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Original Article

Chitosan–Sesbania Gum Mediated pH-Responsive Polyelectrolyte Complexes for Targeted Delivery of Diclofenac Sodium: Preparation and Spectroscopical Evaluation

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ABSTRACT

Background: The implementation of chitosan as an enhanced vehicle for drug delivery is an interesting domain in the pharmaceutical dosage form. The combination of commonly accessible natural polysaccharides like gum may provide a new arrangement of dosage forms such as polyelectrolyte complex. Such modern improvements facilitate the modulated release of active, which can be beneficial in avoiding adverse consequences. There have been no reports on chitosan and sesbania gum-based polyelectrolyte complexes for drug delivery applications to date. **Objectives:** The chitosan-sesbania gum polyelectrolyte complex was developed for modified drug delivery of diclofenac sodium. **Materials and Methods:** pH-responsive polyelectrolyte complexes were accomplished utilizing the coacervation technique. It forms complex due to the capability of chitosan amine groups and sesbania gum carboxylic functionality. **Results:** The SEM analysis assured the aggregated polyhedral shape particles with a smooth surface of the final polyelectrolyte complex. The Diffractogram of the polyelectrolyte complex resulted in an amorphous form of diclofenac. The polyelectrolyte complex batch (B:3) showed satisfactory drug entrapment capabilities. It showed 88.96% of the drug release in 8 hr (pH 6.8). Importantly, it is because of the unprotonated condition of sesbania gum containing hydrophilic functionality that offers boosted hydrogen bonding via interaction with dissolution medium containing water molecules. Therefore, it offers the insertion of water molecules into a complex followed by the swelling of a matrix. **Conclusion:** The developed chitosan-sesbania gum polyelectrolyte complex offers a pH-responsive sustained release of diclofenac sodium. In the future, chitosan and sesbania gum-based polyelectrolyte complex can be preferred as an innovative drug carrier for diclofenac sodium delivery.

Keywords: Chitosan, Sesbania gum, Diclofenac sodium, Polyelectrolyte complex, Drug delivery.

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INTRODUCTION

Presently, the use of polymeric-based systems for the delivery of active is opening a new era that may be because of their prospective applications. These methods control drug delivery rates, maintain therapeutic action, and/or target drugs to tissues. In addition, they enhance and modify physicochemical properties such as stability and solubility, which provide the therapeutic effects of drugs with greater benefits. Due to their bioadhesive nature, they have been utilized as matrices for drug administration via oral, buccal, transdermal, and nasal routes. However, they function as carrier systems for drugs, enzymes, or DNA because charged species may be conveniently incorporated into complex particles. These can be used as membranes, coatings on films and fibers, targeted nucleic acid delivery, nucleic acid isolation and fractionation, pharmaceutical product binding, preparation of microcapsules for drug delivery membranes for dialysis, contact lenses,[1] enzyme mimics,[2] medical applications,[3] nanoparticles for targeted tissue delivery, and the development of biosensors.[4]

Out of several kinds of polymeric systems, polyelectrolytes-based systems are recently reported that solely relied on charged-based components. Interestingly, two oppositely charged polyelectrolytes are simultaneously combined in solution without using any chemical covalent cross-linker leading to the formation of a polyelectrolyte complex.[5] The polyelectrolyte complex has attracted attention due to its nontoxicity and well-tolerated

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properties. In addition, it provides mucoadhesion abilities, biocompatibility, biodegradability, sustainable releases, stability, and sensitivity to changes in environmental conditions, offering significant advantages as a pharmaceutical excipient, for instance in regulating drug release.

A polyelectrolyte complex is formed due to interactions such as electrostatic interactions, hydrogen, and hydrophobic interaction that occur between cationic and anionic polymers.[6] The amino group of chitosan interacts with carboxyl or sulfate groups of other polysaccharides, such as carboxymethyl cellulose,[7] alginate,[8] carrageenan,[9] hyaluronic acid,[10] acacia gum,[11] pectin,[12] dextran sulfate,[13] heparin,[14] promotes the formation of polyelectrolyte complexes. To date, several polyelectrolyte complexes revealed for clindamycin phosphate,[15] diclofenac sodium,[16] clotrimazole,[17] tetracycline,[18] etc. This polyelectrolyte can be converted into modified dosage forms such as a tablet, microcapsule, beads, film, hydrogel, etc. Hence, the use of polyelectrolyte complex for the development of advanced dosage forms will reveal a new path for delivery of active.

Chitosan is a linear polysaccharide composed of glucosamine and N-acetyl glucosamine units linked together by (1–4) links distributed randomly or block-wise throughout the biopolymer chain.[19] Chitin is a naturally occurring polymer primarily found in the exoskeletons of crustaceans, insects, and fungi, and is converted to chitosan through the N-deacetylation process. After deacetylation, the protonation of amino groups on the chitosan backbone helps it to dissolve in acidic solutions, making it the only polysaccharide with a high positive charge density.[20] Chitosan is naturally cationic, and this property is used for the formation of polyelectrolyte complex by interacting with polyanions such as Tripolyphosphate (TPP), other anionic natural polysaccharides such as alginate, pectin, carrageenan, xanthan gum, and gum kondagogu, synthetic anionic polymers such as polyacrylic acids, and semi-synthetic such as carboxymethylcellulose.[21] To date, it has been reported for delivery of bovine serum albumin,[22] amikacin,[23] ciprofloxacin hydrochloride,[24] tetracycline, gentamycin,[25] etc. Hence, we can employ chitosan for the development of polyelectrolyte complexes with naturally obtained polysaccharides.

Presently applications of gum in pharmaceutical dosage form development are extensively revealed that might because of their several merits including biocompatibility, mucoadhesion, drug release modulation potential, etc. In addition, it has been preferred for the development of polyelectrolyte complexes that might be because of their anionic surface functionality. Out of several types of gum, sesbania is not explored in the development of polyelectrolyte complex since it naturally exists. Sesbania gum is synthesized from the endosperm of *Sesbania grandiflora* seeds that belong to the Leguminosae family (Papilionaceous). Galactomannans are heterogeneous polysaccharides made up of a (1-4) D-mannan backbone with α - (1-6) linked D-galactose molecule.[26] It comprises hydro colloidal polysaccharides with a high molecular weight that are made up of galactan and mannan units linked together by glycosidic linkages.[27] The good swelling properties of treated sesbania gum make it suitable for the manufacturing of slower-release tablets, as the swelling of the polymer can control drug release from the matrix. In another investigation, sesbania mucilage was evaluated as a gelling agent for diclofenac topical administration.[28] As per a report, natural gum offers pH-responsive swelling that benefits the targeted release of active.[29] Therefore, we intended to design the pH-responsive polyelectrolyte complex with consideration of sesbania gum functionality.

Diclofenac is widely used around the entire globe for several applications. It is a non-steroidal anti-inflammatory drug suffering from low plasma half-life (1–2 hr). Moreover, gastritis and peptic ulcers are the drug's most common adverse effects of the diclofenac. Literature reported that diclofenac sodium was used as a model drug for novel drug delivery.[30] Therefore, there is a need to develop advanced nanocarriers for the targeted delivery of diclofenac that can help to avoid the adverse effects and overcomes the pharmacokinetics and pharmacodynamics issue. In this case, the use of a pH-responsive sesbania gum-mediated polyelectrolyte complex will provide the alternative to release the drug at the targeted site only. To the best of our knowledge, no pH-responsive polyelectrolyte combination including sesbania gum and chitosan has been described to date.

Therefore, the current study presented the innovative sesbania gum and chitosan-mediated pH-sensitive polyelectrolyte complex for the targeted delivery of diclofenac sodium. In summary, the polyelectrolyte complex was constructed based on the carboxyl and amino functionality of both components, and spectroscopic analysis validated the effective synthesis of the complex. As an outcome, sesbania gum and chitosan-polyelectrolyte complex have good drug entrapment. Furthermore, chitosan-sesbania gum cross-linking aids in the delayed drug release of diclofenac sodium, as well as the conversion of diclofenac sodium from crystalline to amorphous form. Interestingly, the unprotonated condition of sesbania gum containing hydrophilic groups offers a high number of hydrogen bonding via interaction with water molecules present in dissolution media. As an effect, it assists to penetrate the water molecules into a polyelectrolyte complex that offers the swelling of a matrix at pH 6.8. In the future, a polyelectrolyte complex based on chitosan and sesbania gum may be selected as a new drug carrier for diclofenac sodium delivery.

MATERIALS AND METHODS

Materials

Gum sesbania (Mol. wt. 5,00,000 g/mol) was obtained from Badar Enterprises, Jodhpur, India. Chitosan (Mol. wt.: 3800-20,000 Daltons; deacetylation degree: 80%) was obtained from

Sigma–Aldrich Chemie. Diclofenac sodium (Mol. wt. 296.148 g/mol; plasma half-life- 2 hr; MP. 283°C-285°C) was procured from Meditech Chemicals Pvt. Ltd., Gurgaon, India. Glacial acetic acid (Mol. Wt. 60.052 g/mol) and Sodium hydroxide (Mol. Wt. 40 g/mol) was received from Loba Chemie Pvt. Ltd., Mumbai. All other chemicals and reagents were used exactly as they were supplied to us.

Methods

Preparation of diclofenac sodium-loaded gum sesbania and chitosan polyelectrolyte complex

The 20 mL aqueous acetic acid (2% w/v) solution was used for the dissolving of chitosan at a concentration of 0.25-1.5% w/v along with continuous magnetic stirring until completely dissolved. Simultaneously, a 20 mL aqueous dispersion of gum sesbania at a concentration of 0.25-1.25% w/v containing 100 mg diclofenac sodium was prepared under magnetic stirring. Gum sesbania dispersion containing diclofenac sodium was added dropwise into the chitosan solution with continuous stirring for 30 min. After that, the reaction solution was probed sonicated for 15 min and then filtered and dried in the oven at 45°C.[31] The same procedure was preferred for further batches from B2-B6. The formulation concentration of sesbania gum and chitosan-polyelectrolyte complex is shown in (Table 1).

Characterization of Gum Sesbania-Chitosan Polyelectrolyte Complex

Spectrometric analysis

The FTIR analysis of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium–loaded polyelectrolyte complex was performed to study the drug excipients' interaction. In a ratio of 1:100, the sample and potassium bromide were mixed. The samples were analysed by FTIR spectrometer at frequencies ranging from 400 – 4000 cm^{-1}.[32] A Differential Scanning Calorimeter (DSC) obtained thermograms of the diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complexes were obtained using a Differential Scanning Calorimeter (DSC). DSC data were recorded throughout a wide range of temperatures (30-225°C) at a heating rate of 10°C/min with purging nitrogen gas at a 20 mL/min flow rate. The DSC thermogram data of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complexes were obtained.[33] Despite this, Powder X-ray Diffractometers (PXRD) were employed to investigate modifications in drug crystallinity in polyelectrolyte complexes. An X-ray diffraction study was performed to study the crystallinity of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complexes using an X-ray diffractometer. Polymers were scanned from 5° to 80° diffraction angle (2θ).[34] Scanning Electron Microscopy (SEM) with a 15 kV acceleration voltage and a 1-µm resolution was used to study the surface morphology. The study was carried out to distinguish between the surface morphologies of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complexes.[31] At a temperature of 25.2°C and a detector angle of 90°, the polyelectrolyte complex particle size and zeta potential were determined (Nanoplus 3).[35]

Drug Entrapment Efficiency (DEE)

The drug entrapment efficiency of the polyelectrolyte complex was performed as per the previously reported method.[31] In brief, the encapsulation efficiency of the diclofenac sodium-loaded polyelectrolyte complex was measured by centrifugation at 12,000 rpm for 30 min at 25°C to separate the unentrapped drug from the polyelectrolyte complex. The amount of free diclofenac sodium in the supernatant was analysed by using a UV-visible spectrophotometer at 274 nm. The % DEE was determined using equation 1.

$$\text{DEE (\%)} = (\text{DCt-DCs})/\ \text{DCt} \quad \ldots\ldots\ldots\ldots\ldots\ldots \text{(1)}$$

Where, DC_t - total diclofenac sodium, DCs - free diclofenac sodium present in the supernatant

In vitro dissolution study

The *in vitro* release of diclofenac sodium from the chitosan-sesbania gum polyelectrolyte complex was measured by using the dialysis sac method. The dialysis sac was tied to the USP type II dissolution apparatus's paddle (Electrolab dissolution tester, EDT-08Lx), which contained the 5 mL sample of polyelectrolyte complex. Then the paddle was subjected to pH 6.8 phosphate buffer (200 mL) whereas the dissolution media temperature was fixed at 37 ± 0.5°C at 25 rpm. For drug release analysis, a 5 mL sample was collected from the dissolution vessel as per predefined time intervals. Simultaneously, to keep the sink condition 5 mL of fresh pH 6.8 phosphate buffer was added to the dissolution vessel. Finally, the collected samples were examined spectrophotometrically (Shimadzu/UV-1800, Japan) at 274 nm. Percent drug release was calculated using a calibration curve of diclofenac sodium in pH 6.8 phosphate buffer.[35,36] To estimate the drug release mechanism, the drug data were fitted into various kinetic models such as zero order, first order, Higuchi square root, Korsmeyer Peppas, and Hixon-Crowell. To understand the release mechanism by the zero-order kinetics model, the graph was plotted as cumulative drug release versus time. The first-order kinetic model was described by plotting the graph log of the cumulative drug remaining percentage against time. After that, the determination of the release mechanism by Higuchi square root kinetics was plotted as percent cumulative drug release versus square root of time. The Korsmeyer Peppas model was plotted as a log of percent cumulative drug release versus log time. Finally, the Hixon-Crowell kinetic model was explained by the graphical plotting of the cubic root of the remaining fraction of the drug against time.[37]

RESULTS AND DISCUSSION

The interaction between the polymers resulted in the formation of a polyelectrolyte complex. In this study, sesbania gum interacts with cationic chitosan to form a polyelectrolyte complex. Importantly, interaction occurs between the amino group of chitosan and the carboxyl group of sesbania gum mainly driven by electrostatic interaction, hydrogen bond, and hydrophobic interaction. For this, the sesbania gum dispersion was added into the chitosan solution to produce an opalescent suspension. As a response, it indicates the formation of polyelectrolyte complex nanoparticles.[38] Finally, the polyelectrolyte complex formed between the sesbania gum and chitosan was characterized using different spectroscopical analyses such as FTIR, DSC, PXRD, and SEM. Moreover, the entrapment efficiency, particle size, zeta potential, and *in vitro* dissolution were performed to evaluate the designed polyelectrolyte complex for diclofenac sodium.

FTIR

The FTIR spectra of diclofenac sodium (a), sesbania gum (b), chitosan (c), and diclofenac sodium-loaded polyelectrolyte complex (d) are shown in (Figure 1). The spectra of diclofenac sodium showed the N-H stretching peak of secondary amine at 3387 cm^{-1}. Moreover, the typical peaks appeared at 1604 cm^{-1} due to carboxyl stretching. The peak was observed at 746 cm^{-1} and 765 cm^{-1} due to the chloride stretch (Figure 1a). Figure 1b shows the FTIR spectra of sesbania gum. It exhibited a broad absorption peak that occurred because of O-H stretching at 3421 cm^{-1}. The peaks around 1654 cm^{-1} could be due to carbonyl group stretching whereas the C-O stretching band was observed at 1153.47 cm^{-1}. In addition, the peak of the ester's carbonyl group was observed at 1739 cm^{-1} which assured the presence of sesbania gum.[39] Figure 1c shows the FTIR spectrum of chitosan. It showed a broad absorption peak of the O-H group stretching at 3419 cm^{-1} and a peak at 2364 cm^{-1} was observed due to the C-H stretching. Moreover, the peaks at 1153 cm^{-1} and 1085 cm^{-1} correspond to the C-OH stretching and C-O-C stretching of ether, respectively. The doublet peaks of the amide bond show that it was generated from partial N-deacetylation of chitin, and it appeared at 1625 cm^{-1} and 1517 cm^{-1}. Overall, it validates the presence of chitosan.[40] Finally, the polyelectrolyte complex spectra display the typical peaks of diclofenac, sesbania gum, and chitosan with a slight shifting of peaks (Figure 1d). In a polyelectrolyte complex, the carboxyl peak of diclofenac was slightly shifted towards the higher wavenumber at 1666 cm^{-1}. This demonstrates that diclofenac sodium and the polymers used to produce PEC do not interact chemically. The sesbania gum ester's carbonyl group peak at 1739 cm^{-1} was diminished. However, the chitosan amide's doublet peaks were converted into singlet ones and the sharp absorption peak occurred at 1568.18 cm^{-1}. The slight shifting of sesbania gum and chitosan peaks in polyelectrolyte complex spectra revealed the electrostatic interactions between both components. As a result, it confirmed the formation of the polyelectrolyte complex of chitosan and sesbania gum.[34]

Differential Scanning Calorimeter (DSC)

The thermogram of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complex was examined by DSC (Figure 2). The sharp endothermic peak of pure diclofenac sodium was observed at 284.74°C, which corresponded to its melting point (Figure 2a). It assured that the diclofenac was in crystalline form. The broad endothermic peak of sesbania gum was observed at 69.27°C (Figure 2b) assured the presence of polysaccharides in amorphous form. For chitosan, the wide endothermic peak was found to be 77.79°C (Figure 2c), which assured the amorphous nature of chitosan. In the diclofenac sodium-loaded polyelectrolyte complex thermogram, the endothermic peak of diclofenac sodium was

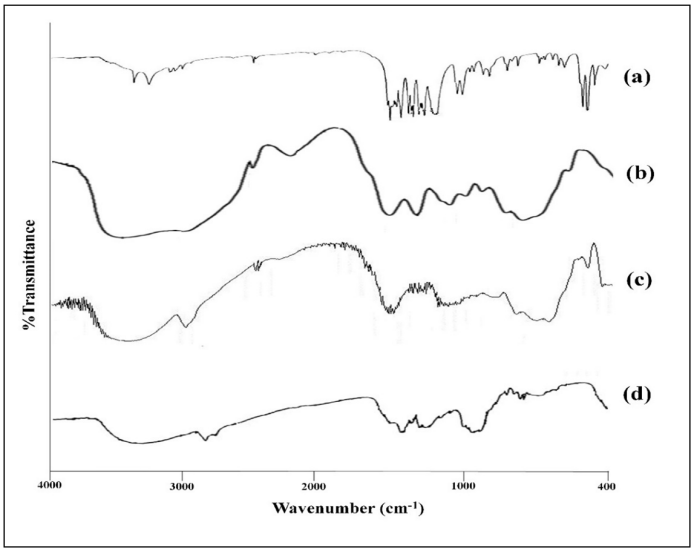

Figure 1: FT-IR spectra of diclofenac sodium (a), sesbania gum (b), chitosan(c), and diclofenac sodium-loaded polyelectrolyte complex (d) (B:3).

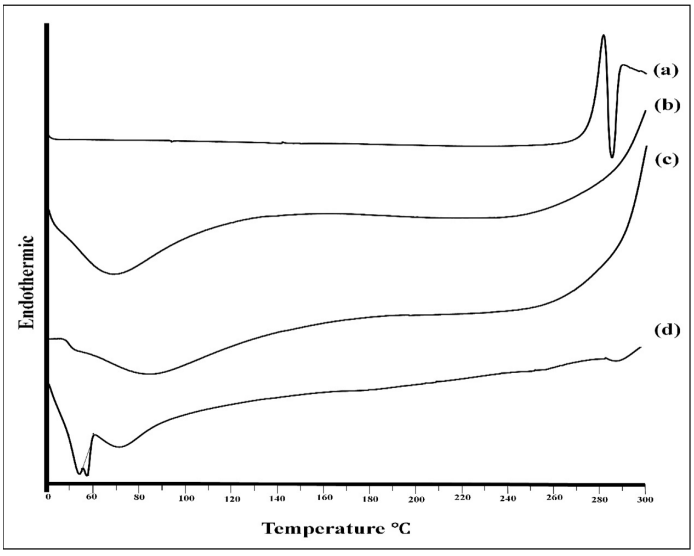

Figure 2: DSC curves of diclofenac sodium (a), sesbania gum (b), chitosan(c), and diclofenac sodium-loaded polyelectrolyte complex (d) (B:3).

shifted towards the lower temperature at 264.74°C (Figure 2d). This could be due to the formation of amorphic dispersion of diclofenac sodium in a polymeric matrix. Possibly, the shifting of the drug's endothermic peak in the diclofenac sodium-loaded polyelectrolyte complex thermogram indicates that the drug was entrapped within a polymer matrix. In addition, because of the formation of the complex the thermal degradation of diclofenac sodium requires less energy. The diclofenac sodium-loaded polyelectrolyte complex showed the shifting of the chitosan endothermic peak at 71.90°C. This might be because of the loss of moisture from chitosan. Similarly, the peak of sesbania gum was also moved towards a lower temperature at 57.20°C. The shifting of the polymer's peak might be occurred due to the formation of the polymeric complex.[33]

Powder X-ray Diffractometers (PXRD)

Figure 3 shows a diffractogram of diclofenac sodium (a), sesbania gum (b), chitosan (c), and diclofenac sodium-loaded polyelectrolyte complex (d). In the diffractogram of the diclofenac sodium (Figure 3a), an intense peak was found at 2θ: 5.10°, 8.70°, 12.10°, 15.31°, 17.34°, and 20.12° indicating the crystallinity of diclofenac sodium. The broad, less sharp peaks of sesbania gum (Figure 3b) were found to be at 5.92° and 20.24° assuring the presence of sesbania gum in less crystalline form. The chitosan diffractogram (Figure 3c) showed two broad peaks at 9.85° and 20.4° (2Θ), indicating the presence of chitosan with a less crystalline nature. The diffractogram of the diclofenac sodium-loaded polyelectrolyte complex showed in Figure 3d. Herein, complete elimination or decrease in peak intensity corresponding to the drug implies a change in drug crystallography and an elevation in amorphic of the drug. As compared to the sesbania gum diffraction peaks, the polyelectrolyte complex showed a lower intensity of sharp peaks or an absence of peaks, indicating that an ionic interaction was formed between a chitosan amino group and a sesbania gum carboxyl group.[41]

Scanning Electron Microscopy (SEM)

In this step, the SEM images of diclofenac sodium, sesbania gum, chitosan, and diclofenac sodium-loaded polyelectrolyte complex are shown in Figure 4. Figure 4a depicts the rough and irregular shape of diclofenac. Figure 4b divulged the strip, smooth on the surface, and irregular particle size for sesbania gum. Figure 4c shows the rough and irregular shape of the chitosan. Figure 4d displayed the surface morphology of the polyelectrolyte complex. It showed aggregated polyhedral shape particles with a smooth surface. The polymer matrix showed the absence of diclofenac sodium particles on the surface of the complex that indicating diclofenac was properly distributed and incorporated into the polyelectrolyte complex.[31,42]

Particle size and zeta potential measurements

The particle size of the chitosan-sesbania gum polyelectrolyte complex containing diclofenac sodium was found to be between 263.3nm to 1898.8 nm (Table 1). In this investigation, the sesbania gum concentration had a much more prominent impact on particle size as compared to chitosan. The particle size of polyelectrolyte complex nanoparticles increases significantly when the concentration of sesbania gum increases. The increased concentration of gum enhanced the viscosity of dispersion, which render to the formation of larger droplets. Importantly, this might cause inadequate cross-linking between cationic polymer and anionic polysaccharide in chitosan solution.[43] Therefore, this could aggregate the particles and increases the particle size.[35] While the concentration of chitosan showed a much lower impact on particle size. From all the formulation batches, the minimum particle size was shown by the B 3 batch (263.3 nm). Possibly, it might be because of the occurrence of optimum cross-linking between gum and chitosan at a selected concentration. Table 1 assured the zeta potential of the complex. As a result, the polyelectrolyte complex-associated zeta potential ranged from +18.22 mV to +33.47 mV. Interestingly, it was revealed that the concentration of chitosan improved the zeta of the formulation batches, and it may assist to boost the stability of the complex. It might be due to electrostatic and steric stabilization caused by chitosan.[43] Conversely, the sesbania gum showed an inverse impact on zeta potential. The zeta of the polyelectrolyte complex is reduced with an increased concentration of sesbania gum. Overall, the optimized batch demonstrated the +30.59 mV of zeta potential. It revealed the good stability of the polyelectrolyte complex.

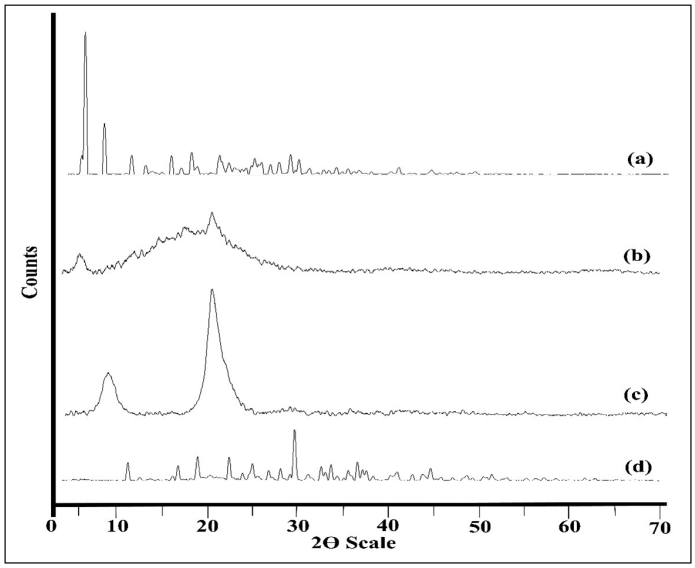

Figure 3: X-ray diffractogram of diclofenac sodium (a), sesbania gum (b), chitosan(c) and diclofenac sodium - loaded polyelectrolyte complex (d) (B:3).

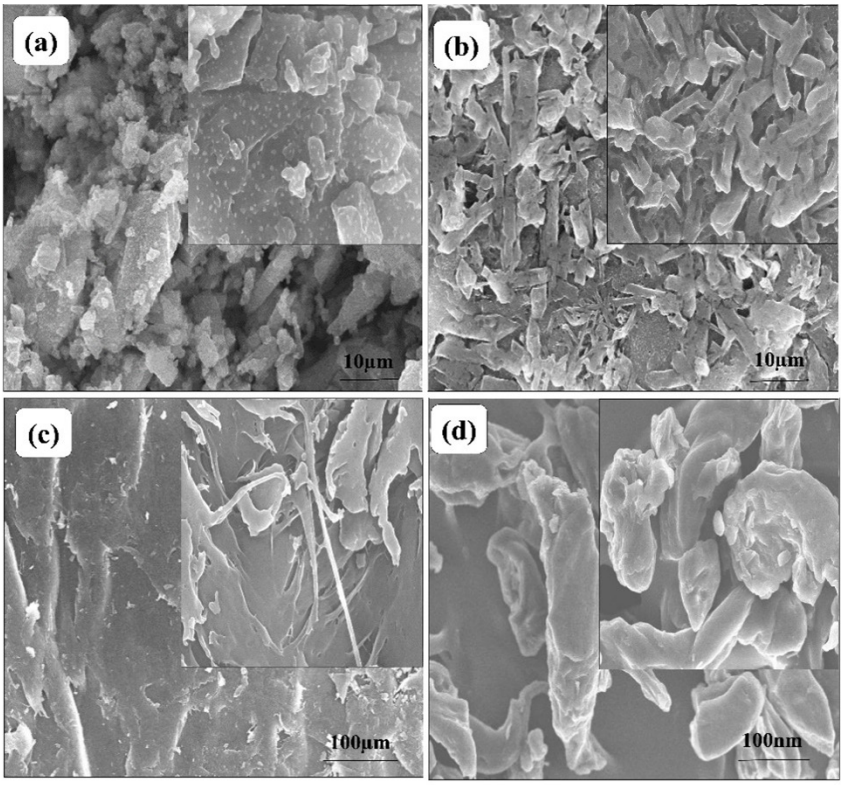

Figure 4: Scanning electron micrographs of diclofenac sodium (a), sesbania gum (b), chitosan(c), and diclofenac sodium -loaded polyelectrolyte complex (d) (B:3).

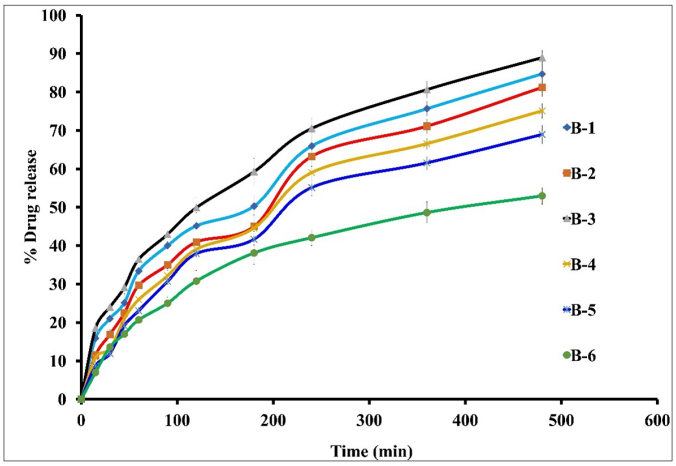

Figure 5: *In vitro* release profile of diclofenac sodium-loaded polyelectrolyte complex B:1-B:6.

Drug entrapment efficiency

The drug entrapment efficiency of polyelectrolyte complex containing diclofenac sodium ranged from 54.40±0.25% to 90.00±0.19% (Table 1). Particularly, the chitosan has shown more prominence than the sesbania gum in entrapment efficiency. On the other hand, the increase in sesbania gum concentration in dispersion increases its viscosity, which might increase the particle size of dispersion. Herein, a decrease in entrapment efficiency was found that may be because of improper interaction between the gum and chitosan.[35,38] However, chitosan had a positive effect on the encapsulation of the drug. Hence, batch B 4 and B: 5 showed maximum entrapment as compared to B: 1 and B: 2 batches. This could be due to increased chitosan concentration, which was enough to form interaction with sesbania gum, and it results in minimum drug loss. Here, the optimized batch B 3 shows maximum entrapment of diclofenac sodium (90.12%) over other batches. Principally, it may be because of efficient interaction between sesbania gum and chitosan that offers results in the formation strong network amongst polymers with less drug leakage.[44]

In vitro dissolution

In vitro drug release of diclofenac sodium in all batches was shown in Figure 5. Herein, the use of the sesbania gum conjugation with chitosan in complex shows the prevention of burst release of diclofenac sodium in acidic media. Importantly, at pH 1.2, sesbania gum containing hydrophilic functionality suffers protonation. As a response, it restricts the association of hydrogen bonds with dissolution media containing water molecules. Therefore, it resulted in the hurdle in penetration of water molecules into the polyelectrolyte complex and finally, prevention of initial burst release in pH 1.2 dissolution media. Therefore, it is a suitable candidate for the targeted delivery of diclofenac. The further dissolution was performed in pH 6.8 buffer. Figure 5 revealed that batch B: 1 and B: 2 showed faster drug release as compared to batch B 4 and B 5. In brief, the concentration of sesbania gum in polyelectrolyte complex

Table 1: Formulation of polyelectrolyte complexes using chitosan and sesbania gum and their evaluations.

Batches	Polymers ratio (CH: SG)	Diclofenac sodium (mg)	Particle size (nm)	PDI	Zeta potential (mV)	DEE (%)
B:1	B:1	100	1898.8	1.038	+22.25	63.23±0.15
B:2	B:2	100	711.9	0.804	+18.22	75.42±0.18
B:3	B:3	100	263.3	0.398	+30.59	90.12±0.22
B:4	B:4	100	580.6	0.404	+33.47	85.01±0.24
B:5	B:5	100	705.3	0.709	+40.78	88.70±0.19
B:6	B:6	100	650.1	0.53	+37.89	54.08±0.25

±: Standard deviation (n=3).

Table 2: Results of *in vitro* drug release data fitted in various release kinetic models.

Batches	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	Hixson- Crowell	Best fit model	% Drug release (8 hr)
B:1	0.9373	0.7978	0.9910	0.9901	0.854	Higuchi	84.72
B:2	0.9369	0.7368	0.9871	0.9883	0.8408	Higuchi	81.2
B:3	0.926	0.793	0.9951	0.9919	0.8451	Higuchi	88.96
B:4	0.9279	0.7593	0.9881	0.9825	0.8275	Higuchi	75.11
B:5	0.9453	0.7255	0.9914	0.9789	0.7998	Higuchi	68.95
B:6	0.9469	0.6915	0.9953	0.9721	0.7711	Higuchi	52.97

increased, which offered an increasing release rate. It may be because of insufficient cross-linking formed between the sesbania gum and chitosan, which can encourage the entry of fluid into the particles. Herein, the release profile of the optimized batch assured the enhanced solubility of the diclofenac sodium, thereby accelerating its dissolution.[45] Conversely, the drug release rate was delayed with an improved concentration of chitosan. Possibly, a maximum concentration of chitosan leads to an increase in cross-linking, which minimizes polyelectrolyte complex free volume of space. Moreover, it restricted the absorption of swelling media resulting in the sustained release of diclofenac sodium from the polyelectrolyte complex.[46] In the optimized (B 3) batch, a promising drug release was found (88.96%) within 8 hr. Herein, enough cross-linking formed between the sesbania gum and chitosan leads to the creation of a strong network amongst polymers that furnishes the prolonged drug release. Moreover, at pH 6.8, the sesbania gum containing hydrophilic functionality remains unprotonated condition. As a response, it offers a large number of hydrogen bonding via interaction with a dissolution medium containing water molecule. Therefore, it offers the inclusion of water molecules into a polyelectrolyte complex followed by the swelling of a matrix. Release kinetics analysis of all designed polyelectrolyte complex release Higuchi matrix release as the best model (Table 2). In this, the diclofenac can be released from the matrix system as the polymer layer was dissolved gradually and the diclofenac gets diffused out or release from the polyelectrolyte complex. Therefore, the anticipated sesbania gum and chitosan-based polyelectrolyte complex for diclofenac intestinal delivery follow the diffusion as a drug transport mechanism.[47]

CONCLUSION

The anticipated novel pH-responsive chitosan and sesbania gum-based polyelectrolyte complex system offer the diclofenac sodium delivery to the small intestine. In brief, the application of chitosan and sesbania gum resulted in electrostatic interaction. Herein, the successful cross-linking among the amine functionality and oxygen functionality resulted in the high entrapment of diclofenac. Diffractogram and thermogram of final polyelectrolyte complex validate the conversion of a crystalline form of diclofenac to the amorphous form which might be because of ionic interaction of chitosan and sesbania gum. There was no release of diclofenac in acidic media because of the protonation of sesbania gum. The case of batch B: 3, showed the maximum drug entrapment efficiency (90.12±0.22%), and 88.96% of drug release in 8 hr. Notably, the unprotonated state of sesbania gum with hydrophilic functionality provides increased hydrogen bonding via contact with dissolving medium comprising water molecules. As a result, it provides the entry of water molecules into complexes proceeded by matrix swelling. As a result, it provides pH-responsive prolonged release of diclofenac sodium. As a result, this innovative chitosan and sesbania gum-based

polyelectrolyte system may reduce gastrointestinal side effects by administering the drug in a sustained manner in the intestinal region. Taken as a whole, the application of chitosan with naturally obtained sesbania gum would be an exceptional substitute for the development of advanced pH-responsive pharmaceutical dosage forms for the targeted delivery of diclofenac sodium.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

API: Active pharmaceutical ingredient; **MP:** Melting point; **TPP:** Tripolyphosphate, **DNA:** Deoxyribonucleic acid; **DEE:** Drug entrapment efficiency; **DR:** Drug release; **XRD:** X-ray diffraction; **FTIR:** Fourier transform infrared spectroscopy; **SEM:** Scanning electron microscopy; **PEC:** Polyelectrolyte complex; **DC_t:** Total diclofenac sodium; **DCs:** Free diclofenac sodium present in the supernatant.

SUMMARY

- First report on pH-responsive chitosan and sesbania gum-mediated polyelectrolyte complex.
- Complex formation between chitosan and sesbania gum follows the Higuchi matrix release kinetics.
- Sesbania gum in polyelectrolyte complex restricts the diclofenac release in acidic pH 1.2.
- The anticipated polyelectrolyte complex can be used as a carrier for the targeted delivery of diclofenac sodium.

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