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Psyllium husk as a hydrophilic matrix agent for the release of a model drug

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Psyllium husk forms the viscous gel by absorbing water. In the present study glipizide was used as a model drug. Swelling behavior study of psyllium was analyzed in 0.1N HCl, phosphate buffer (pH 7.4) and distilled water. Similar medium were used for reconstituted xerogel. Different formulations to analyze the release behavior of glipizide were prepared by using capsule shell '1' and psyllium husk as matrixing agent. The dissolution study of different formulation was performed in six stage dissolution apparatus in phosphate buffer (pH 7.4) and 0.1NHCl for 10 hours. The drug-polymer network thus obtained was characterized for drug polymer interaction by FTIR study. It has been observed that in distilled water could maintain its gel consistency for prolonged time than 0.1NHCl and phosphate buffer ($p<0.05$). It was investigated that 70% of the dispersed drug was released within 10 hours in phosphate buffer. The amount released in 0.1N HCl was significantly different than phosphate buffer ($p<0.05$). Sustaining effect of formulation was obtained very high when large amount of psyllium husk was used. FTIR study revealed that the dispersed drug was unaffected after matrix formation.

Key words : Isabgol husk, Hydrophilic matrix, Xerogel, Glipizide.

INTRODUCTION

Psyllium is the common name used for several members of the plant genus *Plantago ovata* and its seeds are used for the mucilage formation. Mucilage is a white fibrous material, hydrophilic in nature and forms the clear, colorless mucilaginous gel by absorbing water. Laidlaw and Percival (1949) secured evidence for two components, which they characterized as a polyuronoid and a neutral arabinoxylan. Later Kennedy *et al.* (1981) studied the mucilage obtained for plantago seed husk by extraction with alkali and concluded that the preparation although polydisperse, represented a single species of polysaccharide, a highly branched acidic arabinoxylan. Psyllium has been reported as medicinally active polysaccharide including cholesterol lowering capacity, laxative activity, improving insulin sensitivity (Anderson *et al.*, 2000; Song *et al.*, 2000). Psyllium supplementation has also improved blood sugar levels in some people with diabetes (Anderson *et al.*, 1999). In double blind trial, people with ulcerative colitis had a reduction in symptoms such as leading and remained in remission longer when they took 20 gm of psyllium seeds twice daily with water compared to the use of the medications mesalamine alone.

Glipizide is an effective widely used anti diabetic drugs. It has a short biological half-life of 3.4±0.7 hours and is rapidly eliminated due to its short half-life. It is a good candidate or model drug for modified drug delivery system.

The psyllium husk may act as a potential polymer for modified drug delivery. The most popular method of slow release of drug is by forming matrix system that is easy for different formulation development and manufacturing. Hydrophilic swellable matrices are used most commonly than hydrophobic matrices. The release of drug from the matrix regulated by various factors as swelling, dissolution and or erosion. In the present work, the psyllium was used as matrixing agent for Glipizide release and also to analyze the various conditions on gelling behavior.

MATERIALS AND METHODS:

Psyllium husk was procured from the local market (Baidhyanath, Jhansi). Glipizide was provided as a gift sample by Alkem Laboratories Ltd. Mumbai (India). Potassium dihydrogen phosphate was obtained from Ranbaxy Laboratories (New Delhi). All other chemicals and reagents used were of analytical grade and used without further modification.

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Preparation of Psyllium husk dried gel (Xerogel) :
About 5 gram of powdered psyllium husk was (#100) was dispersed in 250 ml distilled water and stirred mechanically (Remi Motors, Mumbai) at 1500 rpm for 5 minutes to disperse homogeneously. The dispersion thus obtained was ultrasonicated for 5 minutes for degassing. The dispersion was taken in glass Petri plates and dried in vacuum oven at 40^0C until dried, grinded and passed through sieve no.100 and then kept in air tight vacuum desiccator until used.

Preparations of capsules containing psyllium husk dried gel (xerogel) loaded with Glipizide:
The batches of controlled release capsules were prepared by mixing Glipizide in psyllium husk. Glipizide was added in psyllium husk and stirred at 1000 rpm for 15 minutes. The dispersion was ultrasonicated for 5 minutes for degassing. The resultant dispersion was dried in vacuum oven (Tempo Bombay) until dried and passed sieve no 100. The drug to psyllium husk ratio was maintained 1:5 in all formulations. About 250mg, accurately weighted and blended powders of each batch were filled in a capsule shell no '1'. The filled capsules were taken in airtight container and kept in desiccator.

Gel behavior of Psyllium husk:
The gelling behavior was determined by modified method of Visavarungroj *et al.* (1990).The gel was prepared in 1%w/v concentration in distilled water, 0.1N HCl and phosphate buffer (pH 7.4). The initial volume was noted down in graduated cylinder kept at room temperature. The volume of the sediment was observed at frequent time interval.

In vitro drug release profile:
Release of Glipizide from the capsules was studied in phosphate buffer (pH 7.4) and 0.1NHCl using an USP XXIII six stage dissolution apparatus (Cambell Electronics, Mumbai) with rotating basket at 100 rpm and 37 ± 0.5 ^{0}C. Samples were withdrawn at different time intervals over a period of 10 hours and after a suitable dilution were analyzed at 224 nm for Glipizide using a Hitachi,U-2001,Japan Double Beam spectrophotometer. The drug release experiments were conducted in triplicate.

Fourier transform infrared measurement (FTIR) study:
The psyllium husk, Glipizide and psyllium-Glipizide matrix were analyzed by FTIR (Perkin Elmer, RXI FTIR SYSTEM) by using KBr pellets for drug-polymer interaction.

RESULTS AND DISCUSSION

Effect of 0.1N HCl and phosphate buffer (pH 7.4) on gelling nature of Psyllium husk:
The separation of the liquid from the swollen gel can be considered as synersis. Separation of a solvent phase is thought to occur because of elastic contraction of the polymeric molecules. In Psylium husk, very few water insoluble components are present (Laidlaw and Percival 1949). The polysaccharide chains can retain plenty of water due to ionic attraction, hydrogen bonding and osmotic capacity as shown in the Fig.1.

The rate of settlement in freshly prepared *Plantago* husk hydrogel was significantly different in distilled water, 0.1N HCl and phosphate buffer pH 7.4 ($p<0.05$). It may indicate the rearrangement of flexible, non-flexible chains in condensed fibers time taking process resulting in dense gel. Consequently, it squeezes out the entrapped water. But in 0.1N HCl and phosphate buffer, the arrangement of (1>3) and (1>4) –â-xylan chains damaged to some extent. The polymeric chains, similar to xanthan exits in solution in a rigid, ordered chain configuration except at high temperature and low ionic concentration (Haque *et al.*,1993).

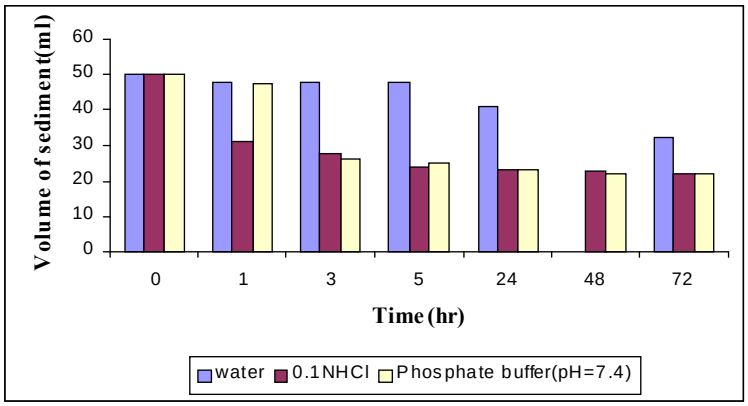

Fig. 1 : Different mediums affecting nature of freshly prepared husk hydrogel

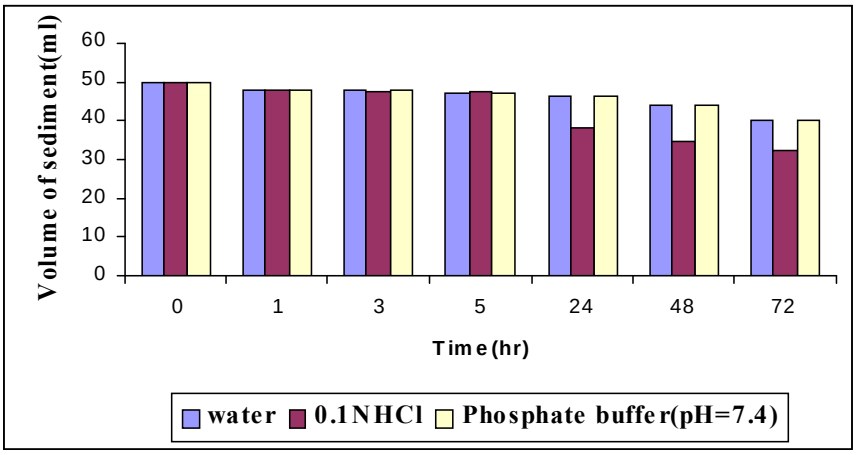

Fig. 2 : Different mediums affecting nature of reconstituted husk Hydrogel

Table 1: Formulations containing glipizide with their respective $t_{50\%}$ in different mediums used for release study

S.No.	Formulation code	Amount of Psylllium husk (%W/V)	$t_{50\%}$(min)	
			In 0.1N HCl	In phosphate buffer (pH 7.4)
1.	A_1	2	150.18	80.88
2.	A_2	4	264.01	131.87
3.	A_3	5	346.50	202.00
4.	A_4	7	713.98	238.76

Effect of phosphate buffer (pH 7.4) and 0.1N HCl on gelling nature of Plantago husk (reconstituted gel): In reconstituted gel of the husk the same effect was observed as shown in the following Fig. 2. But the effect of distilled water, phosphate buffer (pH 7.4) and 0.1NHCl was lower as compared with freshly prepared hydrogel. It seems that during drying operation of freshly prepared gel, most of the water entangled in fibril structures may come out as much as possible. The removal of mostly moisture may increase the entropy, osmotic capacity and chemical potential of the ionic chains present in intermolecular polymeric network of dry gel. When dry husk gel comes in contact with distilled water, phosphate buffer (pH 7.4) and 0.1N HCl, it undergoes more swelling than fresh powder gel. The imbibed distilled water, buffer or HCl may enter into the three fold ribbon like structure of the husk and remain in the husk polymeric network for prolonged time resulting less synersis than freshly husk powdered gel.

In vitro release profile:
A different formulation with their release pattern in acidic and basic medium has been shown in Fig. 3 and the time required for the release of 50% dispersed drug has been shown in Table 1. In the hydrogel system, absorption of water from the environment changes the dimensions and physicochemical properties of the system and thus the release kinetics of the system. There are a large no of mathematical models that can be applied for swellable polymeric system, as single model can not successfully predicts the experimental observations (Lee 1980).The generalized empirical equations has been widely used to describe both the water uptake through the swellable glassy polymers and the drug release from these devices. In case of water uptake, the weight gain, Ms is described by the following empirical equations-

$$Ms=kt^n$$

Where k and n are constant. Normal fickian diffusion is characterized by n=0.5, while Case II diffusion by n=1.0.A value of n between 0.5 and 1.0 indicates a mixture of Fickian and Case II diffusion which is usually called non-fickian or anomalous diffusion (Alfrey *et al.*,1996).

Ritger and Peppas (1987) showed that the above power law expression could be used for the evaluation of drug release from swellable systems. In the above case Mt/Mµ replace Ms in the above equation to give-

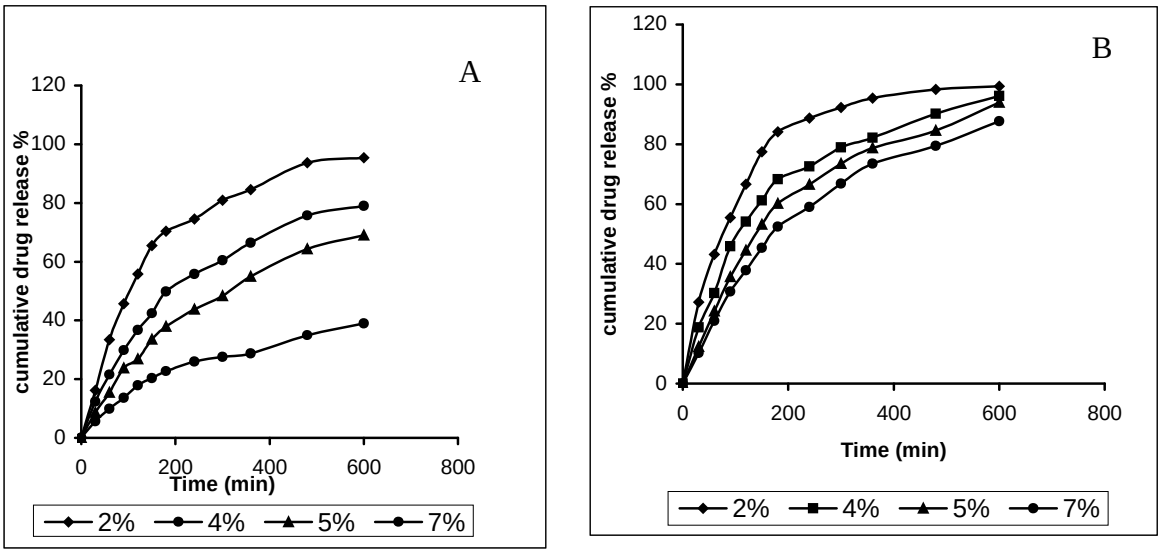

Fig. 3 : Release pattern of different formulations in 0.1N HCl (A) and phosphate buffer (pH 7.4) (B)

$$Mt/ M\alpha = kt^n$$

Where Mt/Má is the fractional release of drug in time t, k is the constant characteristic of drug-polymer system and n is the diffusion exponent characteristics of the release mechanism. When the plot is drawn between In Mt/Má and In t, the slope of the plot gives the value of 'n' and intercept will tell about k.

The diffusion exponent, gel characteristics coefficient and n for different formulations have been shown in the Table 2. According to Alderman *et al.* (1984) and Hodson *et al.* (1995), water-soluble drugs are released from solid dosage forms primarily by diffusion of dissolved drug molecule through the viscous layer, whereas water insoluble drugs are released predominantly by erosion. The value of 'n' for Glipizide, a water insoluble drug was ranged from 0.73 to 0.59 in 0.1N HCl which suggests the fickian diffusion and in case of phosphate buffer, the value of 'n' was significantly different ($p<0.5$). It may be attributable due to breakage of psyllium network in alkaline medium (Haque *et al.*,1993). A greater contribution of fickian diffusion in Glipizide on increasing the amount of husk may be postulated to occur as more water was imbibed as the amount of psyllium was increased. It was also observed that gel coefficient was also decreased on increasing the husk concentration. The drug release depends upon the two simultaneous rate processes, water migration into the device and the drug diffusion through the continuously swelling hydrogels. It is clear from the table that Glipizide release from the psyllium husk hydrogel follows fick's law. Also, the thick gel layer around the dispersed drug on higher psyllium concentration may retard the drug release consequently, resulting in prolonged release.

The FTIR measurements of Glipizide, psyllium husk and Glipizide dispersed husk has been shown in Fig. 4. In FTIR study the characteristics bands due to stretching of-CONH- (16090-1650cm^{-1}),-NH- and C-H (3500-3200cm^{-1}) were appeared in Glipizide dispersed psyllium

Table 2 : Different release kinetics parameters for Glipizide from Psyllium husk.

Formulation code	0.1 N HCl			Phosphate buffer (pH 7.4)		
	n	Diffusion coefficient (min^{-1})	Gel Characteristics constant k	n	Diffusion coefficient (min^{-1})	Gel Characteristics constant k
A_1	0.7316	4.221	0.2822	0.7256	4.2722	0.4778
A_2	0.7007	3.3308	0.1311	0.7229	4.137	0.3069
A_3	0.6827	3.0688	0.0081	0.7134	4.1599	0.7324
A_4	0.5908	1.6559	0.0551	0.7255	3.9339	0.0455

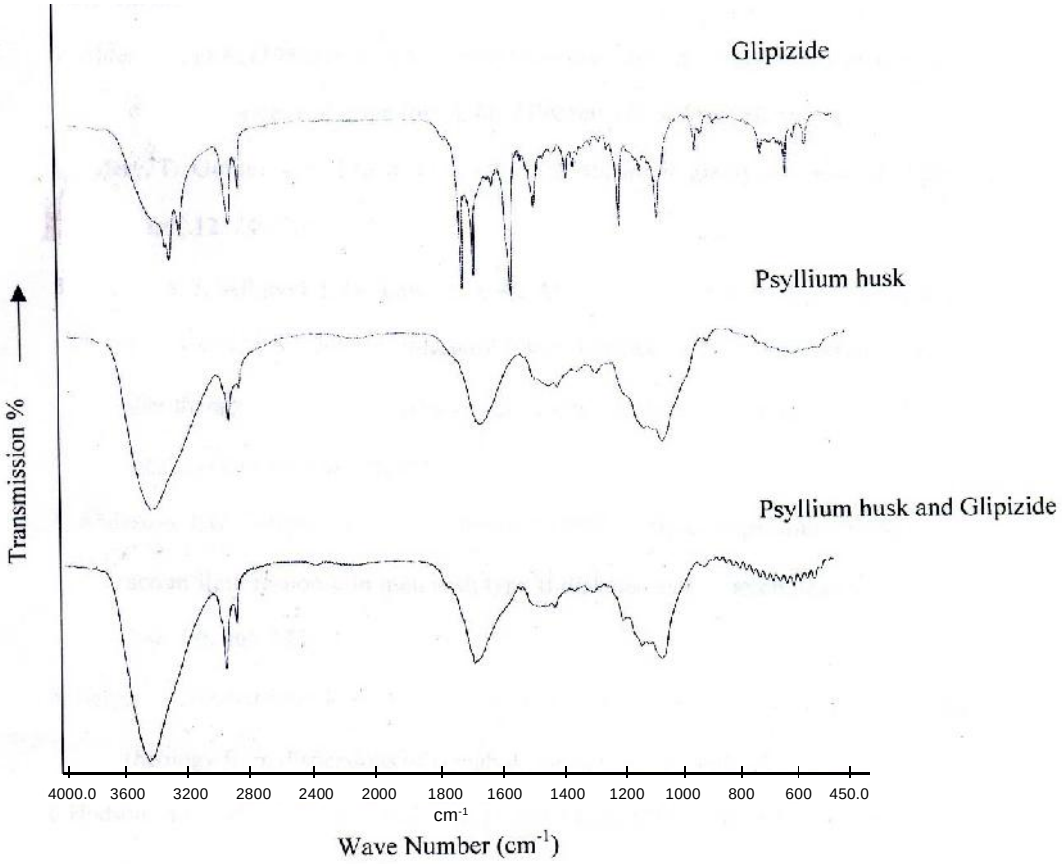

Fig. 4 : FTIR measurements of psyllium husk, glipizide and glipizide dispersed psyllium husk.

husk at 3430cm^{-1} and 1651cm^{-1}. Many bands were observed in the range of 900-650cm^{-1} which was considered due to –NH- bending (Secondary amine). It indicated that Glipizide has maintained its group's identity (the structure of drug has not been shown here) after dispersion in the psyllium husk.

The effect of acidic and alkaline condition on gelling nature of reconstituted and fresh psyllium husk was analyzed. *In vitro* release study of Glipizide from physical mixture of natural psyllium husk and Glipizide was evaluated. On increasing the concentration more profound effect on drug release was observed that might due to thick gel layer formation around the dispersed drug. Chemical stability of Glipizide was shown by FTIR study. Hence natural psyllium husk may be a suitable hydrophilic matrixing candidate modified drug delivery system.

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