

**PSYLLIUM: A POTENTIAL CARRIER TO CONTROL THE DRUG DELIVERY**

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ABSTRACT

Psyllium, the Ispaghula (Isabgol) husk is very well known and widely used from the times of Ayurveda as Laxative to relieve constipation. With the advancement in the technology and research, it is found to be effective to cure some other ailments including colon cancer. Not only that, the scientists have worked upon the use of this biocompatible, inert, easily available and cheap drug as a carrier to control the delivery of other chemicals/drugs. Several studies have been done and reported in the last decade favoring its use as a novel drug delivery carrier. The presented review summarizes the available research studies which were aimed at exploring the use of Psyllium as an excipient in one way or another for the development of novel drug delivery systems.

Key Words: Psyllium, Hydrogels, Sustained release agent, Release retardant, Gastroretentive agent, Superdisintegrant, Microparticals.

INTRODUCTION

Because of its geographical and environmental position India has been a very good source of plants and plant products having medicinal values. The ancient medicinal therapies based on Ayurveda are solely based on the medicines and extracts obtained from the natural sources. Not only the therapeutically active part of the plants are being used from the ancient time, but in the recent years the plant derived polymers have also enjoying the tremendous interest due to their diverse pharmaceutical applications such as diluents, binder, disintegrants in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppositories¹. These plant derived polymers such as natural gums and mucillages are enjoying their incorporation into the pharmaceutical products because of being biocompatible, cheap and easily available. Moreover they are preferred over semi synthetic and synthetic excipient because of their non toxicity, low cost, non irritant nature, soothing action, easy availability and widely acceptance.²⁻⁵

With the advancements in technology these natural products now can also be modified in different ways and can also be incorporated in the final formulations in order to control the release of the drug. Recent trends in the pharmaceutical manufacturing are inclining towards the use of plant based natural products in place of synthetic additives wherever possible due to the above stated properties. Not only in the formulation of the conventional dosage forms, these plant based natural materials are studied and are being explored for their role in the novel drug delivery systems. The most extensively used category of the plant based excipients are polysaccharides and gums (Tamarind Gum, *Hibiscus rosasinensis*, Okra gum, Guar gum, Locust bean gum, Isapgulla husk (Psyllium), *Sterculia foetida*, Aloe Mucilage, Albizia gum, Fenugreek), resins (Gum Copal, Gum Damar) and tannins (Bhara Gum). Among the above listed plant derived excipients, the present review is mainly aimed at the study of Ispaghula husk, briefly as a pharmacologically active agent but largely as an excipient for the development of novel drug delivery.

PSYLLIUM: ROLE AS A DRUG

Although Psyllium is used interchangeably with the term Ispaghula husk, it is the common name used for several members of the plants belonging to the genus *Plantago*. Psyllium and Isabgol are having similar uses but they differ

in their source and doses. Where Psyllium is derived from dried ripe seeds of *Plantago psyllium* and *P. indica*, the Isabgol husk is derived from the ripe seeds of *Plantago ovata*.⁶ The seed and seed coats of *P. ovata* have been studied extensively for its chemical composition and gelling nature and have been reported in the literatures.⁷⁻⁹ It is a very well known, widely accepted and worldly used medicinally active natural polysaccharide used for the treatment of constipation^{10,11} and diarrhea.¹² Different studies by Kumar et. al. and Quitzau et. al. have shown that Psyllium has the paradoxical properties of both improving the constipation by increasing the stool weight¹³ and ameliorating chronic diarrhea.¹⁴ Various studies on the use of Psyllium for the treatment of diarrhea have been done and reported on various animals including calf, leopard and dog.¹⁵⁻¹⁷ Research on humans has also been carried out by Belknap et. al. and the studies suggested that Psyllium increases the number of normal stool and decreases the number of liquid stools.¹⁸

Other well studied and reported pharmacological applications of Psyllium include its use for the treatment of Crohn's disease (inflammatory Bowel-Ulcerative colitis disease),^{19,20} Irritable Bowel's syndrome (IBS)²¹⁻²⁴ with an optimal dose of 20mg/day,²⁵ colon cancer,²⁶ obesity in children and adolescents,^{27,28} diabetes²⁹⁻³⁸ and hypercholesterolemia.³⁹⁻⁴⁶

PSYLLIUM: ROLE AS A NOVEL DRUG DELIVERY CARRIER

Biologically Isabgol is *Plantago ovata* (family-Plantaginaceae). The seed and husk of the Isabgol are widely used in pharmaceutical industry as demulcent, emollient, laxative, as an adjunct to dietary and drug therapy on lipid and glucose levels⁴⁷ and in other above mentioned diseases. The seed and husk of Isabgol contains mucilage which is present in the epidermis of the seed. It is official in IP, BP, and USP. It is used in food and pharmaceuticals at a dose level of 5-6 g twice a day.⁴⁸ The mucilage of isabgol consists of pentosan and aldobionic acid, which on hydrolysis yield arabinose, galactose, galactouronic acid and rhamnose.⁴⁹ The Isabgol mucilage has the property to swell upto 10-14 times of its original volume.

It is just a decade back when some modifications were tried to carry out to the physical and chemical properties of the husk. One such attempt was carried out by Mishra A and coworkers. They synthesized a graft copolymer of Psyllium mucilage and polyacrylamide using ceric-ion induced redox

polymerization. The grafted copolymer was found to dissolve faster than Psyllium mucilage in water and had a higher intrinsic viscosity than the mucilage.⁵⁰ It's only eight years back when Psyllium was reportedly used as a polymer for a sustained release formulation. After that several attempts have been made to explore the potentials of Psyllium to control the drug release rate in one way or another. Some of the available appreciated works have been reviewed and briefly described under the use of Psyllium as

- Hydrogels
- Sustained release agent/Release retardant
- Gastroretentive agent
- Superdisintegrant
- Microparticals

As Hydrogels

In order to utilize the Psyllium husk for the development of a novel hydrogel system for the controlled drug delivery devices, Baljeet Singh et al. synthesized Psyllium and N-hydroxymethylacrylamide based polymeric networks by using N, N methylenebisacrylamide (N,N'MBAAm) as crosslinker and ammonium persulfate (APS) as initiator.⁵¹

The polymeric network thus formed was characterized by various sophisticated analytical methods like SEM, FT-IR and TGA. In order to study the drug release mechanism and diffusion coefficient from the prepared hydrogel, two model drugs, Salicylic acid and Tetracyclin HCl were chosen. The drug release pattern has also been studied at varying pH and in the solution of pH 7.4 buffer, the rate of polymer chain reaction was found out to be more as compared to the rate of drug diffusion from the synthesized hydrogel and also that the rate of drug release followed Fick's Law of diffusion.

In another attempt, Singh B and team also prepared the Psyllium 2-hydroxyethylmethacrylate (HEMA) and acrylamide (AAm)-based polymeric networks by using the same crosslinker and initiator.⁵² The polymeric network thus formed was called psy-cl-poly(HEMA-co-AAm). To evaluate the swelling and drug release mechanism from the hydrogel, the swelling kinetics of the gel and the in vitro release dynamics of Tetracyclin HCl has been studied. The value of diffusion exponent 'n' for both swelling kinetics and drug release dynamics was found out to be 0.5 which showed that Fickian type mechanism has occurred. Also the study concluded that from the drug loaded sample, the rate of release of the drug from hydrogel was slow and the rate of the diffusion of the drug increased with time.

The same team also attempted to explore the double potential of the psyllium for novel drug delivery systems.⁵³ They prepared Psyllium and acrylic acid based pH sensitive hydrogel by using N,N'-methylenebisacrylamide (N,N-MBAAm) as crosslinker and ammonium persulfate (APS) as initiator; this time for the use in colon specific drug delivery. They selected three model drugs-Tetracyclin HCl, Insulin and Tyrosine to target the colon and to study the swelling kinetics of the hydrogel and the release dynamics of the active drug from the drug loaded hydrogel for the evaluation of swelling and drug release mechanism from the polymeric network at varying pH. It was observed that swelling and release of drugs from the hydrogels occurred through non-Fickian or anomalous diffusion mechanism in distilled water and pH 7.4 buffer, which showed that the rate of polymer chain relaxation and the rate of drug diffusion from the prepared hydrogels were comparable.

Singh B and Sharma V in 2010 reported their combined efforts to develop a Psyllium based hydrogel through graft polymerization technique.⁵⁴ They first evaluated the optimum

conditions for the synthesis of Psyllium-poly(vinyl alcohol) (PVA)-poly(acrylic acid) blended hydrogel which have been obtained as 1% v/v acrylic acid; 2% w/v PVA and 1 g of Psyllium and then they characterize the same by SEM, FTIR and swelling studies. Antibiotic Tetracycline HCl was chosen as model drug and its release from the hydrogel was observed more in pH 2.2 buffer than in 7.4 buffer or in distilled water, thus favoring the suitability for peptic ulcer caused by *Helicobacter pylori*. Also, Psyllium has been reported to cure ulcerative colitis, hence the designed system was supposed to have double potential to cure ulcer.

The In vitro release profile of anti-ulcer drug rabeprazole has also been studied from biocompatible Psyllium-PVA hydrogels by Singh B and coworkers.⁵⁵ In this study they first synthesized Psyllium-PVA hydrogels by chemical method in the presence of N,N'-methylenebisacrylamide. Then they characterized the same by Fourier Transform infrared spectroscopy, thermo gravimetric analysis, swelling and drug release studies, and finally they evaluated the haemocompatibility behavior by studying the blood interactions with hydrogels with reference to thrombogenicity and haemolytic potential. Thrombogenicity results indicated that hydrogels were non-thrombogenic. The haemolytic index was found out to be <5%, on the basis of which they concluded that the synthesized hydrogels were haemocompatible and hence could be used for oral administration of antiulcer drugs.

In a quite different research work from already reported one, in the search of an effective and economical material to be used as an effective stimulus sensitive drug delivery device, Parashar D et al.⁵⁶ synthesized a Psyllium based polymer using free radical polymerization mechanism. Psy-cl-poly(AA) thus formed was characterized by scanning electron microscopy (SEM) and the hydrogel was studied for its electrical stimulus sensitive responsive behavior using 5V AC/DC current source at 37°C using artificial biological fluid. Maximum swelling found in artificial biological fluid was 524% under AC and 448% under DC source showing the excellent electrical responsive behavior. From their studies, Prashar D and team suggested that the Psy-cl-poly(AA) may be used for stimulus sensitive drug delivery system as an effective and alternate drug carrier in comparison to synthetic backbone based polymers.

Sustained release agent/Release retardant

The sustained release properties of the psyllium husk has also been explored and evaluated by Desai A et al.⁵⁷ They formulated the sustained release granules of amoxicillin trihydrate using various combinations of psyllium husk and HPMC K4M. They observed a faster release of amoxicillin from the granules containing only psyllium husk while the use of a combination of psyllium husk and HPMC K4M provided a sustained release of the drug. The combination showed this behavior due to the reduction of the immediate swelling of the Psyllium matrix by incorporation of HPMC K4M

Lalwani and Parikh worked upon the preparation and evaluation of an Isabgol based additive to be used as matrix for directly compressible tablets of Acetaminophen using agglomeration technique.⁵⁸ The agglomerates were prepared using varying proportions of Lactose, Calcium hydrogen phosphate dehydrate and Avicel along with Isabgol and Hydroxy methyl propyl cellulose and evaluated for their flow properties. Tablets were directly compressed in different batches using 30% Acetaminophen and 70% of different agglomerates and studied for their controlled release

characteristics of the drug. The findings favored the use of Lactose and Calcium hydrogen phosphate dehydrates in the ratio of 1:2 to get the controlled release up to 12 hours.

Panchal VM successfully formulated the extended release Acetaminophen-Psyllium husk matrix tablets and studied the influence of excipients on the drug release kinetics.⁵⁹ He used Psyllium husk as matrixing agent in drug:polymer ratio of 50:1 and the time taken to release 70% of the drug was found to be 11.6 hrs. He also observed that the increase in the polymer level decreased the drug release from the matrix due to the ability of Psyllium to form a thick gel layer at higher concentration. The addition of the soluble additives in the formulation were reported to increase the drug dissolution rate while the addition of insoluble additives decreased it. The release profile produced a good fit into the first order plot. From his studies, Panchal VM concluded that one can alter the release of Acetaminophen from Psyllium husk matrix by addition of soluble or insoluble additives in relative proportions without altering the amount of Psyllium Husk.

An investigational study was performed by Siahi-Shadbad MR and coworkers to find out the release behavior of Propranolol hydrochloride from Psyllium matrix in the presence of other hydrophilic matrix forming polymers.⁶⁰ Psyllium was used alone and in combination firstly with HPMC, then with Alginate and with Sodium carboxy methyl cellulose. Effects of the addition of different matrix former were studied on the dissolution profiles at pH 1.2 and pH 6.8. The addition of HPMC in increasing concentration was reported to cause a significant decrease in the release rate of Propranolol. On the other hand, Psyllium-Alginate matrices produced lower drug release as compared to the alginate matrix alone and Psyllium with Sodium CMC in the ratio 1:1 was found to slow down the drug release significantly as compared to the matrix formed from only Psyllium or with only Sodium CMC as retardant. From their studies, Siahi revealed that the Psyllium powder has the ability in combination with other hydrophilic polymers to produce the controlled release profile when prepared with good care and consideration.

As Gastroretentive agent

Chavanpatil M et al. in 2005 proposed a new strategy based on sustained release formulation for the development of Gastroretentive dosage form of Ofloxacin for once daily dosing.⁶¹ Different polymers such as Psyllium husk, HPMC K100M and crosspovidone alone and in combination were tried to get the floatable and swellable formulation in order to increase the Gastric residence time and to get the desired sustained release profile over a period of 24 hrs. Effect of different concentrations of the above polymers were studied on the buoyancy lag time, duration of buoyancy, dimensional stability, drug content and invitro release profile of Ofloxacin. They observed that as the concentration of Psyllium husk was increased from 75 mg to 100mg, the formulation was capable to retain its integrity upto 24hrs and the drug release was also reduced. It was thought to be due to the gelling property of the husk as it forms thick gel at higher concentration. Also the formulations containing 100 mg of the Psyllium husk showed similar pattern of the drug release as compared to the marketed formulation. The optimized formulation with composition- Ofloxacin (400mg), Psyllium husk (100mg), HPMC K100M (40mg), Sodium bicarbonate (70mg), crosspovidone (200mg), PVP K30 (20mg) and Betacyclodextrin (100mg) was subjected to stability studies as per the ICH guidelines and in vivo studies in 24 healthy volunteers. The formulation was found to be stable at all the

stability conditions and based on the in vivo performance in a parallel study design in healthy subjects, the developed formulation showed promise to be bioequivalent to the marketed product (Zanocin) with the relative bioavailability of 97.55%.

The same team in 2006 prepared a new gastroretentive sustained release delivery system of Ofloxacin with floating, swellable and bioadhesive properties using crosspovidone as swelling agent and psyllium husk, HPMC K100M to perform dual role as release retarding polymers as well as the mucoadhesive agent to get the release profile for 24 h.⁶² Formulations were evaluated for in vitro drug release profile, swelling characteristics and in vitro bioadhesion property. In vitro tablet bioadhesion studies were done using rabbit stomach tissue. The bioadhesive property of the developed formulation was found to be significant ($P < 0.005$) in combination as compared to HPMC K100M and psyllium husk alone. Effect of different concentrations of psyllium husk on in vitro release of ofloxacin were also studied and they found that as the concentration of psyllium husk increased from 75 mg to 125 mg per tablet, initial drug release as well as drug release in the latter hours was decreased as compared to the marketed formulation. The percent cumulative drug release after 2 h was reported to be 31.23 ± 1.32 (75 mg of husk), $28.98 \pm 1.08\%$ (100 mg husk) and $24.84 \pm 1.68\%$ (125 mg husk). The higher initial drug release at lower concentrations of the polymer might be due to the erosion of the outer surface of the tablet at initial hours while the gelling properties of psyllium husk could have contributed to the slow release at latter hours. The developed optimized formulation with composition Ofloxacin (400 mg) Psyllium husk (100mg) HPMC K100M (40mg) Crosspovidone (200mg) Sodium bicarbonate (70mg) Betacyclodextrin (100mg) per tablet was found to have almost similar in vitro release profile as of the marketed formulation. The similarity factor f_2 was found to be 91.12 for the developed formulation and the marketed formulation, indicating the release was almost similar to that of the marketed formulation (Zanocin). From their studies, they concluded that psyllium husk and HPMC K100M in combination can be promising polymers for gastroretentive drug delivery systems. The optimized formulation followed Higuchi kinetics while the drug release mechanism was found to be anomalous type, controlled by diffusion through the swollen matrix.

Garg R and Gupta GD Prepared and evaluated the gastroretentive floating effervescent as well as non-effervescent tablets of Acyclovir⁶³ and Silymarin⁶⁴ as model drugs for prolongation of gastric residence time.

Floating effervescent tablets were formulated by using hydroxypropyl methylcellulose K 4M, K 15M, psyllium husk as different polymers, crosspovidone and microcrystalline cellulose as swelling agents and gas generating agent like sodium bicarbonate and citric acid. Floating non-effervescent tablets were prepared by polypropylene foam powder and different matrix forming polymers like HPMC K 4M, Carbopol 934P, xanthan gum and sodium alginate. All the formulations were evaluated for floating properties, swelling characteristics and in vitro drug release studies. The drug release kinetics were evaluated using the linear regression method and was found to follow both the Higuchi and the Korsmeyer and Peppas equation. The drug release mechanism was found fickian type in most of the formulations. According to the author The developed floating tablets of Silymarin and acyclovir may be used in clinic for

prolonged drug release for at least 24 h, thereby improving the bioavailability and patient compliance.

A new gastroretentive sustained release delivery system of Atenolol with floating, swellable, and bioadhesive properties was developed by VS Belgamwar and SJ Surana using the novel effervescent agents such as citroglycine and disodium glycine carbonate.⁶⁵ They tried and optimized various release retarding polymers like psyllium husk, HPMC K15M, and a swelling agent crosspovidone in different combinations to get the release profile for 12 hours. The formulations were evaluated for physicochemical characteristics, *in vitro* drug release profile, swelling characteristics, floating capacity, and *in vitro* bioadhesive property. The *in vitro* drug release followed the Higuchi kinetics and the release mechanism was found to be of a non-Fickian type thus favoring the use of psyllium husk, HPMC K15M, and a swelling agent crosspovidone in combination, for getting sustained release of the model drug. The studies also revealed the potential for the use of citroglycine and disodium glycine carbonate as novel effervescent agents to be used in the floating drug delivery system as an alternative to commonly used effervescent agents like sodium bicarbonate and citric acid.

Liquorice along with its antitussive property has the potential for the treatment of *Helicobacter pylori* infection and gastric ulcers. Floating tablets containing aqueous extract of liquorice as drug in order to prolong the gastric residence time of drugs, to improve bioavailability, and to facilitate local drug delivery to the stomach was formulated and evaluated by HN Aswatha Ram et al.⁶⁶ Tablets of liquorice extract using psyllium husk, HPMC K100M, talc, sodium bicarbonate, and magnesium stearate were prepared, physicochemically evaluated and optimized on the basis of buoyancy time and *in vitro* drug release. *In vitro* dissolution studies for the floating tablets were carried out in 0.1N HCl at 37 °C. About 93-99% of the drug was released in 8 h. The optimized formulation released 98.3% of drug in 8 h *in vitro* with the buoyancy lag time of 3.5 min. Formulated floating tablets were found to be best fitted to Korsmeyer-Peppas model and zero-order kinetics. From their studies, Aswatha Ram et al concluded that formulations containing Psyllium husk, sodium bicarbonate and HPMC K100M in combination can be the promising polymers for gastroretentive drug delivery systems. Also that the floating tablets of aqueous extract of liquorice can be formulated as an approach to increase gastric residence time, thereby improving its bioavailability.

In their study, Asnaashari S and coworkers used metronidazole for preparing floating dosage forms that are designed to retain in the stomach for a long time for better eradication of *Helicobacter Pylori* in peptic ulcer diseases.⁶⁷ They designed various formulations using multi-factorial design. HPMC, psyllium and carbopol in different concentrations alone and in combinations were used as floating agents, and sodium bicarbonate was added as effervescent agent. The tablets were assessed for hardness, friability, drug loading; floating ability and release profiles as well as kinetics of drug release. Formulations containing HPMC alone showed prolonged lag times for buoyancy. Adding psyllium to these formulations had significantly reduced relative lag times. The developed formulations were able to float immediately and showed buoyancy for at least 8h. The sustained profiles of the 10 models were assessed and the kinetics of the release pattern of metronidazole from the tablets fitted best to Power law, Weibull model and Higuchi models in respect overall to mean percentage error values of

3.8, 4.73 and 5.77, respectively for calcium carbonate-based tablets and 2.95, 6.39 and 3.9 respectively, for calcium silicate-based tablets. The author suggested that these systems of metronidazole were able to float in the gastric condition and could control the drug release from the tablets.

Kharia AA et al. designed and optimized floating drug delivery systems of acyclovir using psyllium husk and hydroxypropylmethylcellulose K4M as the polymers and sodium bicarbonate as a gas generating agent in order to deliver the drug at a controlled rate to its absorption site so that its oral bioavailability can be enhanced.⁶⁸ The designed floating drug delivery systems were optimized using 3² full factorial design and the tablets from nine different batches were evaluated for all Pharmacopoeial tests and also for swelling index, floating lag time, *in vitro* buoyancy behavior and drug-polymer interaction. The effect of two independent variables i.e. the amount of Psyllium husk and hydroxypropylmethylcellulose K4M were studied on the times required for 50% ($t_{(50\%)}$) and 70% ($t_{(70\%)}$) drug dissolution. Validity of the developed polynomial equation was verified by designing two check point formulations. The predicted and observed values for $t_{(50\%)}$ and $t_{(70\%)}$ were found to be very close which indicated the validity of derived equations for the dependent variables. The optimized formulations followed Higuchi's kinetics while the drug release mechanism was found to be anomalous type, controlled by diffusion through the swollen matrix. Thus the studies revealed that the hydrophilic polymers such as HPMC K4M and Psyllium husk plays an important role in formulation of FDDS. As the amount of the polymers in the formulation increases, the drug release rate decreases. The proper balance between the concentrations of two polymers can produce a drug dissolution profile similar to the predicted one.

As Disintegrant

The disintegrating property of *Plantago ovata* mucilage was evaluated by Prajapati et al.⁶⁹ They prepared dispersible tablet of Nimesulide with wet granulation technique. They found that the mucilage was effective at low concentration as superdisintegrant. Further, the results revealed that disintegrant property of isabgol mucilage was equivalent to Ac-Di-Sol and superior to sodium starch glycolate.

Chakraborty S et al. carried out a comparative study of natural superdisintegrant over the synthetic counterpart and obtained the similar results.⁷⁰ They prepared fast dissolving tablets of aceclofenac by direct compression method employing microcrystalline cellulose as a diluent and isabgol or Ac-Di-Sol or sodium starch glycolate as the disintegrant. The study attributed the better disintegrating property of isabgol mucilage over the Ac-Di-Sol and sodium starch glycolate and also to the higher swelling index of isabgol mucilage as compared to the Ac-Di-Sol and sodium starch glycolate.

The reduction in the disintegration time of conventional tablets from 10 minutes to a minimum of 23 seconds was observed and reported by Tahir MA et al after addition of just 2-5% of dried isabgol extract in their formulation of Diclofenac Sodium tablets.⁷¹ Tablets were formulated by both wet granulation method and direct compression method. Superdisintegrant features of isabgol were further optimized by water absorption and *in vitro* dispersion time. Dissolution profiles suggested that the superdisintegrants action of the dried Isabgol mucilage enhanced the release of the drug from tablets with respect to conventional marketed. Also the studies suggested that directly compressed tablets released

drug more rapidly as compared to those prepared by wet granulation process.

Gokul Ghenge et al. also attempted to develop and characterize Fast Disintegrating Tablet of Amlodipine besylate using mucilage of *Plantago ovata* as a natural Superdisintegrant by direct compression method using different concentrations of Psyllium mucilage.⁷² The optimized formulations showed very less in vitro disintegration time of only 11.69sec with rapid in vitro dissolution within 16 mins. Also they found that In vitro disintegration time decreases with increase in concentration of Psyllium mucilage. From the results of their study, they suggested the use of *Plantago ovata* mucilage as a natural superdisintegrant.

As Microparticals

Unique microparticals of Isoniazid with the walls formed from alkaline extracted Ispaghula husk were prepared by Maurya DP et al. and reported in 2011.⁷³ The team optimized the formulation after studying the effect of four independent variables (viz. Sodium alginate concentration, concentration of alkaline extract of Ispaghula husk, concentration of cross linking agent and stirring speed) on the particle size and entrapment efficiency. The optimized formulation at conditions – Sodium alginate (3.55% w/v), Alkaline extracted Ispaghula Husk (3.60% w/v), cross linker concentration (7.82% w/v) and at stirring speed of 1200rpm was found to exhibit 83.43% of total drug entrapment with validity of 97.80% in the particles of size 51.53 μ m (validity = 96.37%). The drug release profile of the formulated microparticals was studied following Higuchi kinetics and the optimized formulation showed the controlled release of the Isoniazid for more than 12 hrs via non-Fickian diffusion. The In vivo gamma scintigraphy study was also performed on Wister rats and the presence of the microparticals was observed in the intestinal lumen after 1 hr and were retained in the intestine upto 12 hrs. showing decreased radioactivity % age.

CONCLUSION

After reviewing and summarizing the above reported research studies, it can be concluded that the Psyllium possesses the dual potential in pharmaceuticals. Initially its use was limited as a natural drug. But with the need of replacing the synthetic excipients with more economical, renewable, biocompatible and easily available counterparts, Psyllium seems to be promising to modulate drug release in required manner either in the form of hydrogel or microparticals. On one hand it is capable to retard the release rate of the active agent while at the other hand it possesses the superdisintegrant property. Hence its varying potentials can be exploited to design so called tailor made formulations.

REFERENCES

- Zatz JL and Kushla GP. "Gels". In: Pharmaceutical dosage forms- Disperse systems. M. M. Reiger and G.S. Banker, Ed 9 New York: Marcel Dekker Inc. 1996: 399-421.
- Whistler, R.L. "Polysaccharides and their derivatives" In: Industrial gums, 3 Ed, 1999 Academic Press, London. Page 766.
- Kakrani, H.K. and Jain N.K. A study on binding properties of guggal gum. Indian J Hospital Pharmacist 1981 XVIII(3): 100-02.
- Bhunvara, N.S. and Khorana M.L. Studies on suspending properties of *Hypophylla spinosa*. Indian Drugs 1985; 22: 500-02.
- Kulkarni, G.T., Gowthamarajan K, Dhobe R R, Yohanand F and Suresh B. Development of controlled release spheroids using natural polysaccharide as release modifier. Drug Deliv 2005; 12: 201-06.
- Blumenthal M., Goldberg A., Brinkmann J. Herbal Medicine, Expanded Commission E Monographs 2000. Cd-Rom. American Botanical Council, Integrative Medicine, Austin, TX.
- Kennedy JF, Sandhu JS, Southgate DAT. Structural data for the carbohydrate of ispaghula husk ex *Plantago ovata* Forsk. Carbohydr Res 1999; 75: 265-74.
- Laidlaw RA, Purcival EGV. Studies of seed mucilages. Part V. Examination of a polysaccharide extracted from the seeds of *Plantago ovata* Forsk by hot water. J Chem Soc 1950; 528-34.
- Sandhu JS, Hudson GJ, Kennedy JF. The gel nature and structure of the carbohydrate of ispaghula husk ex *Plantago ovata* Forsk. Carbohydr. Res. 1981; 93: 247-59.
- Bouchoucha M, Faye A, Savarieau B, Arsac M. Effect of an oral bulking agent and a rectal laxative administered alone or in combination for the treatment of constipation. Gastroenterol Clin Biol 2004; 28: 438-43.
- Ramkumar D, Rao SS. Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. Am J Gastroenterol 2005; 100: 936-71.
- Washington N, Harris M, Mussellwhite A, Spiller RC. Moderation of lactulose-induced diarrhea by psyllium: effects on motility and fermentation. Am J Clin Nutr 1998; 67: 317-21.
- Kumar A, Kumar N, Vij JC, Sarin SK, Anand BS. Optimum dosage of ispaghula husk in patients with irritable bowel syndrome: correlation of symptom relief with whole gut transit time and stool weight. Gut 1987; 28: 150-55.
- Qvitzau S, Matzen P, Madsen P. Treatment of chronic diarrhoea: loperamide versus ispaghula husk and calcium. Scand J Gastroenterol 1988; 23: 1237-40.
- Cebra ML, Garry FB, Cebra CK, Adams R, McCann JP, Fettman MJ. Treatment of neonatal calf diarrhea with an oral electrolyte solution supplemented with psyllium mucilloid. J Vet Inter Med 1998; 12: 449-55.
- Neiffer DL. Clostridium perfringens enterotoxigenesis in two Amur leopards (*Panthera pardus orientalis*). J Zoo Wildlife Med 2001; 32: 134-35.
- Leib MS. Treatment of chronic idiopathic large-bowel diarrhea in dogs with a highly digestible diet and soluble fiber: a retrospective review of 37 cases. J Vet Intern Med 2000; 14: 27-32.
- Belknap D, Davidson LJ, Smith CR. The effects of psyllium hydrophilic mucilloid on diarrhea in enterally fed patients. Heart Lung 1997; 26: 229-37.
- Hallert C, Kaldma M, Petersson BG. Ispaghula husk may relieve gastrointestinal symptoms in ulcerative colitis in remission. Scand J Gastroenterol 1991; 26: 747-50.
- Fernandez-Banares F, Hinojosa J, Sanchez-Lombrana JL, Navarro E, Martinez-Salmeron JF, Garcia-Puges, A. et. al. Randomized clinical trial of *Plantago ovata* seeds (dietary fiber) as compared with mesalamine in maintaining remission in ulcerative colitis. Spanish Group for the Study of Crohn's Disease and Ulcerative Colitis (GETECCU). Am J Gastroenterol 1999; 94: 427-33.
- Arthurs Y, Fielding JF. Double blind trial of ispaghula/poloxamer in the Irritable Bowel Syndrome. Ir Med J 1983; 76: 253.
- Greenbaum DS, Stein GE. Psyllium and the irritable bowel syndrome. Ann Intern Med 1981; 95: 660.
- Agarwal BD. Irritable bowel syndrome: clinical presentations, enema users and dosage schedules of Ispaghula. J Assoc Phys India 1990; 38: 604.
- Tomas-Ridocci M, Anon R, Minguez M, Zaragoza A, Ballester J, Benages A. The efficacy of *Plantago ovata* as a regulator of intestinal transit. A double-blind study compared to placebo. Rev. Esp. Enferm. Dig. 1992; 82: 17-22.
- Prior A, Whorwell PJ. Double blind study of ispaghula in irritable bowel syndrome. Gut 1987; 28: 1510-13.
- Juarranz M, Calle-Purón ME, Gonzalez-Navarro A, Regidor-Poyatos E, Soriano T, Martinez-Hernandez D et. al. Physical exercise, use of *Plantago ovata* and aspirin, and reduced risk of colon cancer. Eur J Cancer Prev 2002; 11: 465-72.
- Moreno LA, Tresaco B, Bueno G, Fleta J, Rodriguez G, Garagorri JM et. al. Psyllium fibre and the metabolic control of obese children and adolescents. J Physiol Biochem 2003; 59: 235-42.
- Pittler MH, Ernst E. Dietary supplements for body-weight reduction: a systematic review. Am J Clin Nutr 2004; 79: 529-36.
- Florholmen J, Arvidsson-Lenner R, Jorde R, Burhol PG. The effect of Metamucil on postprandial blood glucose and plasma gastric inhibitory peptide in insulin-dependent diabetics. Acta Med Scand 1982; 212: 237-39.
- Uribe M, Dibildox M, Malpica S, Guillermo E, Villalobo, A, Nieto L et. al. Beneficial effect of vegetable protein diet supplemented with psyllium plantago in patients with hepatic encephalopathy and diabetes mellitus. Gastroenterology 1985; 88: 901-07.
- Watters K, Blaisdell P. Reduction of glycemic and lipid levels in db/db diabetic mice by psyllium plant fiber. Diabetes 1989; 38: 1528-33.
- Pastors JG, Blaisdell PW, Balm TK, Asplin CM, Pohl SL. Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in

- patients with non-insulin-dependent diabetes. *Am J Clin Nutr* 1991; 53:1431-35.
33. Wolever TM, Vuksan V, Eshuis H, Spadafora P, Peterson RD, Chao ES, Storey et. al. Effect of method of administration of psyllium on glycemic response and carbohydrate digestibility. *J Am Coll Nutr* 1991;10: 364-71.
 34. Fukagawa NK, Anderson JW, Hageman G, Young VR, Minaker KL. High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. *Am J Clin Nutr* 1990;52: 524-28.
 35. Gupta RR, Argawal CG, Singh GP, Ghatak A. Lipid-lowering efficacy of psyllium hydrophilic mucilloid in non insulin dependent diabetes mellitus with hypercholesterolemia. *Indian J Med Res* 1994;100: 237-41.
 36. Brennan CS. Dietary fibre, glycaemic response, and diabetes. *Mol Nutr Food Res* 2005; 49: 560-70.
 37. Ziai SA, Larijani B, Akhoondzadeh S, Fakhrzadeh H, Dastpak A, Bandarian F et. al. Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J Ethnopharmacol* 2005; 102: 202-07.
 38. Clark CA, Gardiner J, McBurney MI, Anderson S, Weatherspoon LJ, Henry DN et.al. Effects of breakfast meal composition on second meal metabolic responses in adults with type 2 diabetes mellitus. *Eur J Clin Nutr* 2006; 60: 610-16.
 39. Rodriguez-Moran M, Guerrero-Romero F, Lazcano-Burciaga G. Lipid- and glucose-lowering efficacy of *Plantago psyllium* in type II diabetes. *J Diabetes Complicat* 1998; 12: 273-78.
 40. Anderson JW, Allgood LD, Turner J, Oeltgen PR, Daggy BP. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. *Am J Clin Nutr* 1999;70: 466-73.
 41. Anderson JW, Davidson MH, Blonde L, Brown WV, Howard WJ, Ginsberg H et. al. Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. *Am J Clin Nutr* 2006 (a); 71: 1433-38.
 42. Anderson JW, Allgood LD, Lawrence A, Altringer LA, Jerdack GR, Hengehold DA. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia:meta-analysis of 8 controlled trials. *Am J Clin Nutr* 2000 (b); 71: 472-79.
 43. Oliver SD. The long-term safety and tolerability of ispaghula husk. *J. R. Soc. Health* 2000; 120:107-11.
 44. Romero AL, West KL, Zern T, Fernandez ML. The seeds from *Plantago ovata* lower plasma lipids by altering hepatic and bile acid metabolism in guinea pigs. *J. Nutr.* 2002;132: 1194-98.
 45. Moreyra AE, Wilson AC, Koraym A. Effect of combining psyllium fiber with simvastatin in lowering cholesterol. *Arch. Int. Med.* 2005;165: 1161-66.
 46. Van Rosendaal GM, Shaffer EA, Edwards AL, Brant R. Effect of time of administration on cholesterol-lowering by psyllium: a randomized cross-over study in normocholesterolemic or slightly hypercholesterolemic subjects. *Nutr. J.* 2004;28: 17.
 47. Ziai SA, Larijani B, Akhoondzadeh S, Fakhrzadeh H, Dastpak A, Bandarian F et. al. Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J. Ethnopharmacol.* 2005; 102(2):202-07
 48. Reynolds JEF. Martindale- The Extra Pharmacopoeia, 30th ed. 1993; Pharmaceutical Press, London.
 49. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy, 30th ed. 2005; Nirali Prakashan, Pune.
 50. Mishra A, Rajani S, Agarwal M, Dubey R. *P.psyllium*-g-polyacrylamide: Synthesis and characterization. *Polymer Bulletin* 2002;48:439-44.
 51. Singh B, Chauhan GS, Kant A, Gupta I, Chauhan N. The release dynamics of model drugs from the psyllium and N-hydroxymethylacrylamide based hydrogels. *Int J Pharm.* 2006;325(1-2):15-25.
 52. Singh B, Chauhan N, Kumar S, Bala R. Psyllium and copolymers of 2-hydroxyethylmethacrylate and acrylamide-based novel devices for the use in colon specific antibiotic drug delivery. *Int J Pharm.* 2008; 352(1-2):74-80.
 53. Singh B, Bala R, Chauhan N. In vitro release dynamics of model drugs from psyllium and acrylic acid based hydrogels for the use in colon specific drug delivery. *J Mater Sci Mater Med* 2008; 19(8):2771-80.
 54. Singh B, Sharma V. Design of psyllium-PVA-acrylic acid based novel hydrogels for use in antibiotic drug delivery. *Int J Pharm* 2010; 389(1-2):94-106.
 55. Singh B, Lal H, Pal L, Sharma V. In vitro release profile of anti-ulcer drug rabeprazole from biocompatible psyllium-PVA hydrogels. *J Mater Sci Mater Med* 2012 ;23(4):1021-32.
 56. Deepak Prashar, Shalini Sharma, Sukhbir Lal Khokra. Synthesis, characterization and electrical stimulus sensitive behavior of psy-cl-poly(AA) Hydrogel. *Pharma science monitor-An international journal of pharmaceutical sciences* 2011; available at www.pharmasm.com: 1838-45.
 57. Desai A, Shidhaye S, Kadam VJ. Possible use of Psyllium husk as a release retardant. *IJPS* 2007;69(2):206-10.
 58. Lalwani AN, Parikh JR. Preparation and evaluation of an ispaghula based directly compressible matrixing agent for controlled release. *Acta Pharm* 2008;58(3):309-16.
 59. Panchal Vishal M. Extended release acetaminophen-psyllium husk matrix tablets and influence of excipients on drug release kinetics. *ProQuest Dissertations and Theses 2010*; UMI no. 1487604.
 60. Siah-Shadbad MR, Asare-Addo K, Azizian K, Hassanzadeh D, Nokhodchi A. Release behaviour of propranolol HCl from hydrophilic matrix tablets containing psyllium powder in combination with hydrophilic polymers *AAPS PharmSciTech* 2011;12(4):1176-82.
 61. Chavanpatil M, Jain P, Chaudhari S, Shear R, Vavia PV. Development of sustained release gastroretentive drug delivery system for ofloxacin: In vitro and in vivo evaluation. *International Journal of Pharmaceutics* 2005; 304: 178-84.
 62. Chavanpatil M, Jain P, Chaudhari S, Shear R, Vavia PV. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin *International Journal of Pharmaceutics* 2006; 316: 86-92.
 63. Garg R, Gupta GD. Preparation and evaluation of gastroretentive floating tablets of acyclovir. *Curr Drug Deliv* 2009;6(5):437-43.
 64. Garg R, Gupta GD. Preparation and evaluation of gastroretentive floating tablets of Silymarin. *Chem Pharm Bull (Tokyo)* 2009;57(6):545-49.
 65. Belgamwar VS, Surana SJ. Floating bioadhesive drug delivery system using novel effervescent agents. *Asian J Pharm* 2009;3:156-60.
 66. Aswatha Ram HN, Lachake P, Kaushik U, Shreedhara CS. Formulation and evaluation of floating tablets of liquorice extract. *Phcog Res* 2010; 2(5):304-08.
 67. Asnaashari S, Khoei NS, Zarrintan MH, Adibkia K, Javadzadeh Y. Preparation and evaluation of novel metronidazole sustained release and floating matrix tablets *Pharm Dev Technol* 2011;16(4):400-7.
 68. Kharia AA, Hiremath SN, Singhai AK, Omray LK, Jain SK. Design and optimization of floating drug delivery system of acyclovir *Indian J Pharm Sci* 2010;72(5):599-606.
 69. Prajapati ST, Prajapati VD, Acharya SR, Patel CN. Characterization of disintegration properties of *Plantago ovata* mucilage in the formulation of dispersible tablet *Ind. J. Pharm. Edu. Res* 2006;40(3):208-11.
 70. Chakraborty S, Khandai M, Singh SP, Patra NC. Comparative study on effect of natural and synthetic super-disintegrants in the formulation of fast dissolving tablets. *Int. J. Green Pharm* 2008;2(1): 22-25.
 71. Tahir MA, Awadhesh K, Swati S, Sant S, Sajid MA, Pattnaik GD, Farheen. Optimization of fast disintegrating tablets for Diclofenac sodium using Isabgol mucilage as super disintegrant. *Int. J. Ph. Sci.* 2010; 2(2):496-501.
 72. Ghenge G, Pande SD, Ahmad A, Jejurkar L, Birari T. Development and Characterisation of Fast Disintegrating Tablet of Amlodipine besylate using Mucilage of *Plantago ovata* as a Natural Superdisintegrant. *International Journal of PharmTech Research* 2011;3(2):938-45.
 73. Maurya DP, Sultana Y, Aqil M, Kumar D, Chuttani K, Ali A, Mishra AK. Formulation and optimization of alkaline extracted ispaghula husk microparticles of isoniazid - in vitro and in vivo assessment *J Microencapsul* 2011;28(6):472-82.