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## STEADY SHEAR AND DYNAMIC SHEAR RHEOLOGICAL PROPERTIES OF CARBOXY-METHYL LOCUST BEAN GUM INFLUENCING EROSION OF THE POLYSACCHARIDE COAT OF COMPRESSION COATED TABLETS

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### Keywords:

Carboxymethyl locust bean gum, Rheology, Coat-erosion, Polymer concentration, Solution pH

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**ABSTRACT:** Rheological properties of carboxymethyl locust bean gum (CMLBG) solutions having different concentrations and solution pH were evaluated through steady shear and oscillatory measurements and were used to describe the erosion propensity of CMLBG coat of compression coated placebo tablets. CMLBG solutions, irrespective of concentration and solution pH, exhibited predominant viscous character as the viscous modulus ( $G''$ ) > elastic modulus ( $G'$ ) and phase angle ( $\text{Tan } \delta$ ) > 1. The viscous contribution was found to be influenced by both the CMLBG concentration and solution pH. An increase in CMLBG concentration increased the pseudo-plasticity and consistency coefficient and decreased the viscous contribution in all solution pH resulting in a decrease in erosion of CMLBG coat. The higher viscous character of CMLBG in buffer solution of pH 7.4 (Solution B) was responsible for higher erosion of the coat than in acid solution of pH 1.2 (Solution A). When the pH of acid solution of CMLBG was increased dynamically from 1.2 to 7.4, the viscous contribution decreased to some extent than that observed in Solution B leading to a decrease in coat erosion which was albeit more than in Solution A. Rheological parameters could be used as a tool to describe erosion of polysaccharide coated tablets.

**INTRODUCTION:** Locust bean gum (LBG), a galactomannan polysaccharide which is obtained from the endosperm of the seeds of *Ceratonia siliqua* Linn, consists of  $\beta$ -(1-4)-D-mannopyranosyl backbone attached with a side chain of  $\alpha$ -(1-6)-D-galactopyranosyl unit<sup>1</sup>. Because of the absence of toxicity, LBG finds wide applications in the textiles, biomedical, food, cosmetics, and pharmaceutical industries<sup>2,3</sup>.

Frequently, the pristine polysaccharides do not fulfill the requirements of specific applications, and hence, have been modified by introducing ionic functional groups in place of hydroxyl groups along the macromolecular backbone to induce faster and better aqueous solubility and multifunctional characteristics<sup>4</sup>.

Carboxymethylation has been considered as one of the methods to improve the functional properties of many polysaccharides<sup>5-7</sup>. Carboxymethyl LBG (CMLBG) has been found as a suitable excipient for the formulation of matrix tablets for sustained release<sup>8</sup> and compression coated tablets for colon targeting of drugs<sup>9</sup>. When a tablet compression coated with a polysaccharide or its derivatives is brought in contact with aqueous medium, the

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polymer chains present on the surface of the coat hydrate, causing expansion of end-to-end distance and radius of gyration which leads to swelling of the polymer<sup>10</sup>. Subsequently, the polymer undergoes transition from glassy to rubbery state to create a gel layer<sup>11</sup>. Accumulation of sufficient water by progressive hydration initiates disentanglement of the polymer chains<sup>12</sup>, and with time, the gel layer gets so diluted that the polymer network no longer maintains the structural integrity, and the polymer begins to erode<sup>13</sup>.

On a molecular level, the nature of a gel layer, whether it be durable or susceptible to erosion, depends on the extent of entanglement and disentanglement of the polymer chains. The dissolution/or erosion of a polymer is believed to correspond to the disentanglement of the polymer chains that are characterized by a threshold polymer concentration<sup>14</sup>. Since entanglement and disentanglement of the polymer chains, inter-chain interaction, swelling or shrinking of polymer coils depending on the medium, and conformational changes of ionized polymeric chains with a change in pH are involved both in erosion and rheology of polymer solution/gel, rheological study is another approach to characterize the gel layer<sup>15</sup>.

The effect of viscosity of CMLBG solutions having different polymer concentration and solution pH on the erosion propensity of CMLBG coat of compression coated tablets has been recently reported<sup>16</sup>. It was observed that higher viscosity of CMLBG solution, induced by higher polymer concentration and lower solution pH, reduced the erosion propensity of CMLBG coat. However, simple measurement of viscosity of a polymer solution is inadequate, and the viscoelastic properties are more useful to provide greater insight into the rheological properties and hence, on gel structure of polymer<sup>17</sup>. However, neither the detailed study of the viscoelastic properties nor the relation between these parameters and erosion of CMLBG coated tablets have been addressed.

The rheological properties of a polymer solution are generally affected by the polymer concentration, solution pH, temperature, degree of dispersion, dissolution, and electric charge<sup>18</sup>. As a compression coated tablet contains different amount of a polymer for modulation of drug release

and encounters different pH environment in the gastrointestinal tract (G.I.T.), the objective of the present work was to investigate the rheological properties of CMLBG as a function of polymer concentration, solution pH, and under dynamic pH shift condition (simulating that occurring in G.I.T.) and to describe the erosion of CMLBG coated tablets with the support of the rheological parameters. In the present study, 2.5, 3.0, and 3.5% w/w CMLBG in acid solution (Solution A, pH 1.2) and buffer solution (Solution B, pH 7.4) were subjected to steady shear and oscillatory measurements. Also, the viscoelastic properties of CMLBG under dynamic pH shift condition (in Solution A→B) were compared with those in Solution A and Solution B to describe the erosion propensity of CMLBG coat.

## MATERIALS AND METHODS:

**Materials:** Locust bean gum (LBG) (Hi-Media, Mumbai, India), monochloroacetic acid, sodium hydroxide, and tri-sodium orthophosphate dodecahydrate (Loba Chemi, Thane, Mumbai, India), microcrystalline cellulose (Avicel PH 102), sodium starch glycolate (SSG), magnesium stearate, and all other reagents were obtained commercially and used as received.

## Methods:

**Preparation of CMLBG:** LBG was chemically modified to CMLBG through a base-catalyzed reaction between LBG and monochloroacetic acid. The detailed methods of preparation and characterization of CMLBG have been reported previously<sup>8</sup>.

## Preparation of CMLBG Solutions:

**Solution A of CMLBG:** 0.1 (M) HCl solution, the pH of which was adjusted to 1.2, was designated as Solution A. Required amount of CMLBG was dissolved in Solution A at 50 °C. After cooling to room temperature, the solution was adjusted to pH 1.2 with 0.2 (M) HCl solution, and finally, the weight was adjusted with Solution A.

**Solution B of CMLBG:** Solution B was prepared by mixing 700 ml of Solution A with 200 ml of 0.2 (M) trisodium orthophosphate dodecahydrate solution and adjusting to pH 7.4 with 0.2 (M) HCl/NaOH solution<sup>19</sup>. The required amount of CMLBG was dissolved in Solution B at 50 °C.

The solution was cooled to room temperature, the pH was adjusted to 7.4 with 0.2 (M) NaOH solution, and finally, the weight was adjusted with Solution B.

**Solution (A→B) of CMLBG:** Required amount of CMLBG was dissolved in Solution A at 50 °C. After cooling down to room temperature, the solution was kept for 2 h with stirring. 0.5 (M) trisodium orthophosphate dodecahydrate solution was added, mixed for 1 h, and the pH was adjusted to 7.4 with 0.2 (M) NaOH solution. The final weight was adjusted with Solution B.

**Rheological Study:** Various rheological measurements of 2.5% w/w, 3.0% w/w and 3.5% w/w CMLBG in different solution pH were carried out in a Rheometer (Anton Paar, MCR 102, Austria) at 25 °C. The instrument was fitted with a standard cone-plate (CP-40, 40 mm outer diameter, angle 1°) and an air compressor unit to maintain air pressure at 7 kg/cm<sup>2</sup>. Steady shear measurements were performed from 0-100 shear rate (s<sup>-1</sup>) in a rotational mode.

Oscillatory shear measurements involved strain sweep study (0.01 to 100 strain% at a constant angular frequency of 10 rad/s) and frequency sweep study (0.1 to 100 rad/s at 2% strain) in an oscillatory mode. Data were analyzed using Rheoplus Software (US 200, version 3.62).

**Preparation of Core and Compression Coated Tablets:** Placebo (drug-free) core tablets weighing 150 mg were prepared following the method described previously<sup>16</sup>. A blend of Avicel PH 102, 4% SSG (intragranular), and 6% w/w HPMC E15LV was granulated with water. 144.5 mg of the dried granules (# 22 mesh BS screen) were mixed with 4 mg SSG (extra-granular) and 1.5 mg magnesium stearate (for unit tablet) and compressed in a tablet machine (RIMEK, Karnavati Engineering Ltd., Gujarat, India) using 6 mm flat punch. The hardness of the tablets that were measured with a Pfizer type hardness tester (G. T. Scientific Industry, Haryana, India) was close to 3 kg/cm<sup>2</sup>.

The resulting placebo core tablets were compression coated with 250 mg and 350 mg of CMLBG. 40% of powdered CMLBG (#40 mesh) was placed in a 10 mm die cavity; a core tablet was

placed manually in the center, the remaining 60% of powdered CMLBG was placed over the tablet and then compressed with a 10 mm flat punch. The hardness of the compression coated tablets was kept near to 5 kg/cm<sup>2</sup>.

**Erosion Study of Coated Tablet:** Erosion study of placebo CMLBG coated tablets was performed in a tablet dissolution rate test apparatus (TDP 06P, Electro Lab, Mumbai, India). A tablet was weighed in an electronic pan balance (Precissa XB600M-C, Switzerland), placed in a 900 ml solution maintained at 37 ± 0.5 °C, and rotated at 75 rpm with a paddle-type stirrer. The erosion study was conducted in Solution A (acid solution of pH 1.2) and Solution B (buffer solution of pH 7.4). Additionally, to simulate the dynamic pH shift condition prevailing in G.I.T., the erosion study was performed in Solution (A→B) following the method described in Pharmacopoeia for drug release study from delayed-release tablets<sup>19</sup>. The erosion of the tablets was initially studied in 700 ml of Solution A for 2 h, and then the pH of the solution was increased in-situ to pH 7.4 by adding 200 ml of 0.2 (M) trisodium orthophosphate dodecahydrate solution and adjusting the pH with 0.2 (M) HCl/NaOH solution, and the study was continued up to 6 h. At predetermined time periods, the tablet was removed from the liquid and dried to a constant weight at 65 °C to 70 °C in an oven. The weight loss representing the % erosion of the tablet was calculated from the following relationship:

$$\% \text{ Erosion} = W_1 - W_2 \times 100 / W_1$$

Where W<sub>1</sub> and W<sub>2</sub> represent the weight of the tablet at time 0 and time t, respectively, after immersion in the liquid.

## RESULTS AND DISCUSSION:

**Flow Behavior of CMLBG Solutions:** The rheograms of CMLBG solutions having different concentrations and solution pH have been shown in **Fig. 1(A-C)**. The rheograms arose at the origin, were concave towards the shear rate axis, and did not exhibit yield value. This indicated that CMLBG solutions exhibited pseudoplastic flow. An increase in shear stress values was observed with an increase in CMLBG concentration in each solution pH. An increase in shear stress with increase in the concentration of added polymers has been found for yellow passion fruit pulp<sup>20</sup>.

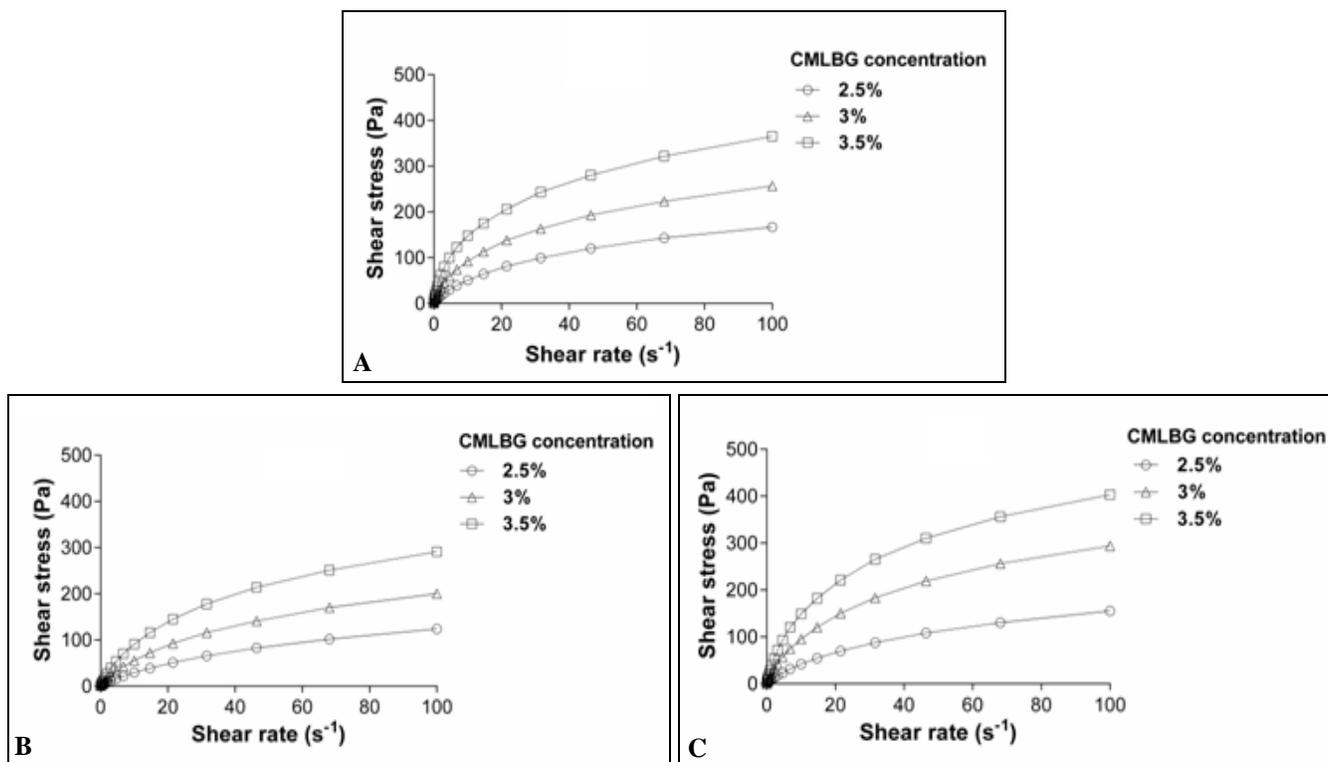


FIG. 1: FLOW CURVES OF 2.5% w/w (O), 3.0% w/w (Δ) AND 3.5% w/w (□) CMLBG IN DIFFERENT SOLUTIONS. KEY: (A) SOLUTION A (ACID SOLUTION OF pH 1.2), (B) SOLUTION B (BUFFER SOLUTION OF pH 7.4), (C) SOLUTION (A→B) (pH 7.4)

Moreover, for each concentration, the values of shear stress were higher in Solution A (pH 1.2), followed by in Solution (A→B) having pH 7.4, and the lowest in Solution B (pH 7.4). To ascertain that the solutions of CMLBG did not follow the plastic flow, the data were fitted in Casson model<sup>21</sup>:

$$\tau^{1/2} = \sigma^{1/2} + (\eta \gamma)^{1/2}$$

Where  $\tau$  is the shear stress,  $\sigma$  = yield stress,  $\eta$  = shear viscosity, and  $\gamma$  = shear rate. The plots were straight lines, almost passing through the origin without showing significant yield stress value **Fig. 2(A-B)**. The results, thus, demonstrated that the solutions of CMLBG did not show plastic flow

which is observed for gel network structure; instead, the solutions exhibited pseudoplastic flow characteristics of simple polymer solution. The shear stress and shear rate data within the shear thinning region were fitted into Ostwald-de Wale equation (Power-law model):

$$\tau = K \gamma^n$$

Where  $\tau$  is the shear stress (Pa),  $\gamma$  is the shear rate ( $s^{-1}$ ),  $K$  is the consistency coefficient ( $Pa \ s^n$ ), and  $n$  represents the flow behavior index (dimensionless). The values of  $n$ ,  $K$ , and regression coefficient ( $R^2$ ) have been shown in **Table 1**.

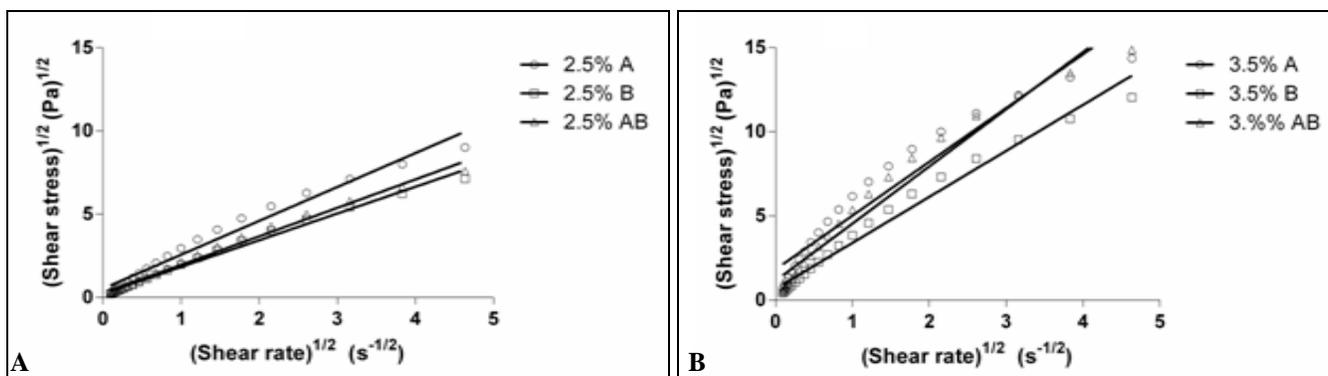


FIG. 2: (SHEAR STRESS)<sup>1/2</sup> vs. (SHEAR RATE)<sup>1/2</sup> PLOT SHOWING COMPLIANCE WITH CASSON MODEL FOR (A) 2.5% w/w AND 3.5% w/w CMLBG IN DIFFERENT SOLUTION pH. KEY: SOLUTION A (A), SOLUTION B (B), SOLUTION (A→B) (AB)

Good linearity with reasonably high regression coefficients ( $R^2$ ) indicated that flow behavior of CMLBG solutions could be adequately described by the Power-law model. While the flow behavior index  $n=1$  indicates Newtonian flow,  $n < 1$  indicates pseudoplastic flow of a liquid<sup>22</sup>. The values of flow behavior index ( $n$ ) were  $< 1$  confirming that CMLBG solutions having different concentrations and solution pH exhibited

pseudoplastic (shear thinning) behavior. Shear-thinning property has been found with many exudates gums<sup>23</sup> as well as with hydroxypropyl and carboxymethyl derivatives of guar gum<sup>24</sup> and is related to the break-down of structural units of the gums and rearrangement of the polymer chains in the direction of hydrodynamic forces generated during shear<sup>25</sup>.

**TABLE 1: EFFECT OF CMLBG CONCENTRATION AND SOLUTION pH ON POWER LAW PARAMETERS**

| Concentration of CMLBG (%)       | Flow Index (n) | Consistency Coefficient (K) (Pa S <sup>n</sup> ) | Regression Coefficient (R <sup>2</sup> ) |
|----------------------------------|----------------|--|--|
| <b>In Solution A (pH 1.2)</b>    |                |  |  |
| 2.5                              | 0.642          | 10.38  | 0.989                                    |
| 3.0                              | 0.555          | 23.28  | 0.988                                    |
| 3.5                              | 0.487          | 44.06  | 0.988                                    |
| <b>In Solution B (pH 7.4)</b>    |                |  |  |
| 2.5                              | 0.752          | 4.67   | 0.991                                    |
| 3.0                              | 0.695          | 9.98   | 0.988                                    |
| 3.5                              | 0.648          | 18.11  | 0.985                                    |
| <b>In Solution (A→B, pH 7.4)</b> |                |  |  |
| 2.5                              | 0.710          | 7.18   | 0.988                                    |
| 3.0                              | 0.629          | 19.82  | 0.986                                    |
| 3.5                              | 0.571          | 35.24  | 0.982                                    |

**Effect of CMLBG Concentration on Flow Behavior:** The flow behavior index ( $n$ ) decreased with an increase in CMLBG concentrations implying that pseudoplastic (shear thinning) behavior increased with increase in the biopolymer concentration. On the other hand, the consistency coefficient ( $K$ ) increased with increase in CMLBG concentration in each solution. Other mucilage<sup>26</sup> and gum<sup>27</sup> have been reported to exhibit similar properties. The consistency coefficient ( $K$ ) is a rheological parameter that gives an idea of the viscosity of a material. An increase in the values of  $K$  indicates an increase in viscosity with increase in polymer concentration and is related to an increase in water binding capacity<sup>28</sup>. We previously reported that steady shear viscosity increased with increase in CMLBG concentration in each solution<sup>16</sup>. An increase in viscosity with polymer concentration is a natural phenomenon and has been found with various polysaccharides such as guar gum, locust bean gum, and modified guar gum derivatives<sup>29</sup> and is attributed to the enhanced degree of molecular chain entanglement<sup>30</sup>.

**Effect of Solution pH on Flow Behavior:** The flow behavior index ( $n$ ) and consistency coefficient ( $K$ ) was also influenced by the pH of CMLBG solutions. The value of  $n$  was high, and that of  $K$

was less in Solution B (pH 7.4) than the values of the corresponding indices in Solution A (pH 1.2). The results indicated that the pseudo-plasticity and consistency coefficient decreased with increase in solution pH. To verify this observation, the values of  $n$  and  $K$  were determined in Solution (A→B) which was prepared by increasing the pH of Solution A of CMLBG in-situ from 1.2 to 7.4 and were compared with those of Solution A (pH 1.2).

The results **Table 1** ascertained that increase in pH even under dynamic condition decreased the pseudo-plasticity and consistency coefficient than in Solution A. It was further noted that, at each of the concentrations, the pseudo-plasticity and consistency coefficient of Solution (A→B) of CMLBG were higher than those of Solution B although both solutions exhibited pH 7.4. Carboxymethylation of neutral locust bean gum imparts anionic character to the resulting CMLBG. In acid solution, suppression of ionization of the carboxylate ions reduced the electrostatic repulsion.

This promoted the formation of intermolecular hydrogen bonds and associated structure producing highly viscous solution<sup>31</sup>. Consequently, the values of  $K$  increased in acid solution. On the other hand, in a solution of higher pH, the molecular

conformation of certain ionic polysaccharides may change<sup>32</sup> or the polymer chains may depolymerize<sup>33</sup> leading to a decrease in viscosity<sup>34</sup>.

As a result, the pseudoplastic behavior and consistency coefficient of CMLBG were found less in Solution B of pH 7.4 than in Solution A of pH 1.2. Interestingly, the pseudoplastic behavior and consistency coefficient of CMLBG in Solution (A→B) were higher than those found in Solution B although the pH of both the solutions was kept the same (pH 7.4). Although unaddressed till date, it is possible that dense network structure or improved topological structure of the polysaccharide chains, which occurred in acid solution (Solution A, pH 1.2), might have persisted to some extent even when the pH of the acid solution of CMLBG was increased in-situ to pH 7.4.

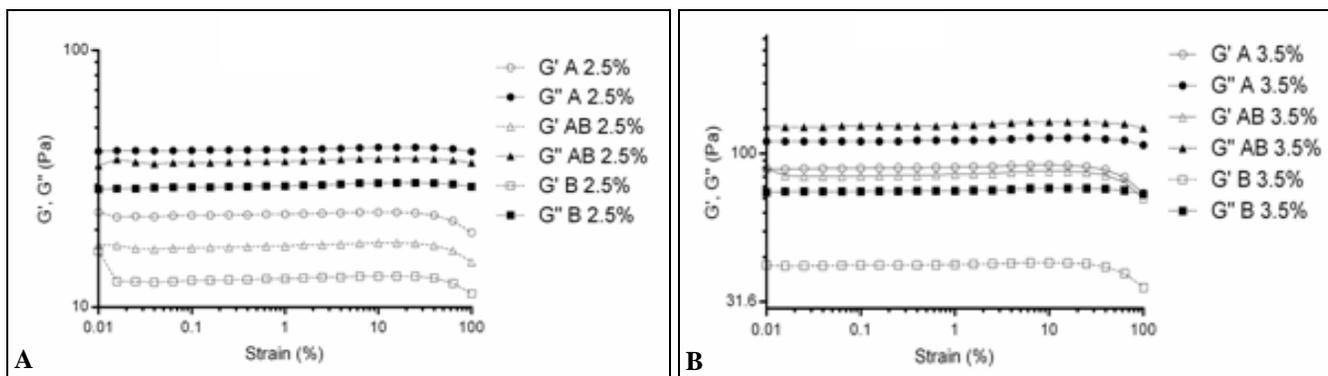
This resulted in a lower flow behavior index ( $n$ ) and higher consistency coefficient ( $K$ ) in Solution (A→B) than in Solution B. The results corroborated well with our previous observation that viscosity of CMLBG in Solution (A→B) was

higher than in Solution B at each polysaccharide concentration<sup>16</sup>.

### Dynamic Rheology:

**Strain Sweep Study:** The predominance of a solid or liquid characteristic of a viscoelastic material could be quantified through dynamic measurements which are performed within the viscoelastic range<sup>35</sup>. A strain sweep study of CMLBG solutions having different concentrations and solution pH was performed from 0.01 to 100% strain at a constant oscillation frequency of 10 rad/s. Representative plots of strain sweep of 2.5% w/w and 3.5% w/w CMLBG solutions having different pH have been shown in **Fig. 3**.

The maximum strain was found to be 10% beyond which the deformation started, and the elastic modulus ( $G'$ ) deviated from linearity sooner and more rapidly than the viscous modulus ( $G''$ ). Hence, the subsequent frequency sweep study was performed at 2% strain, which was well below the maximum strain to retain the structure without significant perturbation of the system.



**FIG. 3: STRAIN DEPENDENCE OF  $G'$  (ELASTIC MODULUS) AND  $G''$  (VISCIOUS MODULUS) AT 10 rad/s OF 2.5% w/w AND 3.5% w/w CMLBG SOLUTIONS. KEY: (A) SOLUTION A (ACID SOLUTION OF pH 1.2), (B) SOLUTION B (BUFFER SOLUTION OF pH 7.4), (AB) SOLUTION (A→B) (pH 7.4)**

**Frequency Sweep Study:** The dispersion of a polysaccharide can be classified or characterized by the information obtained from dynamic measurements wherein the elastic modulus ( $G'$ ) and viscous modulus ( $G''$ ) is plotted against angular frequency ( $\omega$ ) at a constant amplitude within the linear viscoelastic range<sup>34</sup>. The frequency sweep curves of CMLBG solutions having the lowest (2.5% w/w) and the highest (3.5% w/w) concentrations in different solution pH have been shown in **Fig. 4**. The spectra revealed that both moduli were frequency-dependent and increased with an increase in angular frequency.

Moreover, the viscous modulus ( $G''$ ) was higher than elastic modulus ( $G'$ ) over most of the frequency range studied. It appeared from the results that CMLBG solutions exhibited viscous property at a lower frequency and elastic property at a higher frequency.

Plant polysaccharides generally show such property. For a better interpretation of the effect of CMLBG concentration and solution pH on the viscoelastic characteristics, various parameters obtained from the oscillatory measurements were compared at a specific angular frequency **Table 2**.

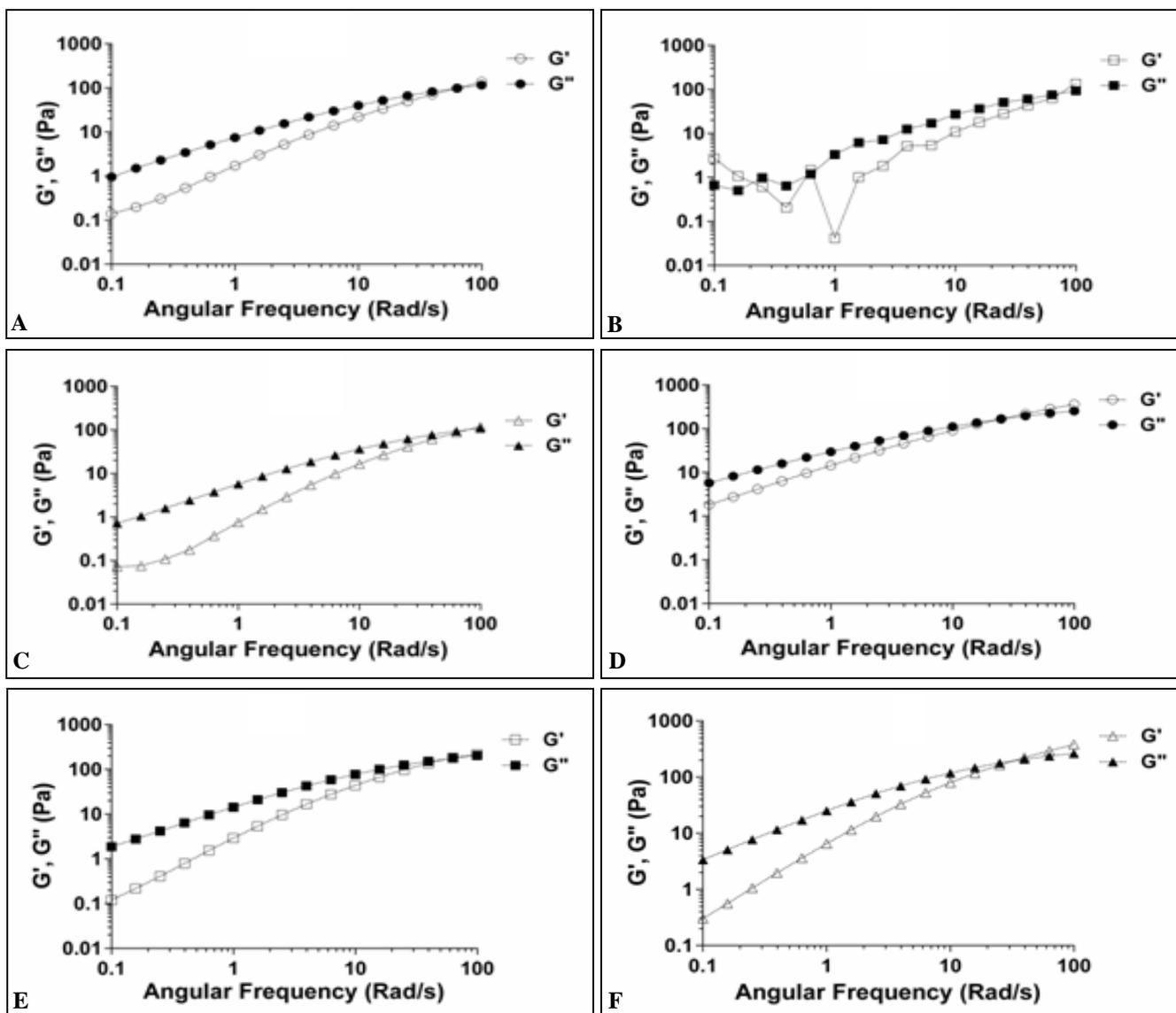


FIG. 4: VARIATION OF G' (ELASTIC MODULUS) AND G'' (VISCOSUS MODULUS) WITH ANGULAR FREQUENCY OF 2.5% w/w CMLBG SOLUTIONS (A – C), 3.5% w/w CMLBG SOLUTIONS (D - F). KEY: (A & D) – SOLUTION A (pH 1.2), (B & E) — SOLUTION B (pH 7.4), (C & F)—SOLUTION (A→B) (pH 7.4)

TABLE 2: EFFECT OF CMLBG CONCENTRATION AND SOLUTION pH ON VARIOUS PARAMETERS OF OSCILLATORY MEASUREMENTS AT 6.31 rad/s

| Concentration of CMLBG Solution (%w/w) | Type of solution | G' G'' | Tan δ | $\omega_c$ | $G_c$ | Relaxation | Time  |
|--|------------------|--------|-------|------------|-------|------------|-------|
| 2.5                                    | Solution A       | 14.10  | 30.00 | 2.12       | 63.74 | 99.37      | 0.016 |
| 3.0                                    | (pH 1.2)         | 34.20  | 56.80 | 1.66       | 41.47 | 138.70     | 0.024 |
| 3.5                                    |                  | 65.50  | 89.20 | 1.36       | 23.97 | 183.30     | 0.042 |
| 2.5                                    | Solution B       | 5.37   | 17.10 | 3.18       | 81.00 | 80.68      | 0.012 |
| 3.0                                    | (pH 7.4)         | 14.30  | 35.10 | 2.46       | 72.82 | 126.30     | 0.014 |
| 3.5                                    |                  | 27.80  | 58.50 | 2.11       | 57.67 | 173.30     | 0.018 |
| 2.5                                    | Solution (A→     | 9.76   | 26.30 | 2.92       | 79.06 | 110.10     | 0.013 |
| 3.0                                    | B) (pH 7.4)      | 28.10  | 57.20 | 2.04       | 43.49 | 146.50     | 0.023 |
| 3.5                                    |                  | 52.50  | 92.30 | 1.76       | 32.24 | 193.50     | 0.031 |

G': Elastic modulus (Pa), G'': Viscous modulus (Pa),  $\omega_c$ : Crossover frequency (rad/s),  $G_c$ : Crossover modulus (Pa), Relaxation time (s/rad).

**Effect of CMLBG Concentration on Viscoelastic Properties:** The results of frequency sweep study of CMLBG having different concentrations

demonstrated that **Fig. 4** the viscous modulus (G'') was higher than the elastic modulus (G'), and a crossover frequency ( $\omega_c$ ) was observed for each of

the CMLBG solutions. This implies that CMLBG solutions having different concentrations behaved like an ordinary polymer solution and not like a gel<sup>17</sup>. The Cox-Merz rule is an empirical relationship in which correspondence is observed between steady shear data and dynamic shear data. This rule states that the steady shear rate viscosity ( $\eta$ ) equals the complex viscosity ( $\eta^*$ ) when the values of shear rate and oscillation frequency are equal<sup>36</sup>. The Cox-Merz rule has been found applicable for many polymer melts and concentrated, and semi dilutes polymer solutions.

However, deviation from this rule has also been reported for high molecular weight polymers, hydrophobically modified polymers, cross-linked or gelling systems, and most particulate dispersions<sup>37</sup> probably due to high-density entanglement or development of structure and intermolecular aggregation. In the present study, when steady shear viscosity ( $\eta$ ) vs. shear rate ( $\dot{\gamma}$ ) and complex viscosity ( $\eta^*$ ) vs. angular viscosity ( $\omega$ ) were plotted on the same logarithmic scales,  $\eta$  were found to be almost superimposed on  $\eta^*$  for all the solutions of CMLBG (figure not shown). This reaffirmed that CMLBG solutions behaved as ordinary polymer solution<sup>17</sup>. The tangent of phase angle ( $\tan \delta$ ) is the ratio of viscous modulus  $G''$  to elastic modulus  $G'$  and can be used to characterize the viscoelastic nature of a material.

As phase angle ranges from  $0^\circ$  (Hookean solid, elastic material) to  $90^\circ$  (Newtonian fluid, viscous material), values of  $\tan \delta < 1$  indicates predominant elastic behavior and  $\tan \delta > 1$  signifies predominantly viscous property<sup>38</sup>. **Table 2** shows that the values of  $\tan \delta$  were  $> 1$  for CMLBG solutions having different concentrations. This confirms that the solutions of CMLBG within the concentration range studied exhibited predominantly viscous character, the contribution of which varied depending on the polymer concentration and solution pH.

It is known that polysaccharides are viscoelastic materials and exhibit solid and liquid characteristics simultaneously<sup>39</sup>. It is, therefore, expected that both the elastic contribution and the viscous contribution may increase or decrease by external factors such as polymer concentration and pH.

An increase in polysaccharide concentration lowered the values of  $\tan \delta$  and thus, tended to decrease the viscous contribution. As a result, the crossover frequency ( $\omega_c$ ), a frequency at which both moduli were same ( $G' = G''$ ), decreased, and the crossover modulus ( $G_c$ ) and the relaxation time, which is the reciprocal of  $\omega_c$ , increased with the concentration of CMLBG. Similar changes in the above rheological parameters with concentration have been reported for amphoteric guar gum derivative due to the formation of dense polymer network structure<sup>40</sup>.

#### **Effect of Solution pH on Viscoelastic Properties:**

The results of the frequency sweep study of CMLBG in different solution pH are also evident in **Fig. 4**, and the various parameters of oscillatory measurements are presented in **Table 2**. An increase in pH of CMLBG solution from pH 1.2 to pH 7.4 produced the phenomena which were opposite to those observed with an increase in the concentration of CMLBG. For each of the concentrations, the magnitudes of both moduli ( $G'$  and  $G''$ ) were less, that of  $\tan \delta$  was high, the crossover frequency ( $\omega_c$ ) increased, and crossover modulus ( $G_c$ ) and relaxation time decreased in a solution of higher pH (Solution B, pH 7.4) than those in a solution of lower pH (Solution A, pH 1.2). The results indicated that the viscous contribution of CMLBG solution increased with increase in solution pH leading to the formation of a more liquid-like system, and the polymer network structure became looser in a solution of higher pH.

These results corroborated well with the findings that the viscosity of CMLBG in Solution B (pH 7.4) was less than that in Solution A (pH 1.2)<sup>16</sup>. It was further observed that the values of  $G'$  and  $G''$  were high,  $\tan \delta$  and crossover frequency ( $\omega_c$ ) were less, and crossover modulus ( $G_c$ ) and relaxation time were more in Solution (A  $\rightarrow$  B) than in Solution B although both solutions exhibited the same pH value (pH 7.4). The results reaffirmed that the denser polymer network structure or the improved topological structure of polysaccharide chains that occurred in acid solution persisted to some extent even when the pH of the acid solution was increased in-situ to pH 7.4.

**Erosion of CMLBG Coat:** The erosion profiles of the placebo tablets coated with 250 mg and 350 mg

of CMLBG in different solution pH have been shown in Fig. 5. While 28.26% and 60.02% erosion were recorded at the end of 6 h from 250 mg CMLBG-coated tablets in Solution A (pH 1.2) and Solution B (pH 7.4), respectively, the erosion of 350 mg CMLBG-coated tablets was 17.52% and 38.57% in Solution A and Solution B, respectively, during the same period. The results indicated that an increase in the amount of CMLBG decreased the erosion of the coated tablets. The erosion of a polymer has been found to vary inversely with molecular weight<sup>41</sup> and viscosity grade<sup>42</sup> of the polymer. The erosion of a polymer also depends on its concentration. An increase in polymer concentration produces a stronger gel layer which

is less susceptible to erosion and vice-versa<sup>43</sup>. It was also noted that erosion of CMLBG in a solution of higher pH (Solution B, pH 7.4) was higher than in a solution of lower pH (Solution A, pH 1.2). When the erosion in two solutions having same pH was compared, the erosion of CMLBG in Solution (A→B), which was prepared by dynamic pH shift condition, was less than that in Solution B, which was a pre-formulated buffer solution of pH 7.4. The erosion of CMLBG from 250 mg and 350 mg coated tablets were 38.54% and 24.11%, respectively, in Solution (A→B) that were considerably less in comparison to the erosion observed in Solution B.

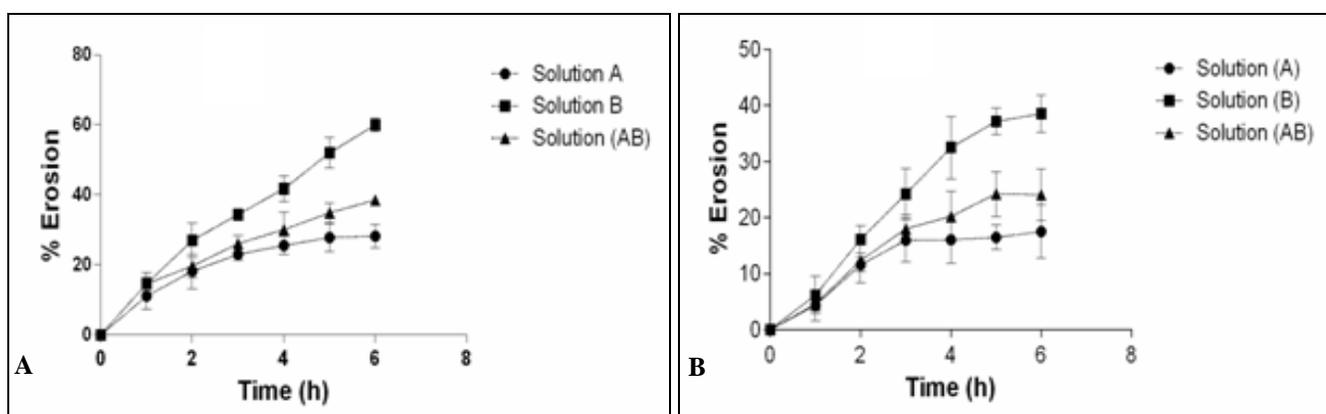


FIG. 5: EROSION PROFILES (MEAN  $\pm$  SD, N = 3) OF TABLETS COMPRESSION COATED WITH (A) 250 mg AND (b) 350 mg OF CMLBG IN DIFFERENT SOLUTIONS. KEY: (●) – SOLUTION A (pH 1.2), (■) – SOLUTION B (pH 7.4), (▲) – SOLUTION (A→B) (pH 7.4)

**Erosion vs. Rheological Parameters:** Increase in CMLBG concentration increased the consistency coefficients and decreased the flow behavior index and viscous contribution because of the formation of a denser or highly aggregated structure. Consequently, the erosion of the matrix decreased with increase in polymer amount. An increase in solution pH made the gel layer less viscous, and the solution appeared to be more liquid-like as evident from the various rheological parameters.

Loose polymer network structure at higher pH produced faster erosion of the matrix. It should, however, be noted that the erosion of the tablets that were studied in a dynamic pH shift condition (in Solution (A→B), pH 7.4) simulating the pH changes in the G.I.T., was less than that observed in Solution B of pH 7.4. Probably, the higher degree of entanglement of the polymer chains which occurred in acid solution persisted to some extent even when the pH was increased *in-situ* to

pH 7.4. This proposition was ascertained by the changes in various rheological parameters.

The results of rheological studies, thus, substantiated our previous observations that CMLBG coated tablets maintained its integrity and minimized the drug release for a period of 6 h during which the tablets might remain in upper G.I.T. following which the coat eroded albeit the susceptibility of erosion and drug release depended on coat weight<sup>16</sup>.

**CONCLUSION:** The results of steady shear and dynamic rheological studies revealed that CMLBG solutions having different concentrations and solution pH exhibited predominant viscous character. However, an increase in polymer concentration tended to decrease the viscous contribution of the hydrated gel layer of CMLBG formed on the surface of the tablet resulting in a decrease in the erosion of the coat. On the other

hand, irrespective of the polymer concentration, the viscous character of CMLBG improved considerably in Solution B of pH 7.4 than that in Solution A (pH 1.2), leading to a higher erosion of CMLBG tablets at higher pH. Interestingly, the viscous contribution of Solution (A→B) of CMLBG was found to be less to some extent than in Solution B although the pH value of both solutions was same. This resulted in a decrease in erosion of the coat in Solution (A→B). It indicates that the erosion of CMLBG coated tablets may be delayed in the *in-vivo* condition where the tablet traverses from an acid solution of gastric fluid to near-neutral solution (pH 7.4) of intestinal fluid. Thus, a detailed investigation of the rheological properties could provide information about the erosion propensity of a polysaccharide coated tablet.

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