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Research Article

NEW POLYMERIC FILM COATING FOR COLON TARGETING AND ITS EVALUATION

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ABSTRACT
The major objective is to optimize the properties of new polymeric films based on blends of cellulose acetate and guar gum. Recently guar gum was shown to be highly promising polymer for the colon targeting drug delivery system. Cellulose acetate, a water-insoluble polymer can protect the core from the small intestinal pH and act as a reservoir type system. However, it is yet unknown how desired membrane properties, especially water uptake and dry mass loss kinetics as well as mechanical stability can be adjusted to the specific needs of particular drug treatment. Variation in the guar gum:cellulose acetate blends were made thereby highly efficient and easy application tools were identified altering the membrane's properties.
KEYWORDS Coating, Guar gum, colon targeting, Cellulose acetate, mechanical stability, water uptake

INTRODUCTION

Oral delivery of drugs to the colon is valuable in the treatment of colonic diseases such as colorectal cancer, Crohn's disease, irritable bowel syndrome, local infectious diseases and spastic colon, whereby high local concentration can be achieved, is more effective than systemic delivery and also reduces toxicity and side effects [1, 2, 3].

Absorption and degradation of the active ingredient in the upper part of the gastrointestinal tract is the major obstacle with the delivery of drugs by the oral route and must be overcome for successful colonic drug delivery.

Coating is an essential part during formulation of pharma ceutical dosage form to achieve superior aesthetic quality (e.g., color, texture mouth feel, and taste masking), physical and chemical protection for the drugs in the dosage form, and modification of drug release characteristics. Film coatings are applied with aqueous or organic based polymer solutions[4].

Different types of polymeric blends of guar gum and cellulose acetate have been investigated. The presence of cellulose acetate avoids premature film dissolution within the small intestine (Guar gum being water-soluble). Due to the presence of inear chain of α- D-mannopyranosyl units linked (1→4) with single member α-D-galactopyranosyl units hydrates quickly to produce viscous pseudoplastic solutions that although shear-thinning generally have greater low-shear viscosity than other hydrocolloids[5]. This gelling property retards release of the drug from the dosage form, and it is susceptible to degradation in the colonic environment. Guar gum composed of galactan and mannan units combined through glycosidic linkages and shows degradation in the large intestine due the presence of microbial enzymes [6, 7, 8,9,10].

However, yet it is unclear whether guar gum:cellulose acetate films provide sufficient to withstand the GIT motility and potentially significant hydrostatic pressure developed within the dosage forms due to the water penetration into the systems upon contact with aqueous media.

The aim of the study was to determine the above aspects and to be able to adapt the film coating properties to the specific needs of a particular type of drug treatment.

MATERIALS AND METHODS

Cellulose acetate and Guar gum (Loba chemie Pvt. Ltd.) were used as polymers. PEG-400 (Qualigens) was used as plasticizer. Acetone (Chemspure) and Methanol (Sisco Research Laboratory) were used as solvents.

METHODS

Preparation of Polymeric Films

The polysaccharide polymeric films were prepared by casting blends of four different concentrations of guar gum in cellulose acetate polymeric solution, using acetone and methanol as solvents with PEG-400 as plasticizer (Table 1). Films were allowed to dry in a closed chamber to control the evaporation of the solvent and dried to constant weight at 30 ± 2°C and stored in

dessicator until used for characterization.

CHARACTERIZATION OF POLYMERIC FILM

The polymeric coating films were taken and evaluated for the following tests

Solubility

500 mg of polymer was mixed with the solvent using a series of blend of solvent (20 ml each) in screw capped test tube. The mixture was shaken at constant speed at room temperature by using a mechanical wrist action shaker. The time used to dissolve the polymer blend was noted (Table 2).

Thickness

Randomly selected films were evaluated for their thickness by using Vernier caliper (Mitotuyo. Japan), (Table 2).

Weight of the Film

The film was cut into 7.5 cm^2 area and its weight was determined by using electronic digital balance (Table 2).

Hardness Determination

The apparatus employed for hardness determination consisted of a sharp needle 12cm long, 2mm thick and tapering to form a pointed end between 11th and 12th cm, passing down a wooden mechanical frame.

The sharp pointed end of the needle rested on a flat surface with metal lining. The upper blunt end of the needle was connected to a circular wooden plate on which increments of weights could be placed.

The upper part of the needle was connected to an electric wire continuous with two 1.5-volt batteries and a three volt electric bulb and the circuit was completed by connecting the wire to the metal plate above which the film is placed. The sharp end of the needle rested on the film.

Increments of weights were added on to the surface of wooden plate and when the hardness of the film is exceeded, the sharp end penetrates across the film, contacts the metal plate and the bulb glow (Table 2).

Folding Endurance

The folding endurance was measured manually. The films were conditioned at 55% relative humidity at 25-30° C for 24 hr before testing. A strip of film (2×2cm) was cut evenly and repeatedly folded at the same place until it breaks. The number of times counted until film could be folded at the same place without breaking, this was gave the exact value of folding endurance[11].

Viscosity

The viscosity of the polysaccharide coating film solution of all the four different batches were determined by using Brookfield Viscometer using LV spindle.

Water Uptake and Erosion Study

Pieces of 1.5×5cm (7.5cm^2) were placed into 120ml plastic containers filled with 100ml of pre-heated medium (0.1M HCl and phosphate buffer pH 6.8, 7.4), followed by horizontal shaking at 37°C (80 rpm). At predetermined time points the films were withdrawn, excess water removed. Films were accurately weighed (wet mass). The water content at various time intervals was calculated. Erosion of the films was calculated by using the initial and final weight of the film after water uptake study[12].

$$\text{Water uptake or water content} = \frac{\text{Wet mass} - \text{dry mass}}{\text{Wet mass}} \times 100$$

$$\text{Erosion of Film} = \frac{\text{Weight loss}}{\text{Initial weight}} \times 100$$

Dry Film Mass

Pieces of 1.5×5cm (7.5cm^2) were cut and dried to constant weight at 60°C (dry mass). The dry film mass at various time intervals were calculated.

$$\text{Dry film mass} = \frac{\text{Dry mass (t)}}{\text{Dry mass (t=0)}} \times 100$$

RESULTS AND DISCUSSION

For colon targeting delivery, various concentrations of the mixture of water soluble (Guar gum) and water insoluble (Cellulose Acetate) polymers were used to prepare the coating material. The various polymer batches were characterized for their solubility and forming properties (Table 2). The prepared films were investigated for their thickness, hardness, and folding endurance, water uptake, erosion and dry mass kinetics.

The different studies revealed that the batches prepared by varying the concentrations of guar gum in cellulose acetate solution showed good film properties. On increasing the concentration of the guar gum from 0.2 to 0.8% the drying time was increased and there was no change in the color. The hardness of the films was found to vary between 1.016 to 1.086 gm.

The folding endurance of films was found to be independent of the thickness but was dependent on the hardness (Table 3). The results clearly explained that the viscosity of polymeric solution was significantly increasing in a linear fashion with that of the increasing concentration of the guar gum (0.2 to 0.8%).

Water uptake and erosion study at various time intervals of all the four different batches of the polysaccharide film were done in different dissolution medium (pH 1.2, 6.8 and 7.4). The results of water uptake and erosion study of the inner coating films showed that Batch A

film was found to have less water uptake and erosion of guar gum, since the concentration of guar gum was less when compared to that of the other three batches. Hence the film Batch A was chosen as good coating mixture to protect the core from small intestinal environment (Figure 4, 5 and 6).

The dry mass of the polysaccharide coating film at various time intervals of all the four different batches was in the range of 91.22 to 98.68%.

The results of this study revealed that Guar gum: Cellulose acetate blends are highly promising film coating material for targeting the colonic site. Mainly, desired system properties, being adapted to the specific needs of a particular treatment can be easily adjusted by varying the polymer:polymer blend ratio as well as the plasticizer content.

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Table 1: Composition of inner (Polysaccharide) coating of tablet

S.No.	Ingredients	A	B	C	D
1	Cellulose Acetate (g)	2	2	2	2
2	Guar gum (g)	0.2	0.4	0.6	0.8
3	PEG-400	0.39	0.39	0.39	0.39
4	Acetone (ml)	80	80	80	80
5	M ethanol (ml)	20	20	20	20

Table 2: Characterization of polymeric films

Batches	Solubility							Appearance of polymeric film	Observation for drying after 24 hours
	S1	S2	S3	S4	S5	S6	S7		
Guar Gum	+	+	+	+	+	+	++	Nil	Nil
Cellulose Acetate	-	+	+	++	+	+	++	Nil	Nil
A	-	-	-	-	-	-	+	White, Flexible and Smooth	Dried
B	-	-	-	-	-	-	+	White, Flexible and Smooth	Dried
C	-	-	-	-	-	-	+	White, Flexible and Smooth	Dried
D	-	-	-	-	-	-	+	White, Flexible and Smooth	Dried

Solubility is determined in various solvents i.e. S1 (Water), S2 (methanol), S3 (ethanol), S4 (Acetone), S5 (chloroform), S6 (Diethyl ether) and S7 (Acetone: methanol 80:20) and indicated by (-) poor solubility, (+) sparingly soluble, (++) very soluble

Table 3: Evaluation of polymeric films

Batches	Thickness (mm)	Weight (gm)	Hardness (gm)	Folding Endurance
A	0.0884±0.0094	0.1334±0.0008	1.016±0.0084	38.0
B	0.0792±0.0009	0.0756±0.4275	1.04±0.0096	42.0
C	0.0796±0.0008	0.1236±0.0018	1.068±0.00394	46.0
D	0.0792±0.0009	0.0792±0.0009	1.086±0.0017	52.0

Each value represents mean±SD (n=5)

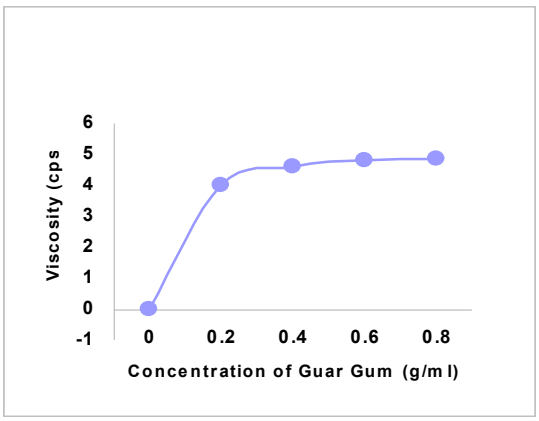

Figure 1: Effect of concentration of Guar gum on the viscosity of polymeric solution at 20°C after 1 hr (Shear Rate at 20 rpm)

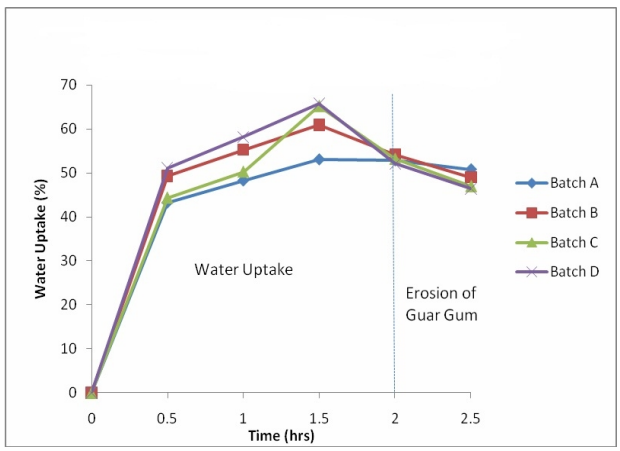

Figure 2: Water uptake and Erosion study of polymeric films in pH 1.2 Buffer

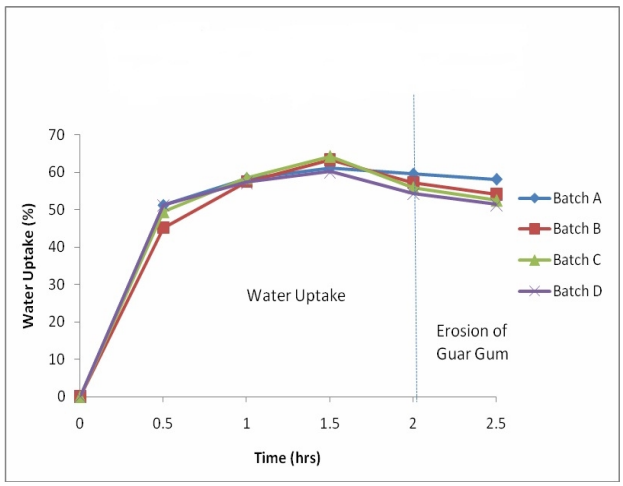

Figure 3: Water uptake and Erosion study of polymeric films in pH 6.8 Buffer

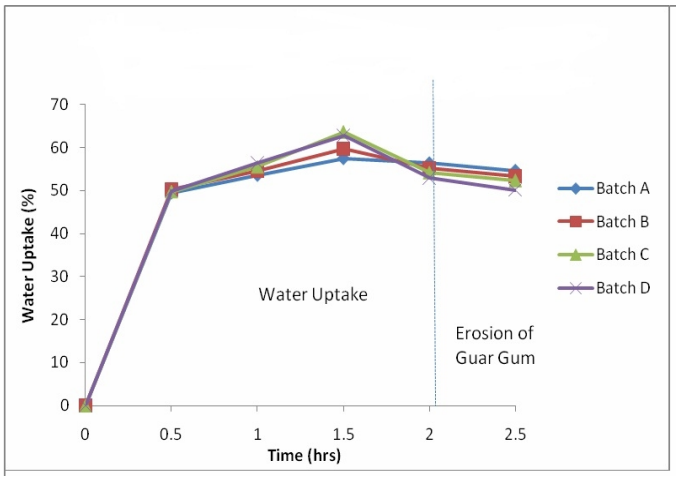

Figure 4: Water uptake and Erosion study of polymeric films in pH 7.4 Buffer

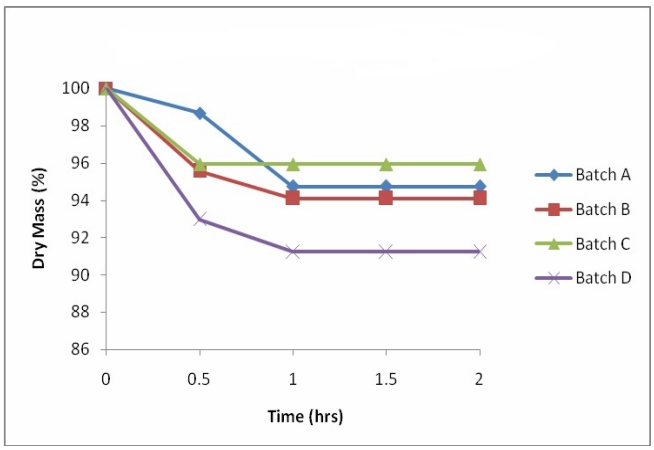

Figure 5: Dry mass kinetics of polymeric films

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