

# Design of dietary fiber psyllium-sterculia gum based hydrogels for use in controlled drug delivery applications

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## Abstract

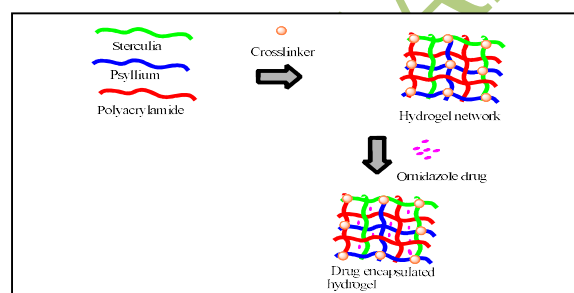
The dietary fibers psyllium-sterculia gum have therapeutic roles in diarrhea, therefore, herein this work, hydrogels were prepared for use as drug delivery devices (DDD) for ornidazole. Grafted copolymers were characterized with SEM, FTIR, EDAX and swelling studies. The drug release was observed in sustained manner with Fickian diffusion. Overall, these hydrogels can act as DDD with enhanced potential due to therapeutic role of psyllium-sterculia and slow release of ornidazole.

**Keywords:** Dietary fiber, Diarrhea, ornidazole, Hydrogels, Drug delivery

## 1. Introduction

Recently, various polysaccharides have been explored for design of controlled DDD to reduce side effects associated with conventional drug formulations [1]. The blending of polysaccharides with other polymers have improved properties of the DDD devices [2,3]. In fact blending adds various properties synergically to the composite material [4]. The drug formulation developed after blending alginate-chitosan has improved the release profile of drug [5]. The high dissolution problem of pectin in upper gastrointestinal tract has been overcome by modifying the pectin with other polysaccharides [6-9]. Addition of the corn starch into grafted pectin has improved the encapsulation efficiency along with the reduction in gastric drug dissolution. The improvement of strength of the hydrogels has also been found by konjac glucomannan with chitosan [10]. The properties of the polysaccharides have been improved by grafting of hydrophilic polymers [11,12]. Both, hydrophilic polymers psyllium and sterculia gum have been functionalized with other polymers for use in CDD applications by Singh et al. [13-16] using chemical and radiation techniques. The degree of grafting during the network formation can be influenced by various factors [17]. The water absorbency property has been improved by addition of humate into the alginate grafted poly(acrylic acid) hydrogels [18].

The percentage grafting affects the swelling and release profile of the drugs. The reaction conditions, types and content of monomers and crosslinkers have exerted strong influence on the grafting/crosslinking of hydrogels [19,20]. Both radiation dose and co-monomer composition have influenced swelling of the copolymers (polyacrylic acid-poly vinyl sulfonic) formed by gamma radiation [21]. The controlled release of active anti-microbial agent metronidazole from the polymer based DDD for the GI tract have been reported in literature [22]. The drug delivery system for gastric ulcer has been developed by Patel and Amiji [23] for the treatment of *Helicobacter pylori*.



Both psyllium and sterculia gums are hydrophilic polymers. The psyllium is extracted from the seed mucilage comprising of xylan-arabinose- rhamnose [24]. It has been reported for its therapeutic value for chronic diarrhea along with other beneficial effects [25,26]. The galacturonic acid-glucuronic acid-rhamnose with some other residues are present in sterculia gum [27]. It has high water retention capacity and high viscosity. It has been used in the treatment of diarrhea [28,29]. It has also been applied in food and pharmaceutical industry [30]. It has also been used as mucoadhesive for the controlled drug delivery [31].

Herein this research, psyllium and sterculia gum were modified with polyacrylamide through grafting to develop hydrogels and anti-diarrhea drug ornidazole was impregnated into these hydrogels for use as DDD. The ornidazole is an antimicrobial agent which is used to treat intestinal infections including amoebic dysentery.

## 2. Experimental

### 2.1 Materials and method

Acrylamide (AAm) [Merck-Schuchardt, Germany], Ammonium persulphate (APS) [Qualigens Fine Chemical Mumbai-India], N, N'-methylenebisacrylamide (N, N'-MBAAm) [S.D. Fine, Mumbai-India], *Psyllium* (psy) [Sidpur Sat Isabgole -Gujarat, India], and ornidazole [ARISTO Pharmaceuticals Pvt. Ltd. Mumbai- India].

### 2.2 Synthesis of hydrogels

The formation of hydrogels was done with graft copolymerization reaction using definite content of psyllium and sterculia gum along with initiator APS and crosslinker NNMBA. Copolymer reaction was done for two hours at 65 °C. The crosslinked product was purified with 1:1 mixture of distilled water and ethanol and finally dried product was named as [psy-co-ster-cl-poly(AAm)] polymer. The optimization was done by varying [AAm] (from  $1.41 \times 10^{-1}$  to

$7.05 \times 10^{-1}$  mol/L) and [N,N'-MBAAm] (from  $6.49 \times 10^{-3}$  to  $32.43 \times 10^{-3}$  mol/L) on the basis of swelling results. The optimized parameters were [AAm]=  $2.82 \times 10^{-1}$  mol/L, [N,N'-MBAAm]= $12.97 \times 10^{-3}$  mol/L, [APS]=  $4.38 \times 10^{-3}$  mol/L, 0.5 g of psyllium and 0.5g sterculia gum.

### 2.3 Characterization

The psy-co-ster-cl-poly(AAm) polymers were characterized by SEM,EDAX, FTIR and swelling studies. SEM and EDAX was recorded on QUANTA 200 FEG-Netherlands and FTIR was taken on Nicolet 5700 FTIR-THERMO.

### 2.4 Swelling and drug release studies

Swelling of psy-co-ster-cl-poly(AAm) network was carried out by gravimetric method [25]. During swelling, the difference in weight of polymer gave gain in weight with time. The ornidazole encapsulation into psy-co-ster-cl-poly(AAm) networks was done in solution of definite drug content [32].The release profile of drug was evaluated from standard curves. The diffusion mechanism of drug was evaluated using Ritger and Peppas equation [33,34] (i)

$$\frac{M_t}{M_\infty} = kt^n \quad (i)$$

where  $M_t$  is ornidazole release in time and  $M_\infty$  is drug release after 24 hrs and their ratio is fractional release in time  $t$  and 'k' is constant and 'n' is diffusion exponent which gives diffusion mechanism.

## 3. Result and discussion:

### 3.1 Characterization

#### 3.1.1 Scanning Electron Micrograph (SEM)

The morphology of psy-co-ster-cl-poly(AAm) polymers was examined by SEM images (Figure 1). It was observed that modified polysaccharides showed structural heterogeneity as compared to a homogeneous structure of un-modified polysaccharides.

#### 3.1.2 Energy dispersion analysis by X-rays (EDAX)

The high energy beams of electrons applied in SEM was also interacted with deep region of polymer sample and emitted X-rays which were characteristics of elements present in polymer sample. It gave EDAX spectra in the form of qualitative results of chemical composition of sample. Presence of nitrogen along with other elements, carbon and oxygen indicated functionalization of psyllium-sterculia gum with poly(AAm) (Figure 2).

#### 3.1.3 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of psy-co-ster-cl-poly(AAm) is shown in Figure 3. The absorption bands at  $1670.3 \text{ cm}^{-1}$  and  $1621.9 \text{ cm}^{-1}$  were due to C=O stretching of Amide-I and N-H in plane bending of Amide-II respectively which indicated grafting of poly(AAm) onto psyllium and sterculia. In addition, in case of modified polymer, absorption bands at  $1041.5 \text{ cm}^{-1}$  and  $1457.5 \text{ cm}^{-1}$  region were recorded due to overlap of C-N and C=O stretching coupled with bending of -OH groups were

also observed along with the bands present in psyllium-sterculia [35,36].

### 3.2 Swelling studies

The influence of monomer [AAm] on crosslinking was determined by taking the swelling of hydrogel network designed with different [AAm] ( $1.41 \times 10^{-1}$ ,  $2.82 \times 10^{-1}$ ,  $4.23 \times 10^{-1}$ ,  $5.64 \times 10^{-1}$  and  $7.05 \times 10^{-1}$  mol/L) (Figure 4 and Table 1). The water uptake was decreased with rise in feed [AAm] during grafting reaction. Maximum swelling was  $(24.96 \pm 3.27)$  g/g in of polymer network formed by  $1.41 \times 10^{-1}$  mol/L. With rise in crosslinker content from  $6.49 \times 10^{-3}$  mol/L to  $32.43 \times 10^{-3}$  mol/L, swelling first increased with increase in crosslinker [NNMBA] and then decreased with some irregular trends. Increment in crosslinker content increased network density which was directly linked with swelling of polymers [37,38]. Maximum water uptake was  $(24.72 \pm 1.25)$ g occurred in case of polymers prepared with  $12.97 \times 10^{-3}$  mol/L of [N,N'-MBAAm]. During swelling, diffusion occurred with non-Fickian diffusion which was confirmed from the diffusion exponent 'n' values observed between 0.5-1.0. It also indicated comparable rate of diffusion of water molecules and relaxation of polymer chains. The values of diffusion coefficients reflected that during later stages rate of diffusion of water was slow.

The higher swelling in pH 7.4 buffer was observed which indicated larger pore size of the network in pH 7.4 buffer as compared to 2.2 buffer. The maximum swelling in pH 7.4 buffer and pH 2.2 buffer was  $11.90 \pm 1.36$  g/g and  $9.66 \pm 0.45$  g/g respectively after 24 hrs. This may be due to opening of pores in network structure due to partial ionization. Swelling in NaCl solution was less as compared to distilled water. Polymers were swelled with Fickian diffusion. The decrease in swelling of psy-co-ster-cl-poly(AAm) hydrogel may be due to rise in [AAm] content which results in formation of denser network structure. Bajpai and coworkers [39] have also found similar results during grafting of polyacrylamide onto polysaccharide. Lv and coworkers [40] have also found higher swelling of polymers in pH 7.4 as compared to pH 1.2 buffer in alginate- carboxymethyl chitosan hydrogels. The increase in de-protonation of -COOH groups in pH 7.4 buffer and thereafter ionic repulsion has opened pores that has expanded network and has enhanced water uptake by hydrogels [41].

### 3.3 Drug release studies

The *ex vivo* release of ornidazole from drug entrapped in psy-co-ster-cl-poly(AAm) hydrogels is shown in Figure 5 and Table 1. The higher release was recorded from drug encapsulated DDD in solution of lower pH as compared to pH 7.4 buffer. The higher solubility of drug in solution of lower pH solution was the main reason for more release in pH 2.2 buffer. Here solubility was the dominating factor for controlling the diffusion from hydrogel DDD. The lower values of late time diffusion coefficients than initial/ average diffusion coefficient reflected that during earlier stages rate of release of drug was higher as compared to later stages. It means after certain time drug release occurred in controlled manner. Drug diffusion by Fickian mechanism reflected that rate of diffusion was much lesser than rate of polymer chain relaxation. The release of encapsulated ornidazole may enhance the potential of DDD to cure diarrhea due to curing action of dietary fiber psyllium-sterculia gum and slow release of ornidazole, a therapeutic agent from DDD. The water holding capacity of psyllium has been used to treat diarrhea along with increase in consistency of diarrheal stools [42,43].

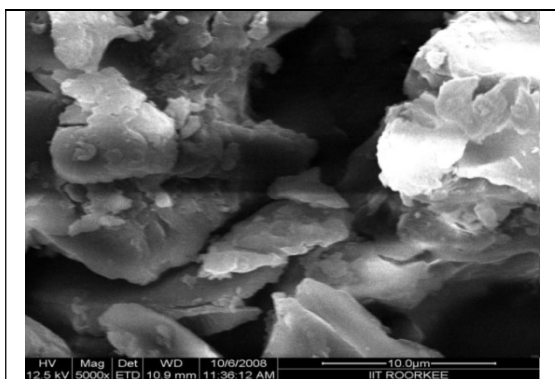


Fig. 1: SEM of psy-co-ster-cl-poly(AAm) polymers.

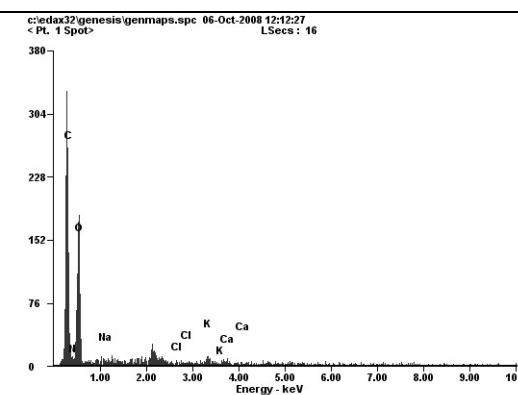


Fig. 2: EDAX of psy-co-ster-cl-poly(AAm) polymers.

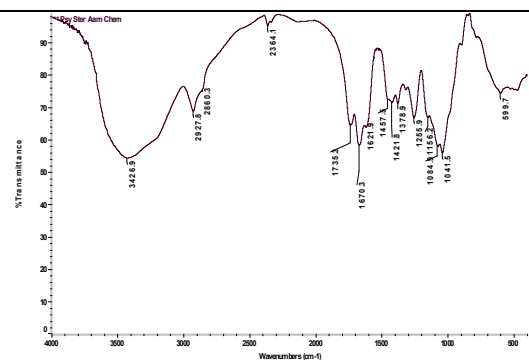
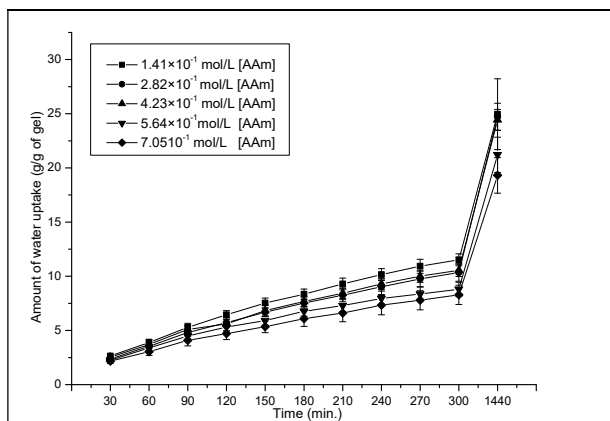
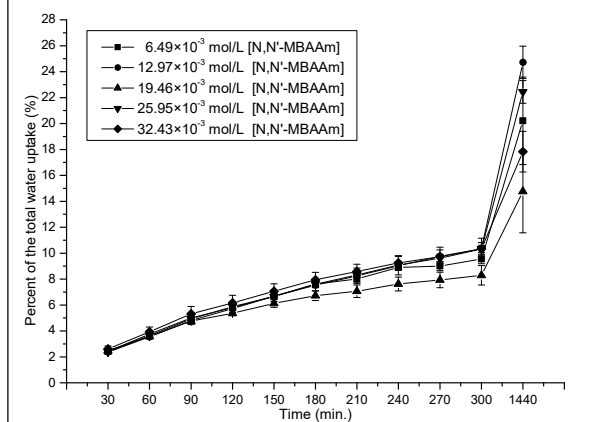


Fig. 3: FTIR spectra of psy-co-ster-cl-poly(AAm) polymers.



(a)



(b)

Fig. 4: Effect of (a) [AAm], and (b) [N,N'-MBAAm] on swelling of psy-co-ster-cl-poly(AAm) polymers at 37 ° C.

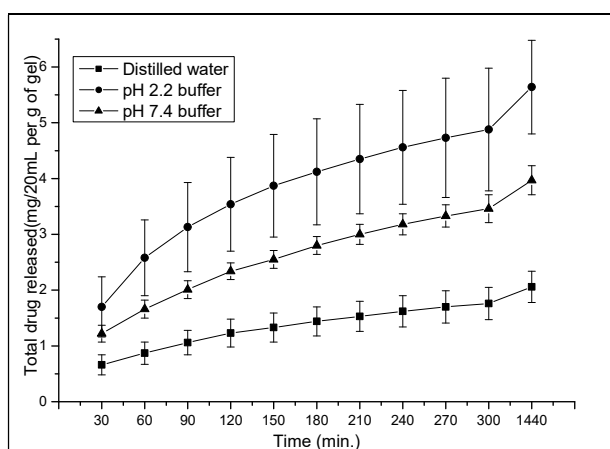


Fig. 5: Release profile of ornidazole from drug loaded psy-co-ster-cl-poly(AAm) polymers at 37 ° C.

**Table 1: Result of diffusion exponent 'n', and gel characteristic constant 'k' for swelling of hydrogels and release of ornidazole from drug loaded psy-co-ster-cl-poly(AAm) hydrogels.**

Parameter	Diffusion exponent 'n'	Gel characteristic constant 'k' × 10 <sup>2</sup>
<b>Swelling studies</b>		
<b>Effect of [AAm] × 10<sup>1</sup> mol/L</b>		
1.41	0.65	1.11
2.82	0.63	0.99
4.23	0.65	1.04
5.64	0.63	0.98
7.05	0.63	1.18
<b>Effect of [N,N'-MBAAm] × 10<sup>-3</sup> mol/L</b>		
6.49	0.50	2.48
12.97	0.63	0.99
19.46	0.61	0.98
25.95	0.60	1.95
32.43	0.57	1.74
<b>Effect of pH</b>		
Distilled water	0.63	0.99
pH 2.2 buffer	0.42	3.70
pH 7.4 buffer	0.44	4.58
<b>Effect of [NaCl]</b>		
Distilled water	0.63	0.99
0.9% NaCl	0.43	3.13
<b>Drug release studies</b>		
Distilled Water	0.43	7.36
pH 2.2 buffer	0.42	6.95
pH 7.4 buffer	0.44	7.18

#### 4. Conclusions

In concluding remarks, copolymer reaction parameters such as content of AAm and NNMBAAm influenced porosity of network structure formed in the form of hydrogels. The rise in AAm and NNMBAAm content in general reduced the swelling of the network hydrogels. The swelling results in different pH medium pH reflected pH responsive nature of psy-co-ster-cl-poly(AAm) hydrogels. The Fickian diffusion of the ornidazole drug was found in sustained manner from Hydrogels. It is a desired feature of the controlled DDD. Overall, these hydrogels can act as DDD with enhanced potential due to therapeutic role of psyllium-sterculia and slow release of ornidazole. Hence, psy-co-ster-cl-poly(AAm) hydrogels can be applied in slow drug delivery uses with enhanced potential to cure diarrhea.

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