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Chitosan — Locust bean gum interpenetrating polymeric network nanocomposites for delivery of aceclofenac

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ABSTRACT

In this study, aceclofenac-loaded IPN nanocomposites were developed based on natural polysaccharides namely chitosan (CS) and locust bean gum (LBG) using glutaraldehyde as cross-linker. Infrared spectroscopy analysis confirmed the formation of composite materials and ensured the chemical compatibility between drug and polymers. The effect of component polymers on the drug entrapment efficiency (DEE) and particle size of the composites was examined. Increasing LBG content actually decreased the DEE from 72% to 40% and produced larger particles of 372–485 nm dimensions. However, an opposite trend was noted as the concentration of CS was increased. Out of these composites, the maximum drug entrapment efficiency of 78.92% and smallest composites of 318 nm-size was obtained at LBG: CS mass ratio of 1:5. However, CS: LBG (1:5) provided the slowest drug release profiles in phosphate buffer solution (pH 6.8) up to 8 h. The drug release data corroborated well with the swelling properties of the nanocomposites. The composite systems efficiently suppressed the burst release of drug in acidic medium (pH 1.2). The drug delivery from the nanocomposites occurred via anomalous transport mechanism in vitro. Overall, this novel chitosan- and LBG-based nanocomposites system could minimize the gastrointestinal side effects of the drug by providing medication in a slow sustained fashion.

1. Introduction

In last few years, a great deal of attention has been paid to the design of interpenetrating polymeric networking (IPN) systems for controlled drug delivery application. IPN is considered as dual polymeric composite, where at least one polymer network is synthesized or cross-linked independently in the immediate presence of the others [1]. Usually, IPN system is preferred over polymer blends because of their improved mechanical strength and ability to prevent the burst, uncontrolled swelling of polymer blends that ultimately controls the release of drug. Therefore, IPN-based drug delivery system appears to be a new avenue in drug delivery research for obtaining sustained drug release profiles [2,3]. Different biopolymer-based IPNs such as gellan gum-polyvinyl alcohol (PVA) [4], xanthan gum-PVA [5], locust bean gum-PVA [6], PVA-guar gum [7], chitosan (CS)-TSP [8], chitosan-hydroxyethyl cellulose [9], CS-methyl cellulose [10], CS-gelatin [11] have been reported for the delivery of different kind of drugs. CS, a cationic polysaccharide obtained by deacetylation of chitin have been extensively studied for developing IPN composites exclusively in conjunction with synthetic polymers such as *N,N′*-dimethylacrylamide [12], poly(*N*-isopropyl acrylamide-co-vinyl pyrrolidone) [13] due to its non-toxic, biodegradable, biocompatible nature [14]. Even, combinations of modified CS and synthetic polymers such as poly (*N*-isopropylacrylamide) [15], poly (methacrylic acid) [16] have been reported. However, the IPN systems of CS with other biopolymers are very uncommon.

CS is composed of α-1, 4-linked 2-amino-2-deoxy- α-D-glucose (*N*-acetyl glucosamine). According to United States Food and Drug Administration (USFDA), it is GRAS (Generally Recognized as Safe) material and hence, finds wide application in pharmaceutical as well as biomedical fields including drug delivery, food technology and tissue engineering [17]. Due to its fast dissolution in gastric fluid, its use is limited as oral sustained drug release carriers [18]. Considering the importance and convenience of oral route, the drug delivery properties of chitosan carriers was modified with the use of other polymer in combination. The drug substance having short biological half-life often requires frequent dosing, which ultimately may lead to toxicity due to accumulation of drug dose [19].

Locust bean gum (LBG) is a natural galactomannan extracted from the seeds of the carob tree (*C. siliqua*), and composed of α (1,4)-linked β-D- mannopyranose backbone with linked to (1,6) α-D-galactose [20]. The non-toxic LBG can be used to monitor the release of drug from its delivery carriers [21,22]. Recently, the

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research scientists are trying to develop biopolymer-based green composites for drug delivery. The green composites are very important due to their simple fabrication methods and low cost [23]. The components are judiciously selected to obtain a green composite system with favorable drug delivery properties, non-attainable by any of the constituents alone [24]. In composites, two or more chemically and physically different phases remain separated by a distinct interface [25,26]. However, chitosan-locust bean gum (LBG) IPN nano-composites are not reported till date.

Aceclofenac (AC) is chemically 2-[2-[2-[(2, 6-dichlorophenyl) amino] phenyl] acetyl] oxyacetic acid and is a non-steroidal anti-inflammatory drug with a short biological half-life of 4 h [27,28]. It is used in the treatment of osteoarthritis, arthritis, rheumatoid arthritis and ankylosing spondylitis [29]. The long-term use of conventional AC formulation is associated with various side effects such as ulcer, gastric irritation and bleeding, abdominal pain, nausea, and flatulence [30]. To overcome these drawbacks, prolonged release CS-LBG IPN nano-composites were developed for AC and characterized in vitro.

2. Materials and methods

2.1. Materials

Chitosan (deacetylation 85%) was obtained from Everest Edward, Kochi, India. Locust bean gum (LBG) (Purity 91.8%; ~M/G = 4:1; Protein ≤7%) was purchased from Hi Media Laboratories Pvt. Ltd., Mumbai, India. Aceclofenac (AC) was obtained as a gift sample from Cipla Pharmaceutical Pvt. Ltd., Sikkim, India. Glutaraldehyde (GA, 25% v/v) was purchased from Merck specialties Pvt. Ltd., Mumbai, India. All other reagents and chemicals were of analytical grade.

2.2. Preparation of AC-loaded CS-LBG IPN nano-composites

Chitosan was first dissolved in 10 ml 1% (v/v) glacial acetic acid solution and added to this; an aqueous LBG dispersion was added. Then pre-weighed aceclofenac (100 mg) was mixed with the polymer blend under continuous magnetic agitation (Remi Equipment Pvt. Ltd., Mumbai, India) until homogeneous drug dispersion was formed. The pH of blended dispersion was adjusted to pH 5.4 using 0.2 M sodium hydroxide (NaOH) solution. Then, 1 ml GA was added to the dispersion and continuously stirred for 1 h. The prepared cross-linked polymer composites were centrifuged at 6000 rpm for 30 min. The drug-loaded IPN nano-composites were washed with glycine-water mixture to remove non-reacted GA. The orange color of the washings disappeared; the final washings were heated with a deep-blue alkaline Fehling's solution. No brick-red precipitate (a negative test) was formed, thus confirming removal of residual GA in the washings [31]. Finally, the drug-loaded nano-composites were stored at −20 °C overnight and lyophilized (Eyela FDU-1200, Japan). The dried samples were stored in desiccators for further use. The composition of different nanocomposite systems is shown in Table 1.

2.3. Fourier transform-infrared (FTIR) spectroscopy

The IR spectral data of AC, CS, LBG, and AC-loaded IPN nano-composites were obtained after scanning of KBr pellets with powder samples using Perkin Elmer FTIR spectrophotometer (Spectrum RX1, USA) in the wave number range 4000–400 cm^{-1} at a resolution of 4 cm^{-1} with scan speed of 2 mm/sec.

Table 1
Composition of chitosan-locust bean gum nanocomposites containing aceclofenac.

IPN composites	Polymers (mass ratio) CS:LBG	Polymers		AC (mg)	GA (ml)
		CS (mg)	LBG (mg)		
CSLBG-1	1:5	50	250	100	1
CSLBG-2	1:2	100	200	100	1
CSLBG-3	1:1	150	150	100	1
CSLBG-4	2:1	200	100	100	1
CSLBG-5	5:1	250	50	100	1
CSLBG-6	3:0	300	–	100	1

2.4. Measurements of particle size & zeta potential

The mean size and zeta potential of the nano-composites were measured by Zetasizer nano ZS90 (Malvern Instruments, UK) at a detector angle of 90° at a temperature of 25.2 °C. The samples were prepared by dilution in deionized water at appropriate concentration. Each sample was measured in triplicate.

2.5. Drug entrapment efficiency (DEE) of CS-LBG IPN nano-composites

Lyophilized CS-LBG IPN nanocomposites (100 mg) were dispersed into 100 ml phosphate buffer solution (pH 6.8), kept overnight and sonicated (FS-600, Frontline Sonicator, Frontline Electronics and Machinery Pvt. Ltd., India) thereafter for 15 min for extraction of the drug. The insoluble polymeric debris was removed by filtration through Whatman® filter paper (No. 40) and the filtrate was analyzed by UV–vis spectrophotometer (Thermo Scientific, Evolution-200, UK) at 274 nm. The DEE of drug-loaded IPN nanocomposites was calculated by the following formula:

$$\text{DEE}\ (\%) = \frac{\text{actual drug present in IPN nanocomposites}}{\text{experimental drug present in IPN nanocomposites}} \times 100$$

2.6. Swelling study

The swelling of the nano-composites was examined in pH 6.8 buffer systems for 1 h. Known amount of composites was immersed in 100 ml of dissolution media and the samples were withdrawn at pre-determined intervals, blotted with tissue paper and weighed. The swelling percentage was calculated by dividing the differential weight between swollen and dry composites with the dry sample weight, followed by multiplication with 100.

2.7. In vitro drug release study

In vitro release of AC from CS-LBG IPN nano-composites was studied as follows. The drug- loaded IPN nano-composites equivalent to 100 mg aceclofenac were placed in dialysis bag (MWCO 12–14 kDa, HiMedia Laboratories Pvt. Ltd., Mumbai, India) containing 5 ml of dissolution medium (phosphate buffer, pH 6.8). Other end of the dialysis bag was tied off and immersed in 900 ml of dissolution medium (Veego VDA-6D, Veego Instruments Co-operation, Mumbai, India) containing. USP type II dissolution apparatus was maintained at 37 ± 1 °C with a paddle speed of 50 rpm. The dialysis bag acted as a donor and that of dissolution vessel as the receptor compartments. An aliquot (5 ml) was collected at predetermined time intervals, and the same volume of fresh buffer was added into dissolution vessel to maintain the sink condition throughout the experiment. The aliquots were then filtered with Whatman® fil-

ter paper (No. 40), suitably diluted and analyzed at 274 nm, using UV–vis spectrophotometer (Thermo Scientific, Evolution-200, UK).

2.8. Drug release kinetics

In order to predict and correlate in vitro drug release behaviour from the nano-composites, the drug release data were fitted into different mathematical models: zero order, first order, Higuchi and Korsmeyer-Peppas [26,32,33]. The highest correlation coefficient was indicative of best-fit model to describe drug release kinetics.

2.9. Statistical analysis

The drug entrapment data for the composite formulations was analyzed by one-way analysis of variance (ANOVA) using Graph Pad Prism software (Trial version 6.00). The release data was analyzed using least square methods in Microsoft excels software and the correlation coefficients were calculated.

3. Results and discussion

Chitosan is an amine group ($-NH_2$) containing polysaccharides [34]. In this study, chitosan was employed to form semi-IPN composites in presence of another bio-polysaccharide LBG. The amine groups ($-NH_2$) of CS reacted with GA and formed covalent imine linkages and thus attributing to the formation of rigid polymer composite structure. A reaction leading to the formation of crosslinks is depicted in Scheme 1.

The characteristic IR peaks of pure aceclofenac due to N—H stretching vibrations of secondary amines at 3319.57 cm^{-1}, aliphatic C—H stretching at 2937.38 cm^{-1}, a sharp band of C=O stretching of carboxylic acid at 1771.82 cm^{-1}, C=O stretching of at 1719.88 cm^{-1} and 1,2, di-substitution of C—Cl stretching at 749.57 cm^{-1} were found in Fig. 1a. Similar peaks of pure aceclofenac were reported earlier [8,26].

The N—H stretching vibration peaks at 3433.17 cm^{-1}, 2924.11 cm^{-1} for aliphatic stretching, N—H deformation at 1656.07 cm^{-1} and C—O—C stretching of glycosidic linkage at 1084.50 cm^{-1} were found in the spectrum of chitosan (Fig. 1b) [8,26]. FTIR spectrum of LBG was observed in Fig. 1c. A broad, stretching of hydroxyl (-OH) groups was noted at 3421.97 cm^{-1}. C—H stretching vibration of —CH and $-CH_2$ groups and a broad peak of C—O—H stretching were evident at 2926.38 cm^{-1} and 1026.38 cm^{-1}, respectively. Similar IR spectrum of LBG was reported by Kaity et al. [6]. The characteristics IR peaks of aceclofenac were also observed in the spectrum of drug-loaded IPN nano-composites with minor fluctuations (Fig. 1d). This suggested that the drug was chemically stable in the nanocomposites and no chemical interaction occurred between AC and IPN polysaccharides. The individual characteristics stretching vibration peaks due to —OH groups of CS and LBG polysaccharides were also identified in the formulated IPN composite. The —C=N stretching peak of the newly formed Schiff base complex between $-NH_2$ group of chitosan and —CHO group of glutaraldehyde was examined in the IR spectrum of the composites (Fig. 1d). A new peak appearing at 1560.11 cm^{-1} was attributed to imine bonds (—C=N) that was formed as a result of cross-linking reaction between amino groups in chitosan and aldehydic groups in glutaraldehyde. Similar peak was assigned to the stretching vibration of imine bonds (—C=N) at ~1563 cm^{-1} [35]. Earlier, it was also reported that CS might be covalently cross-linked with GA through its amino groups [36]. Therefore, the FTIR data suggested that a covalent crosslink was successfully established by GA in the CS-LBG IPN nano-composites.

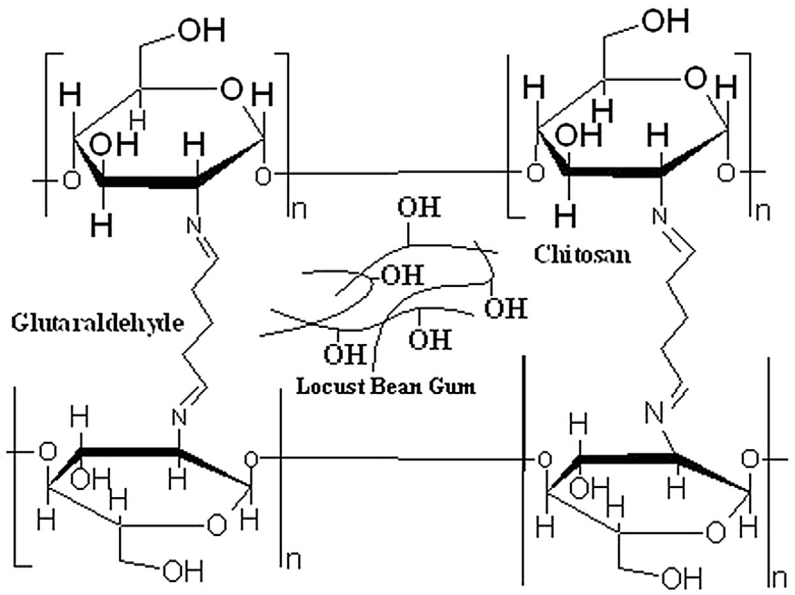
The effect of relative proportion of LBG and CS on the drug entrapment efficiency (DEE), particle size, zeta potential and in vitro drug release properties of AC-loaded CS-LBG IPN nanocomposites was observed. The size of the composites decreased from 485.1 nm to 372.5 nm with corresponding increase in concentration of LBG. On contrary, smaller composites were produced at higher CS concentration (Table 2). Perhaps, with increasing amount of LBG, the numbers of free sites available on chitosan for cross-linking were less such that the size of the composites was also increased with increasing LBG content. Babu et al. [12] observed similar effect for chlorothiazide-loaded chitosan-*N,N'*-dimethylacrylamide IPN microspheres. This was further supported by the lower zeta potential values obtained at higher LBG content. As was evident from Table 2, the surface charge was decreased from +23.5 mV to +10.1 mV.

Table 2
The properties of aceclofenac-loaded chitosan-locust bean gum nanocomposites.

IPN composites	Parameters		
	DEE (%)	Particle size (nm)	Zeta potential (mV)
CSLBG-1	40.38	485.1	+10.1
CSLBG-2	42.88	382.4	+15.6
CSLBG-3	72.60	372.5	+23.5
CSLBG-4	74.56	356.7	+20.3
CSLBG-5	78.92	318.8	+18.1
CSLBG-6	31.48	293.1	+25.9

The drug entrapment efficiency decreased from 72.60 to 40.38% with increasing concentration of LBG in the composites (Table 2). The presence of bulky LBG interfered with the cross-linking process and caused lower entrapment of aceclofenac. Mukhopadhyay et al. [39] reported that the mean size and DEE of the insulin-loaded core-shell CS/alginate nanoparticles decreased with increasing proportion of alginate in the composite from 1:1 to 1:3. On the other hand, higher concentration of CS slightly improved DEE values of the composites i.e. from 72.60% to 78.92% for CSLBG3-CSLBG6 formulations (Table 2). Higher CS content actually increased the number of NH_2 groups available for cross-linking with GA, thus entrapping more drug molecules into the composite structures. Lower values of zeta potential at higher CS strength were indicative of higher extent of cross-linking. More number of NH_2 groups participated in the GA-mediated cross-linking process and therefore, the residual amine groups became less at higher CS concentration and exhibited lower zeta potential values (+23.5 to 18.1 mV). It is important to mention here that the contribution of LBG in developing charge over the composite surface was neglected due to their non-ionic character. Higher degree of cross-linking also affected the size of the nano-composites. The size of the composites dropped from 372.5 nm to 318.8 nm at higher CS. The smallest particles of 293.1 nm-sizes were obtained in absence of LBG in the composites. The size distribution curve for a typical formulation containing 1% GA and CS: LBG (1:1) is displayed in Fig. 2. Obviously, a narrow size distribution was observed.

Only 31.48% DEE was achieved for the only CS particles. Undoubtedly, the incorporation of a second polysaccharide LBG led to greater DEE of the composites than that of the CS alone. The excess amine groups probably generated electrostatic repulsive force and resulted in CS particles of lower mechanical strength. Hence, the ionized fraction of aceclofenac escaped from the loose CS particles into the cross-linking medium, causing most significant reduction in DEE, compared to others ($p < 0.05$). Overall, the drug entrapment efficiency of the composite formulations was low and did not reach to 100%. It was also noted for CS: Boswellia gum resin that the DEE values decreased with increasing CS: gum resin mass ratio and the DEE value did never reach to 100% [26]. We found that the replacement of gum resin with a natural protein egg albumin assisted in achieving the drug entrapment efficiency of CS: albumin (1:1) nanoparticles up to 99.37% [17]. Being phenyl acetic acid



Scheme 1. The reaction mechanism of GA crosslink CS-LBG IPN.

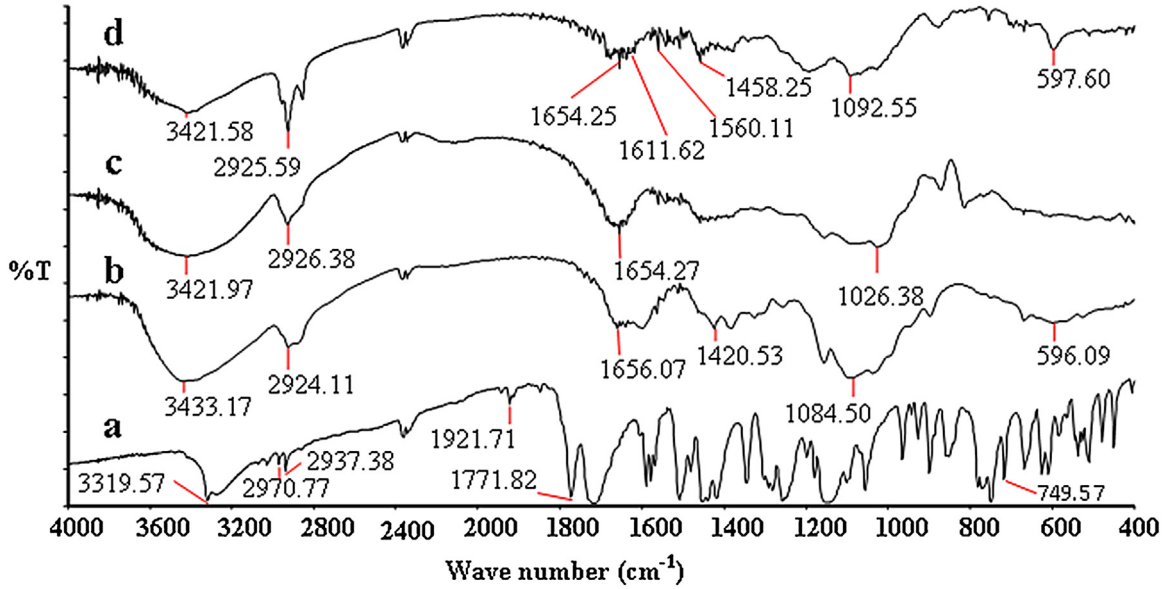


Fig. 1. The FTIR spectra of aceclofenac (a), CS (b), LBG (c) and drug loaded IPN nanocomposite (d).

derivative (pK_a 4.7), aceclofenac was seemed to exist as carboxylate anions and thus, became soluble in the aqueous cross-linking medium and the composites failed to retain 100% of the fed drug during synthesis of the composites.

In vitro drug release profiles of CS-LBG nanocomposites in phosphate buffer (pH 6.8) are illustrated in Fig. 3.

It was evident that the CS composites without LBG (3:0) emptied entire amount of drug in 4 h. As can be seen from Table 2, the highest positive zeta potential value (+25.9 mV) was recorded for this composite formulation. It was possible that the amount of GA was insufficient to crosslink entire CS molecules and the non-reacted CS molecules generated higher surface charge for this system. Therefore, the residual hydrophilic CS molecules created pores in the composite network during dissolution experiments and caused rapid dissolution of AC. Moreover, CS, a cationic polysaccharide has abundant hydroxyl groups necessary for hydrogen interaction with water. More hydration of functional groups (OH and NH_2) on CS chains improved the swelling of CS hydrogels and caused rapid release of drug. In addition, higher solubility of AC at pH 6.8 buffer solution also contributed to that effect.

Irrespective of the variation in composition of CS and LBG, a similar trend in drug profiles was evident. More explicitly, the drug release rate decreased with increasing concentration of either LBG or CS in the composites. Let us explain the possible reasons behind this effect. Keeping the concentration of CS fixed, as the amount of LBG was gradually increased, the composite swelled less. The extent of swelling of the semi-IPN matrix was 59.5, 45.6 and 41.3, for CSLBG-3, CSLBG-2 and CSLBG-1, respectively. The percentage water uptake decreased with an increasing amount of LBG in the semi-IPN matrix. This observation was opposite of that reported by Cui et al. [11] for the genipin-crosslinked CS/gelatin IPN hydrogels at phosphate buffer solution (pH 7.4). They noticed that higher percentage of gelatin caused higher swelling of the hydrogels. This could be due to the fact that as the amount of LBG was increased in

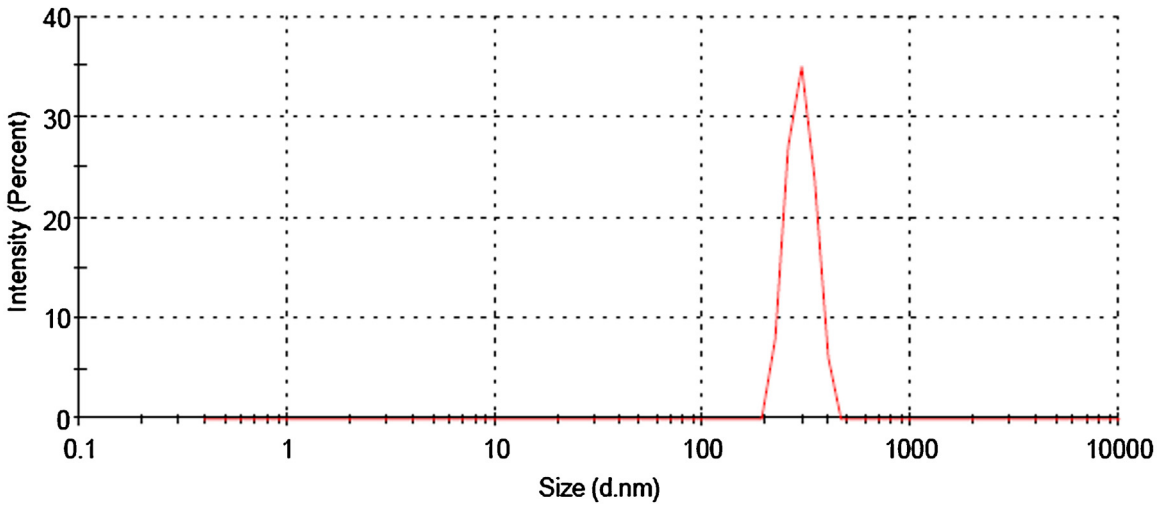


Fig. 2. Particle size distribution of CS: LBG (1:1).

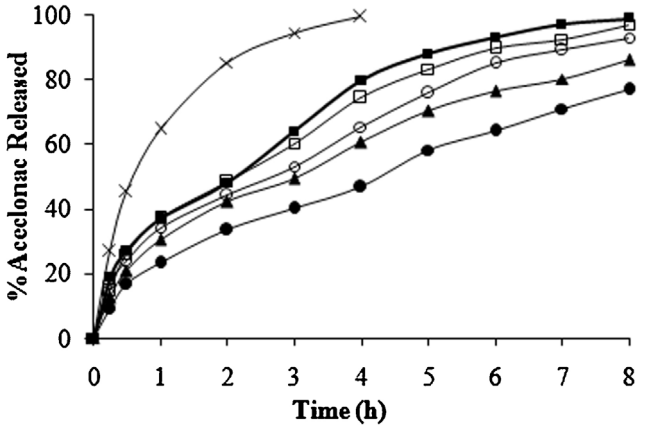


Fig. 3. In vitro drug release curves for the composites in pH 6.8 buffer solution. Key: CSLBG-1 (●); CSLBG-2 (▲); CSLBG-3 (■); CSLBG-4 (□); CSLBG-5 (○) and CSLBG-6 (×).

the matrix, hydrophobicity of the matrix could increase due to the presence of water insoluble LBG. In presence of a higher amount of LBG, a loosely cross-linked network was formed, swelled to a greater extent and consequently released higher amount of AC. Simply, as the amount of LBG was increased, cumulative amount of AC release decreased due to lesser swelling of the LBG chains than chitosan.

The trend of drug release profiles of the formulations prepared at different CS concentration remained almost identical to the formulations containing different amounts of LBG. The data indicated that the degree of swelling was 59.5, 51.3 and 49.8, respectively for the formulations denoted as CSLBG-3, CSLBG-4 and CSLBG-5. At higher CS concentration, the degree of cross-linking might be higher than that observed at low CS concentration. The free volume spaces of the matrix was reduced due to increased cross-linking and prohibited penetration of swelling media and resulted in decreased swelling of the IPN composites with consequent slower drug release rate.

Chitosan (CS) is a weak polybase with pK_b ~6.5 and the amino groups on the CS backbone can be easily protonated in acidic medium [13]. They swelled to an appreciable extent under acidic conditions due to the protonation of amino groups compared to weakly alkaline pH. Therefore, higher amount of drug was encountered at acidic pH 1.2, perhaps due to deformation of the composite structures. For comparison, almost 90% drug was released in 2 h at pH 1.2 for CS particles; however, only ~48% drug was released at pH 6.8 for the CS: LBG (1:5) composites in the same duration. The use of LBG in conjunction with CS in the composite system suppressed the burst release of drug in acidic media. Irrespective of the variations, a maximum of 35% drug release occurred in acidic pH 1.2 in same timeframe. It was seen that the composites were able to provide drug release for a longer duration at least 8 h than the plain CS particles. Nevertheless, there was a drastic difference in the release rates of the formulated blend microspheres in pH 1.2 and pH 6.8 dissolution media. Thus, drug release was dependent upon the composition, nature of the IPN polymer matrix as well as pH of the media. The slowest drug release profile was exhibited by nanocomposites at CS: LBG mass ratio of 1:5. Jana et al. [26] demonstrated that the slowest drug release profile could be achieved at CS: gum resin mass ratio of 1:3. Even, the combination of CS with a natural protein provided sustained release of aceclofenac over a period of 8 h in phosphate buffer solution (pH 7.4) from CS:Egg albumin nanoparticles [40]. The in vitro drug release data obtained in phosphate buffer solution (pH 6.8) were fitted into different mathematical models. The release rate constants and different correlation coefficients are shown in Table 3. The correlation coefficient indicated that the drug release from the nanocomposites did neither follow zero order nor first order kinetics. Again, the values of correlation coefficient were so close for the Higuchi model and Korsmeyer-Peppas model that it became very difficult to suggest a particular model for describing drug release from the nanocomposites.

According to Higuchi model, the release of a solid drug from a polymer matrix involves the simultaneous penetration of the surrounding liquid, dissolution of the drug, and leaching out of the drug through interstitial channels or pores. However, it does account the phenomenon of swelling and matrix dissolution in the process of drug release [37]. However, these are obvious phenomenon observed in case of hydrophilic matrix system. Based on the principles of last two models, it was clear that simple diffusion phenomenon was obviously involved in the drug release process. Korsmeyer-Peppas model can further reveal the contribution of other process that might have involved in the event of drug release. Therefore, the first 60% drug release data were fitted into this model [38]:

$$\frac{M_t}{M_\infty} = kt^n$$

Here, M_t/M_∞ represents the fractional drug release at time t, k is a constant characteristic of the drug-polymer system and n is an

Table 3
Release rate constants and correlation coefficients after fitting drug release data into different mathematical models.

Formulations	Zero order		First order		Higuchi		Korsmeyer-Peppas	
	$^{*}k_0$	r^2	$^{*}k_1$	r^2	$^{*}k_H$	r^2	$^{**}n$	r^2
CSLBG-1	8.957	0.968	0.1681	0.989	25.67	0.984	0.582	0.987
CSLBG-2	9.978	0.941	0.2303	0.993	30.42	0.996	0.543	0.992
CSLBG-3	11.70	0.914	0.5204	0.953	37.15	0.990	0.470	0.994
CSLBG-4	11.35	0.919	0.3961	0.973	35.66	0.994	0.545	0.976
CSLBG-5	10.78	0.943	0.3109	0.981	33.28	0.995	0.465	0.995
CSLBG-6	22.29	0.821	1.2136	0.957	55.23	0.964	0.638	0.988

$^{*}k_0$, k_1, k_H are the release rate constants for zero order, first order, and Higuchi kinetics. r^2 is the correlation coefficient and $^{**}n$ is the diffusion exponent.

empirical parameter characterizing the release mechanism. The values of *n* between 0.43-0.85 indicates anomalous or non-Fickian type drug diffusion mechanism. As was evident from Table 3, the *n* value lied between 0.470 and 0.638 and thus indicated anomalous transport mechanism, i.e. other than simple diffusion, the polymer chain relaxation as well as swelling mechanism was also responsible for providing slower drug release in vitro. Mukhopadhyay et al. [39] indicated that anomalous diffusion mechanism was involved in the process of insulin release from the CS/ALG core-shell nanoparticles, irrespective of polymer ratios. However, Jana et al. [26] found that the diffusion mechanism shifted from anomalous to case II transport as the CS: gum resin ratio was increased from 1:1 to 1:3. This suggested that the drug release kinetics was predominantly controlled by polymer chain relaxation. We further observed anomalous diffusion mechanism for release of aceclofenac from CS-tamarind seed polysaccharide [8] IPN microparticles and that of alprazolam and aceclofenac from CS: egg albumin nanoparticles [17,40]. Non-Fickian diffusion mechanism has also been reported by Thakur et al. [41] for the release of amoxicillin from glutaraldehyde-treated CS and xanthan gum hydrogel films. Overall, it can be said that the drug release kinetics depends on the composition and type of polymers and mostly, both the diffusion and polymer relaxation control the rate of drug release from hydrophilic polymer-based systems.

4. Conclusion

A nanocomposites system of CS and LBG was successfully prepared using glutaraldehyde as a cross-linker. The variation in the polymer composition could tailor the size of the nanocomposites as well as drug entrapment efficiency. The variation of either CS or LBG could be useful in controlling the release rate of drug from the nanocomposites. However, the presence of each polymer component in the composites was inevitable in suppressing the burst release of drug in the stomach and regulating the drug release profiles in variable pH environments of gastrointestinal tract, because only CS particles were insufficient to resist the burst effect at acidic pH of stomach. This novel nanocomposites system had potential for controlled drug delivery application.

Conflicts of interest

The authors declare no conflicts of interest.

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