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Synthesis, characterization and application of borax cross-linked carboxymethyl guar gum

Jay J. Patel[1], Mandar Karve[1], V. A. Patel[2] and Nirmal K. Patel[1*]

[1]*Department of Industrial Chemistry, Institute of Science and Technology for Advanced Studies and Research (ISTAR), V.V. Nagar, Anand*
[2]*A. R. College of Pharmacy & G. H. Patel Institute of Pharmacy, V.V. Nagar, Anand, Gujarat*

ABSTRACT

Control drug delivery is the new way to treat illness. Guar gum (GG) and its derivative viz. Carboxymethyl guar gum (CMGG) find its application in pharmaceutical formulation as binder and disintegrate agent. Further to extend its application second derivatization of CMGG was carried out to improve its properties. CMGG was cross-linked with borax and prepared derivatives was characterized by Fourier Transform Infrared Spectroscopy (FTIR), Thermogravimetry Analysis (TGA) and Scanning Electron Microscope (SEM). Prepared derivatives were used as drug binder in formulation of N-(4-hydroxyphenyl)acetamide (Paracetamol) and (RS)-2-(4-(2-methylpropyl)phenyl) propanoic acid (Ibuprofen). Tablets were prepared by wet granulation method. Prepared tablets were evaluated for hardness, friability, uniformity of weight content, uniformity of drug content and In-Vitro drug release studies.

Key words: Carboxymethyl guar gum, Borax, Cross-linking, *In-Vitro* release

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INTRODUCTION

GG finds important applications in food, oil recovery and personal care industries. The high viscosity of GG solution arised from the high molecular weight of GG (up to 2 million and further) and from the presence of extensive intermolecular associations (entanglements) by means of hydrogen bonds [1].In aqueous solution GG assumed a flexible coil conformation as evidenced by the Mark-Houwink-Sakurada exponent and by the relatively low value of its characteristic ratio and its persistence length [2].

GG, cross-linked with glutaraldehyde, was proposed for colon delivery [3], and it was also tested as a matrix for oral solid dosage forms. Scleroglucan (SCLG), a water soluble polysaccharide produced by fungi of the genus Sclerotium, consists of a main chain of (1→3)-linked β-D-glucopyranosyl units bearing, every third unit, a single β-D-glucopyranosyl unit linked (1→6). It was known that SCLG assumed a triple-stranded helical conformation in aqueous solution and a single coiled disordered conformation in methylsulphoxide or at high pH values (NaOH>0.2 M) [4]. Due to its peculiar properties, SCLG was extensively used for various commercial applications (secondary oil recovery, ceramic glazes, food, paints, cosmetics, etc.) and it was also investigated for modified/sustained release formulations and ophthalmic preparations [5].

Actually, it is well known that borax was an efficient cross-linker for polymers bearing hydroxyl groups but the type of formed linkages is still debated and so far two main models have been proposed. The most popular one implies the existence of pure chemical crosslinks between the polymeric chains and borax [6], and it was proposed for the GG/borax interactions. According to the other model the borax ions hold together the polymeric chains by means of mixed physical/chemical linkages. This model was firstly proposed for poly-(vinylalcohol) and it was recently suggested also for SCLG [7].

The considerable effort devoted to the study of polymer-ion complexes was due to the wide range of application of these systems. A. Tayal et al. studied the complex between GG and borate [8].They investigated the effect of polymer and borate concentration, temperature, environmental pH conditions, and GG molecular weight on the peculiar rheological properties detected by the frequency dependence of relaxation spectra.Furthermore, a detailed study of the crosslinking reaction of borate ion with polyhydroxy polymers was carried out by means of 11B NMR spectroscopy on dilute mixtures of borate ions and GG, for the acquisition of further insight into the complexation mechanism. Thus, the values of complexation equilibrium constants and the complexation enthalpy at various measuring conditions were calculated [9-10].

To extend the application of carboxymethyl guar gum (CMGG) second derivative of CMGG was carried out. There so in present work CMGG was synthesized by method described by N. K. Patel et al. and then it was cross-linked with borax to improve its properties viz. swelling and viscosity. The prepared derivatives were characterized by FTIR, TGA and SEM. The prepared derivatives CMGG and Borax-cross lined CMGG were utilized in formulation of Paracetamol and Ibuprofen tablets. Prepared tablets were evaluated for hardness, friability, uniformity of weight content, uniformity of drug content and *In-Vitro* drug release study.

EXPERIMENTAL SECTION

Guar gum and borax were purchased from Sigma-Aldrich. Methanol was purchased from National chemicals, Baroda. CMGG were prepared by method described by N. K. Patel et al. [11].Paracetamol and Ibuprofen were obtained from Farmson Pharmaceuticals Pvt. Ltd. Gujarat. Starch and lactose was purchased from S.D. Fine Chemicals, Mumbai. Magnesium stearate was purchased from Loba Chemicals, Mumbai. Solvents and other laboratory chemicals were used after routine purification and they were of analytical reagent (AR) grade.

Preparation of borax cross-linked carboxymethyl guar gum

4gms of carboxymethyl guar gum was dispersed for 1hr at room temperature in 400ml of distilled water with the help of mechanical stirrer. The dispersion was kept aside for 2hrs for swelling. 80ml of 1%w/v aqueous solution of borax (disodium tetra borate) was added to the guar gum dispersion and stirred for 30min with the help of mechanical stirrer then kept aside for another 4hrs without stirring. The formed hydrogel was rinsed with distilled water to remove untreated borax and then the hydrogel was dried at room temperature for 3days. The dried Borax cross linked guar gum was triturated in a mortar for size reduction and passed through sieve no 100.

Estimation of free borax and cross linked borax by titration with 0.05N HCl

200mg of carboxymethyl guar gum was taken in conical flasks and dispersed in 30ml of distilled water to make uniform dispersion. To the dispersion, methyl red was added and titrated against 0.05M HCl solution. The guar gum dispersion titrate value was taken as blank value.

200mg of borax cross linked carboxymethyl guar gum was taken in conical flasks and dispersed in 30ml of distilled water to make uniform dispersion. To the dispersion methyl red was added and titrated against 0.05 M HCl solution. Titrate value was taken as free borax value. In the same way again 200mg of borax cross linked carboxymethyl guar gum was taken and dispersed in 30ml of distilled water to make uniform dispersion. The dispersion was heated at 70^0C to break the cross linked bonds of borax with carboxymethyl guar gum and then to the dispersion methyl red was added and titrated against 0.05M HCl solution.

Rheological studies of Carboxymethyl guar gum and Borax cross-linked guar gum

Viscosity of 1%w/v dispersion of carboxymethyl guar gum and Borax cross linked guar gum in water, 0.1N HCl, pH 7.4 and pH 6.8 Phosphate Buffers was measured by using Brookfield viscometer.

Swelling studies of Carboxymethyl guar gum and Borax cross-linked guar gum

Swelling capacity of both carboxymethyl guar gum and Borax cross-linked guar gum was studied in distilled water, 0.1N HCl, pH 7.4 and pH 6.8 phosphate buffers.

1gm of gum was taken in a measuring cylinder to this 10ml of distilled water was added and shaken vigorously for 10min and allowed to stand for 24hrs. Swelling capacity can be determined by,

Swelling Capacity (%v/v) = [Xv / Xi] X 100

Where,
Xv = the final volume occupied by swollen material after 24hrs
Xi = the initial volume of the powder in graduated measuring cylinder

Same procedure was repeated to study the swelling capacity of both gums in 0.1N HCl, pH 6.8 and pH 7.4 phosphate buffers.

FTIR spectroscopy
The IR spectra of CMGG and borax cross-linked CMGG were recorded by Perkin Elmer spectrum GX instrument, by the KBr pallet method.

Thermo gravimetric analysis
TGA of synthesized CMGG and Borax cross-linked CMGG was carried out by heating sample from temperature of 500C to 700^0C at a heating rate of 10^0C using Perkin Elmer Pyris 1 TGA instruments.

Scanning electron microscopy
The SEM micrograph of synthesized carboxymethyl guar gum and borax cross-linked carboxymethyl guar gum were carried out Philips made ESEM EDAX XL-30 model instrument.

Preparation of tablets
Tablets were prepared by wet granulation method. All the ingredients were mixed in mortar and pestle. After mixing all materials were passed through mesh No.60. The granulation was carried out using solution of starch in sufficient amount of water. Wet granules were dried in oven at 60^0C. After drying granules were sized by mesh No.22 followed by mesh No.44 and mixed with magnesium stearate and talc. 250mg tablets were prepared through compressing on a 10-station mini rotary tableting machine.

6 different formulas, having different concentration of carboxymethyl guar gum (1%, 2% and 3%), and borax cross-linked CMGG (1%, 2% and 3%) and paracetamol and ibuprofen where developed to evaluate the drug release. The composition of different formulations is tabulated in table: 1.

Table 1: Composition of different formulation

Ingredients	Formulation											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Paracetamol	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	---	---	---	---	---	---
Ibuprofen	---	---	---	---	---	---	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
CMGG	1%	2%	3%	---	---	---	1%	2%	3%	---	---	---
Borax cross-linked CMGG	---	---	---	1%	2%	3%	---	---	---	1%	2%	3%
Starch	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Diluents	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg
Lubricants (Mgstearate+talc)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%

Evaluation of granules
Prepared granules are evaluated for angle of repose, loose bulk density (LBD), tapped bulk density (TBD), compressibility index.

Angle of repose
The powder is filled into an open-ended cylinder with the bottom resting on a horizontal surface. The cylinder is then lifted vertically allowing the powder to form a heap on the horizontal. The diameter of the base of the cone is determined by measuring the same in more than one direction. The radius is calculated from the diameter. The height of heap is also measured. The angle of repose is calculated from following equation.

$$\theta = \tan^{-1}(\text{height/radius})$$

Bulk density
The powder whose bulk density is to be determined is passed through sieve no. 20. About 20gm is weight accurately and carefully introduced into a 100ml graduated cylinder. The cylinder is dropped at 2sec interval onto a hard surface three times from a height of 1 inch. The volume of powder is noted. Loose bulk density (LBD) and tapped bulk density (TBD) were measured using the following formula:

$$\text{LBD} = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

$$TBD = \frac{\text{Weight of the powder}}{\text{Tapped volume of the packing}}$$

Compressibility index (C.I.) of the granules was determined by using the following formula

$$CI\ (\%) = \frac{TBD - LBD}{TBD} \times 100$$

Evaluation of tablets

All prepared tablets were evaluated for their uniformity of weight, hardness, friability, uniformity of drug content and in vitro drug release.

Hardness

Hardness of the prepared tablets was measured by Monsanto hardness tester. The tablet is placed between the fixed and moving plunger and the reading of the indicator dial arrow is set to zero. Then the screw knob is moved forward and pressure is applied to the edge of the tablet until the tablet breaks. The reading on the indicator dial is noted which is indicated in terms of pressure in Kg/cm^2required to break the tablet.

Uniformity of weight

To determine uniformity of weight 20 tablets were randomly selected and weighed.

Friability

10 tablets are weighed initially and placed in the chamber. The motor is activated and chamber is allowed to tumble for 4min or 100 revolutions. The tablets roll and drop within the chamber. After 100 revolutions or 4min the tablets are removed and weighed again. The difference in weight of tablet within a given time indicates rate of abrasion or friability. A weight loss between 0.5-2% of their weight is considered acceptable.

Uniformity of drug content

20 tablets were powdered in a mortar. An accurately weighed quantity of powdered tablets was extracted with pH 6.8 buffer and the solution was filtered. The absorbance was measured at 249nm after suitable dilution.

***In-vitro* drug release studies**

In-vitro drug release studies were carried out using USP XXII dissolution apparatus type II at 50rpm.The dissolution medium consisted of 900ml of pH 6.8 phosphate buffer, which is maintained at 37 ± 0.5^0C. The drug release at different time intervals was measured using an UV-visible spectrophotometer at 249nm and 264nm

RESULTS AND DISCUSSION

Estimation of free borax and cross linked borax by titration with 0.05N HCl

The results were tabulated in table 2. It is direct titration of strong alkaline borax with strong acid HCl. 1 mole of borax reacts with 2 moles of HCl. Methyl red is used as an indicator because it is not affected by weak acid (Boric acid) end point is yellow to pink.

Table: 2 Amount of borax present in sample

Sr. No.	Contents in conical flask	Burette reading		Titer value (ml)	Amount of borax present (mg)
		V_1 ml	V_2 ml		
1	CMGG + 30ml water	5.7	-----	5.7	-----
2	Borax cross-linked CMGG + 30ml water	5.7	12.3	6.6	0.603mg/200mg of sample
3	Borax cross-linked CMGG + 30ml water at 70^0C	5.7	12.7	7.0	0.639mg/200mg of sample

Unreacted $B_4O_7^{-2}$ present in 200mg of Borax cross-linked carboxymethyl guar gum is 0.603mg and Unreacted $B_4O_7^{-2}$ present in 1gm of Borax cross-linked carboxymethyl guar gum is 3.015mg. Cross-linked $B_4O_7^{-2}$ present in 200mg of Borax cross-linked carboxymethyl guar gum at 70^0C is 0.639mg.

Rheological studies of Carboxymethyl guar gum and Borax cross-linked guar gum

The results were tabulated in table: 3. The viscosity of borax cross-linked CMGG was high compared to CMGG is due to cross-linking of borax onto CMGG backbone.

Table: 3 Viscosity of 1%w/v dispersion of CMGG and borax cross-linked CMGG

1%w/v Dispersion of polymer	Viscosity in water (CPS)	Viscosity in 0.1N HCl (CPS)	Viscosity in pH 6.8 Phosphate Buffer (CPS)	Viscosity in pH 7.4 Phosphate buffer (CPS)
CMGG	102.3	99.5	101.6	107.6
Borax cross-linked CMGG	173.3	168.3	170.0	178.2

Swelling studies of Carboxymethyl guar gum and Borax cross-linked guar gum

The results were tabulated in table:4. The carboxymethyl guar gum displayed a higher swelling ratio relatively to borax cross-linked CMGG. Incorporation of borax onto CMGG backbone decreased swelling index. Due to cross-linking viscosity of borax cross-linked CMGG was increased compared to CMGG.

Table: 4 Swelling index of CMGG and borax cross-linked CMGG

Swelling polymer	Swelling index in water	Swelling index in 0.1N HCl	Swelling index in pH 6.8 Phosphate Buffer	Swelling index in pH 7.4 Phosphate buffer
CMGG	120	128	124	122
Borax cross-linked CMGG	110	114	112	106

FTIR spectroscopy

The IR spectrum of carboxymethyl guar gum and borax cross-linked carboxymethyl guar gum were shown in figure: 1 and figure: 2 respectively.

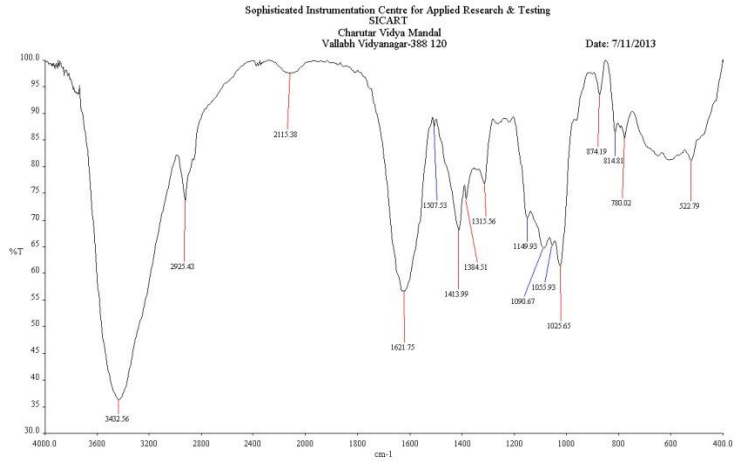

Figure: 1 FTIR spectra of CMGG

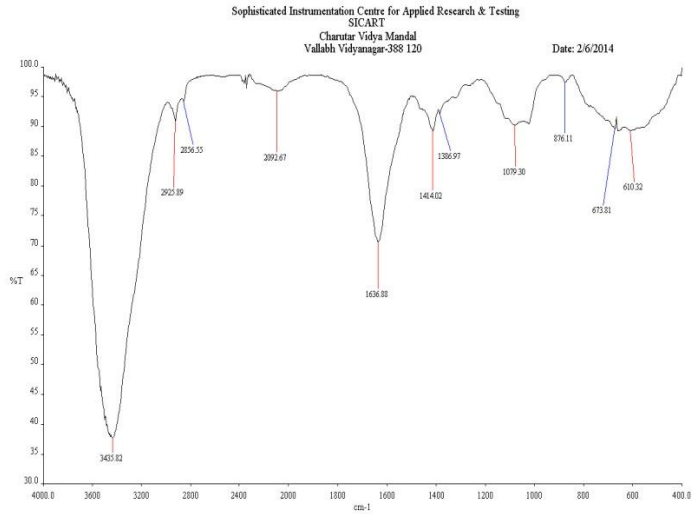

Figure: 2 FTIR spectra of borax cross-linked CMGG

In FTIR spectrum of CMGG a reduced intensity of the absorption band located at 3432.56cm^{-1} due to -OH is stretching, indicating that some -OH group were carboxymethylated. The sharp absorption band located at 2925.43cm^{-1} may be attributed to CH group stretching. TheC-O symmetrical and asymmetrical vibrations at a frequency of 1025.65cm^{-1} and 1149.93cm^{-1} confirms the incorporation of the carboxymethyl group on to the guar gum molecule.

The FTIR spectrum of borax cross-linked carboxymethyl guar gum shows B-O-B bending vibration at 673.81cm^{-1}. It also shows B-O stretching of tetrahedral BO_4^- at 876.211cm^{-1} and B-O stretching of trigonal BO_3 units at 1414.02cm^{-1}. This absorption band in Brox cross-linked carboxymethyl guar gum confirms the cross-linking of borax with CMGG.

Thermo gravimetric analysis

TGA of CMGG and borax cross-linked CMGG were shown in figure: 3 and figure: 4 respectively.

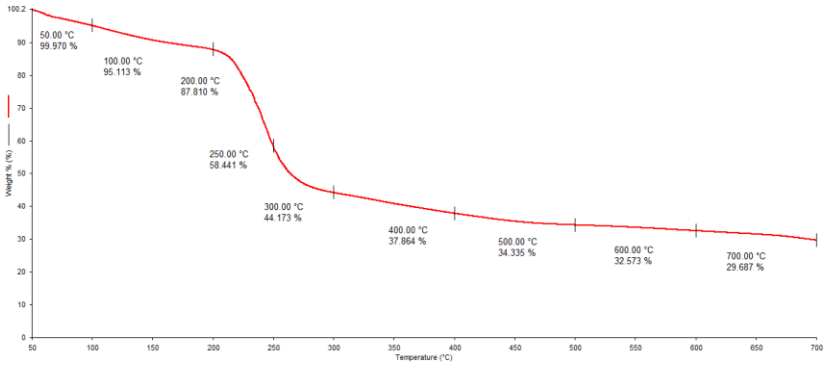

Figure: 3 TGA of CMGG

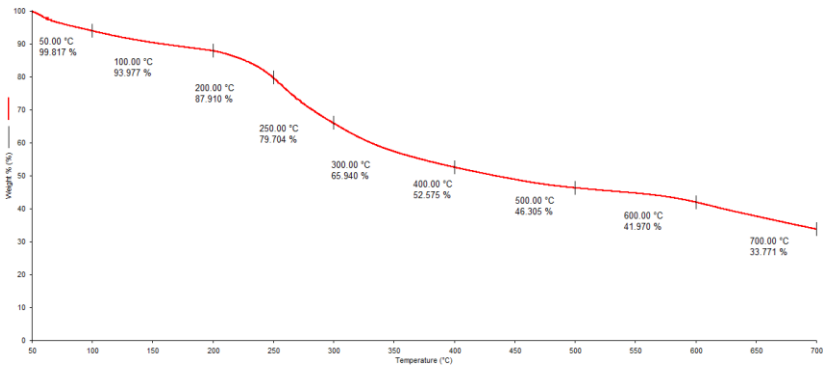

Figure: 4 TGA of borax cross-linked CMGG

Thermo gravimetric analysis of carboxymethyl guar gum essentially reveals two distinct zones of weight loss. The initial weight loss occurred in the 50-100^{0}C range, due to the moisture traces present in the sample. In TGA of CMGG second step represents the degradation of the polymer backbone, having started at 200^{0}C and lasting until 300^{0}C. During this section CMGG lost 55.82% of its weight. In addition to these zones of weight loss, the thermal degradation of carboxymethyl guar gum shown a third zone in the 400-500^{0}C range, due to the degradation of the carboxymethyl groups incorporated in the polymer moiety. Thermo gravimetric analysis of borax cross-linked carboxymethyl guar gum reveals 3 distinct zones of weight loss. The initial weight loss occurred at 100-200^{0}C. The second zones started at 250^{0}C and continue upto 300^{0}C. During this period borax cross-linked CMGG lost 34.06% of its weight. Borax cross-linked CMGG shown third zone started at 400^{0}C and ending at 500^{0}C. After this period borax cross-linked CMGG has retained 53.65% of its weight.

Cross-linking of borax onto the CMGG increased its thermal stability. It can be concluded from TGA curves that at 500^{0}C CMGG lost it 65.67% of its while borax cross-linked CMGG lost 53.7% of its weight. The incorporation of borax onto CMGG backbone provided strength to the polymer hence increased thermal stability of polymer.

TGA analysis shown that borax was cross-linked with CMGG. TGA curve shown the thermal degradation at 600-700^{0}C, due to the incorporation of borax onto CGMM. Thermal stability of borax cross-linked CMGG was improved which can be indicated in TGA.

Scanning electron microscopy

The SEM micrograph of CMGG and borax cross-linked CMGG were shown in figure: 5 and 6 respectively.

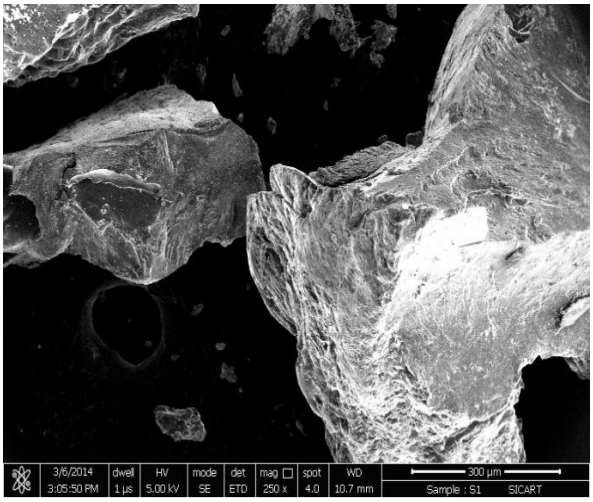

Figure: 5 SEM of GMGG

Figure: 6 SEM of borax cross-linked CMGG

From the SEM micrograph, the surface morphology of CMGG is improved by cross-linking with borax. The most of the porosities present in CMGG are eliminated by cross-linking process. It confirmed the swelling index was decreased by cross-linking CGMM with borax. Incorporation of borax onto the CGMM backbone increased the surface area of the molecule. Cross-inking improved the surface morphology.

Angle of repose

Table: 5 Physical properties of granules

Formulation code	Parameters			
	Angle of repose	LBD (mg/ml)	TBD (mg/ml)	Compressibility index (C.I %)
F1	30.74	0.7571	0.8412	9.997
F2	32.61	0.8130	0.9300	9.996
F3	33.91	0.8587	0.9541	9.998
F4	31.45	0.7761	0.8612	9.986
F5	29.88	0.8236	0.8301	9.931
F6	32.02	0.8336	0.9512	9.899
F7	32.60	0.7768	0.8832	9.397
F8	29.76	0.7982	0.8855	9.858
F9	33.41	0.8212	0.9098	9.738
F10	30.05	0.7912	0.8790	9.988
F11	32.10	0.8112	0.9022	1.008
F12	33.64	0.7723	0.8443	8.527

Results for angle of repose for different formulation were tabulated in table: 5.

The results for angle of repose for formulation F1-F6 and F7-F12 were ranged from 30.84±3.23 and 30.05±3.82 respectively. Best results for angle of repose were 30.74, 29.88, 29.76 and 30.05 for formulation F1, F5, F7 and F10 respectively. The fill weight of tablets depends on flow properties of powder. The poor flow was resulted in with less fill weight. The results of angle of repose for the prepared formulation shows good flow properties and prepared tablets was comply with uniformity of weight requirement.

Bulk density

The results bulk density and compressibility index were tabulated in table: 5. The results for LBD and TBD were ranged from 0.8070±0.0560, 0.9031±0.0682, 0.7923±0.038 and 0.8832±0.023 for formulation F1-F3, F4-F6, F7-F9 and F10-F11 respectively. Compressibility index ranged from 9.995 ± 0.064.

The results of bulk density provided valuable information on tablet porosity and its relation to tablet hardness and disintegration. Bulk density is an important consideration in packing of powders. Low value for compressibility index indicated better flow property of powder. From the value of compressibility index it was said that flow property of powder is excellent.

Hardness

The results were tabulated in table: 6. The hardness of formulation F1, F2, F3, F7, F8, F9 were 5.8, 4.6, 4.3, 5.1, 5.6 and 5.0 kg/cm2 respectively. The hardness of formulation F4, F5, F6, F10, F11 and G12 were 5.6, 6.4, 4.8, 5.8, 5.3 and 5.4 kg/cm2respectively. Hardness of the prepared tablets was compared with standard tablets. Hardness of tablet prepared by using borax cross-linked CMGG was high as compared to CMGG. The value of hardness property insures the tablet is firm enough to withstand handling without breaking, chipping.

Table: 6 Hardness of different formulations

Formulation code	Hardness Kg/cm^2
F1	5.8
F2	4.6
F3	4.3
F4	5.6
F5	6.4
F6	4.8
F7	5.1
F8	5.6
F9	5.0
F10	5.8
F11	5.3
F12	5.4
Standard Paracetamol tablet	7.0
Standard Ibuprofen tablet	6.6

Uniformity of weight

The results were tabulated in table: 7. Resulted were compared with standard tablets. All the formulations were passed the Indian Pharmacopeia (I.P) limits for tablet formulation.

Table: 7 Uniformity of weight

Formulation Code	Average weight of tablet in mg (a)	Average deviation from average weight a-b or b-a	Average % deviation from average weight (*C)	Passes/fails I.P. limits
F1	250.2	1.12	0.7438	Pass
F2	251.4	1.68	1.864	Pass
F3	250.8	0.64	0.3278	Pass
F4	251.9	1.13	0.6552	Pass
F5	250.8	0.72	0.3560	Pass
F6	249.7	1.50	1.0245	Pass
F7	250.1	0.87	0.3478	Pass
F8	250.2	1.02	0.4076	Pass
F9	250.4	1.14	0.4552	Pass
F10	250.3	0.98	0.3915	Pass
F11	250.1	0.88	0.3518	Pass
F12	251.1.	0.77	0.3066	Pass
Std. Paracetamol	250.2	0.200	0.08	Pass
Std. Ibuprofen	250.3	0.300	0.012	Pass

Table: 8 Friability data of formulation

Formulation code	Weight of 20 tablets before test	Weight of 20 tablets after test	Difference in weight = weight loss	% Weight loss	Passes/ Fails I.P. limits
F1	5.008	5.003	0.005	0.39	Pass
F2	5.028	5.008	0.02	1.59	Fail
F3	5.016	4.999	0.017	2.13	Fail
F4	5.012	4.997	0.015	0.29	Pass
F5	5.099	5.081	0.018	0.65	Pass
F6	5.057	5.041	0.016	1.35	Fail
F7	5.012	5.011	0.008	0.68	Pass
F8	5.020	5.018	0.010	0.98	Pass
F9	5.003	5.001	0.006	0.77	Pass
F10	5.012	5.010	0.011	0.88	Pass
F11	5.015	5.013	0.004	0.36	Pass
F12	5.024	5.022	0.005	0.44	Pass
Std. Paracetamol tablet	5.012	5.011	0.001	0.01	Pass
Std. Ibuprofen tablet	5.008	5.006	0.002	0.02	Pass

Friability

The results were tabulated in table: 8. All the formulation passes the limits of Indian Pharmacopeia except formulation F2, F3 and F6. The result was compared to standard tablets. Tablets in which borax cross-linked CMGG were used as binder shown good friability against tablets in which CMGG were used as binder.

Uniformity of drug content

The results were tabulated in table: 9. The uniformity of drug content of all the formulations are in the range of 99.02±1.50. It can be concluded all the formulation has uniformity of drug in the tablet.

Table: 9 Uniformity of drug content

Formulation code	%Drug content
F1	99.02±0.21
F2	99.62±0.12
F3	98.43±0.27
F4	99.10±0.72
F5	99.68±0.40
F6	99.66±0.40
F7	99.06±0.11
F8	99.25±0.15
F9	98.13±0.18
F10	98.22±0.08
F11	99.48±0.22
F12	98.47±0.35
Std. Paracaetamol tablet	99.55±0.11
Std. Ibuprofen tablet	99.02±0.24

***In-vitro* drug release studies**

The cumulative % of drug release of different formulation tablets were shown in figure: 7.

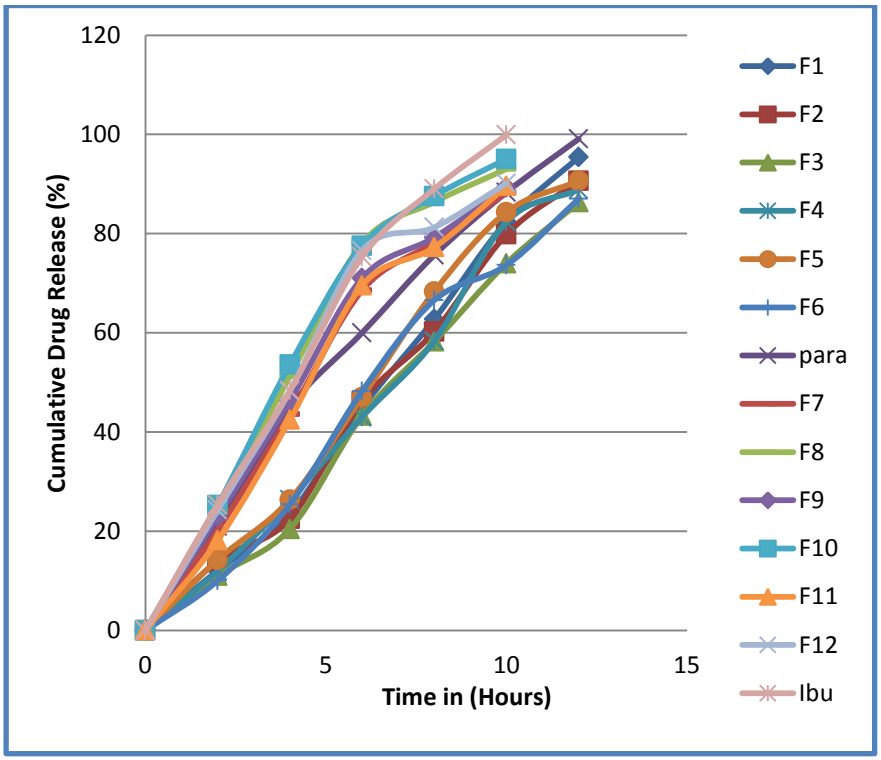

Figure: 7 *In-Vitro* release profile of F1 to F12 formulations

The cumulative % of drug release for F1, F2 and F3 was 95.43%, 90.60% and 86.30% and cumulative % of drug release for F4, F5 and F6 was 88.86%, 90.63% and 87.03% respectively. The cumulative % of drug release for F7, F8, F9 was 88.25%, 93.25% and 89.25 respectively. The Cumulative % of drug release for F10, F11 and F12 was 89.58%, 95.05% and 90.12% respectively. It can be concluded that % release of drug decreases with increase in CMGG concentration. As the concentration of borax cross-linked CMGG increases to 2% from1% %drug release

was increased. Further increased in concentration to 3% the % drug release was decreases. The % of cumulative drug release of standard paracetamol tablet and ibuprofen tablets was 99.09% and 99.90% respectively.

It has been observed that the % cumulative drug release decreases with increasing concentration of CMGG because slow erosion of layer of the tablets containing higher amount of CMGG. The release of drug was slow in the case of borax cross-linked CMGG because formation of a thick gel structure delays the drug release from the tablets, where hydration of individual CMGG particles results in extensive swelling. Thus it maintained the integrity of the tablet.

From the above observations it is concluded that slow and controlled release of paracetamol over a period of 12hrs was obtained from matrix tablets (F1 and F5). Use of derivative of guar gum i.e. CMGG and borax cross-linked CMGG was successful in the formulation of tablets and at the same time it is effective in retarding the drug release. Amongst all the formulation F1 and F5 shows the 95.43% and 90.63% of drug release at the end of 12hrs respectively.

Prepared tablets of ibuprofen were also shown the controlled release over a period of 10hrs. Use of derivatives of CMGG and borax cross-linked CMGG was effective in retarding the drug release. Amongst all formulation F8 and F10 shows the 93.25% and 95.05% of drug release at the end of 10hrs.

The cumulative % drug release was decreased by increase in polymer concentration in both cases. The good results were obtained for flow properties, hardness, friability for the both tablet i.e. paracetamol and ibuprofen.

CONCLUSION

The cross-linking of borax with carboxymethyl guar gum was carried out successfully. The amount of borax cross-linked with CMGG backbone was found by titration method. The cross-linking increased the viscosity of 1%w/v solution of borax cross-linked CMGG. Swelling index of borax cross-linked CMGG is lower as compared to CMGG in all testing medium. The FTIR study reveals the incorporation of borax onto the CMGG backbone. Borax cross-linked CMGG and CMGG were used in pharmaceutical formulation of Paracetamol and Ibuprofen as a drug binder. Prepared tablets were evaluated for Hardness, Friability, Uniformity of weight, Uniformity of content and *In-Vitro* drug release. The results for flow properties, hardness, friability for the both cases are comparatives with standard paracetamol and ibuprofen tablets available in the market also it fulfills the Indian pharmacopeial requirements.

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