Chapter 7

MODIFIED GUAR GUM
AS
FILM FORMER

7.1 INTRODUCTION

Tablet coating is one of the oldest arts employed by the pharmaceutical industry for variety of reasons, including the need to hide an objectionable taste or odor, to protect an unstable core ingredient, to impart an aesthetic appearance or to separate incompatible ingredients by including one in the core tablet and other in the coating (1). The coating of pharmaceutical tablets may be conveniently divided into the traditional sugar or pan-coating procedures and contemporary techniques which include film coating and compression coating. Until about 1950, sugar stood in the foreground as a coating agent for pharmaceutical preparations and much time and effort was spent in perfecting and performing sugar coating techniques. In addition to this, the naturally occurring substance, shellac, played a subordinate role in insulating layers and in enteric coated cores. Zein was also used, though to a smaller extent(2). Film coating evolved in early 1950s because of need to introduce science in the art of tablet coating. It involves the deposition of a thin but uniform membrane of a pharmaceutically acceptable resin onto the surface of the substrate.

The film coating process is simpler, since weight gains of only 2 - 6 % are involved as opposed to more than 60% with sugar coating. The most important raw material for film coating is the film-forming resin. The main prerequisite for the resin is its ability to form a coherent film on the surface of the substrate under the prevailing conditions. Solubility in one or more of the available solvents or solvent combinations is an important factor in determining the suitability of a particular resin. In addition, solubility in most part of the gastrointestinal tract is important if the bioavailability of the active material is not to be impaired. There are many synthetic polymeric materials available, which meet the requirements of a good film former like the lack of toxicity and ability to produce tough, yet elastic, film even in presence of powdered additives such as pigments.

Plasticizers are added to the film former, which prevent the film from becoming brittle with consequent risk of chipping. The choice of plasticizer depends upon the particular film former since the plasticizer essentially functions by modifying polymer-to-polymer molecular bonding. The nature of the solvent system may markedly influence the quality of the film and to optimize various factors, mixed solvents are usually necessary. Alcohols, esters, chlorinated hydrocarbons and ketones have been the most popular choices until recently.

However, as a result of increasing contemporary pressures against undesirable solvents, there has been a pronounced trend towards aqueous film coating. Many of the same polymers can be used but it may be necessary to employ lower molecular weight grades, because of higher viscosity in aqueous systems. This signifies an urgent need to explore newer film formers that can be used as aqueous dispersions/solutions for film coating of the tablets. In the present investigation modified GGs were evaluated as film formers. GG, a naturally occurring galactomannan polysaccharide, has been employed in pharmaceuticals as viscosity builder, tablet disintegrant and such other purposes. GG forms a translucent dispersion on complete hydration in water and the films formed by it lack in clarity and also in tensile strength. Hence GG was modified by hydrolysis, methylation and carboxymethylation as explained. These modified GGs were evaluated as film formers by casting films of the aqueous solutions. NaCMGs were found to be encouraging with respect to film forming characteristics compared to other modified GGs (HGGs, MGGs, OGGs). The type and amount of plasticizers to be used alongwith NaCMGs were optimised using analytical techniques like differential scanning calorimetry (DSC). The films were evaluated for parameters like breaking strength and water vapour transmission rate. Finally aqueous film coating of dummy tablets was done

with NaCMG and the performance compared with commercially available hydroxypropyl methylcellulose 15 cps (HPMC 15 cps).

7.2 MATERIALS

GG and Modified GGs (HGGs, MGGs, and NaCMGs).

Polyethylene glycol 400(PEG), propylene glycol (PG), glycerin (GLY) (National chemicals, Baroda), purified talc I.P., magnesium stearate I.P.(Comet Chemicals, Bombay), titanium dioxide, lactose I.P., microcrystalline cellulose I.P., starch I.P., (Chemical Supply Corporation, Bombay), sodium starch glycollate (D.P. Chemicals, Bombay)

7.3 EQUIPMENTS

Oven (Modern Industrial Corporation, Bombay), Differential Scanning Calorimeter(DSC20 Mettler, Switzerland), Single stroke Compression machine (Cadmach machineries, Ahmedabad), S.S. coating pan (Magumps, Bombay), Spray gun (Pilot Type 59, Manik Machinery Manufacturers Pvt. Ltd., Bombay) Peristaltic pump (Watson-Marlow, Bombay).

7.4 METHODS

7.4.1 Evaluation of GG and modified GGs as Film Former :

Smooth and uniform glass petri plates of 3.5 ± 0.05 inch were used as substrates to cast free films. The glass substrate was coated by hand using disposable wipers with silicon oil, being used as release agent, which was then kept in oven at 250°C for 2 hours. 1% w/v aqueous solutions of GG and modified GGs (HGGs, MGGs, NaCMGs) were prepared. 50ml of these solutions 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°C ± 2°C (drying time about 14 - 16 hours).

The films deposited on the petri plates were removed and cut into circular disks approximately 3 cm diameter and stored in a desiccator containing calcium sulphate. The films were evaluated for physical characteristics like clarity and flexibility. The polymers which formed films of good quality with respect to clarity and flexibility were studied further for application in tablet coating.

7.4.2 Selection and optimisation of concentration of Plasticizers:

1%w/v aqueous solutions of the polymer were prepared.

In 50ml of 1% w/v aqueous solution of polymer, plasticizer (PEG, PG and GLY) was added in the concentration of 30% by weight 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 thermograms are shown in Fig 7.1.

The thickness of the film was measured using a micrometer with least count of 0.01mm .

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 the permeation cell used by Patel *et al*(4). It consisted of a 50ml screw-capped, cylindrical glass bottle with a hole, 1.5cm 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 5ml of supersaturated sodium tartarate solution, which gives an internal humidity of 91% at 30°C, equivalent to a vapour pressure of 28.96 mm Hg (5). The tightly sealed bottles were placed in desiccator over anhydrous calcium sulphate, which was further kept in oven at 30°C ± 0.5°C. The bottles were kept for 12h and weight was recorded. The loss in weight was noted after 72h. The results are recorded in Table 7.1.

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 results are recorded in Table 7.1.

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 tansmission rate. The results are recorded in Table 7.1.

7.4.3 Tabletting :

Dummy tablets of average weight 275mg were prepared on 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	: Smooth , round, biconvex, white tablets
Diameter	: 9.5 ± 0.1 mm
Thickness	: 3.8 ± 0.2 mm
Average weight of tablet	: 275 mg ± 3% w/w
Hardness	: 6.5 ± 0.5 kg/cm^2
Friability loss	: Not more than 0.5% by weight of 20 Tablets
Disintegration time	: 5.0 ± 1.0 min

These dummy tablets were used for film coating.

7.4.4 Film coating of tablets :

Film coating of dummy tablets was done using the solution prepared as per the composition shown in Table 7.2. The polymer was dissolved in sufficient quantity of water (about 60%) and to it PEG was added. Talc, titanium dioxide and sunset yellow lake were mixed and passed through #100 mesh sieve and then dispersed in the polymer-plasticizer solution under continuous stirring(1200 ± 50 rpm). This 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°C ± 2°C
Spray Rate	50ml/min
Spray cycle	15 secs on, 45 secs off

7.5 RESULTS AND DISCUSSION

The selection of a film-forming technique for uniform film 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 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 2h, 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.

7.5.1 Evaluation of GG and modified GGs as Film former :

GG and modified GGs (HGG, MGG, NaCMG) were evaluated as film formers by casting films in petri plates. It was observed that GG and HGG formed translucent and brittle films and could not be removed as intact films from glass petri plates. MGG did not form any film and deposited onto petri plates as powder on drying. 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 Tg of these polymers may be at a temperature much above the room temperature, hence do not form films of required characteristics, and turn into 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.

7.5.2 Selection and Optimisation of concentration of Plasticizer :

The film properties of a polymer are influenced by addition of suitable external plasticizer/s. The incorporation of plasticizer into polymer film reduces Tg of the polymer and enhances molecular mobility of the polymer at lower tempratures (coating temperature). This phenomenon helps in formation of uniform and smooth film on tablet surface.

Many plasticizers are in common use. In this investigation, the selection was made from most commonly available plasticizers viz. Propylene glycol (PG), polyethylene glycol 400 (PEG) and glycerin (GLY). Films of NaCMG were casted using 30% PEG/PG/GLY by weight of polymer as plasticizer. The casted films were dried and then subjected to DSC and the thermograms

Table 7.1 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 15cps	-	-	-	-	-	-	-	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/hour)	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	11.00±0.25	13.50±0.50	14.00±0.50	16.00±0.35	15.50±0.25
Breaking Strength ($Kgcm^{-4}$)	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

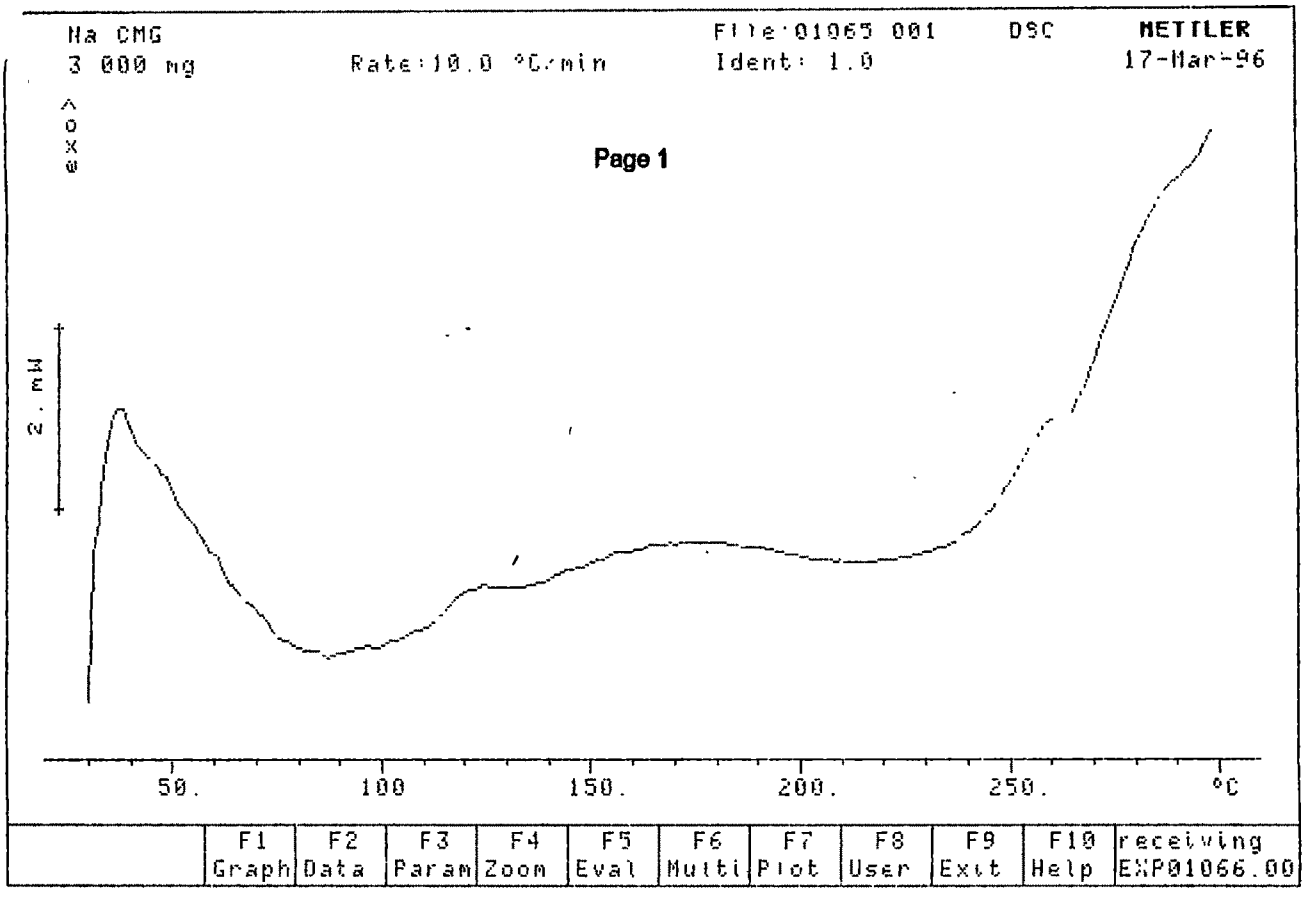
obtained are shown in Fig 7.1. The thermograms show no change in endothermic peak of NaCMG in cases of 30% PG/GLY as plasticizer. In fact, the thermograms show two or more peaks indicating no plasticizing effect and no interaction of these plasticizers with NaCMG. When 30% PEG was used as plasticizer a sharp endothermic peak was observed at lower temperature (78°C - 80°C) compared to broad endothermic peak of NaCMG alone at higher temperature (85°C - 90°C).

The concentration of PEG in NaCMG films was varied from 10% to 40% and casted films were evaluated for water vapour transmission rate (Table 7.1). 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 (4.75mg/h ± 0.50mg/h) and then increases gradually (40% PEG - 5.50mg/h ± 0.75mg/h). Increase in rate of moisture transfer may be attributed to increase of film hydrophilicity.

The breaking strength of the film (Table 7.1) in terms of increase in the hardness of the tablet with respect to that of 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 cm^{-4}). Addition of PEG upto 30% by weight as plasticizer in NaCMG films increases the breaking strength to 6.06 kg cm^{-4} followed by fall in breaking strength of the film at 40% concentration by weight (5.76 kg cm^{-4}). Hence PEG in 30% concentration by weight of NaCMG was used for subsequent investigations.

7.5.3 Film Coating of Tablets :

Film coating of dummy tablets was done using NaCMG and HPMC 15cps as film formers. The composition of the film coating solutions are shown in Table 7.2. the coating was applied to moving bed of tablet in conventional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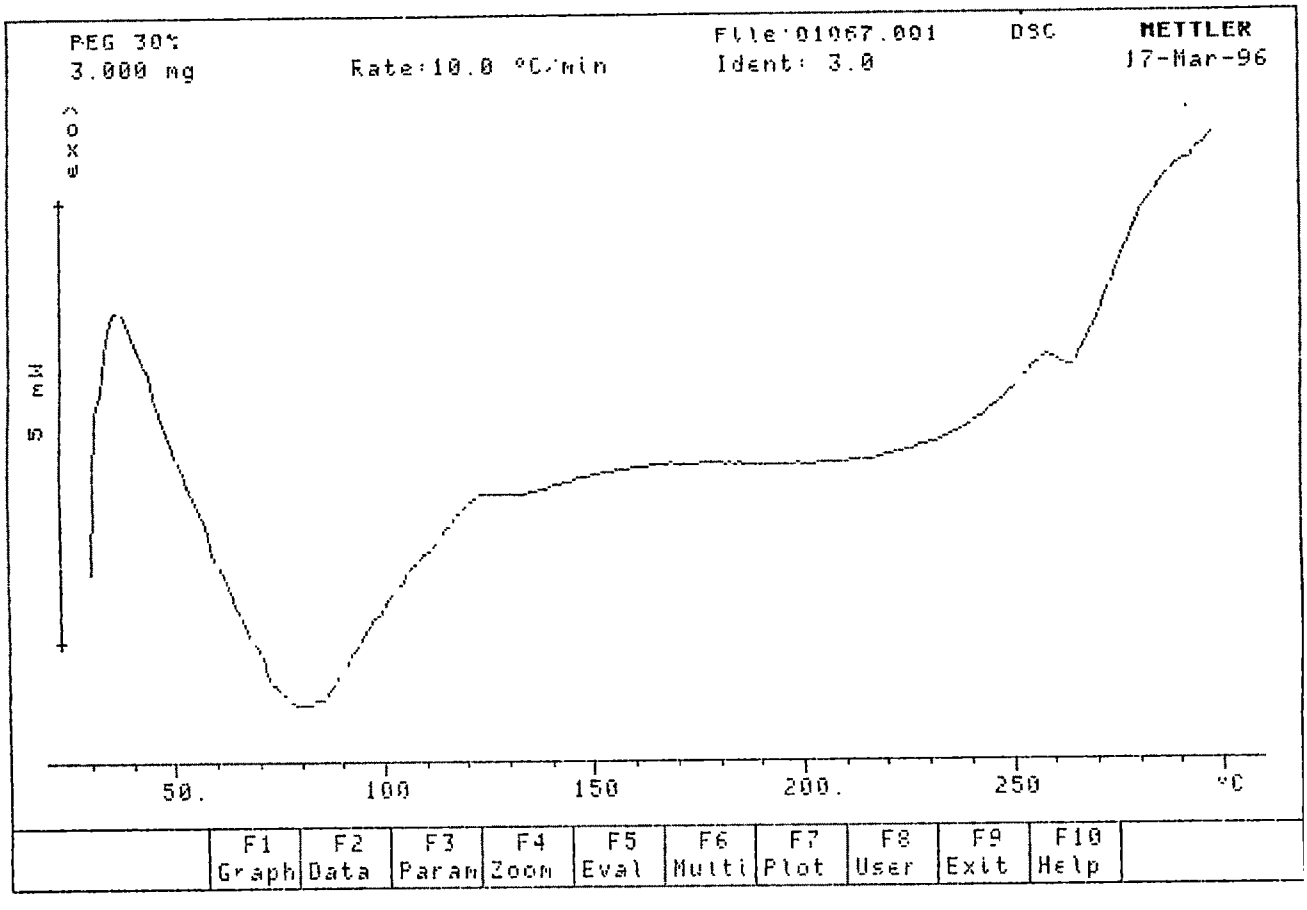
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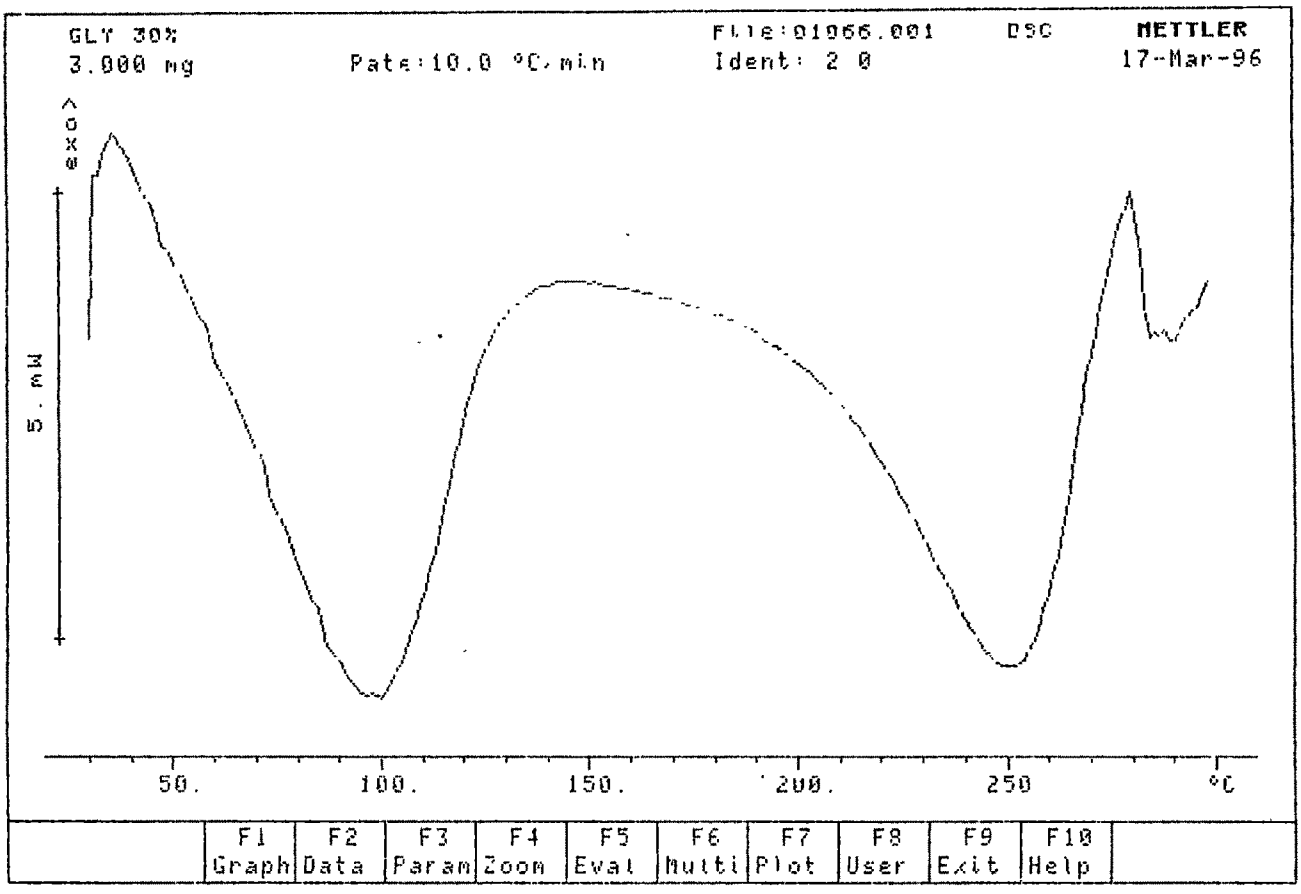
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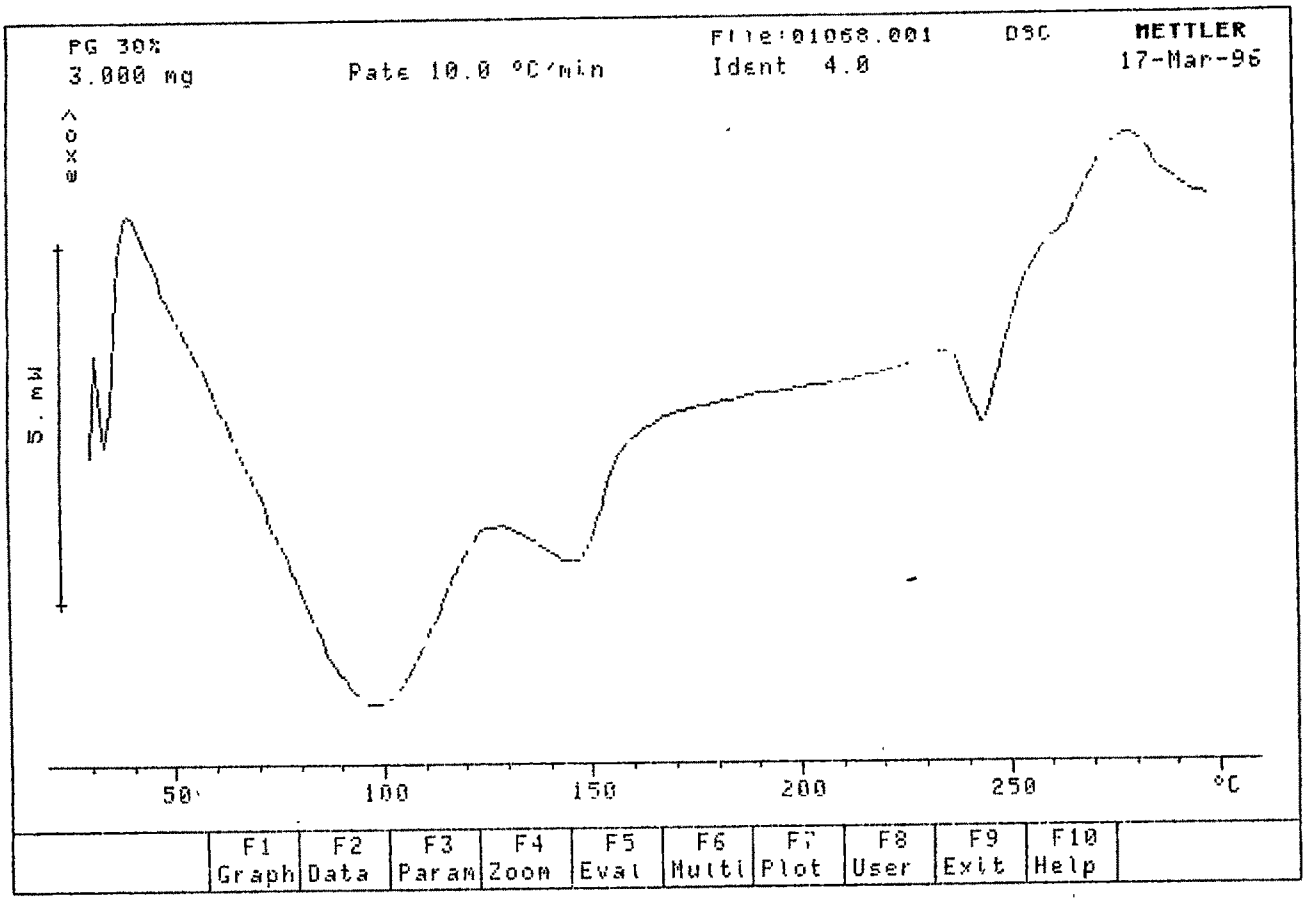
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Table 7.2 Film Coating Solution for coating of Dummy tablets.

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 cm^{-4})		5.50	5.64

*DT of Uncoated tablets was 5.0 ± 1.0 min.

coating pan, spraying the solution in small portions onto the tablets. After distribution of material evenly over the tablet surface, the drying of the film was facilitated by hot air blower at 70°C. Successive applications were made, until a film of 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 15cps were found to be comparable. However, the tablets coated with NaCMG show significant increase (about 7.0 min) in DT, compared to tablets coated with HPMC 15 cps, where no significant change was observed. Comparatively high 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 the 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 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 potential for use in coating of tablets. The higher viscosity grades can also be used to form a barrier layer to increase stability of moisture-sensitive drug.

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