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Modified guar gum as film former

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Guar gum (GG), a naturally occurring galactomannan polysaccharide, produces films that lack in clarity and have poor tensile strength. Hence an attempt was made to modify GG chemically by carboxymethylation to improve its film forming ability. The degree of substitution was altered and the reaction parameters were optimized. Synthesized sodium carboxymethyl derivatives of GG (NaCMGs) were evaluated for their physical and chemical properties. Finally, NaCMGs were evaluated as film formers. The type and amount of plasticizers to be used alongwith NaCMGs were optimised. The results suggest that NaCMGs can be suitable alternatives to the commercially available film formers.

1. Introduction

The most important raw material for film coating is a pharmaceutically acceptable film-forming resin, which should form a coherent film on the surface of the substrate under the prevailing conditions [1]. In the present investigation Guar gum (GG), a naturally occurring galactomannan polysaccharide, has been explored for the possibility of its use as a film former. GG forms a translucent dispersion on complete hydration in water. Films formed by GG lack in clarity and also in tensile strength. Hence GG was modified chemically to improve its film forming characteristics. Sodium carboxymethyl derivatives of GG (NaCMGs) were synthesized and characterised using suitable analytical techniques. NaCMGs, when evaluated as film formers by casting films from its aqueous solutions, were found to give encouraging results with respect to film forming characteristics. The type and amount of plasticizers to be used alongwith NaCMGs were optimised by evaluating the films for parameters like breaking strength and water vapour transmission rate. Finally, aqueous film coating of dummy tablets was done with NaCMG and the performance was compared with commercially available hydroxypropyl methylcellulose 15 cps (HPMC 15 cps). Various tablet parameters, after coating, were determined.

2. Investigations, results and discussion

Film coating of compressed tablets is done for a variety of reasons which include masking of taste, increasing the stability of the active ingredient or improving the elegance of tablets. The first commercial systems were developed in the 1950s but major progress in film coating came in 1960s with the development of low molecular weight cellulose and acrylic polymers and with introduction of spray techniques. Solvent costs, environmental pollution and operator safety have driven the move from organic solvents to aqueous film coating, which is now the method of choice. The polymers most frequently encountered are the cellulose ethers (HPMC, Ethylcellulose, CAP), vinyl polymers (PVAP, PVP) and the methacrylic acid co-polymers. In the present investigation, GG, a naturally occurring galactomannan polysaccharide, has been explored for its potential use as film forming resin. It has been chemically modified to improve its film forming properties.

2.1. Carboxymethylation of GG and characterisation of NaCMGs

GG was treated with a 75% w/v aqueous solution of monochloroacetic acid in a solvent mixture of 40% w/v aqueous sodium hydroxide solution and a polar organic solvent, methanol. The reaction was carried out in a hydroalcoholic medium to control the reaction rate by restricting the hydration of GG. Synthesized NaCMGs were evaluated for bulk and tapped densities, viscosity and were also subjected to differential scanning calorimetry. No significant change in the bulk and tapped densities could be observed (Table 1). A shift in the endothermic peak in thermograms confirmed the formation of new compound after the reaction.

To alter the degree of carboxymethyl substitutes in GG, the reaction was carried out with an increased amount of monochloroacetic acid solution. With the increase in substitution of carboxymethyl groups in GG, a fall in viscos-

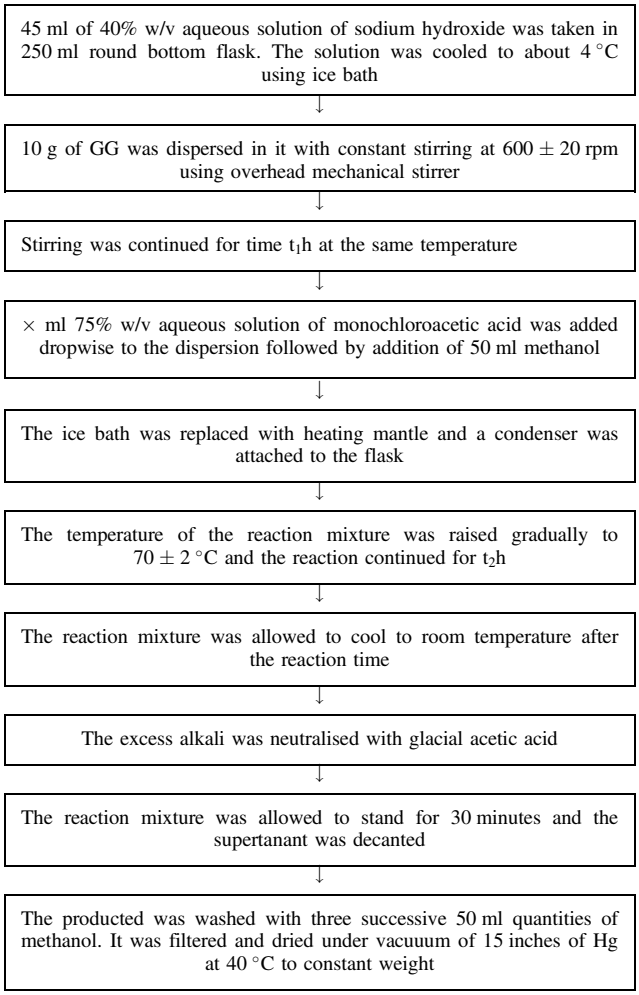

Fig.: Preparation of sodiumcarboxymethyl guar $t_1 = 0.5$, 1.0, 2.0 and 3.0; x = 2, 4, 8, 10, 15, 20, 25 and 30; $t_2 = 3$, 6, 8, 12 and 18

Table 1: Carboxymethylation and characterisation of GG

Sr. No.	Product	Duration in Alkali (h)	Amount of MCAA* solution (ml)	Duration of React. At 70 °C (h)	Viscosity (S.E.) (cps)	Bulk Density (g/ml)	Tapped Density (g/ml)
1.	GG	–	–	–	8266.65 (15.23)	0.40	0.65
2.	NaCMG1	0.50	2	3	6025.50 (15.68)	0.40	0.65
3.	NaCMG2	0.50	4	3	4350.00 (14.77)	0.42	0.667
4.	NaCMG3	0.50	8	3	1015.90 (13.39)	0.41	0.66
5.	NaCMG4	0.50	10	3	800.00 (11.58)	0.42	0.69
6.	NaCMG5	0.50	15	3	475.50 (12.68)	0.40	0.70
7.	NaCMG6	0.50	20	3	300.65 (12.23)	0.41	0.71
8.	NaCMG7	0.50	25	3	–[a]	0.40	0.69
9.	NaCMG8	0.50	30	3	–[a]	0.40	0.69
10.	NaCMG9	0.50	20	6	175.32 (6.12)	0.40	0.70
11.	NaCMG10	0.50	20	8	172.77 (4.78)	0.41	0.71
12.	NaCMG11	0.50	20	12	174.45 (3.98)	0.41	0.71
13.	NaCMG12	0.50	20	18	170.82 (4.13)	0.41	0.71
14.	NaCMG13	1.00	20	6	150.55 (3.77)	0.41	0.70
15.	NaCMG14	2.00	20	6	150.75 (3.82)	0.40	0.69
16.	NaCMG15	3.00	20	6	149.75 (3.76)	0.41	0.70

* 75% w/v aqueous solution of Monochloroacetic acid [a] The product does not form a clear solution but gets dispersed in aqueous medium

ity of aqueous dispersions of NaCMG was observed (Table 1). The fall in viscosity may be attributed to the hydrolysis of GG in basic media along with the formation of sodium salts. This also improved the film forming characteristics of NaCMG and hence efforts were concentrated to modify GG in a way to use NaCMG as a film former.

Polymer viscosity is particularly important in aqueous coating, especially where there is a need to minimise the concentration of water in the coating formulation to achieve reasonable process times and to minimise moisture contact with the dosage form. To maximise drying rate, the maximum possible polymer concentration should be used but the limiting factor is viscosity. Above 500 cps the coating suspension will be difficult to atomise and it will not be possible to produce smooth film coated tablets. Hence low viscosity polymers are needed, particularly where aqueous coating is employed. To meet the objective of lowering viscosity of the NaCMGs and to improve the clarity of cast films, the concentration of monochloroacetic acid solution, duration of reaction and exposure of GG to alkali were altered as follows:

The amount of 75% w/v aqueous solution of monochloroacetic acid used for derivatisation was gradually increased from 2 ml to 30 ml (Table 1). The increase in the amount of monochloroacetic acid solution used for derivatisation caused a significant fall in viscosity of the aqueous solution of NaCMG and the clarity of aqueous dispersion of NaCMG was improved. The fall in viscosity of the aqueous solution of NaCMG was significant when monochloroacetic acid solution was used for the reaction in the amount between 2 ml to 20 ml; thereafter the fall in viscosity values was not-significant.

The reaction time was increased from 3 h to 24 h keeping the amount of monochloroacetic acid solution constant (20 ml). It was observed that when the reaction continues for longer durations, keeping the amount of derivatizing agent constant, the clarity of the aqueous solutions was improved up to 6 h beyond which no significant change could be observed.

To further reduce the viscosity of the aqueous dispersions of NaCMG, exposure time of GG to alkaline medium was increased from 0.5 h to 3 h keeping the reaction procedure and conditions constant (20 ml 75% w/v aqueous monochloroacetic solution and 6 h duration of reaction). This change helped in reducing the viscosity of an 1% w/v aqueous dispersion of NaCMG to 149.75 ± 3.76 cps from 8036 ± 24 cps of GG.

Thus the reaction conditions were optimised as (a) 20 ml of 75 w/v aqueous solution of monochloroacetic acid (b) 6 h duration of reaction and (c) 3 h duration of exposure of GG to alkali.

2.2. GG and NaCMGs as film formers

The selection of a film-forming technique for uniform films is of paramount importance in research where film thickness must be accurately determined and controlled. In the present investigation a glass substrate previously coated with a releasing agent was used to cast films. The releasing agent enhanced the smoothness of the glass substrate in addition to facilitating removal of the dried films from the substrate with minimal stress imparted to the films. The releasing agent was applied in very low quantities and was heated at about 250 °C for 2 h, which reduced the probability of its transfer

to film. The low order of adhesion and ease of film removal from the substrate were of great importance for maintaining the integrity of the film.

GG and NaCMGs were evaluated as film formers by casting films in petri plates. It was observed that GG formed translucent and brittle films and could not be removed as intact films from glass petri plates. The macromolecular mobility of the polymer changes at its glass transition temperature (T_g) and below T_g, polymer chain mobility is severely restricted. The T_g of GG may be at a temperature high above room temperature, hence does not form films of the required characteristics, and gives hard, non-pliable and brittle films on drying. On the contrary, NaCMG formed films with good clarity (transparency), flexibility and sufficient tensile strength. NaCMG with low viscosity (NaCMG15) was taken for further investigation for its possible use in film coating of tablets.

The film properties of a polymer are influenced by addition of suitable external plasticizer/s. The function of the plasticizer is to modify the basic mechanical properties of the polymer. Plasticizers have a high affinity for polymers; the interaction reduces the bonding between adjacent polymer molecules, causing a reduction in elastic modulus. Plasticizer choice depends on identifying a material which has good interaction with the polymer, is miscible with the solvent system and is not lost from the film by evaporation or by partition into the substrate. There are a large number of examples of edible materials with plasticising actions; some of the most commonly used are polyethylene glycols, propylene glycol, glycerol and triacetin. In this investigation, propylene glycol (PG), polyethylene glycol 400 (PEG) and glycerin (GLY) were selected. Films of NaCMG were cast using 30% PEG/PG/GLY by weight of polymer as plasticizer. The cast films were dried and then subjected to DSC. The thermograms show no change in the endothermic peak of NaCMG in cases of 30% PG/GLY as plasticizers. In fact, the thermograms show two or more peaks indicating no plasticizing effect and no interaction of these plasticizers with NaCMG. When 30% PEG was used as plasticizer a sharp endothermic peak was observed at lower temperatures (78 °C–80 °C) compared to a broad endothermic peak of NaCMG alone at higher temperatures (85 °C–90 °C).

The concentration of PEG in NaCMG films was varied from 10% to 40% and cast films were evaluated for water vapour transmission rate (Table 2). The ability of NaCMG films to resist moisture transfer was significantly increased when PEG was used as plasticizer compared to PG and GLY. It further confirms our selection of PEG. The rate of water vapour transmission was minimum with 30% PEG as plasticizer (4.75 ± 0.50 mg/h) and then increases gradually (40% PEG $-$ 5.50 ± 0.75 mg/h). The increase in rate of moisture transfer may be attributed to an increase in film hydrophilicity.

The breaking strength of the film (Table 2) in terms of increase in the hardness of the tablet with respect to that of an uncoated tablet per unit area was calculated. The results suggest a significant increase in the hardness of the tablet after being coated with NaCMG alone ($2.88\ kg \cdot cm^{-2}$). The addition of PEG up to 30% by weight as plasticizer in NaCMG films increases the breaking strength to $6.06\ kg \cdot cm^{-2}$ followed by a fall in breaking strength of the film at 40% concentration by weight ($5.76\ kg \cdot cm^{-2}$). Hence PEG in 30% concentration by weight of NaCMG was used for subsequent investigations.

Film coating of dummy tablets was done using NaCMG and HPMC 15 cps as film formers. The composition of the film coating solutions are shown in Table 3. The coating was applied to a moving bed of tablet in a conventional coating pan, spraying the solution in small portions onto the tablets. After distribution of material evenly over the tablet surface, drying of the film was facilitated by a hot air blower at 70 °C. Successive applications were made, until a film of the desired thickness was achieved (2% weight gain of tablets). The coated tablets were compared for appearance, gloss and disintegration time. General appearance and gloss of the tablets coated with NaCMG and HPMC 15 cps were found to be comparable. However, the tablets coated with NaCMG show a significant increase (about 7.0 min) in DT, compared to tablets coated with HPMC 15 cps, where no significant change was observed. A comparatively higher viscosity of NaCMG (149.75 ± 3.76 cps of 1% w/v aqueous solution) may be the probable reason for the significant increase in DT after coating. The NaCMG film initially gets gelled on surface preventing penetration of the fluid into the tablets causing a delay in disintegration of tablets.

It may be concluded that NaCMG can be employed as film former for tablet coating. NaCMG having lower viscosity may be a better alternative to HPMC 15 cps, as a

Tabelle 2: Composition and evaluation of films

Ingredients	Quantity							
	I	II	III	IV	V	VI	VII	VIII
NaCMG	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	–
HPMC 15 cps	–	–	–	–	–	–	–	5.0%
PG	–	1.5%	–	–	–	–	–	–
PEG	–	–	1.5%	–	0.5%	1.0%	2.0%	–
GLY	–	–	–	1.5%	–	–	–	–
TiO_2	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Talc	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Water q.s. to	100%	100%	100%	100%	100%	100%	100%	100%
Thickness	0.072 ± 0.004	0.074 ± 0.002	0.072 ± 0.003	0.073 ± 0.002	0.074 ± 0.002	0.074 ± 0.002	0.074 ± 0.003	0.073 ± 0.002
Rate of moisture loss (mg/h)	7.00 ± 0.35	7.25 ± 0.25	4.75 ± 0.50	6.00 ± 0.25	6.00 ± 0.50	5.25 ± 0.35	5.50 ± 0.35	5.00 ± 0.50
Hardness of coated tablets (kg/cm^2)	11.25 ± 0.20	12.00 ± 0.25	16.50 ± 0.50	11.0 ± 0.25	13.50 ± 0.50	14.00 ± 0.50	16.00 ± 0.35	15.50 ± 0.25
Breaking strength (kg/cm^4)	2.88	3.33	6.06	2.74	4.24	4.54	5.76	5.45
Times increase in breaking strength	100	115.63	210.42	95.14	147.72	157.64	200.00	189.24

Table 3: Film coating solution for coating of dummy tablets

No.	Ingredients	Quantity (% w/w)	
1.	HPMC 15 cps	5.0	–
2.	NaCMG	–	5.0
3.	PEG	1.5	1.5
4.	Talc	1.0	1.0
5.	Titanium dioxide	2.0	2.0
6.	Sunset yellow lake	0.5	0.5
7.	Purified water q.s. to	100	100
DT of coated tablets (min)*		6.0 ± 0.5	13.0 ± 1.0
Weight gain by tablets after coating		2%	2%
Film thickness (mm)		0.055 ± 0.002	0.064 ± 0.004
Breaking strength of film ($kg \cdot cm^{-2}$)		5.50	5.64

* DT of uncoated tablets was 5.0 ± 1.0 min

film former in aqueous based film coating. The cost effectiveness and possibility of its application in aqueous based film coating are the important factors favouring its use in tablet coating. The higher viscosity grades can also be used to form a barrier layer to increase the stability of moisture-sensitive drugs.

3. Experimental

3.1. Materials

Guar gum (GG) (Sarabhai Chemicals, Baroda, India), sodium hydroxide A.R. (s.d. fine chem. Pvt. Ltd., Boisar, India), monochloroacetic acid G.R. (Apex Chemicals, Ahmedabad, India), glacial acetic acid A.R. (Loba-Chemie, Bombay, India), sodium tartarate A.R. (National Chemicals, Baroda, India), polyethylene glycol 400 (PEG), propylene glycol (PG), glycerin (GLY) (National Chemicals, Baroda, India), purified talc I.P., magnesium stearate I.P. (Comet Chemicals, Bombay, India), titanium dioxide, lactose I.P., microcrystalline cellulose I.P., starch I.P. (Chemical Supply Corporation, Bombay, India), sodium starch glycollate (D.P. Chemicals, Bombay, India), polyvinyl pyrrolidone K-30 (PVP) (BASF (India) Ltd., Bombay), sunset yellow lake (National Chemicals, Baroda, India).

3.2. Equipment

Overhead mechanical stirrer (Remi scientific instruments, Bombay, India), Oven (Modern Industrial Corporation, Bombay), Differential Scanning Calorimeter (DSC20 Mettler, Switzerland), Single stroke Compression machine (Cadmach machineries, Ahmedabad, India), S.S. coating pan (Magumps, Bombay, India), Spray gun (Pilot Type 59, Manik Machinery Manufacturers Pvt. Ltd., Bombay, India), Peristaltic pump (Electrolab, Ahmedabad, India).

3.3. Methods

3.3.1. Synthesis of sodium carboxymethyl guar

Sodium carboxymethyl guar was synthesized using the procedure described in the flow diagram (Fig.). The reaction conditions were altered to optimise the degree of substitution in the derivative.

3.3.2. Characterisation of sodium carboxymethyl guar (NaCMGs)

The NaCMGs were characterised by bulk density, tapped density and viscosity, the values of which are recorded in Table 1. Differential Scanning Calorimetry of NaCMG was performed and the thermograms were recorded.

3.3.3. Evaluation of GG and NaCMGs as film former

Smooth and uniform glass petri plates of 3.5 ± 0.05 inch diameter were used as substrates to cast free films. The glass substrate was coated by hand using disposable wipers with silicon oil. The coated petri plates were then kept in an oven at 250 °C for 2 h. 50 ml of 1% w/v solutions of GG/NaCMGs were poured into separate petri plates. The solutions in petri plates were dried to a moisture content of not more than 3% w/w (Loss on Drying) in oven at 50 ± 2 °C (drying time about 14–16 h).
The films deposited on the petri plates were removed and cut into circular disks of approximately 3 cm diameter and stored in a desiccator containing calcium sulphate. The films were evaluated for physical characteristics like clarity and tensile strength. NaCMGs, which formed films of good quality with respect to clarity and flexibility, were studied further for application in tablet coating and the performance was compared with HPMC films.

3.3.4. Selection and optimisation of concentration of plasticizers

Plasticizer (PEG, PG and GLY) was added in the concentration of 30% by weight of polymer in 50 ml of an 1% w/v aqueous solution of polymer. The polymer solutions containing plasticizers were cast into films in petri plates as described earlier. The recovered films were subjected to DSC. The thickness of the film was measured using a micrometer having a least count of 0.01 mm.
The water vapour transmission rate of the formed films were determined as reported by Parker et al. [3]. The permeation cell used was very similar to that used by Patel et al. [4]. It consisted of a 50 ml screw-capped, cylindrical glass bottle with a hole, 1.5 cm in diameter, in the screw cap. A circular piece of film was placed between two rubber gaskets, which was then fixed into the screw cap. The area of the circular film exposed was 1.65 ± 0.03 cm^2. The bottle contained 5 ml of supersaturated sodium tartarate solution, which gives an internal humidity of 91% at 30 °C, equivalent to a vapour Perser of 28.96 mm Hg [5]. The tightly sealed bottles were placed in a desiccator over anh. calcium sulphate, which was further kept in oven at 30 ± 0.5 °C. The films exposed were kept for 12 h and their weight was recorded. The loss in weight was noted after 72 h.
The breaking strength of the films after coating of tablets was determined as reported by Stern [6]. The hardness of tablets before and after coating was determined to measure the breaking strength of the films.
The promising plasticizer was used in the concentrations of 10%, 20%, 30% and 40% by weight of polymer for film formation. The films, formed as explained earlier, were evaluated for breaking strength and water vapour transmission rate.
All the results are recorded in Table 2.

3.3.5. Tabletting

Dummy tablets (average weight 275 mg) were prepared on a single stroke compression machine, using lactose 35%, microcrystalline cellulose 45%, starch 12.5%, polyvinyl pyrrolidone K-30 2.5%, magnesium stearate 1%, talc 1% and sodium starch glycollate 3% by weight per tablet, with following specifications:

Description:	9.5 ± 0.1 mm round, biconvex
Thickness:	3.8 ± 0.2 mm
Average weight of tablet:	275 mg $\pm$ 3% w/w
Hardness:	6.5 ± 0.5 kg/cm^2
Friability loss:	NMT 0.5% by weight of 20 tablets
Disintegration time:	5.0 ± 1.0 min

These dummy tablets were taken for film coating.

3.3.6. Film coating of tablets

Film coating of dummy tablets was done using the solution composed as shown in Table 3. The polymer was dissolved in sufficient quantity of water (about 60% of total volume used) and to it PEG was added and dissolved. Talc, titanium dioxide and sunset yellow lake were weighed, mixed and passed twice through a #100 mesh sieve. The mix was then dispersed in the polymer-plasticizer solution under continuous stirring (1200 ± 50 rpm). The coating solution was passed through nylon bolting cloth (#200 mesh) to ensure uniform distribution of the dispersed solids. NaCMG and HPMC 15 cps were used as film formers and the tablets were coated under the following coating conditions:

Pan:	8 inch s.s. coating pan.
Pan speed:	20 ± 2 rpm
Spray equipment:	Spray gun of nozzle with 1.0 ± 0.1 mm diameter Peristaltic pump
Atomising pressure:	3.5 ± 0.5 kg/cm^2
Inlet air temperature:	70 ± 2 °C
Spray rate:	50 ml/min
Spray cycle:	15 s on, 45 s off

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Received November 9, 1998
Accepted January 27, 1999

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