EFFECT OF HYDROPHILIC NATURAL GUMS IN FORMULATION OF ORAL-CONTROLLED RELEASE MATRIX TABLETS OF PROPRANOLOL HYDROCHLORIDE

KS RAJESH, MP VENKATARAJU AND DV GOWDA*

Department of Pharmaceutics, Parul Institute of Pharmacy, Limda, Baroda, India
**Department of Pharmaceutics, J.S.S.College of Pharmacy, S.S.Nagar, Mysore, India*

ABSTRACT

In order to develop a controlled delivery of highly water-soluble propranolol hydrochloride (PPHCl) using hydrophilic natural gums (xanthan gum [X] and locust bean gum [LBG]) as cost-effective, nontoxic, easily available. The granules of PPHCl were prepared by wet granulation method using a different ratios drug: gum ratios of X, LBG and XLBG(X and LBG in 1:1 ratios). To increase the flowability and compressibility of the granules, and to prevent its adhesion to punch and die, magnesium stearate and talc were added to the granules in 1:2 ratios before punching. The tablets was analysed to determine hardness, friability, % assay and *invitro* release study was carried out.

The release of PPHCl from a gelatinous swollen mass, which controls the diffusion of drug molecules through the polymeric material into aqueous medium. The XLBG matrices shows precise controlled release than the X and LBG matrices because of burst effect and fast release in case of X and LBG matrices respectively and there was no chemical interaction between drug and polymers in XLBG formulation as confirmed by FTIR studies. First pass effect of PPHCl can be avoided by these formulations. Matrices with XLBG show zero-order release via swelling, diffusion and relaxation mechanism.

The XLBG matrices leads to more precise result than X and LBG alone by the utilization of synergistic interaction between two biopolymers and uniformity in the hydration layer in dissolution media. However, according to the similarity factor (f_2) XLBG3 were the most similar formulation to Lol-SR as the reference standard.

Keywords: Locust bean gum; xanthan gum; propranolol hydrochloride; controlled release.

INTRODUCTION

Hydrophilic polymers are becoming very popular in formulating oral controlled-release tablets. As the dissolution medium or biological fluid penetrates the dosage form, the polymer material swells and drug molecules begin to move out of the system by diffusion at a determined rate by the nature and composition of the polymer as well as formulation type.

The use of naturally occurring hydrophilic biocompatible polymeric materials has been focused in recent research activity in the design of dosage form for oral controlled-release of highly water soluble drugs compare to synthetic polymers like HPMC etc. The use of matrix devices to control the release of a variety of therapeutic agents has become very important in the development of controlled release dosage forms (Bhardwaj *et al*., 2000; Billa and Yuen, 2000; Munday and Cox, 2000; Talukdar *et al*., 1998). The hydrophilic natural gums hydrate and swell on contact with water and these have been used for the preparation of single unit dosage forms. Also, the natural gums selected have an economic importance in being cheaper than many processed synthetic gums available.

The use of hydrophilic polymers like xanthan gum (X) and locust bean gum (LBG) alone and combination was used in this study for oral controlled release dosage forms. The Xanthan gum is water soluble, anionic-bacterial heteropolysaccharide, while LBG is a neutral plant galactomannan. Both materials have been extensively studied (Morris, 1995; Toko, 1991) in a range of environment, with some sensitivity to pH and ionic strength demonstrated. The synergistic gelation of X and LBG has also been reported to decrease dramatically below pH 5, although it is independent of pH within the range of 5-10 (Toko, 1991). Xanthan gum and LBG are water soluble thickening agents, but when they are mixed, an original gelation occurs. The mechanism of gelation of aqueous mixture of xanthan and galactomannan was studied by using rheological, calorimetric and chiroptical methods (Bresolin *et al*., 1997; Bresolin *et al*., 1999). The hydrophilic gels have been shown to produce near zero order drug release kinetics (Colombo *et al*., 1985). The hydrophilic matrix system being investigated that two heteropolysaccharides are the principle of the formulation it utilizes the synergistic interaction of two biopolymers to control the drug release process (Staniforth and Baichwal, 1993).

Corresponding author: Ph.: 02668-263408; Fax: 02668-262327, e-mail: makam_raju@yahoo.co.in

The ideal oral controlled release system should not be or be minimally influenced by the *in vivo* environment of the gastrointestinal tract (GIT), as any significant changes of the product may cause serious therapeutic toxicity (Welling, 1996; Oosterhuis and Jonkman, 1993). Certain hydrophilic matrix formulations have been shown to erode in the GIT much faster postprandially than under fasting conditions, which differ significantly from those pertaining under fed conditions (Abrahamsson *et al*., 1998; Gai *et al*., 1997; Abrahamsson *et al*., 1999). However, there are few reports giving a clear explanation for what caused the modification of drug release and absorption from such hydrophilic matrix systems (Abrahamsson *et al*., 1999).

Xanthan (X) is a commercial hydrophilic polymer, secreted from *Xanthomonas campestris* (N¨urnberg and Retting, 1974). Xanthan gum displayed high degree of swelling due to water uptake and small degree of erosion due to polymer relaxation. In earlier studies, the performance of xanthan gum as a potential excipient for oral controlled release tablet dosage forms was thoroughly evaluated and characterized by *in vitro* tests (Munday and Cox, 2000; Talukdar *et al*., 1998; Cox *et al*., 1999; Sujja-areevath *et al*., 1998; Talukdar and Kinget, 1997) observed that Fickian diffusion was dominant during the first half of the dissolution period of Diclofenac Sodium mini-matrices with xanthan gum of different ratios, while erosion predominates during the latter half, facilitating an approach toward zero-order release.

Locust bean gum (LBG) is a plant seed galactomannan, composed of a 1-4 linked β-D-mannan backbone with 1-6-linked α-D-galactose side groups (Dea and Morrison, 1975). It is a nonionic molecule consists of 2000 residues. It is similar to guar gum but less soluble and lower viscous then guar gum. In LBG the ratio of mannose and galactose is higher then guar gum. It is not affected by ionic strength or pH but will degrade at extremes pH at higher temperature. Physico-chemical properties of galactomannan are strongly influenced by the galactose content (Morris, 1990) and the distribution of the galactose units along the main chain (Launay *et al*., 1986). Locust bean gum Structure Contains long stretches of bare mannose backbone (up to 80 D-mannose units long) which is responsible for synergistic interaction with other polymers (Morris, 1990) and greater functionality (Launay *et al*., 1986). The LBG is also used in the management of elevated plasma cholesterol in healthy subject (Haskell *et al*., 1992).

Propranolol hydrochloride, a highly water soluble nonselective beta adrenergic blocking agent, has been widely used in the treatment of hypertension, angina pectoris, and many other cardiovascular disorders. It is hydrophilic and is almost completely absorbed after oral administration. However, its bioavailability is very limited (30%) due to the hepatic first-pass effect. Its elimination half-life is also relatively short (3-4 hrs) (Rekhi *et al*., 1996; Takayama and Nagai, 1989). Therefore, it was chosen as a model drug for preparation of oral controlled drug delivery.

Drug release from hydrophilic matrices is known to be a complex interaction between swelling, diffusion and erosion mechanisms (Harland *et al*., 1988; Peppas and Sahlin, 1989; Lee and Kim, 1991; Reynolds *et al*., 1998). Previous work has demonstrated that naturally occurring X has useful hydrogels for producing a constant *invitro* drug release (Cox *et al*., 1999; Sujja-areevath *et al*., 1998). This work was an attempt to determine the relative contribution of the drug release mechanisms from propranolol hydrochloride matrix tablets produced with xanthan (X) and the highly hydrophilic locust bean gum (LBG) from the seeds of *ceratonia siliqua*. Different concentrations of gums, alone (X or LBG) and in physical mixture (XLBG) of X and LBG in 1:1 ratio, were tested to evaluate their performance as release-controlling agents.

MATERIALS AND METHODS

Materials

Propranolol hydrochloride (PPHCl) gift sample obtained from Ipca Laboratories Ltd, Mumbai, locust bean gum (LBG) was purchased from Sigma Aldrich, Germany, xanthan gum(X) from Ranbaxy, New Delhi. Dicalcium phosphate (DCP), polyvinylpyrolidinek-30(PVPK-30), alcohol, Talc and Magnesium stearate (Mg. st) were analytical reagent grade and used without further purification.

Preparation of matrix tablets

Matrices were prepared by wet granulation method by using the PVPK-30 as binding agent, alcohol as wetting agent and dicalcium phosphate as diluent, granules were prepared, talc and magnesium stearate was used as a lubricant in 2:1 ratio. 400±5 mg of the prepared granules were compressed using a manesty (Cadmach, India) single punch tablet machine, 9.5 mm flat beveled edge punches producing matrix tablets 4.8 mm in height with a mean crushing strength of 5.8 kg/cm^2 (Pfizer, Mumbai). Under the same condition all the formulations of PPHCl tablets containing X, LBG and XLBG (X:LBG ratio was 1:1) were prepared and the formulation chart is as shown in table 1.

Analysis of tablets

The hardness and friability of tablets were measured in a Hardness Tester (Pfizer, Mumbai) and friabilator (Electrolab, Mumbai), respectively. The uniformity of drug content of all batches (10 units tablets) was analysed in a spectrophotometer (model UVPC 1601, Shimadzu, Japan), in a 1 cm quartz cell, at 290 nm.

Table 1: Composition (mg per tablet) and analysis of PPHCl (80 mg) tablets (400 mg).

Formulation (drug:gum)	Xanthan (mg)	LBG (mg)	DCP (mg)	PVPK-30 (mg)	Talc (mg)	Mg.Starate (mg)	Hardness (kg/cm²)±SD	Friability (%)	% Assay ±SD
X1(1:1)	80	-	216	15	6	3	5.9±0.95	0.3	97±0.83
X2(1:1.5)	120	-	176	15	6	3	5.6±0.63	0.2	96±0.75
X3(1:2)	160	-	136	15	6	3	5.4±0.51	0.2	95±0.71
X4(1:2.5)	200	-	96	15	6	3	5.5±0.45	0.1	97±0.35
LBG1(1:1)	-	80	216	15	6	3	4.9±0.92	Capping	96±0.86
LBG2(1:1.5)	-	120	176	15	6	3	4.6±0.56	Capping	98±0.56
LBG3(1:2)	-	160	136	15	6	3	6.1±0.51	0.4	98±0.38
LBG4(1:2.5)	r	200	96	15	6	3	5.5±0.34	0.3	97±0.58
XLBG1(1:1)	40	40	216	15	6	3	5.7±0.34	0.2	96±0.95
XLBG2(1:1.5)	60	60	176	15	6	3	5.9±0.41	0.1	98±0.71
XLBG3(1:2)	80	80	136	15	6	3	5.6±0.34	0.1	99±0.78
XLBG4(1:2.5)	100	100	96	15	6	3	5.8±0.45	0.2	99±0.69

X (xanthan gum), LBG (locust bean gum), XLBG (xanthan gum and locust bean gum mixture in 1:1 ratio), DCP (dicalciumphosphate), PVPK-30(polyvinylpyrolidineK-30)

Water uptake and erosion determination

Measurement of hydration and erosion rates of XLBG3 were carried out, after the immersion of the tablets in the test medium (Efentakis and Loutlis, 2001), to relate the observed phenomena of drug release with the rates of polymer hydration. Weighed tablets were placed in the baskets of the dissolution apparatus rotating at 50 rpm, with the dissolution medium of phosphate buffer pH 7.2 at 37±0.5ºC. After 0.5, 1, 2, 3, 4, 5, 6, 7 and 8 h, each dissolution basket containing the sample was withdrawn, blotted to remove excess water and weighed on an analytical balance (Shinko Sansui, Japan). The wet samples (basket + sample) were then dried in an oven at 110–120ºC for 24 h time period, allowed to cool in a desicator and finally weighed until constant weight was achieved (final dry weight). The experiment was performed in triplicate for each time point and fresh samples were used for each individual time point. The increase in weight due to absorbed liquid (Q) was estimated at each time point from the following equation

$$Q = \frac{100\,(W_w - W_f)}{W_f}$$

where W_w is the mass of the hydrated sample before drying and W_f the final weight of the same dried and partially eroded sample. The percentage erosion (E) was estimated from the following equation

$$E = \frac{100(W_i - W_f)}{W_f}$$

where W_i is the initial dry sample weight.

In vitro studies

The dissolution test was carried out using apparatus 1 USP (Model No TDT-08L, Electrolab, Mumbai) at 100 rpm. In order to reproduce digestive physiological phases, 900mL of dissolution medium with different pH environments at 37±0.5ºC was performed. The dissolution medium with the pH of 1.2 was changed to 7.2 after 2 h and continued for up to 24 h. At suitable intervals, samples were withdrawn, filtered, diluted when necessary with suitable buffer and analyzed spectrophotometrically (model UVPC 1601, Shimadzu, Japan) at 290 nm. Studies were performed and the mean cumulative percentage of drug was calculated and plotted against time. During the drug release studies, all the formulations were observed for physical integrity at different time.

Drug release kinetics

The Korsmeyer and Peppas equation was used to analyze the data obtained from the *invitro* release studies to evaluate the kinetic models and release mechanism of PPHCl from the matrices. The software PCP Disso V2.08 was used.

Korsmeyer and Peppas equation (Korsmeyer and Peppas, 1981) is:

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

where M_t/M_∞ is the fraction of drug release at time t, k is a constant incorporating the properties of the macromolecular polymeric system and the drug. The n is an exponent used to characterize the transport mechanism. For example, n = 0.45 for Case I or Fickian diffusion, $0.45 < n < 0.89$ for anomalous behaviour or non-Fickian transport, n = 0.89 for Case II transport, and $n > 0.89$ for Super Case II transport (Ritger and Peppas, 1987). Fickian diffusional release occurs by the usual molecular diffusion of the drug due to a chemical potential gradient. Case II relaxational release is the drug transport mechanism associated with stresses and state-transition in hydrophilic glassy polymers, which swell in water or biological fluids. This term also includes polymer disentanglement and erosion (Peppas and Sahlin, 1989).

The similarities between 2 dissolution profiles were assessed by a pair-wise model independent procedure such as similarity factor (f_2) (Eddy *et al*., 2006; Longxiao Liu and Binjie, 2006)

$$f_2 = 50 \log \left\{ \left[1 + \left(\frac{1}{n} \right) \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} \times 100 \right\}$$

where n is the number of pull points, R_t is the reference profile at time point t, and T_t is the test profile at the same time point; the value of f_2 should be between 50 and 100.

RESULTS AND DISCUSSION

Analysis of PPHCl matrices

The tablets with weight of 400 mg, a diameter of 9.5mm and height of 4.8mm were obtained and subjected to quality control tests such as hardness, friability and drug content (table 1). The contents of the formulations were found to be uniform, since the amount of the active ingredient in each of the 10 units tested was within the range of 97.1-100.5% and the relative standard deviations were less than 2.0%, indicating uniform mixing of gums, dicalcium phosphate and drug. The mean values for hardness were over 5.8 kg/cm^2 and all formulations exhibits friability less than 0.5% during the friability determination.

In vitro drug release

The aqueous medium on contact with hydrophilic polymer matrix gradually begins to hydrate from the peripheral towards the centre, forming a gelatinous swollen mass, which controls the diffusion of drug molecules through the polymeric material into aqueous medium. The hydrated gel layer thickness determines the diffusional path length of drug.

The in vitro drug release profiles of PPHCl from tablets containing X, LBG and XLBG in different gum proportions are shown in Fig. 1 respectively. After 2h, the initial pH 1.2 was changed to 7.2 continue the dissolution upto 24 h. It was shown that as the amount of gum in the matrix increased, there would be a greater degree of gum hydration with simultaneous swelling. This resulted in corresponding lengthening of the drug diffusion pathway and drug release rate.

Drug release was generally linear for most of the formulations, especially XLBG matrices. Such linear release was from hydrophilic matrices has been attributed to synchronization between swelling and erosion of the polymer in maintaining a constant gel layer. LBG is a nonionic polysaccharide and their hydration process is independent of pH. During the test, all the formulation swelled and the outer layer of most of tablets appeared to be hydrated after being placed in dissolution medium, with progressive increase in the size of this hydrated layer, specially visualized for matrices containing xanthan, fallowed by a gradual loss of integrity, resulting from the hydrodynamic stress induced by the dissolution apparatus. Thereafter, it remained more or less unchanged until the final stages of dissolution test, when the inner dry core became wetted.

The profiles of the formulation of X, LBG, XLBG, and the erosion and drug release at different drug:gum ratios of 1:1, 1:1.5, 1:2 and 1:2.5 are shown in fig. 1. In each case of X there was an initial burst of xanthan gum erosion from the matrices during the acidic pH thereafter, the erosion of xanthan gum slowed considerably. It follows, therefore, that the hydrated xanthan gum network maintains its tight integrity with drug release by erosion and dissolution of the drug accounting for most of the weight loss during the remainder of the experimental period. Furthermore, there is a greater burst of xanthan gum erosion in the formulation containing the lower proportion of xanthan gum in 1:1 and 1:1.5 drug:gum ratios. LBG tablets formulations showed a higher tendency to loss of integrity than the X and XLBG. The swelling process of LBG tablets was not uniform and the zones of high LBG concentration appeared more swollen. In case of LBG matrix, a rapid erosion of the hydrated layer was observed, releasing the most of the drug content after 4 h. This is because LBG doesn't exhibit a controlled release effect but has a synergistic action along with the xanthan gum and shows precise controlled release effect.

In all the formulations, it has been observed that by increase the concentration of hydrophilic polymers in the formulations there by respectively retard the drug release form the matrices. In order to evaluate the role of XLBG mixture, the drug release of PPHCl tablets with X or LBG alone, in same concentration of polysaccharide, was carried out and the results are shown in fig. 1.

The drug release was slower from the matrices with XLBG compared to X and LBG matrices with the same total polymer concentration. The release of X and XLBG was similar but in case of X the release of PPHCl at low concentration of xanthan gum a starting burst effect of release was seen in acidic pH. In case of XLBG this type of burst effect was not seen in acidic pH. The XLBG formulations exhibits good controlled release effect by the utilization of synergistic interaction between two biopolymers to produce a strong and elastic gel around the core of the matrices in the presence of a ternary component there by control the drug release form the matrices containing XLBG formulation. Thereby XLBG formulations show precise control release then synthetic polymers like HPMC and it is more similar to Lol-SR as reference standard. LBG Structure Contains long stretches of bare mannose backbone which is responsible for

synergistic interaction with other polymers (Morris, 1990) and the LBG is also used in the management of elevated plasma cholesterol in healthy subject (Haskell *et al*., 1992) thereby XLBG is more effective than HPMC.

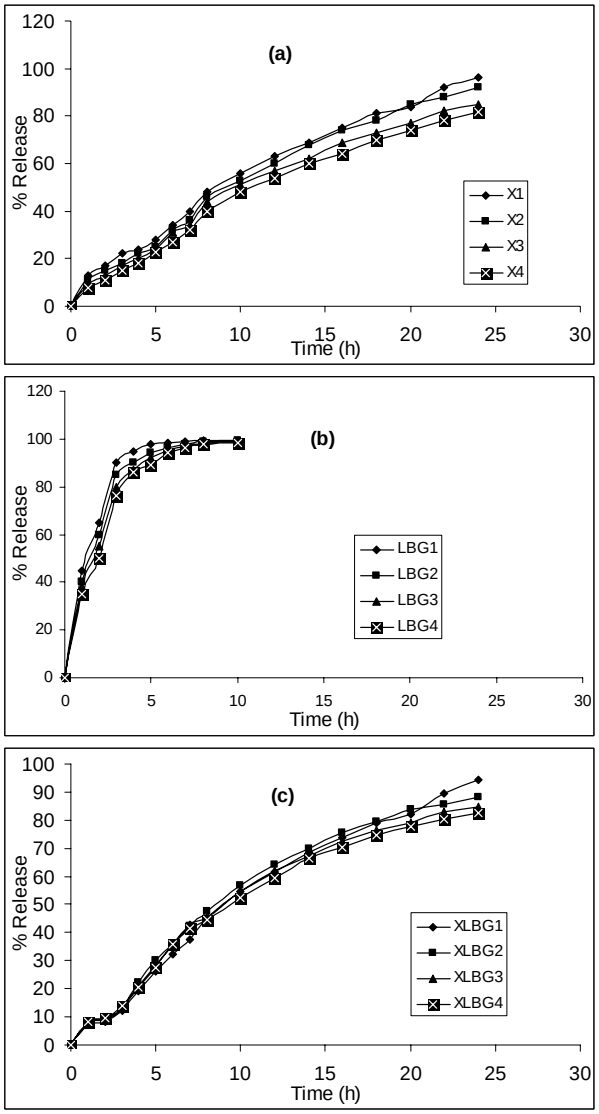

Fig. 1: *In vitro* release profile of PPHCl from tablets containing drug:gum, 1:1, 1:1.5, 1:2 and 1:2.5 ratios of (a) Xanthan gum (b) Locust bean gum and (c) Mixture of Xanthan and Locust bean gum.

Water uptake and erosion studies

The swelling behaviour and erosion studies were carried out with XLBG3 formulation of drug:gum ratio of 1:2, which resulted in the better dissolution profile. The results of swelling and erosion tests were shown in fig.2. The swelling behaviour indicates the rate at which this formulation absorbs water from dissolution media and swells. The change in weight is characteristic of water uptake and swelling, started from the beginning and continued until 8 h of experiment (fig. 2a). This matrix showed a high ability to swell. Visual observation denoted that the matrices appeared swollen almost from the beginning, a viscous gel mass was created when they came into contact with the liquid. The matrix erosion measured the weight loss from matrix tablets immersed in dissolution media as a function of time. The weight loss of the tablets was in constant progression until the end of 8 h (fig. 2b) and was about 70% observed. A similar has been reported with xanthan matrices containing Diclofenac sodium obtained by wet granulation (Billa and Yuen, 2000).

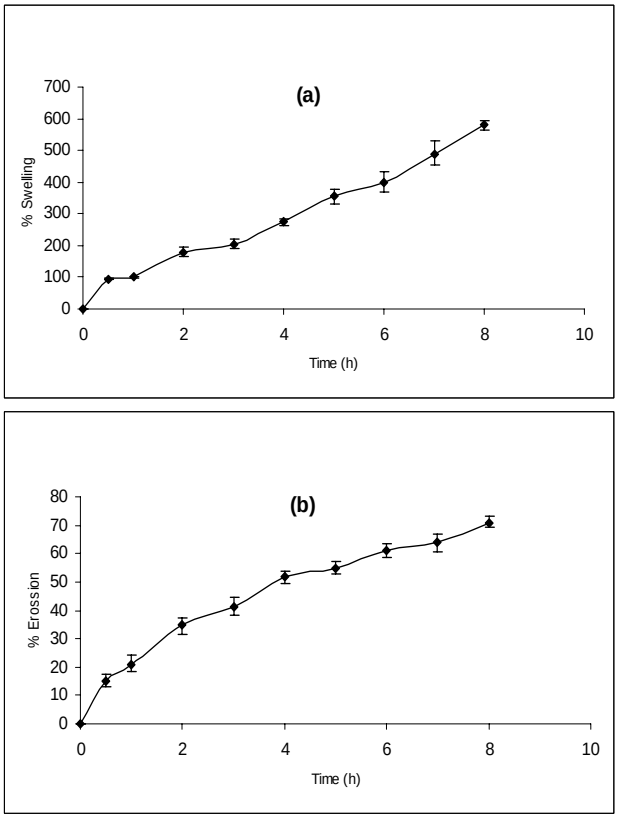

Fig. 2: Analysis of XLBG in drug:gum ratio of 1:2 at pH 7.2: (a) Swelling behaviour; (b) Erosion behaviour. Each point represents the mean value of three samples.

Comparison of dissolution profiles

The similarity factor (f_2) was employed to evaluate the release profiles of various formulations compared with the ideal release profile (Eddy *et al*., 2006; Longxiao Liu and Binjie, 2006). The similarity factor f_2 was a logarithmic transformation of the sum-squared error of differences between the experimental drug release T_t and the ideal release R_t for over all time points 'n'. The similarity factor fit the result between 0 and 100. It approached 0 as the dissimilarity of the test and the reference profile increased, whereas, it attained 100 when the test and the reference profile were identical. The two profiles were believed to be similar when the f_2 value of them was larger than 50 for which the mean deviation

over all time points 'n' was less than 10% based on above equation (table 2). Lol-SR used as a reference standard followed by the value for the similarity factor in XLBG formulations (*f*2 = 62.17-80.70) suggested that the dissolution profile of the prepared formulations and reference standard are more similar. Among the all formulations XLBG3 formulation was more similar to the reference standard with the similarity factor of 80.70 compared to all other formulations. While LBG formulations were the least similar.

Table 2: Similarity factor of various formulations containing Propranolol hydrochloride.

Formulations (drug:gum)	Similarity Factor (*f 2*)
X1 (1:1)	73.90
X2 (1:1.5)	77.56
X3 (1:2)	60.70
X4 (1:2.5)	52.80
LBG1 (1:1)	16.37
LBG2 (1:1.5)	17.37
LBG3 (1:2)	18.13
LBG4 (1:2.5)	18.85
XLBG1 (1:1)	77.13
XLBG2 (1:1.5)	76.90
XLBG3 (1:2)	80.70
XLBG4 (1:2.5)	62.17

Determination of the release kinetics

To evaluate the drug release kinetics, formulations showing a significant slow release were chosen. In general, the mechanism of drug release from polymeric matrices can be described by the swelling phenomenon. The solvent molecules move inside the polymeric matrix like a "front" defined at an exact speed; simultaneously, the thickness of the area increased with time in the opposite direction. The mechanism of drug release can be described by a second phenomenon that involves the disentanglement and erosion of the polymer (Hogan, 1989; Khullar *et al*., 1998) and for guar-galactomannan tablets, the release process involves the penetration of water into dry matrix followed by hydration and swelling of the polymer, and diffusion of the drug dissolved in the matrix.

By using Korsmeyer and Peppas (Korsmeyer and Peppas, 1981) Eq., the *n* values were obtained between 0.46 and 1.19 (table 3) for all formulations. These values are characteristic of anomalous kinetics (non Fickian) and super case –II transport, suggesting that more than one mechanism may be involved in release kinetics. The release pattern of PPHCl from different formulation was obtained by plotting log M_t/M_∞ versus log time was shown in Fig.3. In case of X and XLBG of all formulations shows super case II transport kinetics but in case of LBG both the anomalous (LBG1, LBG2 and LBG3) and super case II(LBG4) transport was found.

For all the PPHCl matrix formulations, the contribution of polymer relaxation occurs throughout the entire dissolution time period. This was also apparent from the *n* values obtained (table 3), which approaches Anomalous and super case-II transport. In general, the relaxational contribution was higher for the formulations with higher *n* values. The XLBG formulation showed the highest contribution of polymer relaxation, and swelling/erosion studies (fig. 3). The formulations of X and LBG, showed the lowest *n* values, respectively then the XLBG approaching less relaxational contribution. In the XLBG3 formulation in the ratio of 1:2 reflects controlled delivery of PPHCl.

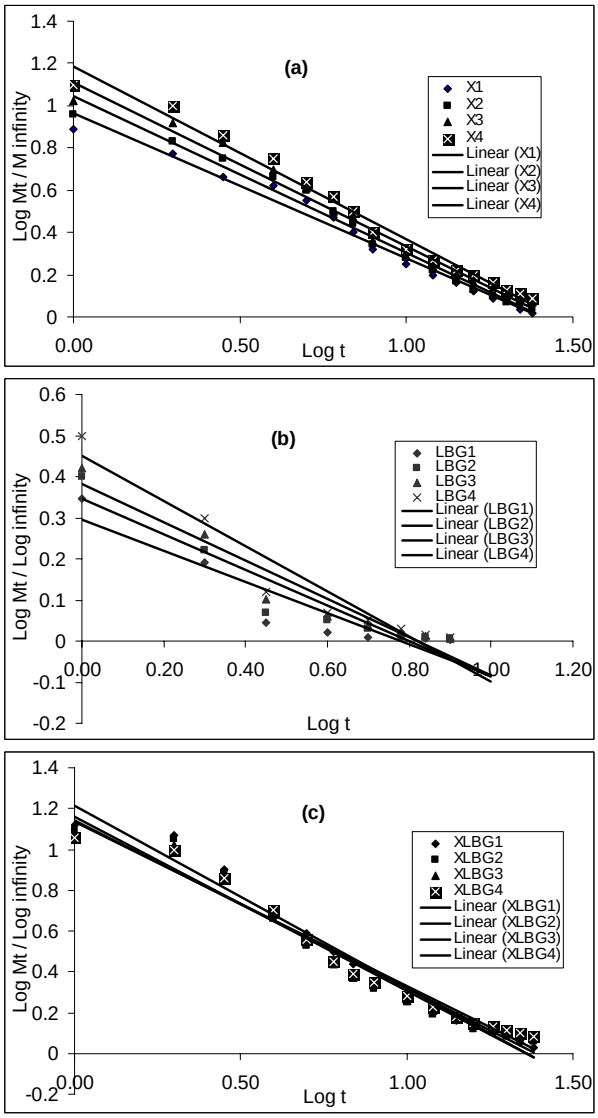

Fig. 3: Release kinetics of PPHCl formulation from (a) Xanthan gum; (b) Locust bean gum and (c) Mixture of Xanthan and Locust bean gum.

Table 3: Values of *n* (exponent for release kinetics).

Formulation (drug:gum)	*n* values	R^2	Transport Mechanism
X1(1:1)	0.97	0.9765	Super case II
X2(1:1.5)	1.00	0.9887	Super case II
X3(1:2)	1.06	0.9939	Super case II
X4(1:2.5)	1.05	0.9980	Super case II
LBG1(1:1)	0.46	0.9797	Anomalous
LBG2(1:1.5)	0.72	0.9982	Anomalous
LBG3(1:2)	0.85	0.9986	Anomalous
LBG4(1:2.5)	0.92	0.9928	Super case II
XLBG1(1:1)	1.12	0.9993	Super case II
XLBG2(1:1.5)	1.16	0.9994	Super case II
XLBG3(1:2)	1.19	0.9980	Super case II
XLBG4(1:2.5)	1.13	0.9979	Super case II

R^2 determination coefficient.
X (xanthan gum), LBG (locust bean gum), XLBG (xanthan gum and locust bean gum mixture in 1:1 ratio).

FTIR studies

The FTIR spectra of pure drug and formulation containing XLBG are shown in fig. 4. From the figure it is clear that the characteristic peaks at 3282(O-H stretching), 1450(C-H bending), 1240(O-H bending), 1100(C-C and C-O stretching), 800(C-H rocking, C-C stretching and C-H bending) cm^{-1} have been appeared in both the pure PPHCl drug and its formulation containing XLBG matrices, without any change in their peak position, indicating no chemical interaction between PPHCl and XLBG as confirmed by the FTIR studies.

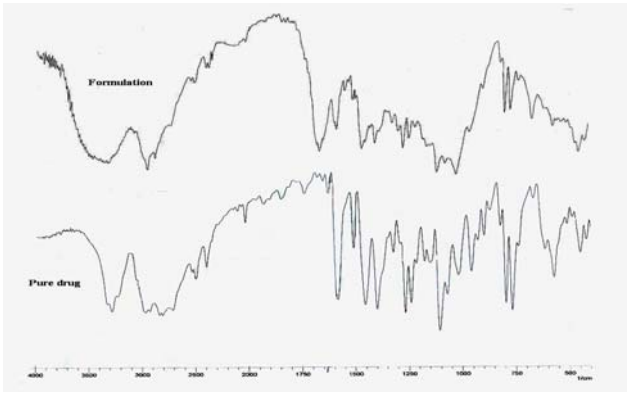

Fig. 4: FITR Spectral obtained for pure drug and formulation containing XLBG.

CONCLUSION

The tablets with XLBG resulted in more uniform controlled drug release matrices than X and LBG, due to the utilization of the synergistic interaction of two biopolymers to produce a strong and elastic gel in the presence of a ternary component to control the drug release process and the smallest average size of the particles. Xanthan gum matrices had marked sustained effect on the release of PPHCl than LBG (*Ceratonia siliqua*) alone matrices. The XLBG formulation was found to provide the required release rate, with zero-order release kinetics, it cost effective and more similar to reference standard. There was no chemical interaction between drug and polymer as been confirmed by FTIR studies. At the same total concentration, the LBG matrices did not show controlled release but the LBG has synergistic action with the xanthan shows precise controlled release effect. The predominant release mechanism varied with matrices composition and drug release was controlled by both diffusion and relaxation, with predominance of the latter mechanism mainly in XLBG tablets.

ACKNOWLEDGEMENT

The authors acknowledge the financial support received from the All India Council for Technical Education (AICTE), New Delhi, India. Parul Arogya Seva Mandal, Boroda and JSS Mahavidyapetha, Mysore for their support and encouragement to carry out this work.

REFERENCES

Abrahamsson B, Alpsten M, Bake B, Jonsson UE, Larsson A, Lepkowaska ME (1998). Drug absorption from nifedipine hydrophilic matrix extended-release (ER) tablet compression with osmotic pump tablet and effect of food. *J. Control Rel*., **52**(3): 301-310.

Abrahamsson B, Roos K and Sjogren J (1999). Investigation of prandial effect on hydrophilic matrix tablets. *Drug Dev. Ind. Pharm*., **25**: 765-771.

Billa N and Yuen KH (2000). Formulation variables affecting drug release from xanthan gum matrices at laboratory scale and pilot scale. *AAPS Pharma. Sci. Tech*., **1**(4): 1-8.

Bhardwaj TR, Kanwar M, Lad R and Gupta A (2000). Natural gums and modified natural gums as sustained-release carriers. *Drug Dev. Ind. Pharm*., **26**(10): 1025-1038.

Bresolin TMB, Sander PC, Reicher F, Sierakowski MR Rinaudo M, Ganter JLMS (1997). Viscometric studies on xanthan and galactomannan systems. *Carbohydr. Polym*., **33**: 131-138.

Bresolin TMB, Milas M, Rinaudo M, Reicher F and Ganter JLMS (1999). Role of galactomannan composition on the binary gel formation with xanthan. *Int. J. Biol. Macromol*., **26**: 225-231.

Colombo P, Conte U, Caramella C, Gazzaniga A and La Manna A (1985). Compressed polymeric mini-matrices for drug release control. *J. Control. Rel*., **1**: 283-289.

Cox PJ, Khan KA, Munday DL and Sujja-areevath J (1999). Development and evaluation of a multiple-unit release dosage form for S (+)-ibuprofen: preparation and release kinetics. *Int. J. Pharm*., **193**: 73-84.

Dea ICM and Morrison A (1975). Chemistry and interactions of seed galactomannans. Adv. *Carbohydrate Chemistry and Bbiochemistry*. **31**: 242-312.

Eddy CG, Antonio IC, Bernard B, Jose LP et.al (2006). Development and optimization of a novel sustained-release dextran tablet formulation for Propranolol hydrochloride. *Int. J. Pharma*., **317**: 32-39.

Efentakis M and Loutlis A (2001). Release of furosemide from multiple-unit and single-unit preparations containing different viscosity grades of sodium alginate. *Pharm. Dev. Technol*., **6**: 91-98.

Gai MN, Isla A, Andonaegui MT, Thielemann AM and Seitz C (1997). Evaluation of the effect of 3 different diets on the bioavailability of 2 sustained release theophylline matrix tablets. *Int. J. Clin. Parmacol. Ther*., **35(12)**: 565-571.

Harland RS, Gazzaniga A, Sanagalli ME, Colombo P and Peppas NA (1988). Drug/polymer matrix swelling and dissolution. *Pharm. Res*., **5**(8): 488-494.

Haskell WL, Spiller GA, Jensen CD, Ellis BK and Gates JE (1992)**.** Role of water-soluble dietary fiber in the management of elevated plasma cholesterol in healthy subjects. *Am. J. Cardiol*., **5**(69): 433-439.

Hogan JE (1989). Hydroxypropylmethylcellulose sustained release technology. *Drug Dev. Ind. Pharm*., **15**: 975-999.

Khullar P, Khar R and Agarwal SP (1998). Evaluation of guar gum in the preparation of sustained-release matrix tablets. *Drug Dev. Ind. Pharm*., **24**(11): 1095-1099.

Korsmeyer RW and Peppas NA (1981). Macromolecular and modeling aspects of swelling-controlled systems. *In*: Roseman TS, Mansdorf SZ ed. *Controlled Release Delivery Systems*. Marcel Dekker. New York, pp.77-90.

Launay B, Doublier JR and Cuvelier G (1986). Flow properties of aqueous solutions and dispersions of polysaccharides. *In*: Mitchell JR, Ledward DA, ed. *Functional properties of food macromolecules.* Elsevier Applied Science. London, pp.1-78.

Lee PL and Kim CJ (1991). Probing the mechanism of drug release from hydrogels. *J. Control. Rel*., **16**: 229-236.

Longxiao Liu and Binjie C (2006). Preparation of monolithic osmotic pump system by coating the indented core tablet. *Eur. J. Pharma*., **64**: 180-184.

Morris ER (1990). Mixed polymer gels. *In*: Harris P ed. *Food gels.* Elsevier Applied Science. London, pp.291-360.

Morris VJ (1995). Bacterial polysaccharides, In: *Food Polysaccharides and Their Applications*. Marcel Dekker Inc., New York, pp.478-493.

Munday DL and Cox PJ (2000). Compressed xanthan and karaya gum matrices: hydration, erosion and drug release mechanisms. *Int. J. Pharm*., **203**: 179-192.

N¨urnberg E and Retting E (1974). On the characterisation of hydrocolloidal slow-release tablets illustrated for the example "Danaden® retard" tablets. *Drugs Made. Germ*., **17**: 26.

Oosterhuis B and Jonkman JLH (1993). Pharmacokinetics studies in healthy volunteers in the context of *in vitro/ in vivo* correlations. *Eur. J. Drug Metab. Pharmaco-kinetics*. **18**: 19-30.

Peppas NA and sahlin JJ (1989). A simple equation for the description of sustained release III Coupling of diffusion and relaxation. *Int. J. Pharm*., **57**: 169-172.

Rekhi SG, Porter SC and Jambhekar SS (1996). Factors affecting the release of propranolol hydrochloride from beads coated with aqueous polymeric dispersion. *Drug dev. Ind. Pham*., **221**: 709-729.

Ritger PL and Peppas NA (1987). A simple equation for description of solute release II Fickian and anomalous from swellable devices. *J. Control. Rel*., **5**: 37-42.

Reynolds TD, Gehrke SH, Hussain AS and Shenouda LS (1998). Polymer erosion and drug release characterization of hydroxypropylmethylcellulose matrices. *J. Pharm. Sci*., **87**(9): 1115-1123.

Staniforth JN and Baichwal AR (1993). Synergistically interacting heterodisperse polysaccharides. In polymer delivery systems, ACS Symposium Series; American Chemical Society. USA, **520**: 327-350.

Sujja-areevath J, Munday DL, Cox PJ and Khan KA (1998). Relationship between swelling, erosion and drug release in hydrophilic natural gum mini-matrix formulations. *Eur. J. Pharm. Sci*., **6**: 207-217.

Takayama K and Nagai T (1989). Novel computer optimization methodology for pharmaceutical formulations investigated by using sustained-release granules of indomethacin. *Chem. Pharm. Bull*., **37**: 160-167.

Talukdar MM and Kinget R (1997). Comparative study on xanthan gum and hydroxypropyl methylcellulose as

matrices for controlled-release drug delivery: II drug diffusion in hydrated matrices. *Int. J. Pharm*., **151**: 99-107.

Talukdar MM, Van den Mooter G, Augustijns P, Tjandra-Maga T, Verbeke N, Kinget R (1998). *In vitro* evaluation of xanthan gum as a potential excipient for oral controlled-release matrix tablet formulation. *Int. J. Pharm*., **169**: 105-113.

Toko M (1991). Synergistic interaction between deacetylated xanthan and galactomannan. *J. Carbohydr*., **10**: 619-633.

Welling PG (1996). Effect of food on drug absorption. *Annu. Rev. Nutri*., **16**: 383-415.