

## Research Article



## INVESTIGATION ON RELEASE PROFILE OF CHITOSAN BASED POLYELECTROLYTE COMPLEXES USING AN ANTIHYPERTENSIVE AGENT

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### ABSTRACT

Atenolol is the most commonly used antihypertensive drug in the management of hypertension. Atenolol is a  $\beta$  blocker with a half life of 6-7 hrs. Administration of conventional tablet has been reported to exhibit fluctuation in the plasma drug level, resulting either in manifestation of side effect or reduction in drug concentration at the receptor site. The aim of the study was to evaluate the possibility of using polyelectrolyte complexes (PEC) in the form of matrix tablets to achieve a prolonged drug release profile of atenolol suitable for peroral administration. The formation of complexes was confirmed by FTIR and DSC studies. Different dissolution profiles were obtained by changing the polymer matrix system. The results showed that lyophilised complexes were better than oven dried complexes in sustaining the release of the drug. In case of PEC (lyophilised) tablets of atenolol, C7 showed highest swelling property with a swelling index of 390.62% and C1 showed least swelling index of 231.64%. In case of lyophilised PEC tablets of atenolol, the best sustained release profile was seen in C7 followed by C3, C1 and C8. In case of oven dried complexes, the tablets of all the complexes were found to disintegrate very fast compared to the lyophilized complexes. This may be due to the loss of the attractive forces at the molecular level, which was lost during drying.

**Keywords:** Polyelectrolyte complex (PEC), Polymer, Drug Delivery, Lyophilised, Oven Dried.

### INTRODUCTION

Recent decade witnessed the appearance of polymers that respond in some desired way to changes in temperature, pH, electric or magnetic field. The driving force behind these transitions include stimuli like neutralisation of charged groups by either a pH shift or the addition of an oppositely charged polymer, changes in the efficiency of hydrogen bonding with an increase in temperature or ionic strength and collapse of hydrogels and interpenetration of polymeric network. These types of polymers not only convert the active substance into a non-deleterious form which can be administered, but also have specific effect on the biodistribution, bioavailability and hence increasingly gaining importance in modern pharmaceutical technology<sup>1</sup>.

Oppositely charged polysaccharides in aqueous solutions interact spontaneously when they are mixed. This interaction between two oppositely charged polymers results in the formation of a complex; termed as polyelectrolyte complex. Polyelectrolytes are polymers that contain a net negative or positive charge at near neutral pH<sup>2</sup>. The formation of polyanion-polycation (polyelectrolyte) complexes is mainly driven by electrostatic mechanism where charge neutralisation and possible local overcompensation or bridging (such as hydrogen bonding, coulomb forces, Vander wall forces and transfer forces) mediated by a multivalent counter ion induces attraction between topologically separated segments of the polyelectrolytes. This avoids the use of chemical cross-linking agents, thereby reducing the possibility of toxicity and other undesirable effects of the reagents<sup>3</sup>. The lower the charge density of the polymer,

the higher is the polymer proportion in the polyelectrolyte complex, since more polymeric chains are required to react with the other polymer, leading to 'bulky' polyelectrolyte complex<sup>4</sup>.

Chitosan, the unique cationic groups-containing polysaccharide is a natural, renewable, non toxic, biodegradable source being considered as an "ecologically- friendly" product. Since chitosan has a rigid, stereo-regular structure containing bulky 'pyranose' rings, the formation of PEC can induce a conformational change of the other polyelectrolyte, if the latter has a non-rigid structure<sup>5</sup>. Chitosan is a weak base and is insoluble in water and organic solvents, however, it is soluble in dilute aqueous acidic solution (pH 6.5), which can convert the glucosamine units  $R-NH_3^+$  which is soluble.

Atenolol, a  $\beta$ -blocker is prescribed widely in diverse cardiovascular diseases, e.g. Hypertension, angina pectoris, arrhythmias, and myocardial infarction. The drug is also indicated in prophylactic treatment of migraine. It has the lowest lipid solubility and a half life of 6-7 hrs. About 50% of the oral dose is absorbed from the gastrointestinal tract, the drug being excreted unchanged in urine<sup>6</sup>. Administration of conventional tablet has been reported to exhibit fluctuation in the plasma drug level, resulting either in manifestation of side effect or reduction in drug concentration at the receptor site. Atenolol has strong absorption throughout GIT as well as in colon. But, it causes GI irritation problem. Hence it is always effective to have absorption of atenolol in the intestine. By formulating a sustained release tablet, the half life of the drug will further be increased thereby



reducing the number of tablets to be taken by the patient and thus enhancing patient compliance.

By use of polymers such as sodium alginate, gaur gum, gellan gum, pectin in the form of polyelectrolyte complexes with chitosan, the release of the drugs in the acidic environment can be protected. These polymers swell and get hydrated on reaching the intestine when in contact with the alkaline medium and release the drug slowly over a period of 8 – 10h.

The aim of this work was to evaluate the possibility to obtain different prolonged dissolution profiles by changing the polymer matrix system (chitosan-sodium alginate, chitosan-pectin, chitosan-gellan gum, chitosan-guar gum) and method used to include the polymers into the formulation was polyelectrolyte complexation. Also, we tried to explain the drug dissolution profiles from the matrices considering the swelling behaviour of polymers used.

## MATERIALS AND METHODS

### Materials

Chitosan was purchased from CIFD, Cochin. Atenolol was procured from Aquila Pharmaceuticals Ltd, Mumbai. Sodium alginate was obtained from CDH Laboratory Ltd, Delhi. Pectin and guar gum were procured from Himedia Laboratories Pvt Ltd, Mumbai and gellan gum purchased from Lobachem pvt Ltd, Mumbai. All chemicals used were of analytical grade.

**Table 1:** Ratios of polymers used in preparation of polyelectrolyte complexes

| F.Code | Chitosan :<br>sodium alginate | Chitosan:<br>pectin | Chitosan:<br>gellan gum | Chitosan:<br>guar gum |
|--------|-------------------------------|---------------------|-------------------------|-----------------------|
| C1     | 1:1                           | -                   | -                       | -                     |
| C2     | 1:4                           | -                   | -                       | -                     |
| C3     | -                             | 1:1                 | -                       | -                     |
| C4     | -                             | 3:7                 | -                       | -                     |
| C5     | -                             | -                   | 1:1                     | -                     |
| C6     | -                             | -                   | 1:4                     | -                     |
| C7     | -                             | -                   | -                       | 1:1                   |
| C8     | -                             | -                   | -                       | 1:0.5                 |

### Methods

#### Preparation of polyelectrolyte complexes of chitosan with sodium alginate, pectin gellan gum and guar gum

For polyelectrolyte complex preparation, 4% w/v of chitosan solution in 1% v/v of acetic acid was mixed with respective quantities of sodium alginate, pectin, gellan gum and guar gum solutions in water<sup>7,8</sup>. Each solution was heated separately at 70 – 80°C. Both the solutions were mixed at 75°C with agitation until it attained room temperature. It was allowed to stand for 2 hours and then the polyelectrolyte complex formed was thoroughly washed with distilled water. It was then separated from water by centrifugation at 10,000 RPM for 30 min. Thereafter, the polyelectrolyte complex was again submerged in distilled water and was kept aside at 9°C for 48 hours. Then the centrifugation step was repeated.

Finally it was dried to a constant weight either by lyophilisation or by vacuum drying at 70°C.<sup>9</sup>

### Characterisation of Polyelectrolyte Complexes

#### FT-IR Studies

The IR spectra were recorded on Thermo Nicolet (Avatar 370) using a thin film of the sample supported on KBr pellets. FTIR spectra of chitosan and all anionic polymers used in combination of chitosan were obtained. All the samples were powdered with KBr to get pellets by applying a pressure of 600 kg/cm<sup>2</sup>. Spectral scanning was done in the range between 4000 and 500 cm<sup>-1</sup>.

#### DSC Studies

Differential scanning calorimetric analysis was used to characterize the thermal behaviour of individual polymers as well as the complexes. DSC thermograms were obtained using an automatic thermal analyzer system (DSC-60, Shimadzu, Japan). Temperature calibration was performed using indium as the standard. Samples were crimped in a standard aluminium pan and heated from 40-300°C at a heating rate of 10°C /min under constant purging of nitrogen at 30 ml/min.

#### Powder Properties

The powders of the polymers and the drug are characterized by bulk density, tapped density, Carr's consolidation index and angle of repose. The flow properties of powders have a great impact on tableting because it requires the flow of materials from a storage container to filling stations<sup>10</sup>.

#### Formulation of Atenolol Tablets from Polyelectrolyte Complexes

In case of oven-dried complexes, the tablets were prepared by wet granulation process and for lyophilised complexes direct compression method was followed. In wet granulation method, starch paste was used as the binder. The drug and polyelectrolyte complex were taken in a ratio of 1:1. Talc and magnesium stearate are used as lubricant and anti-adherent respectively. As the polyelectrolyte complex itself is expected to have binding properties, and control the release of the drug binding agent like starch paste was used in this method. The polyelectrolyte complex and a single dose of the drug were taken in a ratio of 1:1 for both wet granulation as well as direct compression method<sup>11, 12</sup>.

For formulation of atenolol tablets, 100 mg of the drug and 100 mg of the polyelectrolyte complex was taken. The PEC can be used for any dose of the drug, in a drug: complex ratio of 1:1. Hence 100 mg of atenolol tablets was formulated taking into consideration patients with severe hypertension problem.

#### Evaluation of Physicochemical Properties of Tablets

##### Swelling Behaviour

One tablet from each formulation was weighed individually (W<sub>1</sub>) and placed separately in petri dishes



containing 10 ml of simulated gastric fluid (pH 1.2) and at regular intervals (5, 10, 15, 30, 45 and 60 min), the tablets were removed and reweighed ( $W_2$ )<sup>13</sup>. Also swelling study was performed by placing the tablets in 10 ml of phosphate buffer (phosphate buffer of pH 6.8). After regular intervals (1, 2, 4, 6 and 8 h), the tablets were carefully removed from the petri dishes and excess water was removed using a filter paper. The swollen tablets were reweighed ( $W_2$ ). Swelling index of each tablet was calculated using the following equation and expressed in percentage.

$$\text{Swelling index} = \frac{W_2 - W_1}{W_1} \times 100$$

### In Vitro Release Studies

The *in vitro* drug release studies of the tablets were performed using the IP dissolution apparatus type I (Paddle type) using 900 ml of simulated gastric fluid i.e., 0.1N hydrochloric acid (pH 1.2) which after an hour was replaced with phosphate buffer of pH 6.8 as the dissolution medium at a temperature of  $37 \pm 0.5^\circ\text{C}$ <sup>14,15</sup>. The apparatus was immediately operated at a speed of 50 rpm for 30 minutes. 5 ml of the dissolution medium was withdrawn from a zone midway between the surface of the dissolution medium and the top of the rotating blade. The sample was filtered through Whatmann filter paper. The sample was accordingly diluted with phosphate buffer and the absorbance was measured at 272 nm using phosphate buffer as the blank solution. Dissolution studies were performed in a triplicate manner and the mean value was reported. The percentage drug release was calculated and plotted against time and the release profile was studied.

### Stability Study

The stability of all the formulations was carried out at different temperatures using the reported procedure. The tablets were wrapped in aluminium foil and placed in petri dishes. This was placed in stability chamber at accelerated temperature ( $40 \pm 2^\circ\text{C}$ ) and at room temperature ( $25 \pm 2^\circ\text{C}$ ) for a period of 8 weeks. The samples were analysed for physical changes as colour, texture and also other properties.

## RESULTS AND DISCUSSION

### FT-IR studies

The FT-IR spectrum of chitosan (Figure 1) showed a weak band of C-H stretching at  $2852\text{ cm}^{-1}$ , the absorption band of the carbonyl (C=O) stretching of the secondary amide (amide I band) at  $1645\text{ cm}^{-1}$ , the bending vibration of the N-H of non-acetylated 2-amino glucosamine primary amines at  $1570\text{ cm}^{-1}$  and the bending vibrations of N-H (N-acetylated residues, amide II band) at  $1587\text{ cm}^{-1}$ . The peaks at  $1417$  and  $1321\text{ cm}^{-1}$  belong to N-H stretching of the amide and the ether bonds and N-H stretching (amide III band), respectively. The bridge oxygen (C-O-C, cyclic ether) stretching bands at  $1153$ ,  $1070$ ,  $1020$  and  $895\text{ cm}^{-1}$  were observed as well. Sodium alginate being a carboxyl

salt showed strong absorption bands (Figure 2) at  $1601$  and  $1407\text{ cm}^{-1}$  due to carboxyl anions (asymmetric and symmetric vibration).

For chitosan- sodium alginate polyelectrolyte complex, the band (figure 3) around  $3500\text{--}2900\text{ cm}^{-1}$  becomes broader, which indicates hydrogen bonding is enhanced. Moreover, the N-H bending vibration of non-acetylated 2-amino glucose primary amines (band at  $1571\text{ cm}^{-1}$ ) and asymmetric and symmetric C-O stretching at  $1601$  and  $1407\text{ cm}^{-1}$  respectively disappeared, indicating that ( $\text{NH}_3^+$ ) of chitosan has reacted with  $\text{--COO}^-$  of sodium alginate.

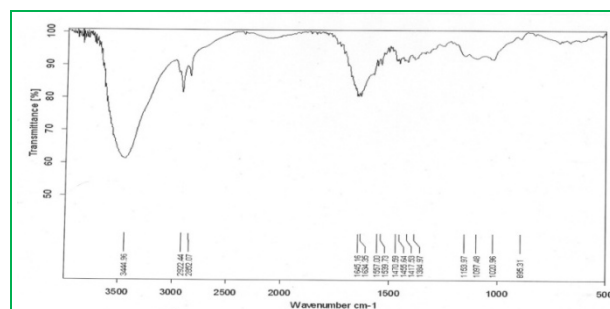


Figure 1: FT-IR spectrum of chitosan

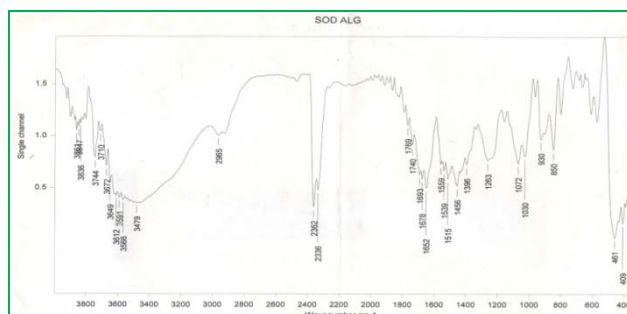


Figure 2: FT-IR spectrum of sodium alginate

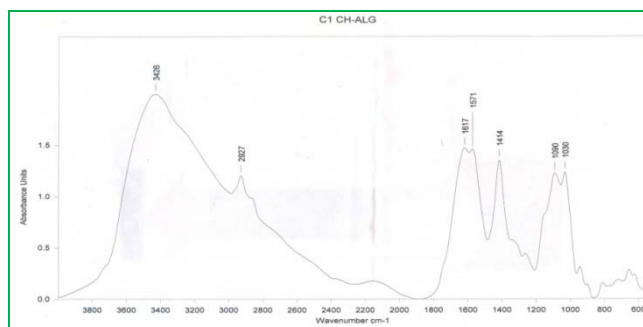
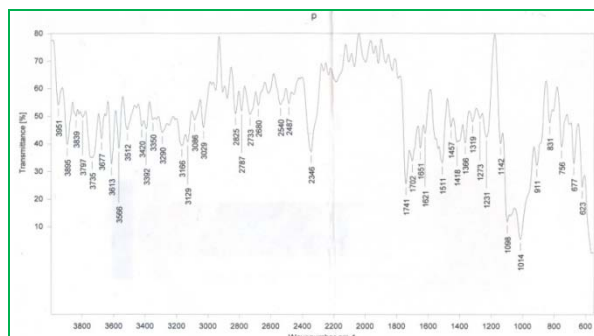
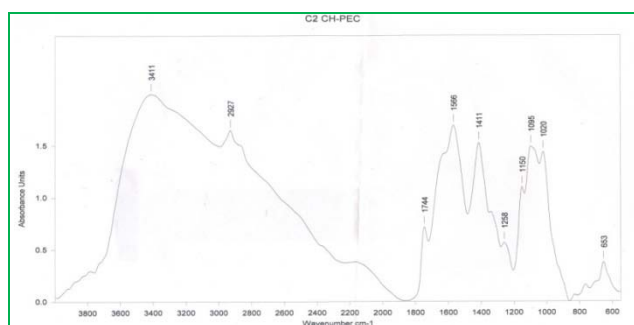


Figure 3: FT-IR spectrum of chitosan-sodium alginate complex (lyophilised)

FT-IR spectrum of pectin (figure 4) showed a typical  $>\text{C}=\text{O}$  band of methyl ester group and undissociated carboxyl group at  $1741\text{ cm}^{-1}$  and  $>\text{C}=\text{O}$  band of carboxylate at  $1621\text{ cm}^{-1}$ . Chitosan showed characteristic C=O band of amide at  $1645\text{ cm}^{-1}$  and N-H band of amine at  $1587\text{ cm}^{-1}$ . The shift in amine band to  $1566\text{ cm}^{-1}$  in spectrum of complexes indicates a change in the environment of amine group through its interaction with pectin. The complexes were stabilised by electrostatic interaction by positively charged chitosan ( $\text{NH}_3^+$ ) and negatively charged pectin ( $\text{COO}^-$ ).



**Figure 4:** FT-IR spectrum of Pectin



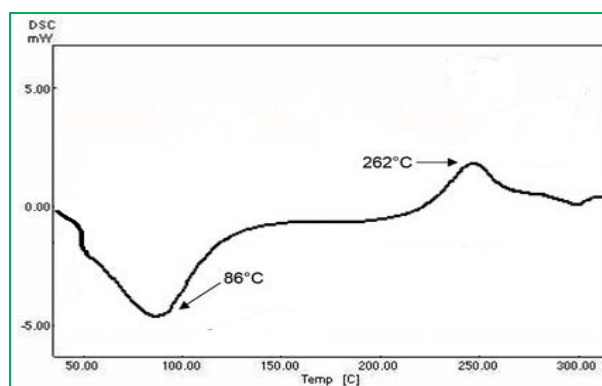
**Figure 5:** FT-IR spectrum of chitosan-pectin complex (lyophilised)

### DSC Studies

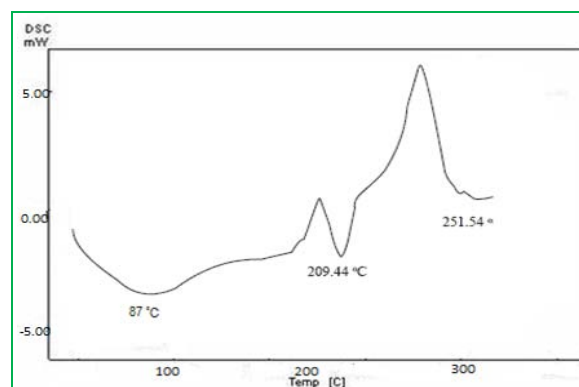
The thermogram of chitosan polymer exhibited an endothermic peak at about 86°C (Figure 6) that has been attributed to the evaporation of absorbed water. It showed an exothermic peak at 262°C. The exothermic baseline deviation beginning around 250°C indicates the onset of chitosan degradation. A broad endothermic peak at 87°C in the thermogram of sodium alginate (figure 7) was similarly attributed to the presence of water molecules. It showed an exothermic peak at 251.2°C and an endothermic peak at 209.44°C. The chitosan alginate interaction can be characterised by the disappearance of the exothermic peak of alginate at 262°C (figure 8) An endothermic peak at 113°C which was not observed in the DSC thermogram of chitosan or sodium alginate may be assigned to the formation of ionic pair between  $\text{NH}_3^+$  of chitosan and  $\text{COO}^-$  of sodium alginate.

The DSC thermogram of Pectin showed exothermic peaks at 163.7°C and 148.4°C and an endothermic peak at 233.9°C (figure 9) which may be attributed to the presence of water molecules. Chitosan as mentioned earlier exhibited an endothermic peak at 86°C (figure 6) that has been attributed to the evaporation of adsorbed water and an exothermic peak at 262°C. The exothermic baseline deviation beginning at around 250°C indicates the onset of degradation of chitosan. The chitosan pectin interaction was characterised by appearance of an endothermic peak at 101.6°C and 226°C (figure 10) which is not observed in the DSC thermogram of chitosan and pectin. This may be attributed to the interaction between  $\text{NH}_3^+$  of chitosan and  $\text{COO}^-$  of pectin which may be due to the formation of ionic bond by evaporation of water molecules.

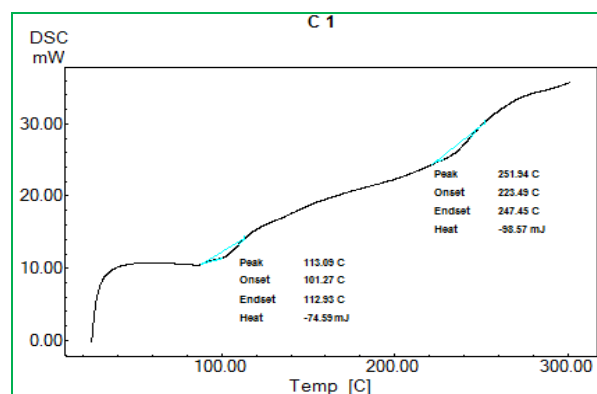
Chitosan on complexing with sodium alginate, pectin, guar gum and gellan gum gave maximum solid precipitate in a 1:1 ratio of the two polymers at a pH of 5.0-5.5. At a pH of 3.5-4.0, chitosan-sodium alginate and chitosan-gellan gum in a ratio of 1:4, chitosan-pectin in a ratio of 3:7 and chitosan-guar gum in a ratio of 1:0.5 gave high solid precipitate. But the solid precipitate obtained was lesser than that obtained at pH 5.0 in a 1:1 ratio of the polymers. Since the  $\text{pK}_a$  value of chitosan was 6.3, in the 2.0-5.0 range most of the chitosan amine groups were protonated. In contrast the  $\text{pK}_a$  values of sodium alginate ( $\text{pK}_a$  3.38), pectin ( $\text{pK}_a$  4.0), gellan gum ( $\text{pK}_a$  3.06) and guar gum ( $\text{pK}_a$  3.68) decreased with decreasing pH values in the media. This suggests that much larger amounts of anionic polymer molecules were required to interact with chitosan at low pH values. At a pH below 3.0, the poor ionisation of anionic polymer limited solid complex formation at any ratio.



**Figure 6:** DSC thermogram of pure chitosan



**Figure 7:** DSC thermogram of pure sodium alginate



**Figure 8:** DSC thermogram of chitosan-sodium alginate complex (lyophilised)



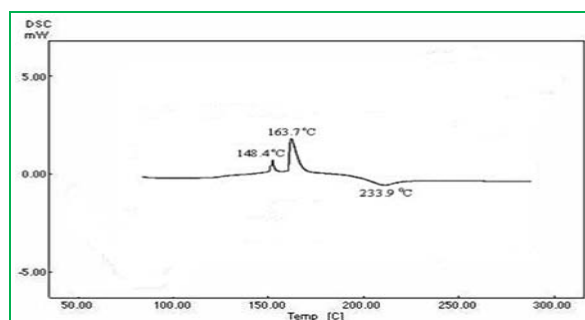


Figure 9: DSC thermogram of pure pectin

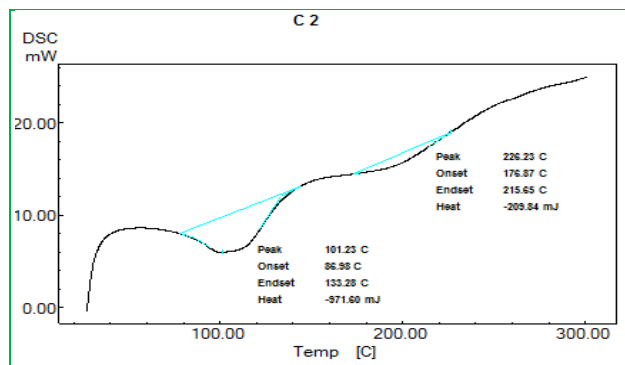


Figure 10: DSC thermogram of chitosan-pectin complex (lyophilised)

Table 2: Powder properties of polyelectrolyte complexes (lyophilised)

| Powder properties     | C1           | C2         | C3         | C4         | C5         | C6         | C7         | C8         |
|-----------------------|--------------|------------|------------|------------|------------|------------|------------|------------|
| Bulk density (g/cc)   | 0.695        | 0.614      | 0.721      | 0.684      | 0.703      | 0.659      | 0.675      | 0.723      |
| Tapped density (g/cc) | 0.754        | 0.659      | 0.791      | 0.746      | 0.761      | 0.715      | 0.728      | 0.783      |
| Angle of repose       | 24.98 ± 0.35 | 25.93±0.16 | 25.85±0.23 | 24.88±0.47 | 23.09±0.09 | 25.73±0.56 | 24.15±0.41 | 25.39±0.57 |
| Carr's index          | 7.82         | 7.32       | 8.84       | 8.31       | 7.62       | 7.83       | 7.28       | 7.66       |

Table 3: Powder properties of polyelectrolyte complexes (oven dried)

| Powder properties     | C1          | C2         | C3         | C4         | C5         | C6         | C7         | C8         |
|-----------------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| Bulk density (g/cc)   | 0.863       | 0.795      | 0.821      | 0.874      | 0.783      | 0.856      | 0.814      | 0.791      |
| Tapped density (g/cc) | 0.945       | 0.876      | 0.906      | 0.956      | 0.861      | 0.949      | 0.896      | 0.873      |
| Angle of repose       | 33.09± 0.25 | 35.81±0.05 | 34.98±0.51 | 35.66±0.47 | 33.21±0.17 | 34.66±0.27 | 35.79±0.89 | 36.73±0.74 |
| Carr's index          | 8.67        | 9.24       | 9.27       | 8.57       | 9.05       | 9.79       | 9.15       | 9.39       |

### Swelling behaviour studies

Chitosan showed good swelling properties in acidic pH but on forming a complex with sodium alginate, pectin, gellan gum and guar gum showed extremely poor swelling at pH 1.2. In case of PEC (lyophilised) tablets of atenolol, C7 showed highest swelling property with a swelling index of 390.62% and least swelling index was 231.64% (C1). Oven dried PECs rapidly disintegrated within 30 – 60 min without showing any good swelling properties.

Chitosan PECs' with sodium alginate, pectin, gellan gum and guar gum presented ionic interactions between positively charged chitosan and negatively charged anionic polymer and exhibited pH sensitive swelling in basic condition. As swelling medium pH changes, the charge balance inside the gelling network and therefore the degree of interaction between chitosan and

### Powder properties

The bulk density, tapped density, Carr's consolidation index and angle of repose were determined as described in methodology and the results were reported in the tables 2 and 3. Directly compressible forms of powders coupled with good flow properties make them suitable candidates for employing direct compression as the method of tablet preparation. This helps to achieve good tablet properties. This was proved to be true in case of lyophilised polyelectrolyte complexes, whereas oven dried polyelectrolyte complexes were not self compressible and had to be granulated using starch as binder. It was observed that oven drying of the complexes made them brittle in nature due to which they lost their self compressibility properties as well as binding properties. Whereas, it was observed that the lyophilised polyelectrolyte complexes did not lose their binding properties as a small amount of moisture content was retained in it.

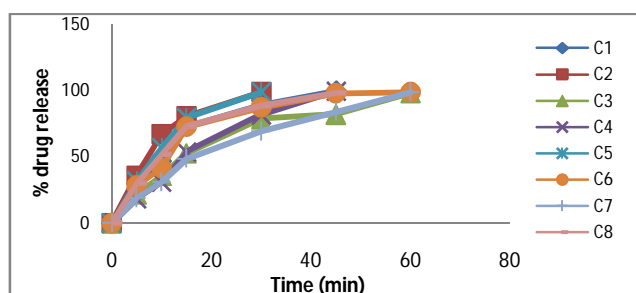
negatively charged polymers is modified and swelling occurs because of dissociation of the complex. In alkaline medium, chitosan is neutralised and free negative charges appear inside the gel. The mutual repulsion between positive and negative charges and the entry of water together with counter ions to neutralise this charge causes swelling. Moreover, the swelling ability of different polymers can be modulated by adequate selection of preparative conditions.

### In Vitro Release Studies

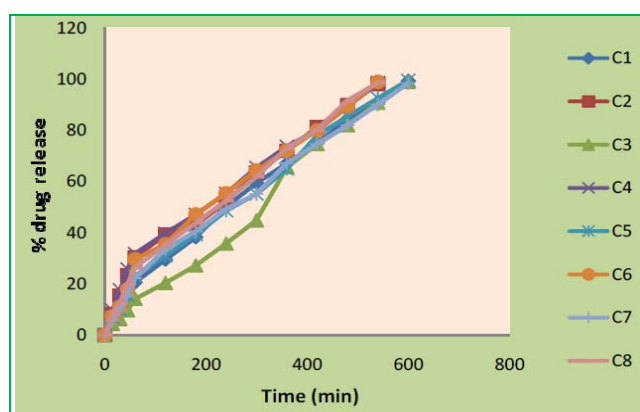
The *in vitro* release studies of atenolol from different formulations were carried out in 0.1N hydrochloric acid (pH 1.2) and in phosphate buffer of Ph 6.8. The percentage drug release was calculated and plotted against time and the release profiles were obtained.



It was evident from the above release profiles that the lyophilised PEC tablet of atenolol showed maximum release and sustained over 8-10 hours whereas tablets prepared from oven dried PECs completed the profile within 1 hour. In the case of lyophilised atenolol tablets the best sustained release was seen in C7 followed by C3, C1 and C8. As the oven dried PECs completed their release profile within an hour we can conclude that the oven dried PECs did not possess any sustaining properties which may be due to the brittle nature of the complexes on vacuum drying, the loss of binding properties. From the release profile data of the tablets prepared from lyophilised PECs, it was observed that the formulation C7 which is chitosan-guar gum (1:1) PECs' tablet released least percentage of the drug in the acidic environment of the stomach thereby sustaining the release of the drug in the alkaline environment of the intestine. Also the chitosan-guar gum PEC (C7) showed extremely high swelling properties thereby prolonging the release of the drug for about 10 hrs. Hence it can be considered to be the best formulation of all the above formulations prepared. The tablets were formulated by taking the drug and the complex in a ratio of 1:1 because too much of the complex made the tablet hard in nature and too little of the complex caused it to disintegrate soon resulting in the immediate release of the drug.



**Figure 11:** Comparative percentage release profile of polyelectrolyte complex (lyophilised) tablets of atenolol pH 1.2



**Figure 12:** Comparative percentage release profile of polyelectrolyte complex (lyophilised) tablets of atenolol pH 6.8

### Drug Release Mechanism

To understand the influence of swelling of the matrix (upon hydration) and gradual erosion of the matrix Korsmeyer Peppas model was studied. Therefore, the

dissolution data was fitted according to the well known exponential equation (1), which is often used to describe the drug release behaviour from polymeric system.

$$M_t / M_\infty = kt^n$$

Where,  $M_t / M_\infty$  is the fractional drug release at time  $t$ ;  $k$  is a constant incorporating the properties of the macromolecular polymeric systems and the drug, and  $n$  is a kinetic constant which depends on and is used to characterize the transport mechanism. The values of  $n$  for a tablet are,

$n = 0.45$  Fickian (case I) release

$0.45 < n < 0.89$  Non Fickian (Anomalous) release

$n = 0.89$  Case II (zero order) release

$> 0.89$  Super case II type release

The data was processed for regression analysis using Microsoft excel statistical function. The value of release exponent ( $n$ ) was found to be a function of the polymer used and the physicochemical properties of the drug molecule itself.

The hydrophilic polymers sodium alginate, gellan gum, guar gum and pectin highly swell on reaching the intestine due to polymer relaxation and is characterised by formation of a gel-like network surrounding the system. The charges inside the complex balance and the degree of interaction between  $\text{NH}_3^+$  and  $\text{COO}^-$  is modified inside the gelling network and swelling occurs because of dissociation of complex. The mechanical property of the surface hydrated gelatinous barrier plays an important role in overall drug release. As it is desirable for a sustained release drug to deliver drug in zero order kinetics, the results of this investigation showed high correlation coefficient among the formulation for zero order release. In our formulations it was found that the fluid enters through the cracks and pores of the matrix with diffusion of the drug from the matrix. All the formulations showed zero release kinetics and found to be best fitting the Higuchi's model. The regression was seen closest to 1 in Higuchi's model and confirmed to be diffusion assisted mechanism of release.

### Stability Study

The stability of the drug in the formulation was confirmed by UV scanning and no spectral change was observed. The drug content obtained for every 2 weeks showed that drug content did not differ from initial drug content by more than 3%, indicating that the formulations are stable.

### CONCLUSION

The scope of polymers used in dosage form design can be increased by several approaches such as modification of their chemical structure, by combining different polymers in physical mixtures or by formation of polymer-polymer associations such as polyelectrolyte complexes. Polyelectrolyte complexes combine unique physicochemical properties of different polymers with the



advantage of retaining high biocompatibility. It is therefore not surprising that polyelectrolyte complexes are gaining importance in modern pharmaceutical technology. Release profile indicated that the lyophilised PEC tablets of atenolol prolonged the release of the drug for 8 – 10 h with only a small percentage of the drug being released in the stomach. From the *in vitro* studies conducted on chitosan – based polyelectrolyte complexes, it is clear that they are valuable excipients with specific properties for efficient dosage form design, which may be valuable in the development of modified drug delivery systems.

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