DERIVATIZATION OF GUAR TO SODIUM CARBOXY METHYL HYDROXY PROPYL DERIVATIVE; CHARACTERIZATION AND EVALUATION

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ABSTRACT

Guar gum is derived from the seeds of *Cyamopsis tetragonolobus* (Linn, Family Leguminosae). Guar has extensive pharmaceutical applications; however; it has certain draw- backs like uncontrolled rate of hydration, fall in viscosity on storage, susceptibility to microbial degradation and turbidity in aqueous dispersion. Many of these drawbacks can be over come by effecting chemical derivatization of guar gum molecule to Sodiumcarboxymethyl hydroxypropyl guar; the derivatization was ascertained by spectral characterization. In aqueous dispersion, the derivative was subjected to the effect of electrolytes, varied pH conditions and storage at elevated temperatures. The sodium carboxymethyl hydroxypropyl guar derivative revealed superior viscosity retaining qualities when compared to guar gum. The derivative was subjected for detailed rheological investigation and rate of hydration studies. In 1% w/v dispersion the derivative revealed pronounced pseudoplastic behavior and in 2 % w/v dispersion, a distinct pseudoplastic behavior with slight thixotropic effect is seen. In contrast to guar gum, the derivative revealed a more controlled rate of hydration. The derivative revealed sodium content of 10.4% w/w and Degree of substitution of 1.5.

Keywords: Sodium carboxymethyl hydroxypropyl guar, Pseudoplastic behavior, rate of hydration, alkali slurry method, degree of substitution, rheological studies.

INTRODUCTION

Guar gum (Whistler, 1973) is a polygalactomannan gum with the structural chain made up of D-mannose units with 1-4 linkages whereas D-galactose unit is linked 1-6 on an average to every second D-mannose unit of the chain. The cyclic neutral structure contains numerous hydroxyl groups (an average of 3 per sugar unit). The primary C-6 hydroxyl position is highly active but the secondary hydroxyls are also sites for substitution. Guar dispersion are turbid and colored. Improved clarity results from derivatization and solubilization of insoluble seed impurities. Upon incorporation of substituent groups such as hydroxy alkyl, sodium carboxy alkyl, changes in solubility occur. Further, increased hydrolytic resistance is also seen. These changes enable the derivative to impart clarity to the formulation and help in retention of viscosity of aqueous dispersion upon storage for prolonged periods of time. Various authors have reported on the synthesis of guar derivatives (Patel S.P *et al*., 1988; Prabhanjan *et al.*, 1989; Yea 1990; Tathem *et al.*, 1995; Paranjyothi *et al.*, 1992; Swamy *et al.*, 2006).

MATERIALS

Guar gum: was obtained as a gift sample from Ace gum Industries Ltd Bombay. Propylene oxide (Juggat Pharma Pvt. Ltd.), Sodium boro-hydride (Aldrich), Mono-chloroacetic acid (Nice). Sodium hydroxide pellets, glacial acetic acid, and isopropyl alcohol (Qualigens).

METHOD

50 gms (Lawerence, 1973) of guar gum was added little by little with agitation to 75ml of isopropyl alcohol taken in a round bottom flask with a B-19 ground glass joint.1.5gms of sodium hydroxide pellets was dissolved in 35ml of ice-cold water and the Ice-cold solution was added little by little with continuous agitation to guar dispersion in isopropyl alcohol; 1.45 gms of monochloro sodium acetate was added and mixed well.17.68 ml of chilled propylene oxide was added dropwise with continuous swirling of the contents; 5 mg of Sodium Boro Hydride was added and stirred well. The flask was stoppered and secured with cellophane adhesive tape. The flask was allowed to rise to the laboratory temperature with intermittent agitation. The flask was clamped to a reciprocating shaker in thermostatic water bath; the temperature was maintained at 58^{o}C with constant agitation for 6 hrs. At the end of 6 hrs, the contents were cooled to laboratory temperature; 100ml of isopropyl alcohol was added, mixed thoroughly and neutralized to pH-7 with glacial acetic acid. The slurry was filtered; the precipitate was re-suspended in a 80:20 mixture of isopropyl alcohol and water, stirred and filtered. This process of washing the precipitate was repeated two more times; the precipitate was allowed to dry at the laboratory temperature for 24 hours; further dried at 45^{o}C for 5 hours. The derivative was stored in closed container until subjected to various characterization tests. Yield of the product: 58 gm.

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Table 1: Effect of temperature on viscosity of guar gum and Sodium carboxymethyl hydroxypropyl guar dispersion

Time (weeks)	Viscosity (CPS)							
	S1	S2	S3	S4	S5	S6	S7	S8
0	17.44	17.44	17.44	17.44	7.45	7.45	7.45	7.45
1	14.85	15.98	15.52	13.49	7.39	7.42	7.44	7.35
2	13.25	14.5	14.48	11.72	7.39	7.41	7.41	7.33
3	12.05	13.03	12.66	9.68	7.36	7.4	7.32	7.21
4	10.19	12.09	10.54	7.54	7.25	7.4	7.32	7.1
5	8.33	10.94	8.78	5.58	7.19	7.31	7.25	7.03
6	6.78	9.17	7.24	3.91	7.15	7.3	7.22	6.95
7	4.69	8.29	5.15	2.11	7.05	7.28	7.05	6.88
8	2	4.19	3.01	1.01	6.94	7.15	6.99	6.82

S1, S2, S3 S4 are guar dispersion stored at 5^{o}C, 25^{o}C, 45^{o}C, and 60^{o}C; S5, S6, S7, S8 are Sodium carboxymethyl hydroxypropyl guar dispersion stored at 5^{o}C, 25^{o}C, 45^{o}C, and 60^{o}C.

Table 2: Effect of electrolyte on viscosity of guar gum and Sodium carboxymethyl hydroxypropyl guar dispersion

Time (weeks)	Viscosity (CPS)					
	S1	S2	S3	S4	S5	S6
24 hrs	17.44	17.44	17.44	7.44	7.44	7.44
1	15.98	17.85	18.25	7.42	7.58	7.56
2	14.5	17.95	19.15	7.42	7.62	7.64
3	13.03	18.05	20.58	7.42	7.62	7.69
4	12.09	18.39	22.97	7.41	7.68	7.74
5	10.94	18.95	25.35	7.41	7.7	7.81
6	9.17	19.25	29.44	7.41	7.78	7.95
7	8.29	19.65	35.42	7.4	7.85	8.02
8	6.54	22.05	39.8	7.35	7.9	8.15

S1, S2, S3 are Guar dispersion using NaCl, $CaCl_2$ and $AlCl_3$, S4, S5, S6, are Sodium carboxymethyl hydroxypropyl guar dispersion using NaCl, $CaCl_2$ and Al_2Cl_3

CHARACTERIZATION

1. IR spectra of the derivative were recorded using Shimadzu FT IR 8400 Spectrophotometer by mull technique. Additional bands were seen between 1070 to 1170 cm^{-1} (-C-O-C- ether linkage) and 1550 to 1610 cm^{-1} (Carboxylate anion). Substitution of carboxy methyl and hydroxypropyl grouping is thus confirmed.
2. Determination of sodium content (Beckett and Stenlake, 2002): This was carried out in order to asses the extent of sodium carboxy methyl grouping incorporated into the guar structure. This was carried out by non-aqueous titration method. Sodium carboxymethyl hydroxypropyl (0.5 gm) derivative of guar was dispersed in glacial acetic acid; 2 ml of acetic anhydride was added and heated on the water bath for a period of 2 hours. The contents were cooled to laboratory temperature and titrated against 0.1N perchloric acid using crystal violet as the indicator. Each ml of 0.1 N Perchloric acid ≈ 0.003 gm of sodium. A sodium content of 10.4 %w/w was obtained.
3. Degree of substitution: Abbreviated as D.S. It represents the number of hydroxyl groups per moles of sugar in guar gum that has been substituted by Hydroxy Propyl grouping. D.S values range from 0-3. D.S. values are usually not integer numbers, because they represent the average values over an entire sample. The method of Lawrence R Jones and John A Riddick was adapted to obtain the degree of substitution; the derivative possessed D.S value of 1.5 (Lawerence and Riddick, 1957).
4. Effect of temperature: 0.25 w/v dispersions of Guar gum and Sodium carboxymethyl hydroxypropyl derivative of guar stabilized with 0.18% w/v of methyl paraben and 0.02% w/v of propyl paraben were stored at 5^{o}C, 37^{o}C, 45^{o}C, and 60^{o}C, and the

viscosity (Tathem *et al.*, 1995) was recorded at weekly intervals for 8 weeks. The data for viscosity is recorded in table 1 and graphical representation shown in fig. 1.

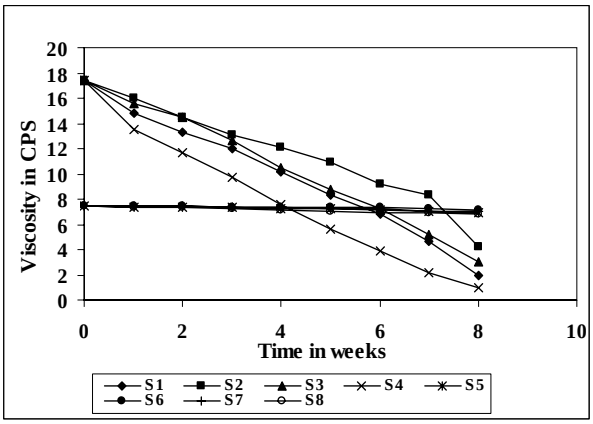

Fig. 1: Effect of temperature on viscosity of Guar gum and Sodium carboxymethyl hydroxypropyl guar dispersion.
S1, S2, S3 S4 are Guar dispersion stored at 5°C, 25°C, 45°C, and 60°C, S5, S6, S7, S8 are Sodium carboxymethyl hydroxypropyl guar dispersion stored at 5°C, 25°C, 45°C and 60°C.

5. Effect of Electrolyte: 2% w/v of electrolyte viz; sodium chloride, calcium chloride, and aluminum chloride, were added to 0.25% w/v aqueous dispersion of guar gum and sodium carboxymethyl hydroxypropyl guar stabilized with parabens as mentioned above. Viscosities were recorded at weekly intervals of time using Ostwalds U-tube viscometer. The data is recorded in table 2 and graph shown in fig. 2.

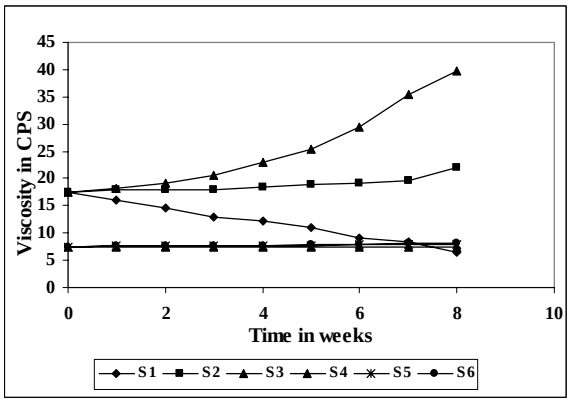

Fig. 2: Effect of electrolyte on viscosity of guar gum and Sodiumcarboxymethyl hydroxypropyl guar dispersion.
S1, S2, S3 are guar dispersion using NaCl, $CaCl_2$ and $AlCl_3$, S4, S5, S6, are Sodium carboxymethyl hydroxypropyl guar dispersion using NaCl, $CaCl_2$ and Al_2Cl_3

6. Influence of pH: 0.25% w/v aqueous dispersion of sodium carboxymethyl hydroxypropyl guar and that of guar gum were prepared in a preservative solution (0.18% w/v of methyl parabens and 0.02% w/v of propyl parabens in water) and allowed to hydrate for a period of 8 weeks. The viscosities were recorded with Ostwald's U-tube viscometer. The optimum hydration in case of guar was at pH -6 where as in case of derivative it was at pH-7. The data for recording pH is complied in table 3 and graphical representation shown in fig. 3.

Table 3: Effect of pH on the viscosity of 0.25% w/v aqueous dispersion of guar gum and Sodium carboxymethyl hydroxypropyl guar

pH	Viscosity (CPS)	
	S1	S2
2	16.39	6.22
3	18.94	6.22
4	18.77	7.06
5	17.38	6.01
7	18.70	7.63
8	14.45	7.59
9	14.21	7.45

S1 is Guar dispersion S2 is Sodium carboxymethyl hydroxypropyl guar dispersion.

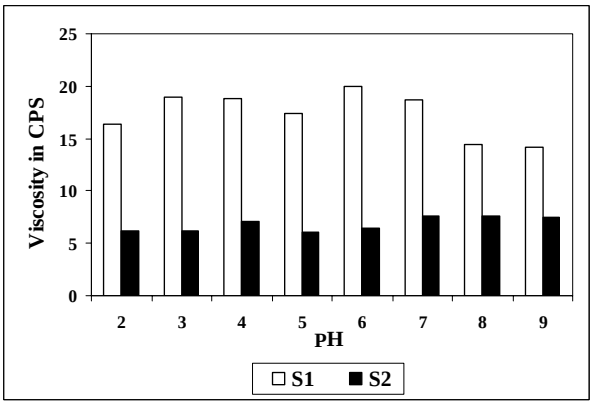

Fig. 3: Effect of pH on the viscosity of 0.25% w/v aqueous dispersion of guar gum and sodium carboxymethyl hydroxypropyl guar
S1 is guar gum dispersion and S2 is Sodium carboxymethyl hydroxypropyl guar dispersion.

7. Rate of hydration (Robert Davidson, 1980): Rate of hydration studies were carried out in 500ml aqueous dispersions of guar and sodium carboxymethyl hydroxypropyl guar in 0.25%w/v strengths. As soon as the polymers were added to the vehicle, the time was recorded and the dial readings were recorded using Brookfield Synchrolectric L.V.T model viscometer (Analog model) at the end of 1, 2, 3, 4, 5, 6 and 24 hours. The data for rate of hydration is contained in table 4 and graphical representation is shown in fig. 4. In case of guar gum, the rate of

hydration proceeded pretty fast; whereas the rate of hydration proceeded at controlled rate in case of sodium carboxymethyl hydroxypropyl guar, which is an advantage for making dispersion.

Table 4: Rate of hydration of guar gum and sodium carboxymethyl hydroxypropyl guar

Time(Hrs)	Dial Reading	
	S1	**S2**
0	15	6
0.5	26	13
1	38	17.5
2	42	19.5
3	49	22.5
4	57	24
5	65	26.5
6	74	29.5
7	82	32
24	98.5	36

S1 is guar dispersion and, S2 is sodium carboxymethyl hydroxypropyl guar dispersion

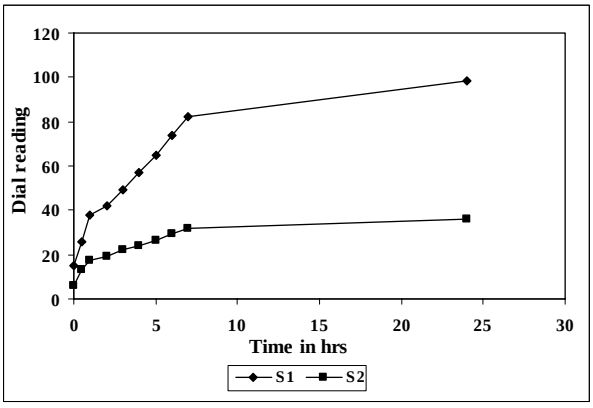

Fig. 4: Rate of hydration of guar gum and sodium carboxymethyl hydroxypropyl guar.
S1 is guar dispersion and, S2 is sodium carboxymethyl hydroxypropyl guar dispersion.

8. Detailed rheological study (Tantry *et al.*, 2001): The rheological studies were carried out on 0.5% w/v, 1% w/v and 2% w/v guar and the sodium carboxymethyl hydroxypropyl guar dispersions in preservative solution using Brookfield Synchrolectric LVT model viscometer. The data is compiled in table 5 and graphical representation is shown in fig. 5.

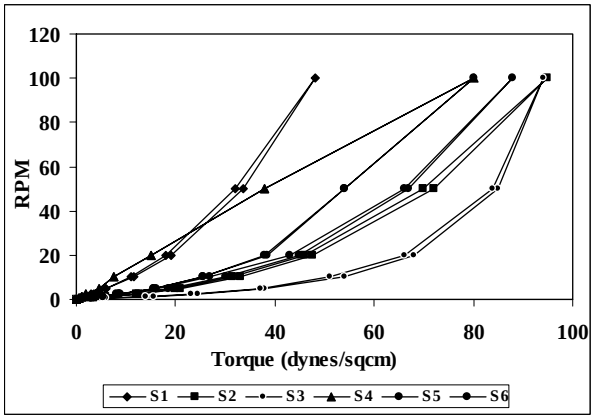

Fig. 5: Rheological behavior of guar gum and Sodium carboxymethyl hydroxypropyl guar dispersion.
S1, S2, S3 are guar dispersion using 0.5% 1% and 2% w/v S4, S5, S6, are sodium carboxymethyl hydroxypropyl guar dispersion using 0.5% 1% and 2% w/v.

RESULTS AND DISCUSSIONS

Alkali slurry method was employed to derivatize Guar gum to Sodiumcarboxymethyl hydroxypropyl derivative. The derivative was found to have a D.S value of 1.5 and Sodium content of 10.4% w/w. The derivative revealed a very good resistance against hydrolytic attack when stored at 5°, 25°, 45° and 60°C at the end of 8 weeks. It is observed that the derivative did not reveal any significant variation in viscosity in presence of electrolytes such as NaCl, $CaCl_2$ and Al_2Cl_3 at the end of 8 weeks. Howerever, guar dispersions while retaining viscosity in presence of NaCl, revealed increase in viscosities in presence of $CaCl_2$ and Al_2Cl_3 from first week onwards. These observations are indicative of better stability for guar derivative in presence of electrolytes. Guar revealed an optimum hydration at a pH value of 6 where as the derivative revealed an optimum hydration at pH-7 (neutral pH). From the Rheological studies, it is observed that the derivative revealed pseudoplastic flow behavior and thixotropic effect only at 1 % w/v and above strength in contrast to guar which exhibited pseudoplastic as well as thixotropy effect at 0.5 w/v strength. From the rate of hydration studies, it is observed that the derivative revealed a more controlled rate of hydration in contrast to guar gum (Misra *et al.*, 1997). This observation along with increased resistance of the derivative to hydrolytic attack and retention of viscosity for derivative in presence of divalent and trivalent electrolytes makes the Sodium carboxymethyl hydroxypropyl derivative of guar a promising derivative for being used as a viscosity-imparting agent in pharmaceutical suspensions. Further, since the derivative undergoes controlled rater of hydration, it claims a berth as a promising pharmaceutical adjuvant in the formulation of controlled release tablets and possibly as a hydrophilic gelling material.

Table 5: Rheological behavior of guar gum and sodium carboxymethyl hydroxypropyl guar dispersion

RPM	Dial Reading					
	S1	S2	S3	S4	S5	S6
0.5	0.5	3.5	6	0.5	2	3
1	1.5	6	15.5	1	4	5.5
2.5	3.5	12.5	24.5	2	8.5	9
5	6	21	38	4.5	15.5	18.5
10	11.5	33	54	7.5	25.5	30
20	19	47.5	68	15	38	45
50	33.5	72	85	38	54	67
100	48	95	94	80	80	88
50	32	70	84	38	54	66
20	18	46	66	15	38.5	43
10	11	31.5	51	7.5	25.5	27
5	6	20	37	4.5	15.5	16
2.5	3	12	23	2	8.5	8
1	1	5.5	14	1	4	4
0.5	0.5	3	5.5	0.5	2	3

S1, S2, S3 are guar dispersion using 0.5%, 1% and 2% w/v S4, S5, S6, are sodium carboxymethyl hydroxypropyl guar dispersion using 0.5% 1% and 2% w/v.

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