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Development of Alginate Based Aqueous Film Coating Formula for Tablets

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Sodium alginate was selected as film-forming polymer because of its water solubility and low cost. Metronidazole tablets were coated to mask their bitter taste. The present work was carried out by initially developing aqueous film coating formulae with various concentrations of sodium alginate (4, 6 and 8% w/v). Secondly, the properties of the cast films were evaluated. When compared with dilute solutions, concentrated solutions gave thick films, as the density was more. UV light transmission, water vapour transmission and gas permeability of the films decreased with the increase in the thickness of the films. They were freely soluble in distilled water and simulated intestinal fluids but precipitated in simulated gastric fluid. Thirdly, 2 kg of tablets were coated using solutions of the above concentrations. Some tablets were withdrawn after application of 400, 600 and 800 ml of coating solutions, respectively. Coated and uncoated tablets were evaluated for weight variation, hardness and friability, which were all within the acceptable limits. Coating increased hardness and decreased friability. All the coated and uncoated tablets disintegrated within 10 min in water and complied with the USP and BP limits for the assay. The rate of drug release decreased as the concentration of sodium alginate increased. Only 400, 600 and 800 ml coats of 4% w/v solution and 400 ml coats of 6% and 8% w/v solutions in buffer pH 1.2 met USP dissolution requirements. Based on the results of above work along with statistical analysis and accelerated stability studies, 400 ml coat of 6% w/v solution was chosen as the best.

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The objective of the present work is to develop an aqueous film coating formula for tablets as it avoids the use of organic solvents which are associated with many problems[1] such as toxicity hazards, flammability hazards, environmental pollution and higher cost. Sodium alginate[2] was used as film forming polymer, which is water soluble, easily available and cheap. Also, much work has not been done using sodium alginate as aqueous film coating material for tablets. Metronidazole tablets were chosen for coating, as they are bitter in taste.

Film coating formulae and coating conditions such as 40° for drying tablet bed while coating from among 30°, 35° and 40° and 14 as the coating pan rpm from among 12, 14 and 16, were selected based on initial trials of coating dummy tablets with various concentrations of the chosen ingredients. Plain films were cast using 10 ml of each of 4%, 6% and 8% coating solutions on lubricated glass plates of equal areas of 10 cm^2. They were then dried by infrared lamp and the films were peeled off to evaluate their physicochemical properties[3].

Metronidazole tablets (200 mg) were coated using the selected coating solutions and coating conditions. Coating pan with 8 baffles was loaded with 2 kg of metronidazole tablets. The rotation of the coating pan was adjusted to 14 rpm. Coating solution was sprayed using low pressure air-atomized system at the rate of about 15 ml/min over pre-warmed tablets at a pressure of 3-5 kg/cm^2 while the temperature of the drying air was maintained at 70-80°. The temperature of the tablet bed was maintained at 40° through out the coating process. Around 300 tablets were withdrawn every time after applying 400, 600 and 800 ml coats with all the above concentrations of the coating solutions. At the end of spraying process, tablets were dried at 40° for 2 h in a hot air oven. Coated and uncoated tablets were then evaluated according to official requirements. Finally, accelerated stability studies were carried out for 6 w on the best coat (400 ml coat of 6% w/v) along with uncoated tablets and were analyzed every two weeks to compare the effect of coating on the stability of the tablets.

The various selected film coating formulae are given in Table 1. The physicochemical properties of the plain films are given in the Table 2. It was observed that the thickness

TABLE 1: FILM COATING FORMULAE

Ingredients	4% w/v	6% w/v	8% w/v
Sodium alginate	40 g	60 g	80 g
PEG 6000	30 g	30 g	30 g
Titanium dioxide	12.5 g	12.5 g	12.5 g
Brilliant blue	250 mg	250 mg	250 mg
Castor oil	5 ml	5 ml	5 ml
Distilled water sufficient to	1000 ml	1000 ml	1000 ml

The above coating formulae were selected based on initial trials of coating dummy tablets with various concentrations of the chosen ingredients.

TABLE 2: PHYSICOCHEMICAL PROPERTIES OF PLAIN FILMS

SA % w/v	Thickness* (cm)	Density* (g/cm^3)	Gas permeability* (g/cm/h)	Water vapour transmission* (g/cm)		Solubility (At 37°)		
				RH 51%	RH 79.3%	DW	SGF	SIF
4%	0.013 (±0.0007)	0.5882 (±0.0044)	0.00003612	0.0004154	0.0005994	S	NS	S
6%	0.014 (±0.0008)	0.6521 (±0.0025)	0.00002835	0.0003764	0.0005242	S	NS	S
8%	0.015 (±0.0007)	0.7430 (±0.0031)	0.00001396	0.0003424	0.0004419	S	NS	S

SA=Sodium alginate; RH=Relative humidity; DW=Distilled water; SGF=Simulated gastric fluid; SIF=Simulated intestinal fluid; S=Soluble; NS=Not soluble. Variation in the concentration of film former has direct influence on the properties of the films obtained. The values in the parenthesis indicate standard deviation. *Average of 6 determinations.

of the film increased with the increase in the concentration of sodium alginate due to increased density of coating solution. Gas permeability and water vapour transmission of the films decreased with increase in the film thickness. The films were soluble in simulated intestinal fluid and water but precipitated in simulated gastric fluid. The results obtained on evaluating the coated and uncoated tablets according to official requirements are given in Table 3. The average tablet thickness, diameter, weight of the tablets, hardness and disintegration time (all coated and uncoated tablets disintegrated within 10 min) had all increased after coating with increasing volume and concentration of the coating solutions. Friability and weight gain on exposure to relative humidities (51% and 79.3%) decreased after coating with increasing volume and concentration of the coating solutions. The assay values for coated and uncoated tablets remained the same proving that the coating had not interfered with the assay method. Dissolution studies[4] were carried out to analyze the drug concentration in the solution every 20 min for 1 h. The results of which are given in Table 4. Only tablets coated with 400, 600 and 800 ml of 4 % w/v sodium alginate solution and 400 ml of 6% and 8% w/v sodium alginate solutions met the USP dissolution requirements.

The reduction in drug release observed with increasing

TABLE 3: PHYSICOCHEMICAL PARAMETERS OF UNCOATED AND COATED TABLETS

Parameters	UT	Coated tablets (with various coating polymer concentrations)								
		4% w/v			6% w/v			8% w/v		
		400 ml coat	600 ml coat	800 ml coat	400 ml coat	600 ml coat	800 ml coat	400 ml coat	600 ml coat	800 ml coat
Thickness* (mm)	3.8	3.9	3.9	3.9	3.9	3.9	3.9	3.9	3.9	4.0
Diameter* (mm)	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1	11.1
Weight# (mg)	0.43	0.44	0.44	0.45	0.44	0.44	0.45	0.44	0.45	0.45
Hardness* (kg/cm^2)	5	6	6	6	6	6	6	6	6	6
Friability (%)	0.42	0.07	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.05
DT* (min)	5	5.5	6	6.1	6.1	6.1	6.3	6.2	6.3	6.4
WG(mg)*										
RH: 51%	10	3.7	2.5	1.6	2.8	1.9	1.2	1.7	1.4	0.9
RH: 79.3%	20.9	12.2	11.0	10.1	10.9	10.3	9.1	10.4	8.9	7.4
Assay* (%)	101	101	101	101	101	101	101	101	101	101

UT=Uncoated tablets; DT=Disintegration time; WG=Weight gain on exposure to relative humidities of 51% and 79.3%, respectively. Coating has beneficial effect on the properties of the tablets without altering the disintegration time to any significant extent. *Average of 6 determinations. #Average of 10 determinations.

the sodium alginate concentration in the coat may be due to increased drug trapping resulting from the precipitation of sodium alginate in acidic medium. The results of accelerated stability studies obtained at the end of 6th w were presented in Table 5. It was observed that coating had not adversely affected the properties of the tablets on exposure to higher temperature.

TABLE 4: DISSOLUTION STUDIES ON UNCOATED AND COATED TABLETS

Time (Min)	Uncoated Tablets*	Tablets coated with various coating polymer concentrations*								
		4% w/v			6% w/v			8% w/v		
		400 ml coat	600 ml coat	800 ml coat	400 ml coat	600 ml coat	800 ml coat	400 ml coat	600 ml coat	800 ml coat
20	97.1	19.0	17.9	15.7	17.2	16.3	14.0	15.8	14.1	9.8
	(±0.44)	(±1.7)	(±0.7)	(±0.8)	(±0.8)	(±0.8)	(±0.9)	(±1.5)	(±0.6)	(±0.8)
40	97.1	97.2	82.1	65.9	81.1	60.9	42.4	65.6	41.3	19.0
	(±0.44)	(±0.6)	(±1.2)	(±1.3)	(±0.8)	(±0.9)	(±1.4)	(±1.1)	(±1.4)	(±1.4)
60	97.2	97.2	97.2	88.3	97.2	82.9	59.3	87.8	62.4	38.0
	(±0.5)	(±0.6)	(±0.6)	(±1.1)	(±0.6)	(±1.2)	(±1.5)	(±1.1)	(±1.5)	(±1.5)

The decreased drug release with increase in the sodium alginate concentration may be due to its increased drug trapping as sodium alginate gets precipitated in the acidic medium. The values in the parenthesis indicate standard deviation. *Average of 6 determinations.

TABLE 5: ACCELERATED STABILITY STUDIES ON UNCOATED AND COATED TABLETS

Parameters (At the end of 6th week)	Temperature	Uncoated tablets	Coated tablets#
Disintegration time* (min)	RT	5.16	6.20
	37°	5.27	6.29
	45°	5.36	6.34
% Drug release* (USP method)	RT	96.9	96.8
		(±0.96)	(±0.45)
	37°	96.6	96.7
		(±0.53)	(±0.32)
	45°	96.2	96.2
		(±0.43)	(±0.7)
Assay*(%)	RT	100.4	100.4
	37°	100.1	100.1
	45°	99.8	99.9

Exposure to higher temperature for 6 weeks had the same effect on the properties of both uncoated and coated tablets. #Tablets coated with 400 ml of 6% w/v sodium alginate were taken for comparison with uncoated tablets as it was the most satisfactory coating solution formula. The values in the parenthesis indicate standard deviation. *Average of 6 determinations.

Based on the above results and the statistical analysis[5] of dissolution data using ANOVA and 't' test, the best coat was selected. The 't' test was carried out only if ANOVA was significant at 5% level. Statistical analysis had showed that for the 400 ml coats, the difference in the dissolution rate (Table 4) at 60 min between 4% and 6% w/v solutions was insignificant at 5% level. But, 400 ml coat of 6% w/v solution were considered as the best since 400 ml coat of 4% w/v solution was dilute and took long time to dry during coating. Thus, drying time was also taken into consideration while choosing the best coating formula. Even though the tablets coated with 400 ml of 8% w/v solution had just passed (approximately 87%) the USP dissolution requirements [85% (Q)] in 60 min, it is not recommended to use this concentration for coating as the value is on the border. In the light of the above results, aqueous film coating with sodium alginate can be employed for cost effectiveness and competitiveness especially for export markets in addition to the associated safety. The 400 ml coat of 6% w/v aqueous film coating formula, which was chosen as the best, could be used for coating any extremely unpalatable tablets in addition to metronidazole tablets.

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A New Reverse Phase High Performance Liquid Chromatographic Method for Analysis of Rofecoxib in Tablets

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A simple, selective, rapid, precise and economical reverse phase HPLC method has been developed for the determination of rofecoxib in tablets. The analyte is resolved by using a mobile phase (methanol and water in the ratio 50:50) at a flow rate of 1 ml/min on an isocratic HPLC system (Shimadzu) consisting of LC 10AT liquid pump, SPD 10A UV-Visible detector, a ODS C-18 RP column (4.6 mm I.DX25 cm) at a wavelength of 230 nm. The linear dynamic range for rofecoxib was 2-40 μg/ml by this method. Paracetamol was used as an internal standard.

Rofecoxib is a new non-steroidal antiinflammatory drug. It is commonly prescribed in the treatment of osteoarthritis and chemically it is 4-[4-(methyl sulfonyl) phenyl]-3-phenyl-2 (5H)-furanone[1]. A survey of literature reveals that two HPLC methods[2-3] are reported for the determination of rofecoxib in biological fluids and in tablets[4]. In the present investigation, a new RPHPLC method is reported for the

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