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Research Article

NATURALLY OCCURRING BIODEGRADABLE POLYMERS FOR CONTROLLED RELEASE OF CIPROFLOXACIN FOR TREATMENT OF INFLAMMATORY BOWEL DISEASE

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ABSTRACT

Naturally occurring biodegradable polymers were evaluated as carriers for colon targeted controlled release formulations. Films were prepared by mucilage of different natural gums with variability in concentration, combination of polymers and solvent with triethyl citrate (5%) as plasticizer. Films containing natural biodegradable polymers were characterized for their physical appearance, solubility, film forming properties and effect of colon micro flora on different combinations of polymers. Films were also evaluated for parameters like water uptake, tensile strength and folding endurance. The results showed that natural gums can be used as film material for colon targeting system(s). Results of rheological studies demonstrated that effects of galactomannan on the viscosity of naturally occurring polymeric gum solution are concentration-dependent. A significant increase in the viscosity was noted in the presence of galactomannan at a concentration of 2.5 to 15 mg/ml, indicating that the properties of polysaccharide mucilage can effected by addition of another enzymatic degradable polymers. The purpose of the study is development of targeted system bearing ciprofloxacin using various natural biodegradable polymers for delivery of ciprofloxacin to the colon for treatment of inflammatory bowel disease.

Keywords: Coating system, Natural biodegradable polymers, Colon targeting carrier.

INTRODUCTION

The development of pharmaceutical coating technology is useful for the preparation of controlled release formulations. The film forming materials used mainly natural or synthetic polymers. There are several patents made for selective drug delivery with various polymeric coating materials. Natural polymer blends have colon specific properties with film-forming properties suggested by various researchers as coating material, because these polymers contain cellulose derivatives[1,2].

Coating is an essential part during formulation of pharmaceutical 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 forms, and modification of drug release characteristics. Film coatings are applied with aqueous or organic-based polymer solutions. Modern pharmaceutical coating began in the 19th century with sugar coating, which was mainly used to increase the palatability of bitter medicaments. Sugar coating has a long processing time (up to 5 days), a high level of required operator expertise, and difficulty in standardizing the procedure.

The possibility of bacterial and mold growth in sugar solutions, sealing of tablets before coating have restrictions of tablet shape, and a lack of automation in the process led to the search for alternative coating methods[3]. The introduction of film coating greatly reduced the processing time. Film coating rapidly changed the coating technology. This transformation was facilitated by the introduction of many polymer alternatives and also by the development of more precise and efficient coating equipment. Film coating offered better reproducibility of the process, ability of the film coating to be applied on a wide range of pharmaceutical dosage forms, process automation, increased process control, and improved batch-to-batch uniformity of the product[4].

Aqueous film coating which is largely used has certain disadvantages viz.[5], heat is required for aqueous-based systems to evaporate the water present in the coating dispersion. For aqueous film-coating systems, the slow drying rate of the coating is a problem due to the relatively high latent heat of vaporization (539.4cal/g) of water[6]. Aqueous film coating includes a wide variety of solutions and dispersions of cellulose ether and ester derivatives and polymethacrylates[7,8]. Drug delivery systems for colon targeting based on the use of polysaccharides offer superiority over other systems. Polysaccharides retain their integrity and prevent the release of drug during its passage through the GIT. But when it comes in contact with colonic fluid, degraded by the action of microorganisms and consequently entrapped drug is librated[9].

Naturally occurring biodegradable polysaccharides also show great promise in pharmaceutical applications.

These polymers are extensively used for the development of coated solid dosage forms mainly for targeted drug delivery of drugs [10,11]. Present study deals with naturally occurring biodegradable polymers for preparing films as carrier or coating material for colon drug delivery.

There are several reports published about the successful use of natural biodegradable gums in various pharmaceutical preparations [12-14]. During the past two decades, much attention has been paid to the development of aqueous and organic solvent film coatings for pharmaceuticals due to safety, economic and environmental reasons. Today, a number of films coating technology are most commonly used as coating systems for masking, barrier and controlled release applications.

MATERIALS AND METHODS

Guar gum (Loba chemicals Pvt. Ltd., India), xanthan gum (Hi-media laboratory Pvt. Ltd., India), pectin (Sisco laboratory Pvt. Ltd., India) were used as naturally occurring polysaccharide polymers. Triethyl citrate (Thomas baker chemicals Pvt. Ltd., India) was used as plasticizer and mercury extra pure (metal) (Thomas baker chemicals Pvt. Ltd., India) was used as casting solvent.

Preparation of films

Dispersion containing 4% w/v of different polymeric gums prepared by dispersing gum in pure distilled water or 1:1 ethanol-water mixture containing plasticizer TEC (5% w/v, based on amount of solvent) (Table 1).

Before addition of plasticizer in gum mucilage, dispersion was allowed to equilibrate for period of 6 h. Gum mucilage stirred gently for a period of 10min with magnetic stirrer. Dispersion was transferred to a filtering flask for removal of air bubbles by using a vacuum pump after complete homogenization.

The mixture was poured on mercury substrate within limited area of a petridish. A glass ring of constant diameter was used to control the area of the film during casting. Films were allowed to dry in a closed chamber to control the evaporation of the solvent and dried to constant weight at 30 ± 2^{0}C and stored in desiccator until used for characterization.

Table 1: Formulations of Natural Biodegradable Polymeric Films

F.Code	Water (100 % ml)	1:1 Ethanol : Water mixture (ml)	Triethyl Citrate (% v/v of solvent)	Guar gum (% w/v of solvent)	Xanthan gum (% w/v of solvent)	Pectin (% w/v ofsolvent)
F1	20	-	5	2	-	-
F2	-	20	5	2	-	-
F3	20	-	5	4	-	-
F4	-	20	5	4	-	-
F5	20	-	5	-	2	-
F6	-	20	5	-	2	-
F7	20	-	5	-	4	-
F8	-	20	5	-	4	-
F9	20	-	5	-	-	2
F10	-	20	5	-	-	2
F11	20	-	5	-	-	4
F12	-	20	5	-	-	4
F13	20	-	5	1	3	-
F14	-	20	5	1	3	-
F15	20	-	5	3	1	-
F16	-	20	5	3	1	-
F17	20	-	5	1	1	2
F18	-	20	5	1	1	2
F19	20	-	5	1	-	3
F20	-	20	5	1	-	3

Table 2: Composition of Ciprofloxacin (250 mg) core or uncoated tablet formulations prepared by wet granulation method

Formulation code	Ingredients							
	MCC (Avicel pH 102)	**DBP (di basisc calcium phosphate dehydrate)**	**Lctose anhydrous**	**Potato starch**	**Talc**	**Magnesium stearate**	**Disintegration agent (SSG)**	**Binder polyvinyl pyrrolidone K-30**
F1	90	210	150	-	30	30	24	(10% w/v in iso
F2	48	252	150	-	30	30	24	propyl alcohol)
F3	90 (10%)	360 (50%)	-	-	30	30	24	
F4	115	120	110	50	30	30	-	

Table 3: Composition of Ciprofloxacin (250 mg) coated tablet formulations prepared by spray pan coating techniques on F4 core tablet and polymeric films

Formulation code (Tablet)	Polymers Guar gum (%)	Solvent system Xanthan gum (%)	Pectin (%)	
F5	3	1	-	Water 100%
F6	1	1	2	Water 100%
F7	3	1	-	Ethanol:Water mixture (50:50)
F8	1	1	2	Ethanol:Water mixture (50:50)
F9	-	1	3	Ethanol:Water mixture (50:50)
F10	1	-	3	Ethanol:Water mixture (50:50)

Table 5: Evaluations of Polymeric Films

Formulations	Thickness (mm)	Tensile strength(kg/cm2)	Folding endurance	Water uptake (%)
F1	0.230	2.75	45.0	5.65
F2	0.227	2.94	55.0	3.65
F3	0.574	1.91	31.0	5.36
F4	0.590	2.08	33.0	4.36
F5	0.256	2.96	58.0	5.42
F6	0.288	3.32	68.0	5.22
F7	0.322	1.21	6.0	4.44
F8	0.316	1.28	10.0	4.23
F9	0.380	1.94	23.0	5.14
F10	0.366	2.22	28.0	4.78
F11	0.389	3.88	22.0	7.10
F12	0.408	4.02	27.0	6.10
F13	0.584	4.08	110.0	5.90
F14	0.556	4.22	118.0	4.77
F15	0.290	4.18	120.0	5.96
F16	0.272	4.65	128.0	4.88
F17	0.426	3.96	90.0	5.85
F18	0.411	4.28	102.0	4.56
F19	0.410	3.86	95.0	5.43
F20	0.402	4.11	99.0	4.92

Table 4: Characterizations of Polymeric Films

Formulations	Solubility							Appearance of polymer film	Polymer degradation	Observation for drying after 24 h
	S1	S2	S3	S4	S5	S6	S7			
Xanthan gum	-	*	*	*	*	*	**	Nil	Nil	Nil
Guar gum	-	*	*	*	*	*	**	Nil	Nil	Nil
Pectin	*	*	*	*	*	*	**	Nil	Nil	Nil
F1	-	-	-	-	-	-	-	Brownish, Flexible and Smooth	Density of pores is less	Satisfactorily Dried
F2	-	-	-	-	-	-	-	Whitish-Brown, Flexible and Smooth	Density of pores is less	Dried
F3	-	-	-	-	-	-	-	Brownish, Flexible and Transparent	Density of pores is medium	Satisfactorily Dried
F4	-	-	-	-	-	-	-	Brownish-White, Flexible and Transparent	Density of pores is medium	Dried
F5	-	-	-	-	-	-	-	Brownish, More flexible and Smooth	Density of pores is medium	Satisfactorily Dried
F6	-	-	-	-	-	-	-	Brownish, More flexible and Smooth	Density of pores is more	Dried
F7	-	-	-	-	-	-	-	White, flexible and Smooth	Density of pores is more	Dried
F8	-	-	-	-	-	-	-	White, hard and Smooth	Density of pores is more	Dried
F9	-	-	-	-	-	-	-	White, hard and Smooth	Density of pores is less	Dried
F10								White, hard and Smooth	Density of pores is less	Dried
F11								White, very hard and Smooth	Density of pores is medium	Dried
F12	-	-	-	-	-	-	-	White, very hard and Smooth	Density of pores is medium	Dried
F13	-	-	-	-	-	-	-	Brownish, Flexible and rough	Density of pores is medium	Wet
F14	-	-	-	-	-	-	-	Brownish, Hard, Flexible and rough	Density of pores is medium	Satisfactorily Dried
F15	-	-	-	-	-	-	-	Brownish, Flexible and Smooth	Density of pores is more	Wet
F16	-	-	-	-	-	-	-	Brownish, Hard, Flexible and Smooth	Density of pores is more	Satisfactorily Dried
F17	-	-	-	-	-	-	-	Whitish-Brown, Hard and Smooth	Density of pores is high	Satisfactorily Dried
F18	-	-	-	-	-	-	-	Whitish-Brown, Hard, transparent and Smooth	Density of pores is high	Dried
F19	-	-	-	-	-	-	-	Yellow-Whitish, Less hard and Smooth	Density of pores is medium	Wet
F20	-	-	-	-	-	-	-	Yellow-Whitish, hard and Smooth	Density of pores is medium	Wet

Solubility was determined in various solvents i.e. water (S1); ethanol (S2); methanol (S3); toluene (S4); chloroform (S5); diethyl ether (S6) and ethanol: water 50:50 (S7) and indicate by – as polymer insoluble or viscous, * as sparingly soluble, ** very soluble.

Table 6: Physical characteristics of Uncoated and Coated tablet

Parameters	Uncoated cores				Coated cores					
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Weight (mg)	780	780	780	780	860	856	862	860	858	865
Weight gain (%)	-	-	-	-	10.1	9.98	10.2	10.1	9.9	10.3
Diameter average (mm)	1.2	1.2	1.2	1.2	1.4	1.4	1.4	1.4	1.4	1.4
Thickness average (mm)	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5
Coat thickness (%)	-	-	-	-	10	10	10	10	10	10
Friability (%)	<0.1	<0.2	<0.1	<0.1	0	0	0	0	0	0
Hardness (kg)	0.42	0.50	0.56	0.61	0.64	0.66	0.66	0.68	0.71	0.70
Disintegration time average (min)	1.34	1.56	1.14	1.10	268	280	272	320	286	274
Ciprofloxacin content average (%)	99.43	99.51	99.44	99.42	99.53	99.50	99.54	99.56	99.52	99.53

Table 7: In-Vitro release kinetic parameters of ciprofloxacin

Formulation code	Zero-order		First-order		Korsemeyer-peppas		$t_{50\%}$ (min)
	K_0 (mg/h)	R^2	K^{-1} (h^{-1})	R^2	n	R^2	
F1	1.5584	0.9054	1.5589	0.9054	0.7885	0.9350	22
F2	1.5504	0.8956	1.5501	0.8956	0.7004	0.9404	16
F3	1.4647	0.8053	1.4647	0.8053	0.5812	0.8364	16
F4	1.6351	0.9491	1.6351	0.9491	0.9948	0.9483	23
F5	0.2031	0.9042	0.2031	0.9042	1.1668	0.9335	312
F6	0.2036	0.9202	0.2036	0.9202	1.2123	0.9477	314
F7	0.2068	0.8977	0.2068	0.8977	1.1554	0.9296	320
F8	0.1893	0.8730	0.1893	0.8730	1.1255	0.9119	341
F9	0.2047	0.8633	0.2047	0.8633	1.1393	0.9189	315
F10	0.2041	0.8639	0.2041	0.8639	1.1170	0.9007	316

Fig. 1: Photograph of Fabricated Spray Pan Coater

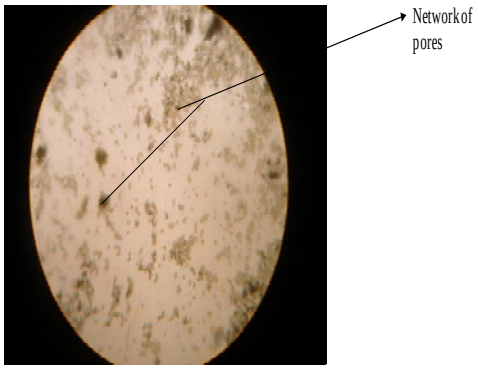

Fig. 2: Microbial degradation on polymeric film containing guar gum, xanthan gum and pectin in ratio of 1:1:2

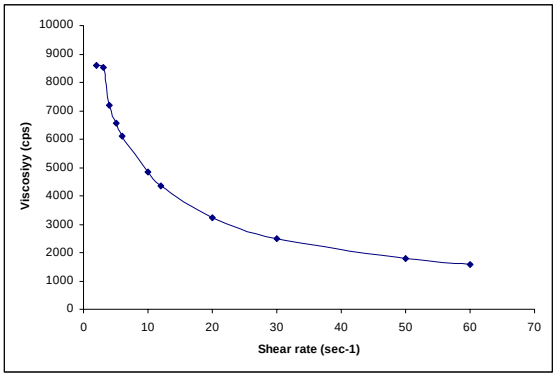

Fig. 3: Effect of shear rate on the viscosity of 1% aqueous Guar gum (galactomannase) solution at 25ºC

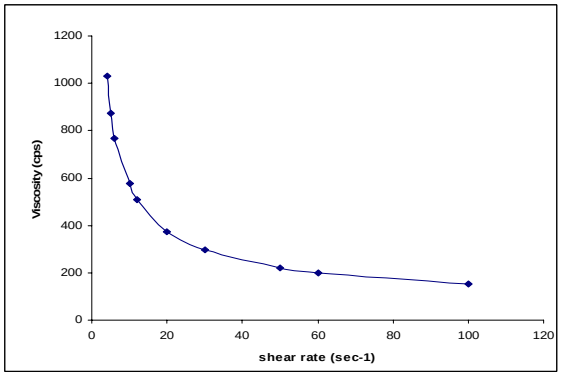

Fig. 4: Effect of shear rate on the viscosity of 1% aqueous Xanthan gum solution at 25ºC

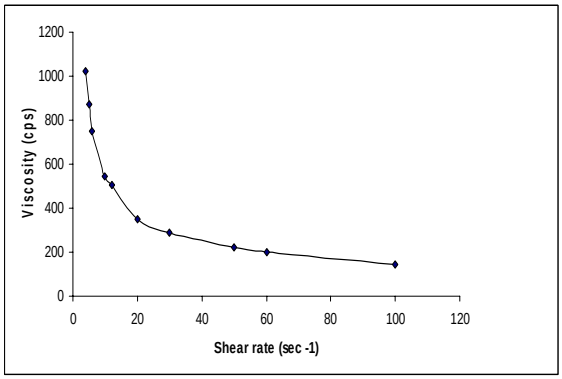

Fig. 5: Effect of shear rate on the viscosity of 8% aqueous Pectin solution at 25ºC

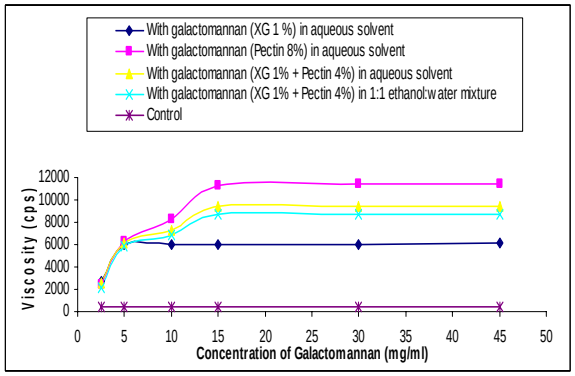

Fig. 6: Effect of concentration of galactomannan on the viscosity of polymers at 25ºC after 1 h (shear rate = 20 rpm)

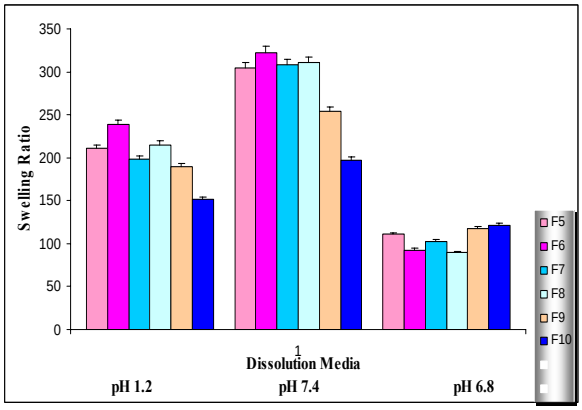

Fig. 7: The swelling ratio of the tablets at three different pH media

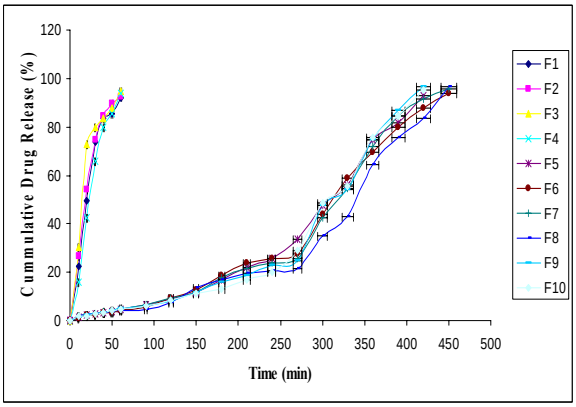

Fig. 8: Zero-Order Kinetic Plot, In-Vitro drug release profile of ciprofloxacin 250 mg, n = 3

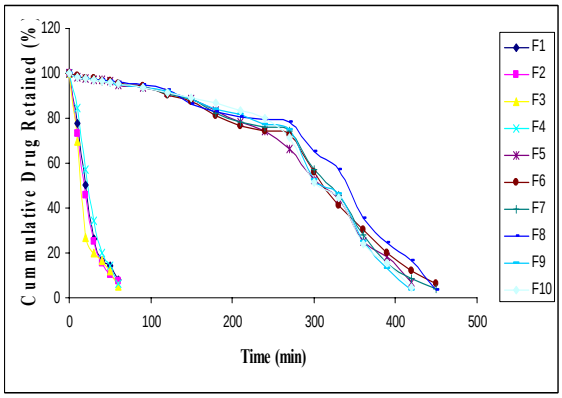

Fig. 9: First-Order Kinetic Plot, In-Vitro drug release profile of ciprofloxacin 250 mg

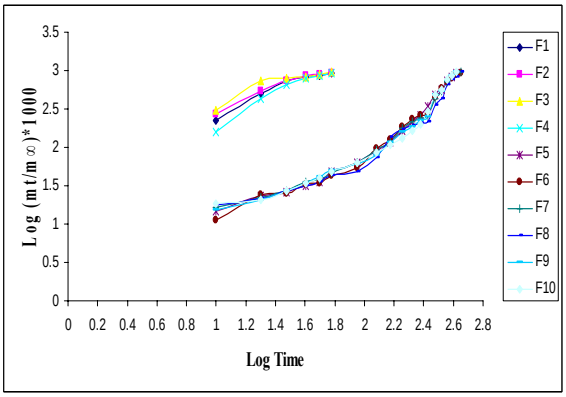

Fig. 10: Korsmeyer-Peppas equation, In-Vitro drug release profile of ciprofloxacin 250 mg

Evaluation of films:

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.

Effect of microbial flora of colon on polymeric materials: This was evaluated by inoculating the polymer coated glass cover slips in 10ml sterilized media (nutrient agar broth) with 2-3 ml freshly voided human fecal suspension and 2ml of liquid paraffin to ensure anaerobic conditions (Table 2). The incubation was done at 37 ± 0.5^{0}C for 8 days.

Water uptake: Water uptake was determined by drying the films at 60^{0}C with a current of air, after drying films were subjected to desiccation over calcium chloride at 40^{0}C for 24 h. Samples were weighed and exposed to 75 ± 0.5% relative humidity at room temperature. This relative humidity was achieved by saturated solution of sodium chloride. After equilibration of system under this humidity, films were weighed for determining the increase in weight and increase of weight percent was calculated.

Thickness of polymeric films: Thickness was measured by using a micrometer (India) having least count 0.02 mm. The films were conditioned at 55% relative humidity at 30^{0}C for 24 h. The polymeric films were pulled by pulley system; weights were gradually added to the pan, this increase the force until the films were broken.

The folding endurance: The folding endurance was measured manually. The films were conditioned at 55% relative humidity at 25-30 ^{0}C for 24 h before testing. A strip of film (2 x 2 cm) 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 [15].

Rheological Studies of Gum mucilage: Solution was prepared by dissolving polysaccharide gum (1% guar gum, 1% xanthan gum and 8% pectin) in purified water heated to 90ºC. Sodium citrate 0.6% was added as a sequestering agent for preventing gelation of gum solution at room temperature. 1% solution of guar gum in water was used as controlled during study; because guar gum acts as galactomannan.

Basically galactomannan are polysaccharides consisting of a mannose backbone with galactose side groups (more specifically, a (1-4)-linked beta-D-mannopyranose backbone with branch points from their 6-positions linked to alpha-D-galactose, i.e. 1-6-linked alpha-D-galactopyranose). Several aliquots (in triplicates) of this solution were incubated at 25ºC with different concentrations (2.5, 5, 10, 15, 30 and 45 mg/mL) of galactomannanan for 1h.

The effect of galactomannan on viscosity was determined by addition of different concentration of galactomannan in same concentration of polymeric dispersion. The viscosities of solutions were measured by using Brookfield digital RVDV-E viscometer at a fixed rpm of = 20. Prior to each measurement, the instrument was calibrated using a Brookfield Viscosity Standard Fluid 5000 (Brookfield Engineering Laboratories, Inc., MA, and USA) [16].

Preparation of Core or uncoated tablets:

The core tablets containing 250 mg of ciprofloxacin were prepared by wet granulation technique. All additional ingredients with

sodium starch glycollate as disintegrating agent were weighed and granulated with polyvinyl pyrrolidone K-30 (10% w/v in iso propyl alcohol). Granules were passed through sieve # 10. Added talc and magnesium stearate (5% w/w) with granules and compressed into tablets at an applied force of 4000-kg using 1.2 cm diameter, round and flat punches on a single station tabletting machine (Table 2).

Preparation of Coating tablets:

Compressed tablets were coated by the coating solution containing Guar gum, Xanthan gum and Pectin respectively alone or in combination at ratio of 1:1:2 was prepared in a solvent system (Table 3) using TEC (5% w/v) as plasticizer. Gums containing mucilage stirred gently for a period of 10 min with magnetic stirrer. Dispersion was transferred to a filtering flask for air bubble removal by using a vacuum pump after complete homogenization. The core tablets containing ciprofloxacin were coated at different levels of coating by using spray pan-coat (Fig. 1). Coating solution containing 5% TEC as plasticizer used to reduce film brittleness. The coating process was repeated until the desired level coating weight was achieved.

Evaluation of tablets:

The tablets were evaluated for their organoleptic properties (size, shape, texture, and colour), coating thickness, weight variation, friability, hardness, water uptake percentage, disintegration time3, drug content uniformity, swelling studies3, and in-vitro release study[17].

RESULT AND DISCUSSION

Various natural biodegradable polymers (guar gum, xanthan gum and pectin) are investigated as film coating material for colon targeted delivery. The polymers were characterized for their solubility, film forming properties and effect of microbial flora of colon on polymers (Table 4). The prepared films were investigated for their thicknesss, tensile strength, and folding endurance and for water uptake properties (Table 5).

The different studies revealed that the formulations prepared with 2% w/v gum in water as solvent showed satisfactorily film properties. On increasing the concentration of gum from 2% to 4%, the drying time was increased and the films were noted to be brown in colour with some what lower tensile strength. The tensile strength of all the films was found to vary between 1.21 to 4.81 kg/cm^2. The tensile strength of the formulation F1 was 32% more than F3, because of increase polymeric concentration.

The problems arised due to increase in the concentration could be overcome by using 1:1 ethanol water mixture instead of water. The effect of solvent could be attributed due to the difference in rate of drying and the total time required for the drying as the latent heat for 1:1 ehanol: water mixture being low, the vaporization may be uniform at room temperature. Whereas incase of water uniform drying could be achieved at a higher temperature.

The folding endurance of films was found to independent of the thickness but was dependent on the tensile strength. Tensile strength and folding endurance were depending (F13, F15 & F17) on the concentration of xanthan gum (Table 5). As the concentration of xanthan gum change with increase guar gum (F13 & F15), the tensile strength and folding endurance were increased of films. But in case of formulation F17, on addition of pectin with equal ratio of guar gum and xanthan gum showed significantly same tensile strength, the film prepared with more concentration of xanthan gum. The water uptake capacity of the films was found to be dependent on the nature of the polymers and solvent system used. Water uptake percentage was between 4.23% and 6.10%. The films prepared in 1:1 ethanol: water mixture showed less water uptake percent than with aqueous solvent.

The effect of microbial flora on prepared polymeric films is as shown in microphotograph at magnification 400 times (Fig. 2). The formation of pores in polymeric films was due to microbial degradation of the polymer by microbial flora present in the colon. The photomicrograph No. 2 shows the effect of microflora of colon on the polymeric film of composition F18.

The low density (less no. of pores per unit area) of pores formed by microbial flora indicate that less amount of drug is released from this composition may be due to presence of guar gum as galactomannan, which increase the viscosity of polymeric solution containing xanthan gum, pectin, and gives more uniform coating. Pectin is almost completely degraded by the colonic bacterial enzymes to produce a series of soluble oligalactorunates but it is highly soluble in water, which posse's problem in the development of colon targeted drug delivery systems. Pectin if used alone swells on contact with G.I.T. fluid and release the drug by diffusion.

This problem can be overcome by using galctomannan, which restricts the entry of water and consequently swelling of polymer. The viscosity of guar gum (1%), xanthan gum (1%), pectin (8%) in purified water was measured at 25ºC (Fig. 3, 4 and 5) for investigation the properties of polymeric dispersion during spray coating. A curvilinear decrease of the viscosity was suggested pseudoplastic flow properties of polymeric solution. The effect of galactomannan concentration on the viscosity of other polysaccharide solution was performed at a low but constant shear rate 20 rpm (= 3.4 sec^{-1}). Because the viscosity might change due to sequential (increasing or decreasing order) applications of various shear rates. The rheological profile obtained with the aqueous solution or 1:1 ethanol:water mixture containing 1% xanthan gum and 4% pectin in the presence of various concentrations of galactomannan is given in Fig. 6.

The results clearly shows that the viscosity of polymeric solution was significantly increased in a linear fashion with increasing the concentration of galactomannan from 2.5 to 15 mg/mL, but no further increasing was noted over the concentration range from15 to 45 mg/mL. The result identified polymeric properties of gums was change due to presence of galactomannan. The viscosity of combination of coating dispersion containing xanthan gum, pectin and galactomannan was reduced with using 1:1 ethanol: water mixture during spray coating. From the above results it is concluded, that natural biodegradable gums have enormous potential for use as film coating in preparation of colon targeted systems. These can also be used as a water-imprevious film coating agent for tablets and capsules with satisfactory tensile strength of films.

Tablet formulations (F1 - F4) were prepared using various compositions as shown in table 2 and the formulation (F4) was selected for coating by using different polymers as shown in table 3. In formulation (F4) Avicel pH 102 was used with dibasic calcium phosphate dihydrate, lactose anhydrous, and potato starch for controlled drug delivery as diluent. Formulation F-4 was selected on the basis of its hardness, friability, and disintegration time (Table 6). Swelling ratio was found to be directly related to the coating thickness of polymers on surface of tablets (Fig. 7). The result indicated that the swelling ratios of tablet were affected by pH of dissolution media.

In-vitro dissolution studies showed that release from tablets coated with guar gum, xanthan gum, and pectin polymer in combination in 1:1 ethanol-water mixture was drastically reduced up to 27% (Fig. 8, 9 and 10). The other site specific dosage form coated with guar gum in water as solvent was unable to retard drug release under similar conditions. The drug release data fit to Korsmeyer-Peppas equation (r2 = 0.9007 to 0.9477) of all coated tablets (F5 - F10). The release exponent (n) was in the range of 1.117 to 1.2123 or _ 1.0 indicating **supercase-II type or zero-order kinetics** but the nature of drug transport was non-fickinon type in case of uncoated formulations (F1 - F4). As illustrated in table 6, t50% of various batches is in accordance with the drug release rate. Uncoated tablets exhibited lower t50%, but as the combination of coating was changed a substantial increase in t50% was observed (Table 7). Statistical analysis of release data indicated that release pattern of ciprofloxacin is significantly affected by the nature and composition of polysaccharide used for coating.

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