Chapter 4

MODIFICATION

AND

CHARACTERISATION

OF

GUAR GUM

4.1 INTRODUCTION

Chemical modification of polysaccharides is useful for altering physico-chemical properties of polysaccharides to give them new pharmaceutical applications. GG, a naturally occurring galactomannan polysaccharide, has very high intrinsic viscosity (1) and relatively higher rate of hydration compared to other available natural gums like gum acacia, gum tragacanth, etc. GG is indigenously available at low cost and has widespread established applications. It has hot and cold water swellability, non-ionic nature and no toxicity. These properties make it a good candidate for use as disintegrant, viscosity builder, hydrophilic matrix former for sustained/controlled release tablets and for other pharmaceutical applications(2).

Despite the advantages, there are certain limitations in the use of GG in pharmaceuticals such as non-uniform rate of hydration, microbial contamination, loss of viscosity on storage and non-reproducibility. In the present work, naturally occurring GG was procured, characterised and modified to overcome its limitations and also to improve its interaction coefficient. GG was chemically modified by partial acid hydrolysis, methylation, oxidation and carboxymethylation, to overcome its limitations in its use as a hydrophilic matrix for controlled release tablets. Modified GG products were characterised using suitable analytical techniques and investigated for their applications.

4.2 MATERIALS

Guar gum I.P. (Prince Chemicals, Mumbai), methanol A.R. (Emerck (India) Limited, Mumbai), hydrochloric acid (Ranbaxy Chemicals, Indore), ammonia solution (SRL Chemicals, Mumbai), galactose, phenol I.P. (Sarabhai M. Chemicals, Baroda), sulphuric acid A.R. (Qualigens Fine Chemicals, Mumbai), sodium hydroxide A.R., potassium acetate A.R.,

potassium iodide A.R., sodium metaperiodate A.R. (S.D. Fine Chem Pvt. Ltd., Boisar), dimethylsulphate A.R. (SRL Laboratories, Mumbai), glacial acetic acid A.R. (Loba-Chemie, Mumbai), monochloroacetic acid G.R., sodium thiosulphate (Apex Chemicals, Ahmedabad),

4.3 EQUIPMENTS

Overhead mechanical stirrer (Remi Scientific Instruments, Mumbai), vacuum oven (INSREF, United Engineers, Mumbai) Vacuum pump (Baysinth Rotary Pumps, Mumbai), UV-Visible Spectrophotometer (Hitachi U-2000, Japan), Densitometer (Electrolab Instruments, Ahmedabad), Brooke field synchro-lectric viscometer LVT model (Brookefield Engineering Equipments, Stoughton, Massuchetts, U.S.A.), Analytical balance (National Scientific Works Ltd., Bombay), Carver Laboratory press (Fred S. Carver Inc., U.S.A.).

4.4 HYDROLYSIS OF GG

4.4.1 Reagents :

(i) Water : Purified Water.

(ii) Hydrochloric acid, xN : As per I.P. 1985 (3).

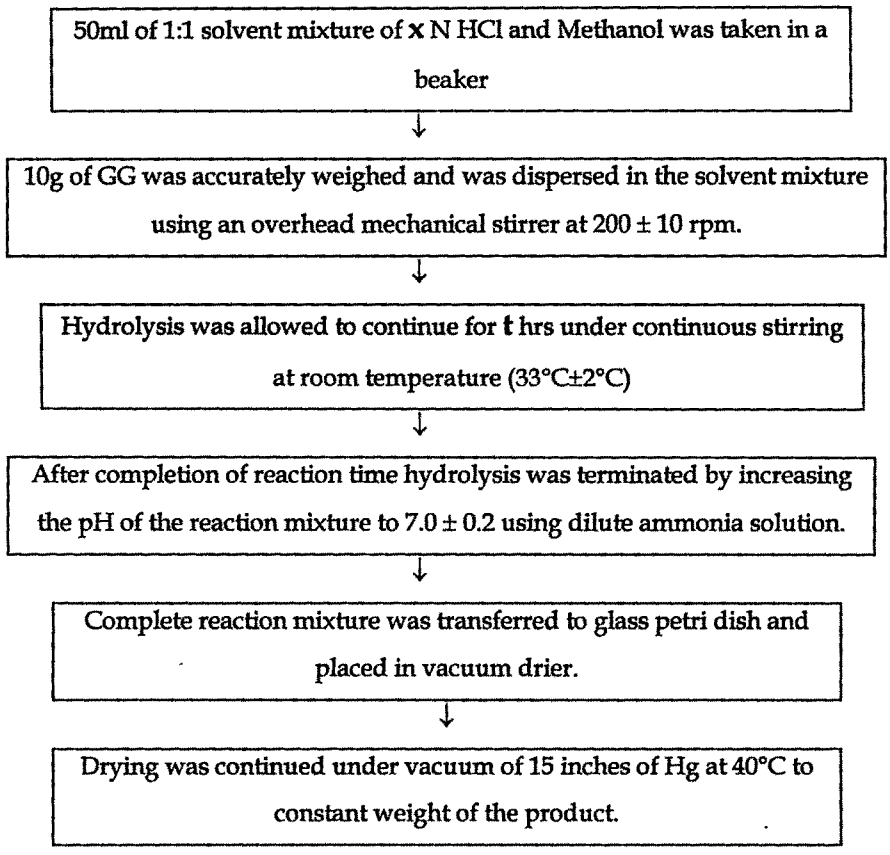
(iii)Dilute Ammonia solution : As per I.P. 1985 (4).

(iv)Acidified alcohol : 25 ml of xN HCl was transferred to a 50 ml clean volumetric flask using a 25 ml volumetric pipette and the volume was made up with methanol. 0.1N, 0.2N, 0.3N and 0.5N HCl were used.

4.4.2 Method :

The hydrolysis of GG was carried out by dispersing GG in 1 : 1 solvent mixture of diluted hydrochloric acid and methanol and stirring for a fixed time period. The method for hydrolysing GG is described in the flow chart shown in Fig 4.1.

Fig 4.1 Flow diagram of procedure for hydrolysis of GG.



Where,

x = 0.1, 0.2, 0.3 or 0.5 ; **t** = 1.0, 2.0, 3.0, 4.0 or 5.0

The degree of hydrolysis was varied by changing the strength of the acid used for hydrolysis and the duration for hydrolysis. Hydrolysis was done using dilute HCl of strengths 0.1N, 0.2N, 0.3N and 0.5N. Stirring was continued for a period varying from 1h to 5h at room temperature (33°C ± 2°C).

4.4.3 Characterisation of hydrolysed GG products (HGGs):

The HGGs were characterised with respect to viscosity, bulk density and tapped density as per the method described earlier (Chapter 3, section 3.4). The results are recorded in Table 4.1. The amount of sugars liberated on hydrolysis (Table 4.1) was used as a measure of degree of hydrolysis.

4.5 METHYLATION OF GG

4.5.1 Reagents :

(i) Sodium hydroxide solution, 40 % w/v : 40g of carbondioxide free sodium hydroxide was accurately weighed and was dissolved in sufficient water and the volume was made to 100 ml with water.

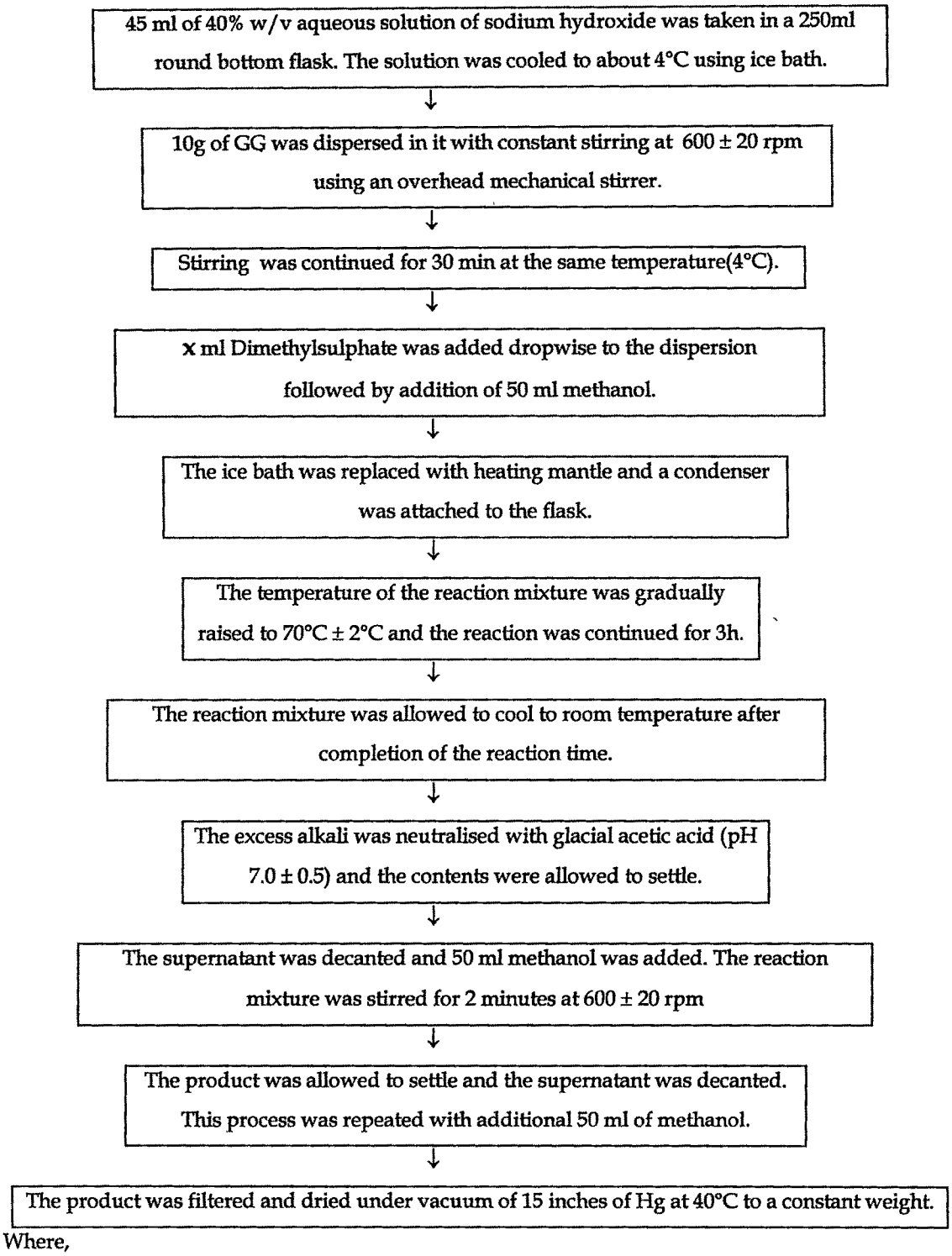
(ii) Sodium thiosulphate solution, 0.1N : Sodium thiosulphate was dissolved in water so as to contain 2.482g in 100ml (6).

4.5.2 Method :

GG was methylated with dimethylsulphate in presence of strong alkali (40% w/v aqueous sodium hydroxide solution) as per the procedure described in the flow diagram (Fig 4.2).

The degree of methylation was altered by varying the amount of methylating agent, dimethylsulphate, and the obtained products were characterised.

Fig 4.2 Flow diagram of procedure for methylation of GG.



Where,

x = 5, 10, 15, 20, 25 or 30

4.5.3 Characterisation of methylated GG products (MGGs):

The MGGs were characterised with respect to I.R. spectra, methoxy content, viscosity and differential scanning calorimetry as per the procedure described in chapter 3. The I.R. spectra of GG/MGG are shown in Fig 4.5. Viscosity (section 3.4.2) and the methoxy content values of MGGs, determined using semi-micro Zeisel method (section 3.5.2), are recorded in Table 4.2. The differential scanning calorimetry thermograms of MGGs are shown in Fig 4.6.

4.6 OXIDATION OF GG

4.6.1 Reagents :

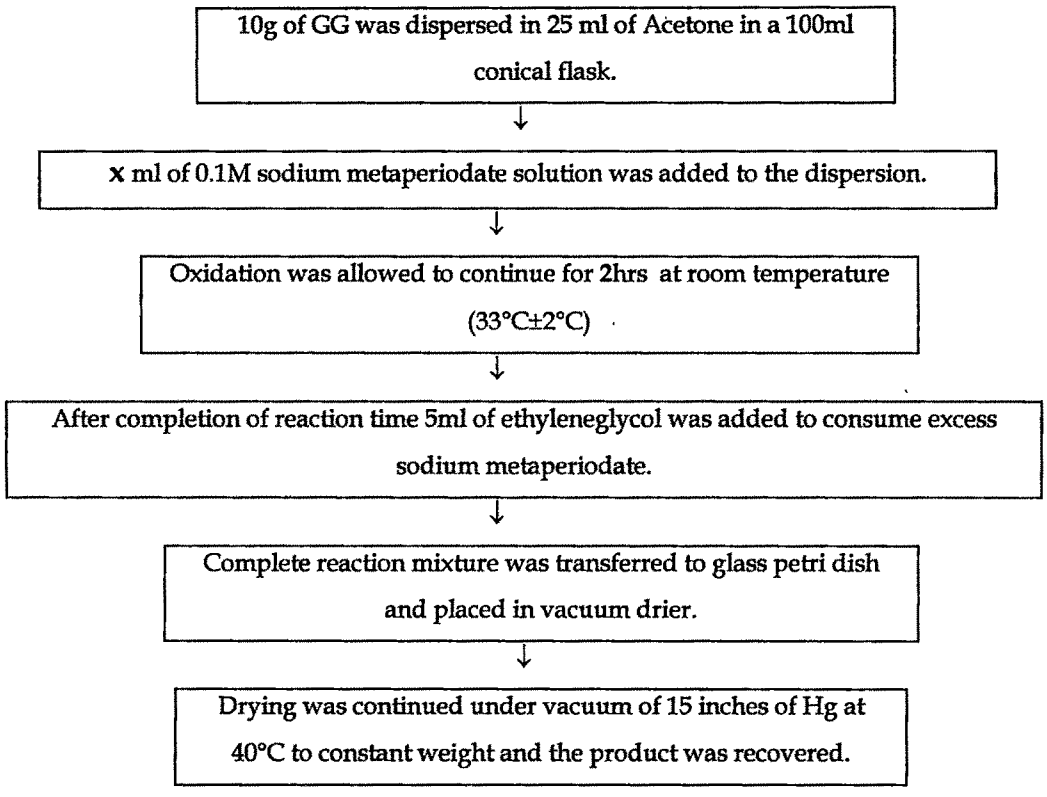
(i) Sodium metaperiodate, 0.1M: 21.389g of sodium periodate was accurately weighed and transferred to a 1000ml volumetric flask, dissolved in sufficient quantity of water, and the volume was made up with water.

4.6.2 Method :

Aqueous solution of sodium metaperiodate was used for oxidation of GG. The procedure employed for oxidation of GG is described in the flow chart shown in Fig 4.3.

The amount of 0.1M sodium metaperiodate solution was varied (Table 4.3) to alter the degree of oxidation of GG. The reaction was carried out at room temperature (33°C ± 2°C). The oxidised products were recovered by drying, under vacuum of 15 inches of Hg at 40°C ,to a constant weight.

Fig 4.3 Flow diagram of procedure for oxidation of GG



Where,

x = 0.5, 1.0, 1.5, 2.0, 2.5 or 3.0

4.6.3 Characterisation of oxidised GG products (OGGs) :

The OGGs were characterised with respect to bulk density, tapped density, carboxyl content and viscosity as per the procedures described in chapter 3. The results are recorded in Table 4.3.

4.7 CARBOXYMETHYLATION OF GG

4.7.1 Reagents :

(i) Sodium hydroxide solution, 40% w/v: as described earlier.

(ii) Monochloroacetic acid, 75% w/v: 75g of monochloroacetic acid was carefully transferred from a tared 100ml beaker to a clean 100ml volumetric flask. Sufficient quantity of water (about 25 ml) was added to dissolve it and finally the volume was made up with water.

4.7.2 Method :

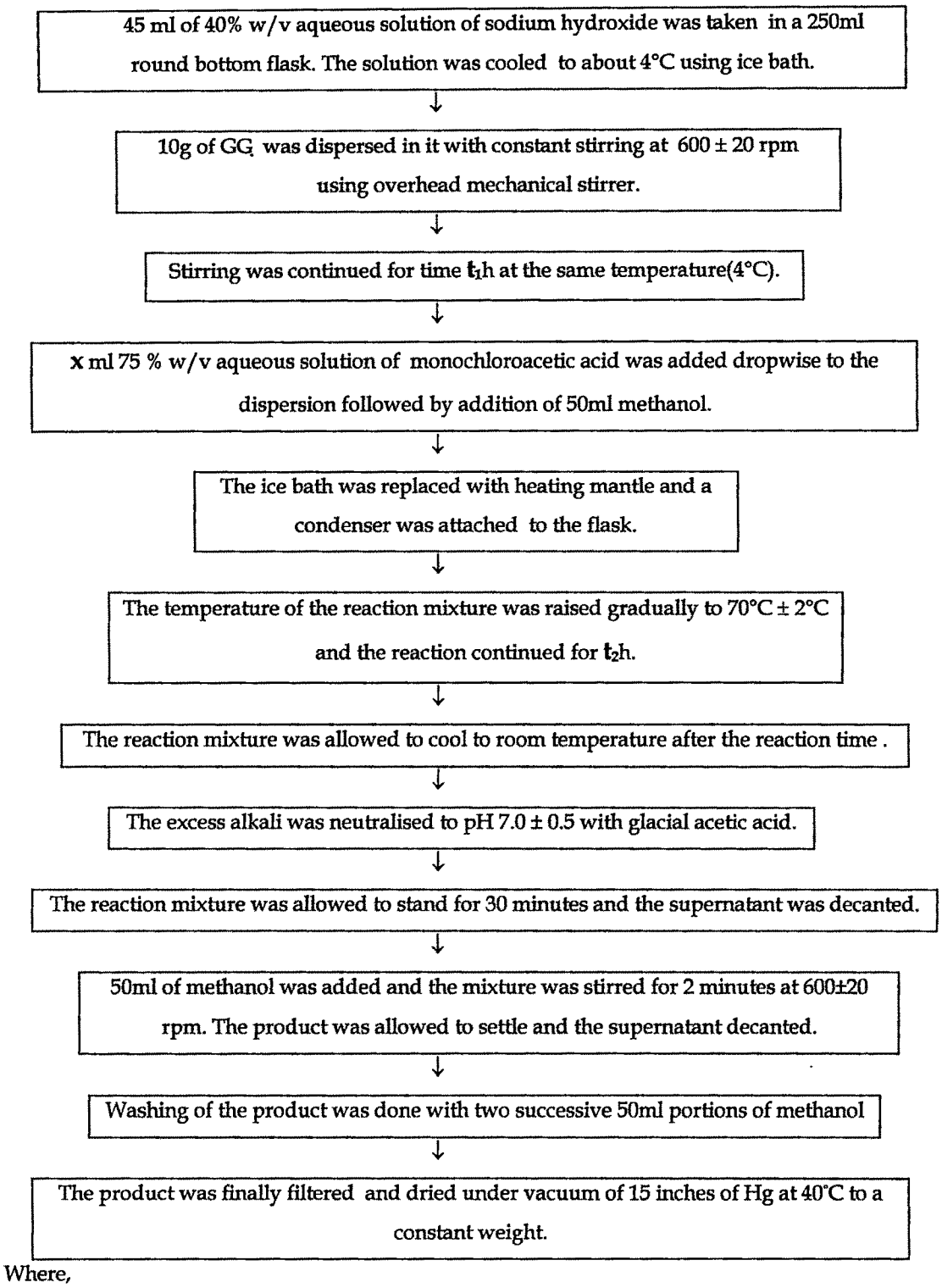
Sodium carboxymethylguar was synthesized by dispersing GG in 40%w/v aqueous solution of sodium hydroxide and reacting it with 75%w/v aqueous solution of monochloroacetic acid, as described in the flow diagram (Fig. 4.4.)

The reaction parameters were altered to change the degree of substitution. The amount of 75% w/v solution of monochloroacetic acid was increased from 2 ml to 4, 8, 10, 15, 20, 25 and 30 ml ; the reaction time after addition of reagent was varied from 3h to 6h, 8h, 12h and 18h and the time of exposure of GG to strong alkali was changed from 0.5h to 1h, 2h and 3h.

4.7.3 Characterisation of sodium carboxymethyl guars (NaCMGs):

The NaCMGs were characterised by the bulk density, tapped density and viscosity as per the procedure described in chapter 3, the values of which are recorded in Table 4.4. Differential scanning calorimetry

Fig. 4.4. Flow diagram of procedure for preparation of Sodiumcarboxymethyl Guar.



Where,

t_1 = 0.5, 1.0, 2.0 or 3.0 ; x = 2, 4, 8, 10, 15, 20, 25 or 30 ; t_2 = 3, 6, 8, 12 or 18.

of NaCMG was performed and the thermograms were recorded (Fig. 4.7).

4.8 RESULTS AND DISCUSSION

GG is a naturally occurring macromolecular galactomannan polysaccharide. There are certain limitations in the use of GG in pharmaceuticals such as non-uniform rate of hydration, microbial contamination, loss of viscosity on storage and non-reproducibility. Naturally occurring GG has been chemically modified to overcome the limitations in its use in pharmaceuticals, specifically as a matrix former. Chemical modifications were done by partial acid hydrolysis, methylation, oxidation and carboxymethylation. These modified GG products were characterised using suitable analytical techniques such as bulk density, tapped density, viscosity, I.R. spectra and differential scanning calorimetry. The modified GG products were also characterised with specific tests for each type of modification such as degree of hydrolysis for HGGs, methoxy content for MGGs and carboxy content for OGGs. Results have been recorded and discussed.

4.8.1 Hydrolysis of GG and Characterisation of HGGs :

Acidic, enzymatic and alkaline hydrolytic methods are commonly employed for hydrolysing polysaccharides. Hydrolysis of a complex polysaccharide is done by stepwise degradation with acids of increasing strengths(10). Enzyme α-d-galactosidase specifically hydrolyses GG producing galactose. Enzymatically modified gums are able to form gels due to smooth unsubstituted mannan regions in the modified galactomannan(11). Enzymatic hydrolysis could not be performed due to nonavailability of the α-d-galactosidase enzyme, which can reduce the galactose-mannose ratio. Partial acid hydrolysis of GG was performed to improve its interaction coefficient without significantly affecting its viscosity. Various weak organic acids viz. benzoic acid, salicylic acid,

acetic acid were tried for partial hydrolysis of GG. These acids failed to produce the necessary change in the gum characteristics. Subsequently a mineral acid, hydrochloric acid, was tried for hydrolysing GG. These attempts also failed to hydrolyse GG in controlled manner. The use of dilute HCl (0.1N, 0.2N and 0.5N) alone resulted in gelling of the reaction mixture due to high intrinsic viscosity of GG . This made the recovery of the product very difficult and could not produce the desired quality of product.

Finally, partial acid hydrolysis of GG was performed using mixture of dilute hydrochloric acid with a polar organic solvent, methanol, in 1:1 ratio. The presence of a polar O-containing organic solvent like methanol provides resistance to hydrolysis(12). It also prevents complete hydration of gum, resulting in controlled hydrolysis of GG, by restricting it to the surface only.

The degree of hydrolysis was varied by using hydrochloric acid of varying strengths (0.1N, 0.2N, 0.3N and 0.5N) and allowing the reaction to continue for varying durations (1h, 2h, 3h, and 5h). The product was recovered by drying under vacuum (15 inches of Hg) at 40°C. The presence of organic solvent, which prevents complete hydration of gum, also results in faster drying and easier recovery of the hydrolysed GG. The rate of hydrolysis of GG was controlled by optimising the reaction conditions such as temperature, pH, ionic strength and nature and intensity of agitation.

HGGs were characterised with respect to their bulk and tapped densities, viscosity and the degree of hydrolysis in terms of the amount of reducing sugars liberated on hydrolysis. The results are recorded in Table 4.1.

Table 4.1 Hydrolysis and Characterisation of GG.

Sr. No.	Product	Normality of HCl (N)	Duration of Hydrolysis (H)	Amount of Red.Sugar (S.E) (mg/10g)	Viscosity (S.E.) (cps)	Bulk Density (g/ml)	Tapped Density (g/ml)
1.	GG	-	-	33.75 (1.71)	8266.65 (15.23)	0.40	0.65
2.	HG11	0.10	1.00	261.00 (3.56)	6230.50 (14.48)	0.40	0.66
3.	HG12	0.10	2.00	400.45 (3.56)	6093.00 (14.94)	0.39	0.65
4.	HG13	0.10	3.00	420.65 (7.08)	5585.90 (12.27)	0.41	0.64
5.	HG14	0.10	4.00	490.80 (4.20)	5383.00 (12.83)	0.40	0.64
6.	HG15	0.10	5.00	510.45 (6.25)	5230.50 (12.99)	0.40	0.63
7.	HG21	0.20	1.00	423.55 (5.07)	5746.36 (14.77)	0.41	0.64
8.	HG22	0.20	2.00	429.45 (4.34)	5536.77 (12.28)	0.40	0.64
9.	HG23	0.20	3.00	534.95 (4.85)	4908.01 (14.96)	0.41	0.63
10.	HG24	0.20	4.00	559.50 (5.68)	4646.03 (15.72)	0.40	0.63
11.	HG25	0.20	5.00	633.60 (3.84)	4305.45 (12.28)	0.40	0.63
12.	HG31	0.30	1.00	579.14 (5.77)	3305.45 (10.24)	0.41	0.63
13.	HG32	0.30	2.00	662.60 (5.23)	2881.82 (9.73)	0.40	0.64
14.	HG51	0.50	1.00	697.35 (5.23)	2122.06 (10.71)	0.40	0.62
15.	HG52	0.50	2.00	856.90 (5.79)	1448.91 (11.22)	0.39	0.63

No significant change in the bulk densities of the HGGs was observed as compared to GG. Although a decrease in the tapped densities was observed with increase in the degree of hydrolysis, it was non-significant and also no definite correlation could be made with the degree of hydrolysis.

Results reveal a decrease in the viscosity values of 1% w/v aqueous dispersions of the HGGs compared to GG. The viscosity values show a tendency to decrease with increase in the degree of hydrolysis, either by increased duration of hydrolysis or by increased strength of acid used for hydrolysis. It was observed that using weaker acid for longer duration results in product with higher viscosities compared to those prepared using concentrated acid for shorter durations (HG12 - 6093.0 ± 14.94 cps, HG21 - 5746.36 ± 14.77 cps; Table 4.1). This shows that a better control over the degree of hydrolysis could be obtained by using lower strength acid for longer durations. Optimum strength of acid and time was used for controlled hydrolysis of gum.

Similar observation was made with the results of total amount of sugars liberated. The amount of sugars liberated increases with increase in the duration and strength of acid used for hydrolysis.

4.8.2 Methylation of GG and Characterisation of MGGs :

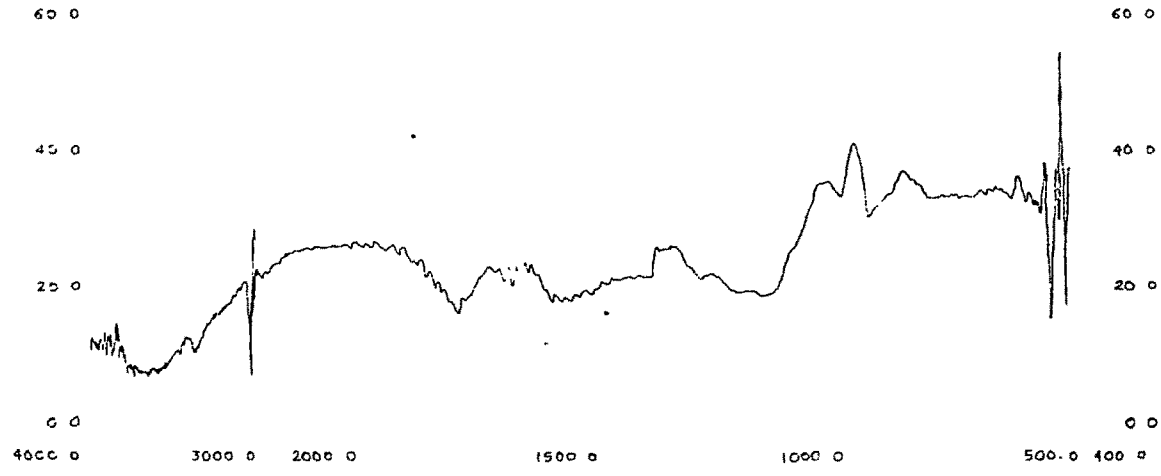
GG was methylated with dimethylsulphate in conjunction with strong alkali, 40%w/v sodium hydroxide solution, which serves to promote ionization of pertinent hydroxyl function for methylation. GG has very high intrinsic viscosity, which on hydration leads to gelling of the reaction mixture. The gelling of the reaction mixture was prevented by dispersing GG at low temperature (4° ± 0.5°C) and high pH, which depresses the hydration of GG. To prevent hydration of gum on raising the temperature (70°C) of reaction mixture after addition of dimethylsulphate, a polar organic solvent,

methanol was added to the reaction mixture. This also restricts the rate of hydrolysis of the gum due to alkali. Furthermore, the presence of polar O-containing organic solvent, methanol, which does not solvate the hydroxyl groups, permits the reaction to proceed with favorable kinetic rates under relatively mild conditions. The degree of substitution of the methoxy groups was altered by changing the amount of methylating agent, dimethylsulphate, from 5ml to 30 ml. Three batches of each type (similar methoxy content) were prepared and characterised.

I.R. spectra of MGGs reveal a peak at $1080cm^{-1}$ - $1100cm^{-1}$ confirming the presence of methoxy group (Fig 4.5).

Methoxy content of the MGGs was determined using semi-micro Zeisel method (7) with suitable modifications. The results are recorded in Table 4.3. It can be observed that with the increase in the amount of dimethylsulphate used for methylation, there is an increase in methoxy content (MG1 - 2.20 % ± 0.05 to MG6 - 4.04% ± 0.02). With an increase of about 0.04 moles of dimethylsulphate an increase of approximately 0.4 % in methoxy content was observed.

Viscosity measurements of 1 % w/v aqueous solutions of MGGs were made using Brookefield Viscometer spindle no. 2 (Table 4.3). A sharp decline in viscosity of MGGs was observed (from 8066 ± 15.28 cps of GG to 327 ± 14 cps of MG6). This reflects the problem involved in methylation of natural products. It includes the liability of the compound to the methylating condition. The fall in viscosity shows some chain cleavage of the GG polysaccharide molecule. Hence, methylation of GG was done at relatively mild conditions and in presence of polar organic solvent, which also made the recovery of the product faster and easier.



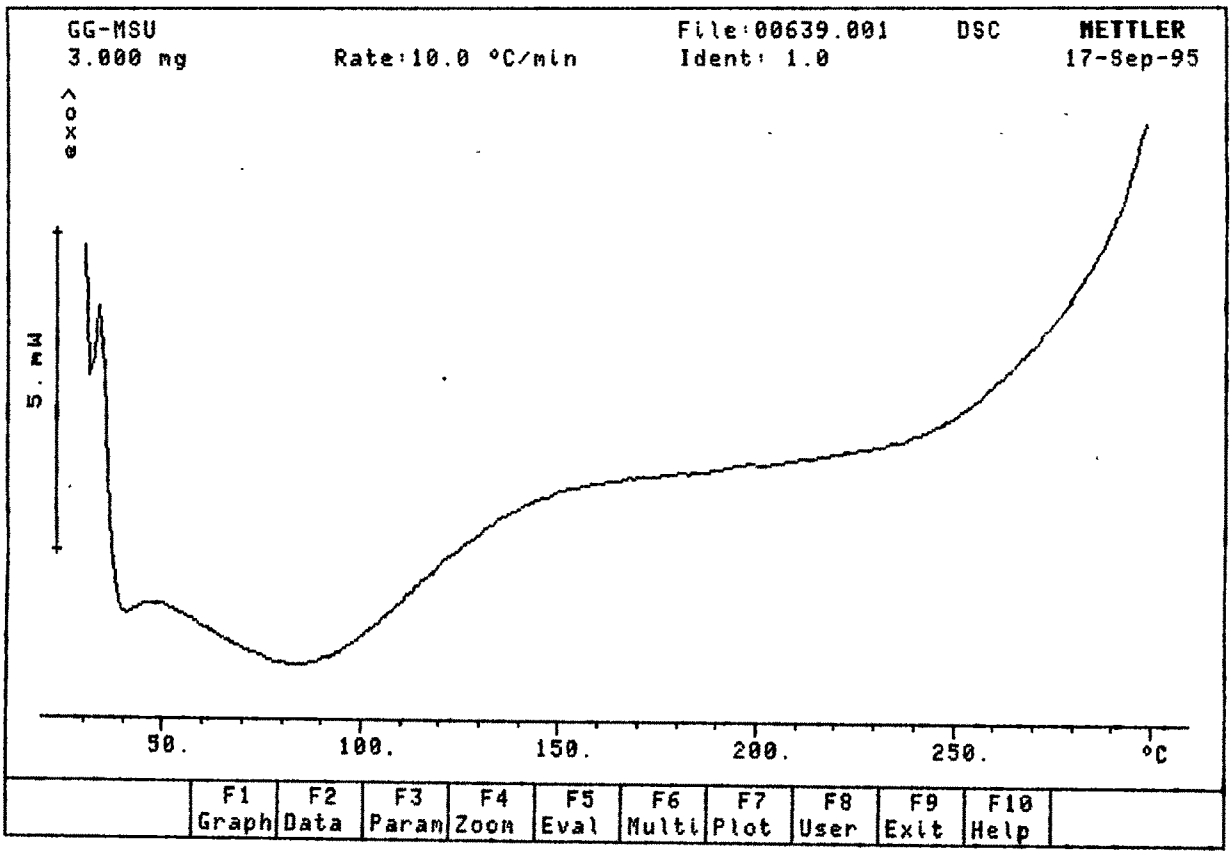
A

B

Fig 4.5 A → GG B → MGG

Table 4.2 Methylation and Characterisation of GG.

Sr.No.	Product	Amount of DMS (ml)	Methoxy Cont. ± S.E. (%)	Viscosity ± S.E. (cps)	Bulk Density (g/ml)	Tapped Density (g/ml)
1.	GG	-	-	8266.65 ± 15.23	0.40	0.65
2.	MG1	5.0	2.20 ± 0.05	6078.01 ± 22.71	0.40	0.64
3.	MG2	10.0	2.69 ± 0.05	2541.24 ± 15.62	0.41	0.66
4.	MG3	15.0	3.05 ± 0.02	2436.44 ± 20.27	0.39	0.67
5.	MG4	20.0	3.29 ± 0.07	916.95 ± 16.43	0.40	0.66
6.	MG5	25.0	3.60 ± 0.02	419.17 ± 07.71	0.42	0.67
7.	MG6	30.0	4.04 ± 0.02	327.48 ± 14.28	0.41	0.67


GG-MSU
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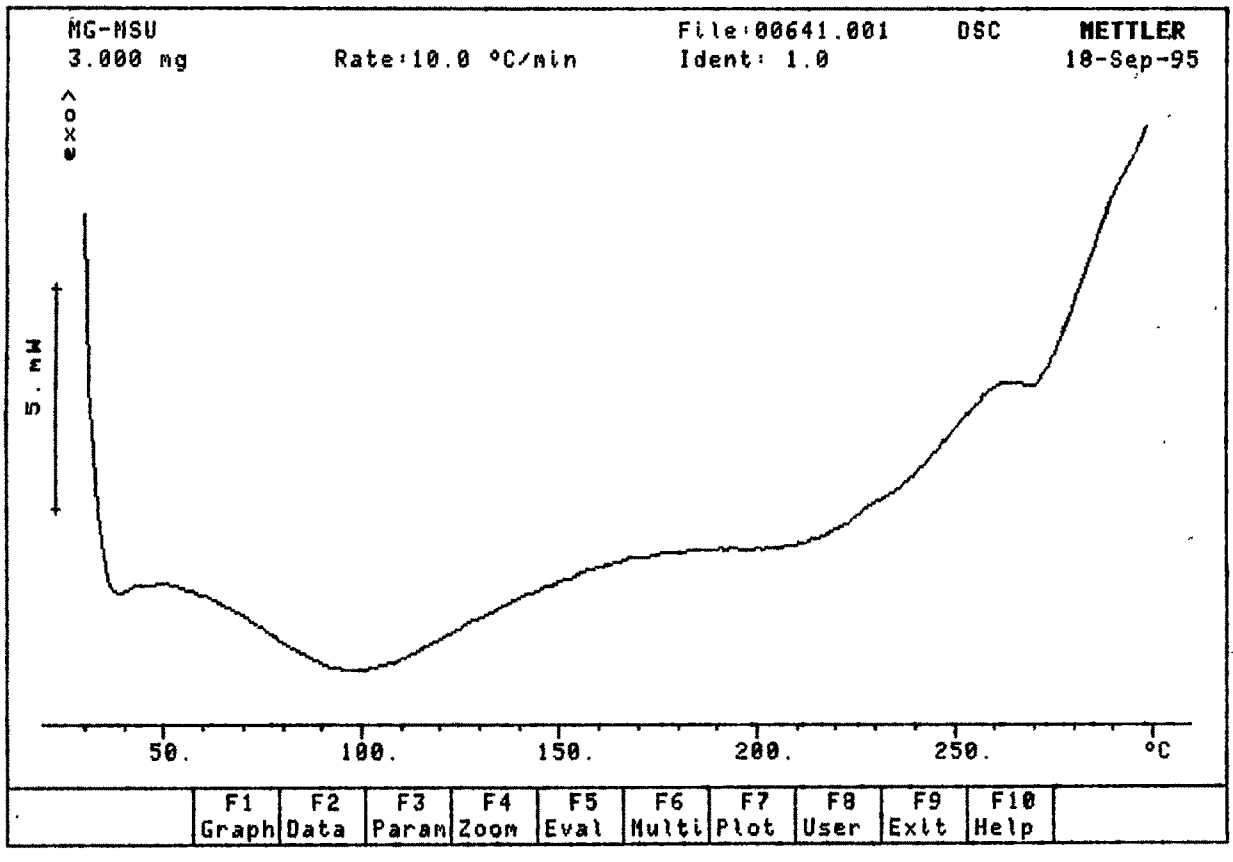
MG-MSU
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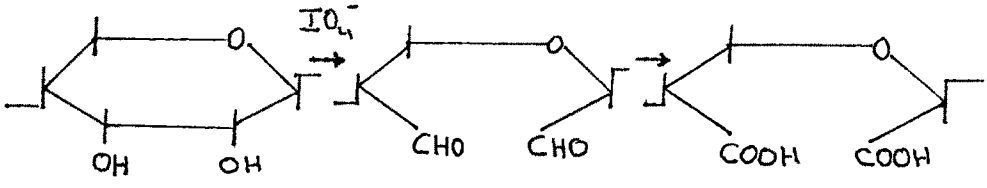
F10 Help

The products were also characterised by thermal analysis (Differential Scanning Calorimetry). A shift on the higher side of the endothermic peak of MGGs compared to the GG was observed (Fig 4.6).

4.8.3 Oxidation of GG and Characterisation of OGGs :

Periodic acid and its salts are mainly used in the carbohydrate chemistry for the oxidation of α-glycol groups (14). GG consists of chain of d-mannose units with pendant d-galactose groups(13). Small amounts of periodate preferentially oxidises the galactose group leaving the mannose chain intact. The reaction takes place as-



Taking this fact into consideration along with the report that reduction of galactose-mannose ratio increases the interaction coefficient of GG, periodate oxidation of GG was carried out using 0.1M aqueous solution of sodium metaperiodate. The aqueous solution causes hydration of gum which makes both the recovery of the product and control over the degree of oxidation, difficult. The reaction was, therefore, carried out in a solvent mixture of water and an unreactive water-miscible organic solvent, acetone. The products of the reaction were easily recovered by filtration and the costly precipitation method for recovery of gum product was eliminated. The presence of organic solvent also helped in controlling the degree of oxidation by preventing complete hydration of the gum.

The amount of periodate ion used for oxidation of GG was altered for changing the degree of oxidation of GG by varying the amount of 0.1M

Table 4.3 Oxidation and Characterisation of GG.

Sr.No.	Product	Amount of Sod. meta-periodate (ml)	Bulk Density (g/ml)	Tapped Density (g/ml)	Carboxy content ± S.E. (meq/g)	Viscosity ± S.E. (cps)
1.	GG	-	0.40	0.65	6.28 ± 0.29	8266.65 ± 15.23
2.	OGG1	5.0	0.43	0.71	60.53 ± 1.65	6585.61 ± 13.48
3.	OGG2	10.0	0.39	0.71	71.38 ± 1.54	5971.91 ± 12.34
4.	OGG3	15.0	0.40	0.67	79.34 ± 0.94	3565.63 ± 12.45
5.	OGG4	20.0	0.38	0.64	94.90 ± 1.36	3248.07 ± 9.67
6.	OGG5	25.0	0.41	0.66	112.80 ± 1.85	2977.48 ± 9.71

sodium metaperiodate solution from 5.0 ml to 30.0 ml and the obtained products were characterised.

Bulk and tapped densities were determined before and after oxidation and no significant change was observed.

The results of carboxy content of GG/OGGs (Table 4.4) indicate an increase in the degree of oxidation of GG. However no definite correlation could be established in the amount of periodate ions used for oxidation and the carboxy content value.

Oxidation of GG results in a product which is soluble at basic pH. 1 % w/v aqueous solution of OGGs was prepared by accurately weighing 1g and dispersing in about 70 ml of water in glass beaker. To this 5 ml of 0.1N NaOH solution was added to solubilize the product. Viscosity measurements of these solutions of OGGs were made, after allowing the solutions to stand for 2 hours, using Brookefield viscometer, at room temperature. The values (Table 4.4) show a decrease in the viscosity with increased degree of oxidation. It can also be observed that there is a sharp decline in viscosity after OGG2 (5871.91± 112.34cps) to OGG3 (3565.63 ± 12.45 cps) and further. This sharp decline in viscosity may be attributed to the oxidation of mannose backbone alongwith the galactose moiety, resulting in chain cleavage and hence reduction in the molecular weight. Therefore the reaction conditions should be optimised to get controlled oxidation of GG.

4.8.4 Carboxymethylation of GG and Characterisation of NaCMGs

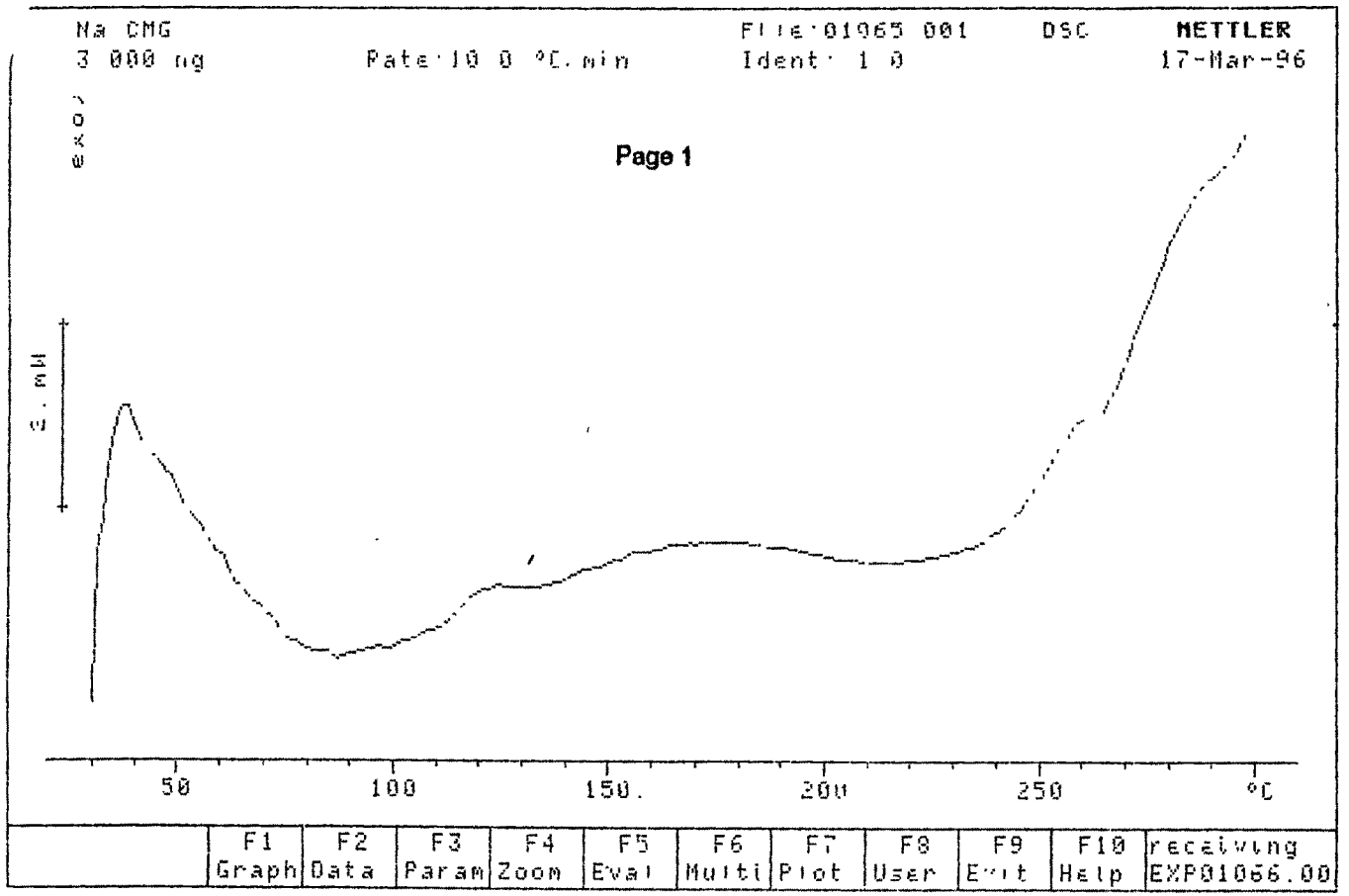
GG was treated with 75% w/v aqueous solution of monochloroacetic acid in a solvent mixture of 40%w/v aqueous sodium hydroxide solution and a polar organic solvent, methanol, as per the procedure described in the flow chart (Fig 4.4) to carboxymethylate GG. The reaction was carried out in a

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 as described in the chapter 3. No significant change in the bulk and tapped densities could be observed (Table 4.4). A shift in endothermic peak in thermograms confirmed the formation of new compound after the reaction (Fig 4.7).

To alter the degree of carboxymethyl substitutes in GG, the reaction was carried out with increased amount of monochloroacetic acid solution. With increase in substitution of carboxymethyl groups in GG, fall in viscosity of aqueous dispersions of NaCMG was observed (Table 4.4). The fall in viscosity may be attributed to the hydrolysis of GG in basic medium alongwith the formation of sodium salts. This also improved film forming characteristics of NaCMG and hence efforts were concentrated to modify GG in a way to use NaCMG as a film former.

The major objective was to control the viscosity, so as to use the polymer in aqueous dispersion as a film former. It was also felt important to improve the clarity of the film. To achieve the desired goals, the concentration of monochloroacetic acid solution, exposure of GG to alkali and duration of reaction were altered as under -

(i) The amount of 75% w/v aqueous solution of monochloroacetic acid used for derivatisation was gradually increased from 2ml to 30 ml (Table 4.4). The increase in the amount of monochloroacetic acid solution used for derivatisation caused a significant fall in viscosity of the aqueous solution of NaCMG. The solution was found to be clear compared to the aqueous dispersions of GG. The fall in viscosity of aqueous solution of NaCMG was significant when monochloroacetic acid solution was used for the reaction


Na CMG
3 000 mg
Rate 10 0 °C.min
File 01965 001
Ident 1 0
DSC
METTLER
17-Mar-96
exo
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3 . mW
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F1 Graph
F2 Data
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F6 Multi
F7 Plot
F8 User
F9 Exit
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receiving EXP01066.00

Table 4.4 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.

in the amount between 2ml to 20 ml and thereafter the fall in viscosity values were non-significant.

(ii) The time of the reaction was increased from 3h to 24h 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, clarity of the aqueous solutions was improved. However reaction times beyond 6h failed to produce NaCMG with significantly improved solution characteristics.

(iii) To further reduce the viscosity of the aqueous dispersions of NaCMG, exposure time of GG to alkaline medium was increased from 0.5h to 3h keeping the reaction procedure and conditions same (20ml 75% w/v aqueous monochloroacetic solution and 6h duration of reaction). This change helped in reducing the viscosity of 1% w/v aqueous dispersion of NaCMG to 149.75 ± 3.76cps from that of GG (8036 ± 24 cps). The products were found to be very encouraging with respect to their use as film formers, when films were cast in petri plates.

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

4.9 REFERENCES

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