerization is a well-established technique for producing polymeric materials that combine the chemical and physical properties of both the base polymer and the grafted monomer[21-23]. In this work, hydrogels based on CS and Polyvenylalcohol (hydrophilic material) grafted N-isopropylacrylamide were prepared by ^{60}Co gamma radiation, the thermo sensitivity and swelling properties of the polymers were also investigated.

MATERIAL AND METHODS

Materials

Chitosan was purchased from Fluka company (degree of deacetylation = 98%, molecular weight =1.5 _ 105 g/mol). PVA was purchased from Merck company. N-Isopropylacrylamide (NIPAM, Aldrich) were recrystallized from nhexane and methanol freshly before use.

A series of CS-g-PVA-g-NIPA hydrogels were prepared in the following procedures: pure CS (in 5% aqueous acetic acid) and PVA (in water) dissolved in a glass reaction bottle, the monomer was added to the CS solution (W% different ratios. Mohr's salt (ammonium ferrous sulphate) was added to the mixture to minimize homopolymerization during irradiation. The solution was deoxygenated by purging with nitrogen for 30 min. The sealed reaction bottles were irradiated at different doses 10 and 20 kGy. After irradiation, the product was extracted with methanol in a Soxhlet extractor for 48 h, in order to remove the unreacted monomer, homopolymer and other impurities. The hydrogel was dried at 40 °C in a vacuum oven overnight. table 1 shows prepared samples and concentrations.

Characterization

Swelling measurement

Swelling of the hydrogels were determined gravimetrically after immersing the grafted product in water for an hour for different NIPAAm concentrations and temperatures and two doses, the surface of the hydrogels were wiped with filter paper in order to remove the free water and weighed. The swelling ratio was determined as:

Swelling ratio

Ws/Wd

Where Ws and Wd are the weights of swollen and dry hydrogels, respectively.

Differential scanning calorimetry (DSC)

The samples were investigated by thermal analysis using the DSC device (Netzschdsc200F3) with the heating rate of 5 degree per minute from 0°C to 60°C in a nitrogen gas atmosphere.

Solubility measurement

Grafting of between the NIPAAm/PVA/ Chitosan were determined gravimetrically after immersing the grafted product in ethanol (PNIPAAm solvent) and water (PVA solvent) and acetic acid (Chitosan solvent) for an 48 hour in shaker separately.

RESULTS

Swelling measurement

Swelling ratio of the hydrogels in different doses and concentrations showed in tables and figures 2 and 3. Results show swelling increased with to PVA increasing. The high swelling obtained for sample with to 0.067-0.0066-0.0264 ratio.

Also in the tables 4 and 5 indicated swelling ratio of the hydrogels in different temperatures (10 -25-35 and 40°C) in the distilled water for 1 hours. Tables Swelling ratio for 35 and 40 were calculated which demonstrated hydrophobicity of samples and for 10 and 25 °C were showed hydrophilicity of the samples. The Figures 4 and 5 showed swelling ratio / temperature of hydrogels . The curve slop related

Table 1. Ratio of samples with different concentration

No	Samples	Ratio	Concentration
1	N/C	1/1	0.05-0.05
2	N/C	3/1	0.067-0.033
3	N/C/P	1/0.8/0.2	0.05-0.04-0.01
4	N/C/P	3/0.8/0.2	0.067-0.0264-0.0066
5	N/C/P	1/0.5/0.5	0.05-0.025-0.025
6	N/C/P	3/0.5/0.5	0.067-0.016-0.016
7	N/C/P	1/0.2/0.8	0.05-0.01-0.04
8	N/P	3/0.2/0.8	0.067-0.0066-0.0264
9	N/P	1/1	0.05-0.05
10	N/P	3/1	0.067-0.033

(N:NIPAAm , C:Chitosan , P:Polyvenylalcohol)

Table 2. Swelling ratio of copolymers with to NIPAAm : 0.067 and two doses 10 and 20 KGy in 25 °C for 1 hours and 1 week

Samples	2/10	2/20	4/10	4/20	6/10	6/20	8/10	8/20	10/10	10/20
Ws/Wd (1 hour)	5/5	5/4	9/8	6	12/5	6/63	14/1	9/9	11/1	10/6
Ws/Wd (1 week)	11/1	10/8	27/1	15/4	41	20/5	44/6	24/3	14/6	14/1

Table 3: Swelling ratio of copolymers with to NIPAAm : 0.05 and two doses 10 and 20 KGy in 25 °C for 1 hours and 1 week

Samples	1/10	1/20	3/10	3/20	5/10	5/20	7/10	7/20	9/10	9/20
Ws/Wd (1 hour)	7/6	7/1	19/3	11/2	24/3	18/2	28/9	19/4	31/2	23/1
Ws/Wd (1 week)	14/1	14	34/1	24/6	39/1	29/8	44/2	34/6	34/8	28/1

Table 4: Swelling ratio of copolymers with to NIPAAm : 0.067 and two doses 10 and 20 KGy in different temperatures for 1 hours

Temperature°C	2/10	2/20	6/10	6/20	8/10	8/20	10/10	10/20
10	0.85	0.82	1/206	1/103	1/245	1/141	0.95	0.92
25	0.82	0.8	1/179	1/1	1/216	1/133	0.94	0.9
35	0.225	0.222	0.154	0.121	0.208	0.187	0.171	0.176
40	0.225	0.223	0.151	0.122	0.211	0.189	0.171	0.177

Table 5: Swelling ratio of copolymers with to NIPAAm : 0.05 and two doses 10 and 20 KGy in different temperatures for 1 hours

Temperature°C	1/10	1/20	5/10	5/20	7/10	7/20	9/10	9/20
10	0.89	0.87	1/412	1/301	1/555	1/411	1.95	1.322
25	0.84	0.83	1/379	1/290	1/546	1/403	1.94	1.320
35	0.232	0.230	0.174	0.172	0.225	0.199	0.182	0.189
40	0.231	0.232	0.170	0.172	0.227	0.201	0.182	0.190

to critical temperature of the gels and this demonstrated presence of PNIPAAm in the hydrogels during radiation and graft process.

Solubility results

The gravimetric results of immersed samples in the solvents at 48 hour show that the samples dissolved in solvents also acetic acid (solvent for chitosan) and water (solvent for PVA) and ethanol (solvent for NIPAAm). This result well demonstrated grafting between the polymers.

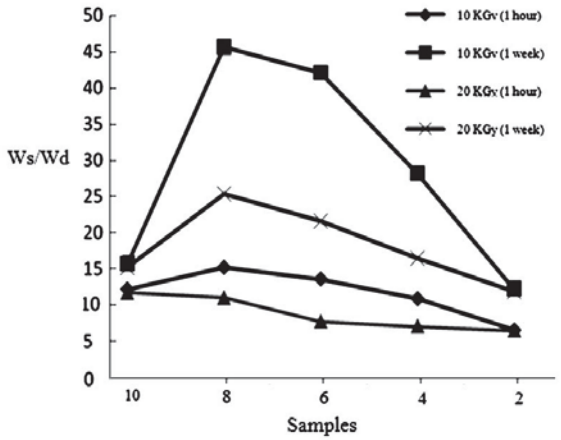

Fig. 2: Swelling ratio of copolymers with to NIPAAm : 0.067 and two doses 10 and 20 KGy in 25 °C for 1 hours and 1 week

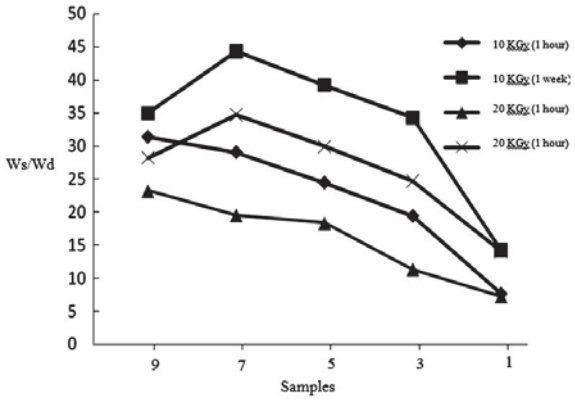

Fig. 3: Swelling ratio of copolymers with to NIPAAm : 0.05 and two doses 10 and 20 KGy in 25 °C for 1 hours and 1 week

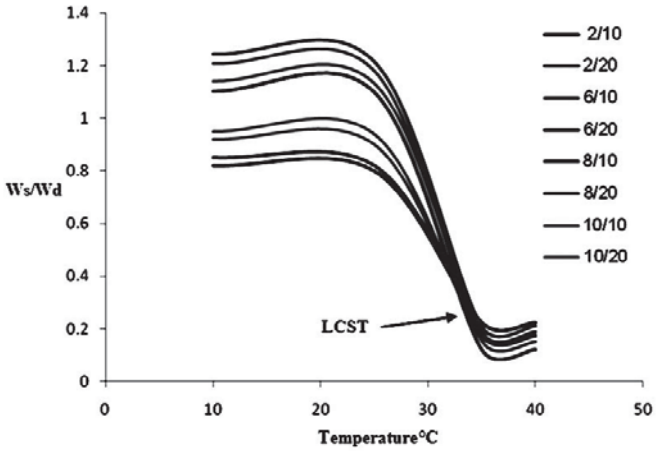

Fig. 4: Swelling ratio of copolymers with to NIPAAm : 0.067 and two doses 10 and 20 KGy in different temperatures for 1 hours

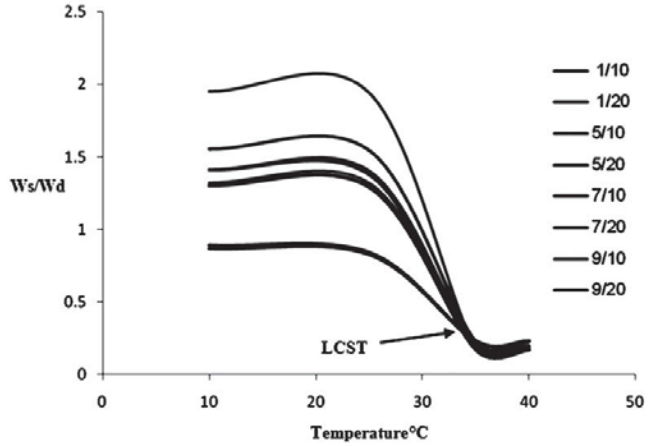

Fig. 5: Swelling ratio of copolymers with to NIPAAm : 0.05 and two doses 10 and 20 KGy in different temperatures for 1 hours

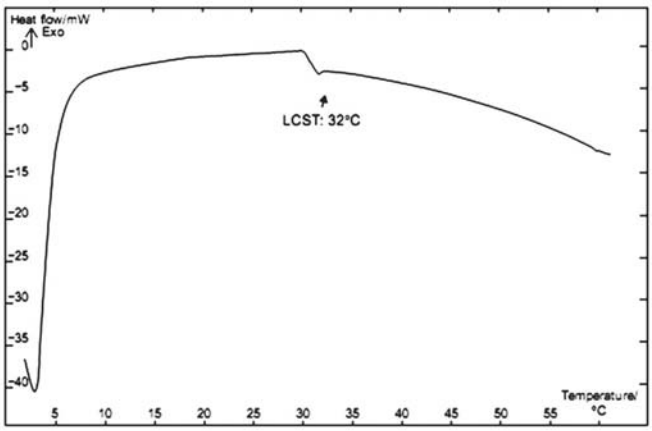

Fig. 6: DSC spectra of the hydrogel grafted by gamma radiation

Differential scanning calorimetry (DSC)

The samples were investigated by thermal analysis using the DSC device (NETZSCHD SC200F3), with the heating rate of 5 degree per minute from 0°C to 60°C in a nitrogen gas atmosphere. The grafted samples' DSC analysis review showed a critical temperature of the grafted PNIPAAm. Figure 6 shows the DSC thermogram in which the curve slope in 32°C is obtained. This shows no significant change in the smart polymer critical temperature during radiation and graft process and different concentration.

CONCLUSION

In this work, hydrogels based on CS and PVA grafted N-isopropylacrylamide were prepared by 60Co gamma radiation, the thermo sensitivity and swelling and structural properties of the polymers were also investigated . the CS-g-PVA-g-NIPA hydrogels showed good thermosensitivity and swelling property. Results show swelling of samples increased with PVA increasing also swelling ratio of samples decreased with radiation dose increasing due to more cross linking between polymeric chains. Swelling ratio and curves results administrated hydrophilicity / hydrophobicity of hydrogel that this property is due to presence of PNIPAAm in different temperatures. These unique properties of the hydrogel would make it a promising support for drug delivery systems and tissue regeneration.

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