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Swelling properties of Cross linked chitosan & L-alanine semi-Interpenetrating Polymer Network (semi-IPN)

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ABSTRACT

Semi-Interpenetrating Polymer Networks (semi-IPN) were prepared by cross linking chitosan and L-alanine with glutaraldehyde as cross linker. A viscous solution of chitosan–alanine was prepared in 2 % acetic acid solution, extruded in the form of droplets by a syringe to NaOH – methanol solution and cross linked with glutaraldehyde. The swelling behavior of cross linked beads in different pH solutions was measured at different time intervals. The swelling behavior was observed to be dependent on the degree of cross linking, concentration of chitosan and swelling environment. The structural and morphological studies of beads were carried out by using a scanning electron microscope (SEM).

Key words: Chitosan; Controlled drug release; interpenetrating polymer networks; Beads; Crosslinking.

INTRODUCTION

In the recent years, much attention has been paid on the development of Interpenetrating polymer networks (IPNs) from natural, biocompatible and biodegradable polymeric materials. An interpenetrating polymer network (IPN) is a combination of two polymers, in network form, of which at least one is synthesized and/or cross-linked in the immediate presence of the other without any covalent bonds between them. IPNs that have only one polymer cross linked (where the polymers are synthesized separately) or where the polymers have vastly different kinetics are

still considered to be IPNs / semi-IPNs [1]. An IPN has a potential for carriers of bioactive macromolecules, wound dressing and controlled drug release in the swollen state.

A wide range of hydrophilic polymers has been examined for preparing IPNs and chitosan is one of them. Chitosan is the deacetylated derivative of chitin which is a water insoluble polymer, (N-acetyl-d-glucosamine), found in nature, present in insect exoskeletons, outer shells of crabs, shrimps, lobsters etc. and fungal cell walls. The difference between chitin and chitosan lies in the degree of deacetylation. Blending of chitosan with other polymers [2-4] and cross linking are both convenient and effective methods of improving the physical and mechanical properties of chitosan for practical applications. Chemical cross linking agents such as glutaraldehyde, ethyleneglycol diglycidyl ether and poly (ethyleneglycol), are used to enhance the controlled release of drugs from the chitosan based microparticles [5-6]. However, the addition of these chemical substances can be limited due to their toxicity. The cross linker is removed by repeated washing with suitable solvent followed by the drying of particles.

L alanine is an organic compound, one of the twenty amino acids commonly found in animal proteins. It is hydrophobic, with nonpolar methyl group side chain, and is the second–smallest of the twenty after glycine. The alpha-carbon in alanine is substituted with a methyl group, making it one of the simplest amino acids with respect to the molecular structure and is one of the most widely used in protein construction [7-9]. The biocompatibility is the reason behind the use of L-alanine along with chitosan [10].

In the present study the beads consisting of chitosan and L-alanine are cross linked with different amounts of glutaraldehyde to form semi-IPN. The swelling behavior of the semi-IPNs in acidic and basic environment has been examined. The effect of concentration of chitosan and the cross linker on swelling of beads has also been studied.

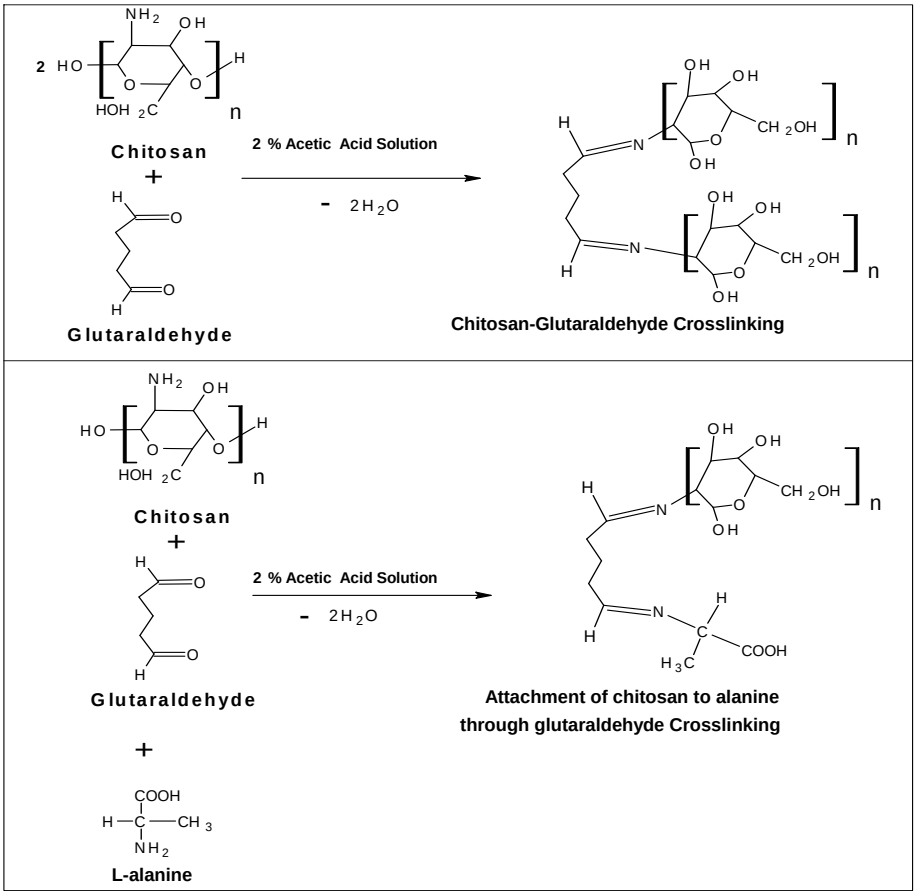
EXPERIMENTAL SECTION

Materials

Chitosan (percentage of deacetylation after drying was 80 %; total nitrogen: 7% minimum, loss on drying < 15% and ignition residue (sulfate) : <2 %) was purchased from Tokyo Kasei Kogyo Co., Ltd. Japan and was used as received. Glutaraldehyde ($C_5H_8O_2$) (MW=100.11), acetic acid and L-alanine ($CH_3CH(NH_2)COOH$) (MW= 89.09) were procured from CDH, New Delhi.

Preparation of cross linked chitosan –alanine beads

Purified chitosan and alanine were dissolved in 2 % acetic acid solution by stirring conditions for three hours at room temperature. The concentration of 2 % acetic acid solution was varied just to make a uniform extrude able mixture. The homogeneous mixture was extruded in the form of droplets using a 0.56mm diameter syringe into NaOH- methnol solution (1:20 w/w) under stirring conditions. The beads were washed thrice with hot (50 ^oC) and cold (25 ^oC) water and it generally took two to three minute, respectively. The resultant beads were allowed to react with glutaraldehyde solution at 50 ^oC for about 10 min for cross linking. The formation of cross linked chitosan – alanine IPN is shown in scheme 1. Finally, the cross linked beads were successively washed with hot (50 ^oC) and cold (25 ^oC) water respectively and vacuum dried for thirty minutes at -700 mmHg and 55 ^oC. The composition of the prepared beads is given in the Table 1.



Scheme 1 Cross linking of chitosan and l-alanine by glutaraldehyde for the formation of Semi-IPN

Table 1 Designation and composition of the synthesized cross linked chitosan – lysine semi-IPN beads

	S. No.	Chitosan (g)	L-alanine (g)	2% Acetic acid (ml)	Glutaraldehyde 10 ml (%)
(a)	S1	0.1	0.5	5	25
	S2	0.1	0.5	5	12.5
	S3	0.1	0.5	5	6.25
(b)	S1	0.2	0.5	10	25
	S2	0.2	0.5	10	12.5
	S3	0.2	0.5	10	6.25
(c)	S1	0.3	0.5	15	25
	S2	0.3	0.5	15	12.5
	S3	0.3	0.5	15	6.25
(d)	S1	0.4	0.5	20	25
	S2	0.4	0.5	20	12.5
	S3	0.4	0.5	20	6.25

Swelling studies

Swelling behavior of the cross linked chitosan-alanine beads was measured by allowing the beads to swell in medium of different pH. The pre- weighed dried cross linked chitosan-alanine beads were immersed in solutions of pH = 2.0 and 7.4. The immersion time was eight days. The beads were withdrawn from the solution at different time intervals and their wet weight were determined after first blotting with a filter paper to remove the surface water and immediately weighing the beads. The degree of swelling for each sample at time t was calculated using the relationship:

$$\text{Degree of swelling} = (W_t - W_d) / W_d$$

Where W_t and W_d are the weights of the samples at time t and in the dry state, respectively.

Scanning Electron Microscopy (SEM)

A JEOL JSM-6100 scanning electron microscope was used to study the shape and surface morphology of the cross linked beads. For SEM studies, the samples were mounted on metal stubs using double – sided adhesive tape and each one was submitted to gold sputtering before analysis. Magnifications of 40X to 3000X were applied to each sample in order to estimate the size and surface morphology.

RESULTS AND DISCUSSION

Swelling Studies

Swelling response of the glutaraldehyde cross linked chitosan-alanine beads in solutions of pH 2.0 and pH 7.4 is shown in Figure 1-4. The observed swelling rates of the cross linked beads followed the order S3>S2>S1 in all the samples. Generally, the swelling process of the beads in pH<6 involves the protonation of amino / imine groups in the beads and mechanical relaxation of the coiled polymeric chains. The process of protonation is expected to be completed in two stages. In the first stage, amino/imine groups of the bead surface were protonized, that led to dissociation of the hydrogen bonding between amino/imine groups and other groups. The protonation resulted in solvent invading the polymer from the sample surface and forming a sharp boundary or moving front separating the unsolvated polymer region with that of the swollen portion of the beads. In the second stage, protons and counterions diffused into the bead to protonate the amino/imine groups inside the beads and dissociating the hydrogen bonds. This process of protonation continued until the whole structure of the beads was collapsed and solvated [11-12]. It has been observed that the swelling rates are directly proportional to the degree of crosslinking and concentration of chitosan. In both cases, the degree of swelling is very high in solution of pH 7.4 compared to that of pH 2. Sample S1 (of Set a) has lesser composition of chitosan as compared to sample S1 (of Set b). The lesser cross linked density resulted due to the decrease in chitosan composition is the main reason of higher degree of swelling of S1 (of Set a) in both the mediums. It is observed that as the concentration of chitosan as well as of glutaraldehyde increased, the degree of cross linking increases and the rate of swelling decreases.

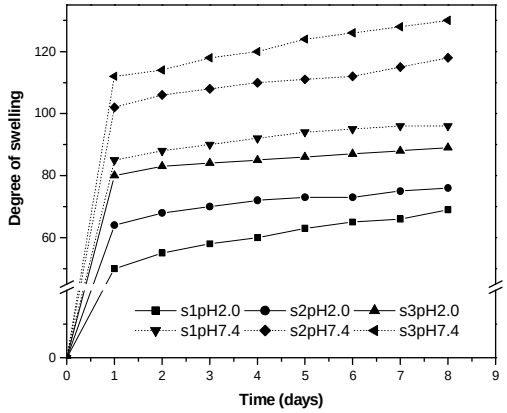


Figure 1 Swelling kinetics of air-dried chitosan/alanine (1/5 wt %) cross linked beads in solution of pH= 7.4 and 2.0.

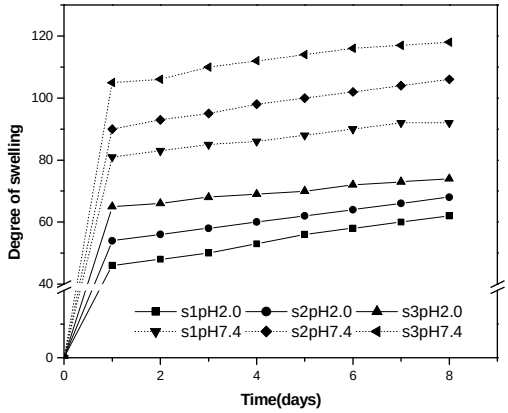


Figure 2 Swelling kinetics of air-dried chitosan/alanine (2/5 wt %) cross linked beads in solution of pH= 7.4 and 2.0.

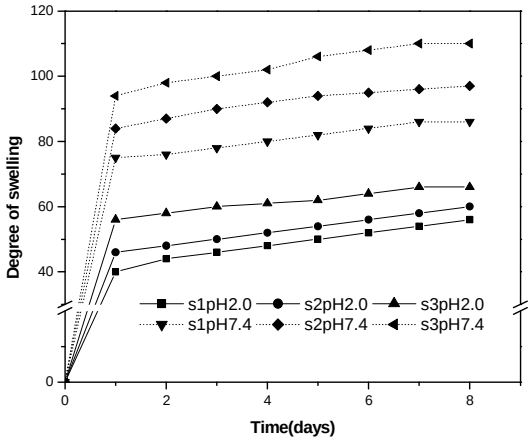


Figure 3 Swelling kinetics of air-dried chitosan/alanine (3/5 wt %) cross linked beads in solution of pH= 7.4 and 2.0.

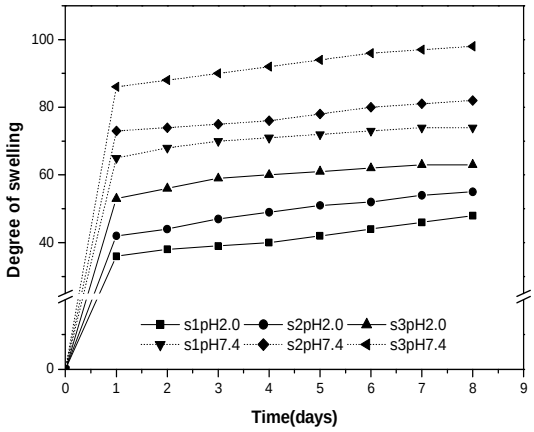


Figure 4 Swelling kinetics of air-dried chitosan/alanine (4/5 wt %) cross linked beads in solution of pH= 7.4 and 2.0.

Similar studies [13] have been reported for chitosan–glycine system, but the release rates in the two systems are entirely different. According to the earlier report, the amount and percentage of drug released is higher in acidic media, where as we observed that it is the basic medium in which the release rate is higher. This may be due to the different chemical structures of glycine and alanine. In case of alanine, steric hindrance is more as

compared to glycine due to presence of an additional CH_3. As a result of which carboxylic group in alanine is free from such hindrance and alkaline group can easily penetrate into the system. In the case of glycine, due to the higher electron density, more electrons are available for the reaction with acid and they will form NH_3^+ (ammonium ions), but the same is not facilitated in case of alanine.

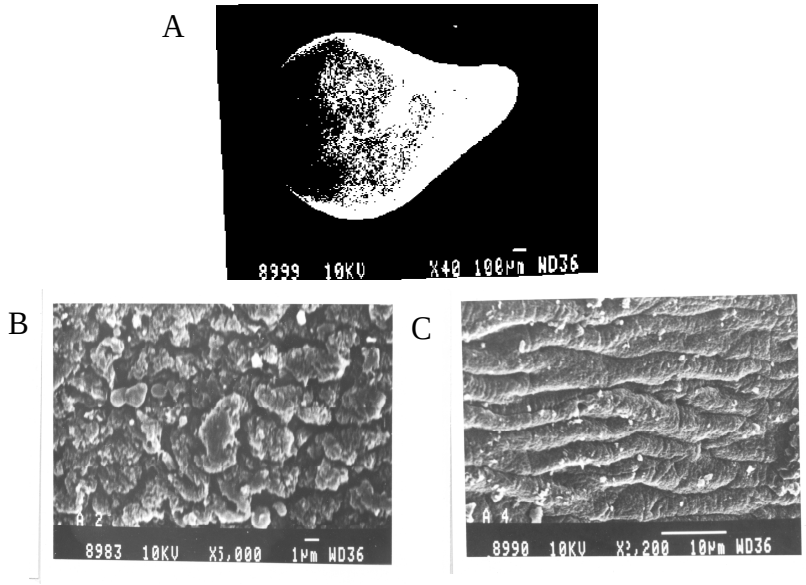


Figure 5 SEM photographs of (A) the cross linked bead showing shape and (B, C) surface morphology of samples S3 and S1 of set (d), respectively.

SEM studies

Crosslinked chitosan- alanine beads prepared by using different concentrations of glutaraldehyde have rough and dense surfaces. The observed shape of the bead was like a droplet and is shown in Figure 5 A. The reason for non-spherical size may be due to higher viscosity of the chitosan –alanine solution. The approximate size of the beads is in the range of 0.8-1.2 mm. From the morphology of the beads shown in Figure 5B, one can observe rough and folded surfaces of the beads. With the higher concentration of crosslinker the chains come closer to each other and give a regular, fibrous structure (Figure 5C).

CONCLUSION

Beads of chitosan-alanine having different weight ratios were cross linked with varying concentrations of glutaraldehyde to form IPNs with different degrees of cross linking. The morphological studies of the samples were carried out by using a scanning electron microscope (SEM). The swelling of beads in different pH solutions were studied. It was observed that the percentage of swelling was more in basic medium than in acidic

medium. It has been observed that the swelling rates are directly proportional to the degree of cross linking. Cross linking hinders the mobility of the polymer chain, hence lowering the swelling ratio. Highly cross linked IPNs have a tighter structure, and will swell less compared to the same IPNs with lower cross linking ratios. From these investigations, it is evident that the rate of swelling of matrix is dependent on the degree of cross linking, concentration of chitosan and the pH of solution. Therefore, by varying the crosslink densities and concentration of chitosan, the desired rates of swelling can be achieved from diffusion-controlled chitosan – alanine semi-IPN. Further, it can also be helpful in drug entrapping capacity and its sustained release for an extended period of time.

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