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Research Article

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EFFECT OF PSYLIUM HUSK ON FLOATING BEHAVIOUR OF ATENOLOL BILAYER TABLETS

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ABSTRACT

The purpose of this study was to develop gastroretentive floating bilayer tablets of atenolol. A natural excipient, psyllium husk, was utilized for development of floating layer of bilayer tablet. Tablets were prepared by compression of separate layers of drug release controlling granules and floating granules. All tablets were subjected to buoyancy lag time, floating duration and in-vitro drug release studies. The buoyancy lag time was found dependent on sodium bicarbonate concentration. The presence of psyllium husk was found suitable for maintaining buoyancy of bilayer tablets for long duration without affecting drug release kinetics. Thus psyllium husk inclusion in floating layer of bilayer tablets was improved the floating behaviour of bilayer tablets of atenolol.

Keywords: Psyllium husk, bilayer tablets, gastroretention, floating dosage form.

INTRODUCTION

The gastroretention of dosage form has been successfully utilized for drug delivery of narrow absorption window drugs[1,2]. In addition to retention in stomach region, the drug release can also be controlled for longer duration.[3] Several approaches have been utilized for gastroretention of dosage form like, floating tablets, *in-situ* gelling gums[4], multiunit systems[5] etc. Both matrix[6] and bilayer tablets[7] have been successfully developed and evaluated by several authors earlier. Bilayer tablets contain separate drug release layer and floating layer. Floating layer generally contains mixture of hydrophilic polymer and sodium bicarbonate. Sodium bicarbonate particles provide buoyancy by carbon dioxide bubble formation whereas gel matrix of hydrophilic polymer tries to entrap carbon dioxide bubbles.

In this research work, floating bilayer tablets using psyllium husk and HPMC K4M in floating layer with sodium bicarbonate were developed. Psyllium husk can form gel and was utilized by Chavhanpatil et al.[8] in development of floating matrix tablets. In this study psyllium husk was usd in floating bilayer tablets as gelling agent. Atenolol was selected as model drug for this study. Atenolol is beta-1 adrenoreceptor blocker and poorly absorbed through lower part of gastrointestinal tract.[9] Thus bioavailability of atenolol can be improved by gastroretention.

MATERIALS AND METHODS

Chemicals and Reagents

Atenolol and HPMC K4M were obtained as gift sample from Sanjivani Parenteral Ltd Dehradun. Sodium bicarbonate and PVP K30 were purchased from CDH Ltd. Psyllium husk was purchased from local vendor. Other solvents were also purchased from CDH Ltd.

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Preparation of Bilayer Tablets

Preparation of release controlling granules: The appropriate quantities of atenolol and HPMC (Table **1**) were weighed and mixed thoroughly. Granules were prepared by wet granulation technique using 5% PVP K30 solution in IPA as binder solution.

Table 1. Composition of Atenolol floating bilayer tablets.

Drug release Layer	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
Atenolol (mg)	50	50	50	50	50	50	50
HPMC K4M (mg)	350	350	350	350	350	300	250
PVP K30 (mg)	20	20	20	20	20	20	20
Floating Layer	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
Psyllium husk (mg)	-	50	100	100	100	100	100
HPMC K4M (mg)	300	250	200	200	200	200	200
Sodium bicarbonate (mg)	10	10	10	15	25	25	25
PVP K30 (mg)	30	30	30	30	30	30	30

Preparation of floating granules: The appropriate quantities of psyllium husk, HPMC and sodium bicarbonate were weighed and mixed thoroughly. Again wet granulation was performed using 5% PVP K30 solution in IPA as binder solution.

Compression: Granules were compressed on sixteen station single rotary compression machine (Cadmach Machinery Co. Pvt. Ltd., Ahmedabad, India) at the constant compression pressure using 12 mm flat punches. The hardness of tablets kept constant at 5 kg/cm^2.

Floating Behaviour

The floating behaviour of bilayer tablets was determined by evaluating tablets for buoyancy lag time (BLT) and floating duration (FD). BLT was the time taken by tablets to reach the surface of release medium and floating duration was the time for which tablets remain buoyant. These experiments were done in USP XXVI Dissolution apparatus II (Lab India Disso 2000) using 900 ml 0.1 N HCl as release medium at 100 rpm.

In-vitro Drug Release

In-vitro drug release study of matrix floating tablets was conducted for a period of 12 h using USP XXVI dissolution apparatus 1 (Lab India Disso 2000) at 37± 0.5°C and 100 rpm speed. For dissolution study, 900 ml 0.1 N HCl was selected as medium and aliquots of 5 ml. were withdrawn at predetermined time intervals of 1, 2, 3, 4, 6, 8 and 12 h. After filtration and appropriate dilution, the samples were analyzed by a UV spectrophotometer (Shimadzu UV-250 1PC double beam spectrometer) at 272.8 nm. The total content of atenolol in the sample was determined using the appropriate calibration curve.

Drug Release Kinetics

Drug release data was fitted with different release kinetics models. Zero order, First order, Higuchi model and Koresmeyer-Peppas model were utilized for release kinetic determination.[10] Further Ritger-Peppas equation was utilized for determination of release mechanism.

$$\frac{M_t}{M_\infty} = kt^n \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where, M_t/M_∞ is fraction of drug release, t is time, k is the constant incorporating structural and geometrical characteristics of dosage form and n is release exponent.[11,12] The value of n was calculated only for the portion of drug release curve where $M_t/M_\infty \leq 0.6$.

RESULTS AND DISCUSSION

Floating Behaviour

The floating layer of tablet was responsible for the floating profile of bilayer tablets. In this study the psyllium husk is used in combination with HPMC K4M as a hydrophilic polymer. As the acidic medium came in contact with sodium bicarbonate molecules the carbon dioxide gas bubbles formed rapidly and propel the tablet in upward direction (Figure **1**). In case of formulation having combination of psyllium husk and HPMC K4M were having BLT value less than 3 minutes (Table **2**). Further as the proportion of sodium bicarbonate was increased in floating layer the value of BLT was also reduced (Figure **2**). With 15 mg sodium bicarbonate the BLT was 3.3 ± 0.06 minutes whereas with 25 mg sodium bicarbonate the BLT was 0.5 ± 0.02 minutes. Thus high content of bicarbonate was found favourable for initial buoyancy of dosage form. Further the change in psyllium husk concentration was not resulted in significant change in BLT value of tablets which indicates that BLT value was depend only on sodium bicarbonate concentration.

Figure 1. Floating behaviour of bilayer matrix tablet formulation F5 at (a) one minute and (b) 5 hr.

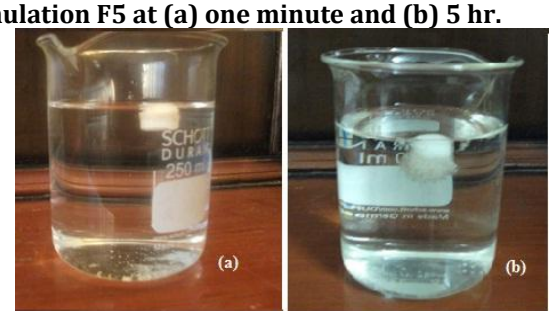


Figure 2. Effect of sodium bicarbonate on BLT (n=3).

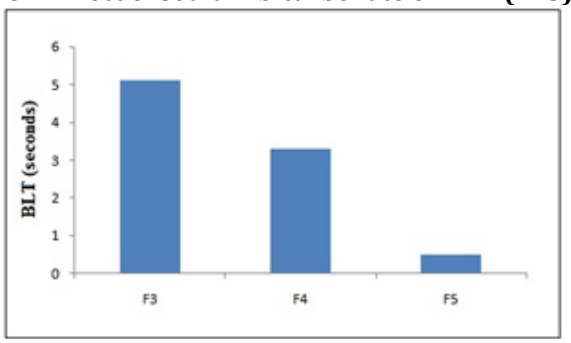


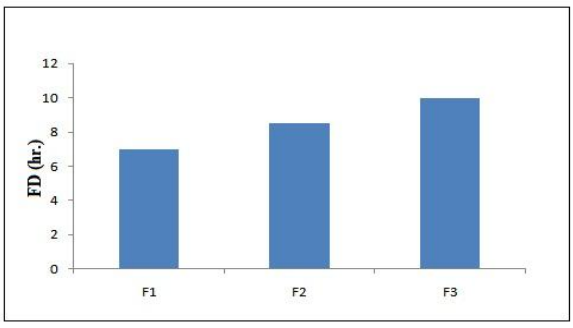
Table 2. Physicochemical properties of the prepared Atenolol floating bilyer tablets.

Formulation code	Tablet weight mg	Drug content %	Friability %	Buoyancy Lag Time (BLT, min)	Floating Duration (FD, hr)
F1	760.13 ± 0.54	99.21 ± 0.92	0.45 ± .02	5 ± 0.04	7
F2	760.12 ± 0.12	99.59 ± 0.11	0.31 ± 0.03	4.7 ± 0.02	8.5
F3	760.68 ± 0.32	101.17 ± 0.54	0.45 ± 0.12	5.1 ± 0.04	10
F4	766.01 ± 0.23	102.56 ± 0.75	0.38 ± 0.19	3.3 ± 0.06	> 12
F5	775.23 ± 0.57	100.31 ± 0.01	0.42 ± 0.09	0.5 ± 0.02	> 12
F6	775.89 ± 0.21	98.99 ± 0.35	0.38 ± 0.21	0.3 ± 0.03	> 12
F7	775.15 ± 0.33	99.35 ± 0.73	0.41 ± 0.08	0.3 ± 0.04	> 12

In addition to initial buoyancy behaviour long term floating duration for 10 hours was also desired for bilayer tablets. As the release medium penetrates the matrix of floating layer and resulted in hydration of hydrophilic polymeric chains of polymers.[13] The entrapment of carbon dioxide bubbles inside the gel matrix of hydrophilic polymers was reduced the density of tablets and provide long term buoyancy. As the concentration of sodium bicarbonate was increase from 10 mg to 25 mg (F3-F5) the floating duration of bilayer tablets was increased from 10 hours to 12 hours. Thus higher floating duration was achieved with higher concentration of sodium bicarbonates.

The effect of psyllium husk on floating duration was also studied (Figure **3**). In formulation F1 only HPMC was used as the hydrophilic polymer in floating layers. After initial buoyancy F1 was not floated constantly and irregular up and down pattern was observed. This might be due to escape of carbon dioxide from floating layer. Initially the bubble formation by sodium bicarbonate provided buoyancy but once bubble detached from tablet the irregular pattern was observed.

Figure 3. Effect of psyllium husk on FD (n=3).



In formulation F2 the pysllium husk and HPMC were taken in combination. The floating duration of 8.5 hours was observed for F2. Formulation F2 was remained afloat after initial buoyancy and no irregular pattern was observed for pysllium husk containing formulations. This might be due to the rapid gel formation ability of psyllium husk. The rapid gel formation resulted in entrapment of carbon

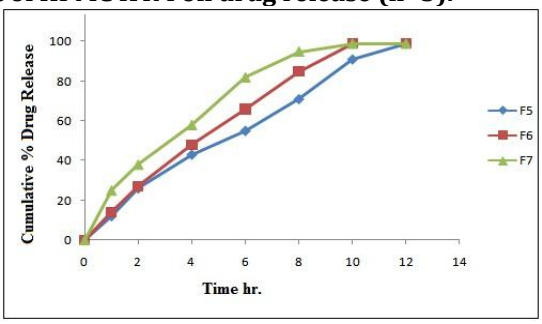
dioxide bubbles right from the beginning and provided constant buoyancy to dosage form. Further, with 100 mg psyllium husk (F3) the 10 hr. floating duration was observed. Thus with higher concentration of psyllium husk the higher floating duration was achieved.

Drug Release Study

The drug release pattern was depended on the release controlling layer of bilayer tablet. The drug release from matrix of hydrophilic polymer depends on the hydration of polymeric chains by the release medium.[14] As the release medium hydrate the polymeric chains the swollen gel matrix was formed. This viscous swollen gel matrix of hydrophilic polymer controlled the drug release. At 250 mg concentration of HPMC in release controlling layer, the complete drug release was achieved within 8 hours. With 350 mg concentration of HPMC the drug release was further sustained upto 12 hours (Figure **4**). Thus the drug release rate was reduced with increase in HPMC concentration.

The drug release data was further subjected to the various models in order to understand the kinetics of drug release. The swelling of polymeric chains resulted in gel formation which further reduces the diffusion of drug according to its viscosity.[15,16] The zero order, first order, Higuchi model and Koresmeyer - Peppas model were utilized. The best model was selected on the basis of highest value of regression coefficient (R^2). The initial burst release and slower drug release later on were found associated with bilayer tablets. Thus, the release data was best fitted with Koresmeyer-Peppas (KP) model (Table **3**).

Figure 4. Cumulative drug release profiles showing effect of HPMC K4M on drug release (n=3).



Further the mechanism of drug release was determined by using Ritger-Peppas model (considering $M_t/M_\infty \leq 0.6$). The value of diffusion constant (n) is shown in table **3**. The value of n was found between 0.45-0.89 which indicates for anomalous drug transport. Thus both diffusion and polymeric chain relaxation were found responsible for drug release.[17,18] After complete hydration of polymeric chains the erosion of chains was occurs.

Table 3. R^2 for different release kinetics models with n for various matrix tablets.

Formulation Code	Zero Order R^2	First Order R^2	Higuchi R^2	Korsmeyer Pepass		Best Model
				R^2	n	
F5	0.988	0.814	0.921	0.992	0.840	Pepass
F6	0.959	0.88	0.945	0.991	0.864	Pepass
F7	0.901	0.952	0.989	0.981	0.607	Pepass

Notes: R^2 - Regression coefficient; n - Diffusion exponent

CONCLUSION

The psyllium husk was utilized in combination with HPMC K4M in floating layer of bilayer tablets. In the absence of psyllium husk the tablets were not having constant floating behaviour for 10 hr duration. With inclusion of psyllium husk the constant floating behaviour was successfully achieved. Also, drug release pattern was not affected with inclusion of psyllium husk due to bilayer nature of dosage form. Thus, both sustained drug release and constant floating pattern were achieved with psyllium husk inclusion in floating layer of bilayer tablets.

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