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Dual Potential of Dietary Fiber Psyllium as a Laxative for Constipation Relief and Healthy Bowel Function

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Abstract:

The beneficial effects of dietary fibre on bowel function have long been recognized. In addition to promoting regular bowel movements, dietary fibre provides several health benefits that have attracted considerable interest from researchers, healthcare professionals, and the food and pharmaceutical industries. Non-digestible polysaccharides (NDPs) and non-digestible oligosaccharides (NDOs), naturally present in many foods, possess unique physicochemical and biological properties that support physiological functions in both the small and large intestines. These properties also improve the organoleptic characteristics and nutritional quality of food products.Psyllium is a natural polysaccharide-based dietary fibre obtained from the dried, ripe seeds of *Plantago* species. It is a white, fibrous, hydrophilic material that absorbs water to form a colourless mucilaginous gel. Due to its high water-holding capacity, psyllium is widely used as a bulk-forming laxative for relieving constipation and maintaining healthy bowel function.The present study investigates the dual potential of psyllium-based hydrogels (Psy-cl-poly(AAM)) as a controlled drug delivery system for the model drug Dulcoflex (bisacodyl). Bisacodyl(BD) is a stimulant laxative that enhances bowel evacuation by stimulating intestinal muscle contractions. The prepared hydrogels were characterized for their swelling behaviour and drug release properties. In vitro release studies were performed to evaluate the cumulative release profile of bisacodyl. The results demonstrated that Psy-c*l*-poly(AAM) hydrogels exhibit excellent swelling capacity and sustained drug release, indicating their potential as effective carriers for controlled drug delivery to the lower intestine and colon.

Keywords: *Polysaccharides, Slow release formulations, Controlled Release, Dietary Fiber*

INTRODUCTION

Constipation is a prevalent gastrointestinal disorder affecting approximately 20% of the global population and is associated with reduced quality of life and an increased risk of colon cancer [1,2]. Current management strategies include lifestyle modifications, such as increased fluid intake and regular physical activity, as first-line interventions; however, evidence supporting their efficacy remains limited [3]. Although laxatives are the mainstay of pharmacological treatment, their prolonged use may be associated with adverse effects, highlighting the need for safer and more effective therapeutic alternatives [4,5].

Dietary fiber has emerged as a promising non-pharmacological intervention for constipation. Soluble fiber absorbs water to form a viscous gel that is fermented by the gut microbiota, whereas insoluble fiber increases stool bulk and accelerates intestinal transit [6]. Owing to these physiological

effects, increased dietary fiber intake is widely recommended for the prevention and management of constipation in both children and adults [7–9]. Consistent with these recommendations, a large population-based case–control study by Rome et al. reported an independent inverse association between dietary fiber intake and chronic constipation, irrespective of age or age at symptom onset [10].

Psyllium polysaccharides, due to their therapeutic importance, can be effectively utilized in polymeric hydrogel-based drug delivery systems when suitably modified. Graft polymerization of vinyl monomers enables the incorporation of functional polymer chains into the backbone structure.In this study, psyllium-based and poly(acrylamide) [poly(AAm)] hydrogels were synthesized using N,N′-methylenebisacrylamide (MBAAm) as a crosslinker and ammonium persulfate (APS) as an initiator. These hydrogels were evaluated as drug delivery systems using bisacodyl (Dulcoflex) as a model drug. The in vitro drug release behavior was analyzed in different media to understand the release mechanism and diffusion characteristics.

2. EXPERIMENTAL

2.1 Materials and Methods

Plantago psyllium mucilage (Psy) was procured from Sidpur Sat Isabgol Factory, Gujarat, India. Acrylamide was obtained from Merck-Schuchardt, Germany. Ammonium persulfate (APS) and N,N′-methylenebisacrylamide (NN-MBAAm) were purchased from S.D. Fine Chemicals, Mumbai, India, and used without further purification. Drug powder (purity over 99%) was purchased from Dishman (Ahmedabad, India).

2.2. Synthesis of Psy-*cl*-poly(AAM) Hydrogel

The optimum reaction conditions for the modification of psyllium to hydrogels have been discussed somewhere else [12]. Reaction was carried out with 1g of psyllium husk, 1.095×10^{-2} moles/L of APS, 3.52×10^{-1} moles /L of AAm, 9.73×10^{-3} moles /L of N,N-MBAAm in the aqueous reaction system at 65^{o}C temperature for 2h. Polymer thus former was stirred for two hour in distilled water and for two hour in ethanol to remove the soluble fraction and then was dried in air oven at 40^{o}C. The resultant polymeric network Psy-*cl*-poly(AAM)hydrogel , was used to study the release dynamics of the Dulcoflex from the drug loaded hydrogels.

2.3 Swelling Kinetics

Swelling kinetics of the polymeric networks was carried out in different pH solution by gravimetric method. Known weight of polymers were taken and immersed in excess of solvent for different time intervals at 37^{o}C and then polymers were removed, wiped with tissue paper to remove excess of solvent, and weighed immediately. The difference in weight will give the gain in weight at different time intervals.

2.4 Preparation Calibration Curves

The absorbance of a number of standard solutions of the reference substance at concentrations encompassing the sample concentrations were measured on the UV-Visible Spectrophotometer and calibration graph was constructed. The concentration of the drug in the sample solution was read from the graph as the concentration corresponding to the absorbance of the solution. Three calibration graphs of Dulcoflex were made to determine the amount of drug release from the drug loaded polymeric matrix in different medium (distilled water, pH2.2 buffer and pH7.4 buffer).

2.5 Drug loading to the polymeric hydrogels

The loading of a drug onto hydrogels was carried out by swelling equilibrium method. The hydrogel**s** were allowed to swell in the drug solution of known concentration for 24h at 37ºC and dried to obtain the release device.

2.6 Drug release from the hydrogels

In the release dynamics studies of the drug have been carried out by keeping dried and loaded sample in definite volume of releasing medium at 37ºC temperature. The amount of insulin released was assayed using Lowry methods and measured spectrophotometrically by taking the absorbance of the solution after every 30min. at wavelength 264nm in acidic medium (pH2.2buffer) and at 268nm for release in distilled water and pH7.4 buffer. The drug release was measured after fixed interval of time and release dynamics of drug was studied.

3. RESULTS AND DISCUSSION

Hydrogels were synthesized chemically by free radical polymerization technique. APS has generated the reactive sites, both on the psyllium and monomers, leading to the propagation of the reaction. In the presence of crosslinker NN-MBAAm (CH_2=CHCONHCH$_2$ NHCOCH=CH_2), because of its poly-functionality, a new macro-radical get formed that has four reactive sites and these sites can be linked both with the radical on the psyllium and the poly(AAm).The resultant three-dimensional polymeric networks i.e Psy-*cl*-poly(AAm)hydrogel, were used to study the in vitro release dynamics of the model drug Dulcoflex (bisacodyl**)**

3.1. Mechanism for swelling and drug release from hydrogels

In the hydrogels system, absorption of water from the environment changes the dimensions and physicochemical properties of the system and thus the drug release kinetics. Polymeric matrix consists of three zones that is adjacent to the bulk water is a layer of completely swollen gel and then there is a thin layer in which the polymer chains are slowly hydrating and relaxing. The third zone is un-swollen, completely dried, rigid polymer. The diffusion of water in hydrogels was classified into three different types based on the relative rates of diffusion and polymer relaxation. This classification of the diffusion of water in hydrogels can also be used to classify the drug release profiles from the swelling polymer .This classification is given as follows [11].

3.2. Mathematical modeling of drug release

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 the case of water uptake, the weight gain, M_s, is described by the following empirical equations:

$$M_S = kt^n \qquad (1)$$

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 . Ritger and Peppas [12] showed that the above power law expression could be used for the evaluation of drug release from swellable systems. In this case, M_t/ M_∞ replace M_s in above equation to give

$$\frac{M_t}{M_\infty} = kt^n \qquad (2)$$

Where M_t/M_∞ is the fractional release of drug in time *t, 'k' is* the constant characteristic of the drug-polymer system, and 'n' is the diffusion exponent characteristic of the release mechanism. When the plot is drawn between ln M_t/M_∞ and ln t, the slope of the Plot gives the value of 'n' and intercept will tell about k. This equation applies until 60% of the total amount of drug is released. It predicts that the fractional release of drug is exponentially related to the release time and it adequately describes the release of drug from slabs, spheres, cylinders and discs from both swellable and non-swellable matrices. The values of 'n' and 'k' have been evaluated for the release dynamics drug and results are presented in Table 1.

3.3. Diffusion coefficients

Fick's first and second laws of diffusion adequately describe the most diffusion processes. For cylindrical shaped hydrogels the integral diffusion is given in simple equation (3) by Ritger and Peppas [12]

$$\frac{M_t}{M_\infty} = 4\left(\frac{Dt}{\pi \ell^2}\right)^{0.5} \qquad (3)$$

Where (M_t/ M_∞) is the fractional release and M_t and M_∞ is drug released at time 't' and at equilibrium respectively, D is the diffusion coefficient and l is the thickness of the sample. In equation (3) the slope of linear plot between (M_t/ M_∞) and $t^{1/2}$ yield diffusion coefficient D. Therefore, initial diffusion coefficient D_i was evaluated from the slope of the plot.

The average diffusion coefficient D_A may also be calculated for 50% of the total release by putting $M_t/M_\infty = 0.5$ in the equation (3), which finally yields (4)

$$D_A = \frac{0.049\ell^2}{t^{1/2}} \qquad (4)$$

Where $t^{1/2}$ is the time required for 50% release of drug.

Late diffusion coefficients were calculated using the late-time approximation as described by Peppas et al.given in equation 5 .

$$\frac{M_t}{M_\infty} = 1 - \left(\frac{8}{\pi^2}\right)\exp\left[\frac{(-\pi^2 Dt)}{\ell^2}\right] \qquad (5)$$

The slope of the plot between ln(1-M_t/M_∞) and t was used for the evaluation of D_L.

The values of Diffusion coefficients for the drug release dynamics have been evaluated and results are presented in Table 1.

3.5 Release dynamics of model drug Dulcoflex (bisacodyl), from drug loaded hydrogels:

The release of model drug, entrapped in a polymeric hydrogels, occur only after water penetrates the network to swell the polymer and dissolve the drug, Dulcoflex (bisacodyl)followed by diffusion along the aqueous pathways to the surface of the device. The release profile of Dulcoflex (bisacodyl) from per grams of the drug-loaded hydrogels has been shown in the fig.1. The amount of drug release in pH 7.4 buffer and distilled water was higher than the release medium of pH2.2 buffer. The swelling of hydrogels [psy-*cl*-poly(AAm) increased when the pH of the medium changed from pH2.2 to pH7.4 At lower pH the -$CONH_2$ groups does not ionized and keep the network at its collapsed state. At high pH values, it gets partially ionized, and the charged -COO^- groups repel each other, leading to the higher swelling of the polymer and resultant to more drug release. From the slope and intercept of the plot of ln M_t/M_∞ versus ln t, the diffusion exponent 'n' and gel characteristic constant 'k' .

As the values of 'n' are between 0.5 and 1.0 for the release of drug in distilled water and pH7.4 buffer which indicates a non- Fickian or anomalous diffusion mechanism for the release of drug from the polymer matrix in these mediums. It means that the rate of polymer chain relaxation and the rate of drug diffusion from these hydrogels are comparable. The values of the initial diffusion coefficient for the release of drug(BD) was observed to be higher than the value of average and late time diffusion coefficient in each release medium indicating that in the start, rate of diffusion of drug from the polymeric matrix was higher Table 1.

4. CONCLUSION

In summary, the development of acrylamide based Psyllium-*cl*-poly(acrylamide) [Psy-cl-poly(AAm)] hydrogels for the delivery of the model drug Dulcoflex highlights their potential as effective carriers for colon-specific drug delivery of laxatives. The combination of psyllium and acrylamide results in a hydrogel system capable of providing controlled and sustained release of therapeutic agents, making it well-suited for targeted delivery to the colon. Additionally, the drug release behavior reveals that the release mechanism follows a non-Fickian diffusion pattern in both distilled water and pH 7.4 buffer solutions. This indicates that the rates of drug diffusion and polymer chain relaxation are comparable, thereby contributing to the overall controlled release characteristics of the hydrogel system.

REFERENCES

[1].Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. Am J Gastroenterol. 2004;99:750–759. doi: 10.1111/j.1572-0241.2004.04114.x. [DOI] [PubMed] [Google Scholar]

[2].Watanabe T, Nakaya N, Kurashima K, Kuriyama S, Tsubono Y, Tsuji I. Constipation, laxative use and risk of colorectal cancer: The Miyagi Cohort Study. Eur J Cancer. 2004;40:2109–2115. doi: 10.1016/j.ejca.2004.06.014. [DOI] [PubMed] [Google Scholar]

[3].Johanson JF. Review of the treatment options for chronic constipation. MedGenMed. 2007;9:25. [PMC free article] [PubMed] [Google Scholar]

[4].Xing JH, Soffer EE. Adverse effects of laxatives. Dis Colon Rectum. 2001;44:1201–1209. doi: 10.1007/BF02234645. [DOI] [PubMed] [Google Scholar]

[5].Wald A. Is chronic use of stimulant laxatives harmful to the colon? J Clin Gastroenterol. 2003;36:386–389. doi: 10.1097/00004836-200305000-00004. [DOI] [PubMed] [Google Scholar]

[6].Anderson JW, Baird P, Davis RH, Ferreri S, Knudtson M, Koraym A, Waters V, Williams CL. Health benefits of dietary fiber. Nutr Rev. 2009;67:188–205. doi: 10.1111/j.1753-4887.2009.00189.x. [DOI] [PubMed] [Google Scholar]

[7].Loening-Baucke V. Chronic constipation in children. Gastroenterology. 1993;105:1557–1564. doi: 10.1016/0016-5085(93)90166-a. [DOI] [PubMed] [Google Scholar]

[8].Marlett JA, McBurney MI, Slavin JL. Position of the American Dietetic Association: health implications of dietary fiber. J Am Diet Assoc. 2002;102:993–1000. doi: 10.1016/s0002-8223(02)90228-2. [DOI] [PubMed] [Google Scholar]

[9].Jenkins DJ, Jenkins AL. The clinical implications of dietary fiber. Adv Nutr Res. 1984;6:169–202. doi: 10.1007/978-1-4613-2801-8_7. [DOI] [PubMed] [Google Scholar]

[10].Roma E, Adamidis D, Nikolara R, Constantopoulos A, Messaritakis J. Diet and chronic constipation in children: the role of fiber. J Pediatr Gastroenterol Nutr. 1999;28:169–174. doi: 10.1097/00005176-199902000-00015. [DOI] [PubMed] [Google Scholar]

[11]. Baljit S, Nirmala C, Modification of psyllium polysaccharides for use in oral insulin delivery"Food Hydrocolloids 23 (2009) 928–935.
[12]. Ritger. P.L, Peppas,N.A, A simple Equation for Description of Solute Release I. Fickian and Non-Fickian Release from Non-Swellable Devices in the Form of Slabs, Spheres, Cylinders or Discs" J. Contr. Rel. 5 (1987) 23-36.

FIGURE AND TABLE:

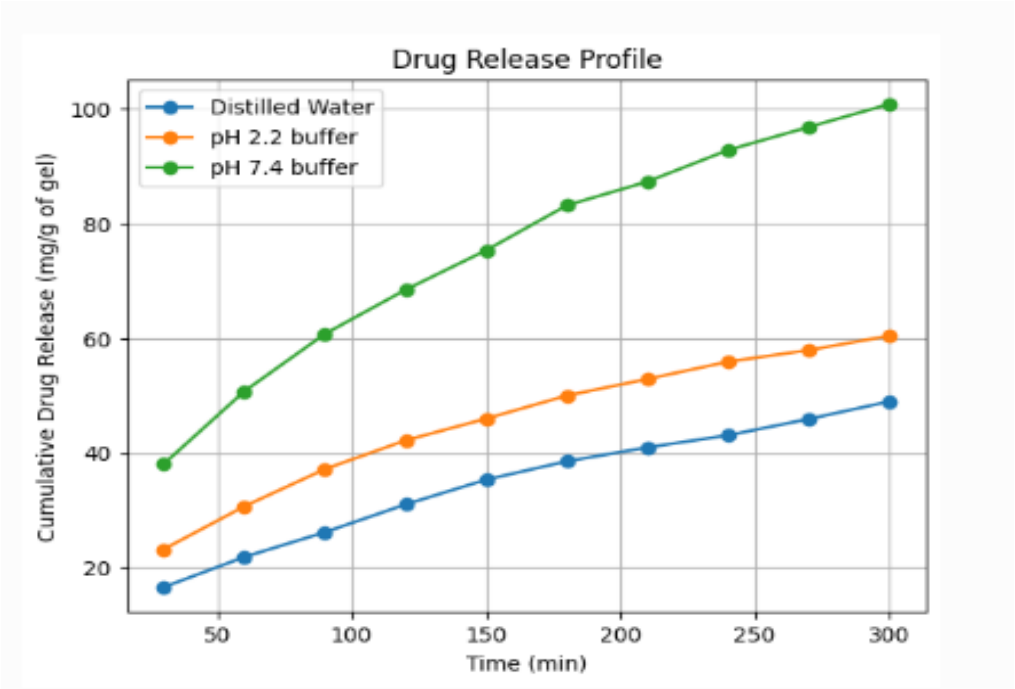

Fig.1. Cumulative release of model drug Dulcoflex (bisacodyl)from Psy-*cl*-Poly(AAm)hydrogels

Table 1: Results of diffusion exponent 'n', gel characteristic constant 'k' and various diffusion coefficients for the release of model drug Dulcoflex (bisacodyl) from drug loaded psy-*cl*-poly(AAm) based hydrogels in different medium at 37^0C.

Drug in releasing medium	Diffusion exponent 'n'	Gel characteristic constant 'k'×10^2	Diffusion coefficients (cm^2/min)		
			Initial $D_i \times 10^4$	Average $D_A \times 10^4$	Late Time $D_L \times 10^4$
Distilled Water	1.20	0.06	2.15	11.50	1.43
pH 2.2 buffer	0.70	0.91	1.37	10.11	1.25
pH 7.4 buffer	0.61	2.0	1.05	9.52	1.05

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