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Research Paper

EVALUATION OF GUAR GUM AS SUSPENSION AGENT IN COMPARISON WITH XANTHAN GUM USING METRONIDAZOLE BENZOATE AS MODEL OF DRUG TO ESTIMATE THE EFFECTS OF TEMPERATURES AND STORAGE ON ITS SUSPENSION ABILITY

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Abstract

This study is aimed to evaluate the Guar gum (GG) local and natural compound to be used as an alternative for the formulation of pharmaceutical suspensions, and evaluate its tolerance to time and temperatures. The suspending properties of the Guar gum (GG) was evaluated at different concentrations ranged between 0.1%, 0.3%, 0.5% to 0.7% comparatively with Xanthan gum (XG) at concentrations range from 0.2%, 0.4%, 0.6% to 0.8% in Metronidazole Benzoate (M. B.). Then, both suspensions were putted in different degrees of temperatures; 30°C, 40°C and 50°C. Moreover, the characterization tests were carried out on the formulated suspensions of GG and XG, using sedimentation volume, re-suspendability and viscosity. In the mean time, the values obtained from these parameters were used as basis for comparison of the suspending agents studied. The study revealed that GG is not stable at temperatures above 30°C, the flow behavior of GG showed Newtonian, which was not desirable for suspensions, except the formulated suspension containing 0.7% of GG concentration showed non-Newtonian behavior at temperature of 30°C. On the other hand, the study found that Xanthan gum (XG) was stable at temperatures above 30°C, in that the flow behavior produced was Non-Newtonian. Regarding the sedimentation rate produced by GG in formulated suspensions was higher than that produced by XG. So the formulated suspensions containing GG as suspending agent was less aesthetic appearance than those containing XG. But the formulated suspensions containing GG were dispersed easily with shaking and cake sediment was formed upon storage at temperatures above 30°C. The study concluded that GG had weaker suspending ability relative to XG due to Newtonian behavior, less aesthetic appearance and un-stability at higher temperatures above 30°C.

Key words: Guar gum, Xanthan gum, Metronidazole Benzoate, Sedimentation volume, Re-suspend ability, Viscosity, Newtonian, Non-Newtonian.

INTRODUCTION

Herbal medicine was used around the world in folkloric medicine for prevention and treatment of diseases; recently many medicinal plants were studied and characterized for using in modern medicine. Moreover, Guar gum (GG) was taken as good example for this purpose. Guar gum is a galactomannan, obtained from plant *Cyamopsis tetragonolobus*. Guar gum is obtained by ground endosperm of *Cyamopsis tetragonolobus*. It is native to the Indian subcontinent and used as a green vegetable. Also, GG widely used in food and industrial applications, as natural gum, is an edible thickening agent extracted from the Guar bean, which possess a large endosperm which contains galactomannan gum which forms a gel in water [1]. In the mean time, Guar was used in wide range of industrial applications like food, pharmaceuticals, paint, textiles, paper, constructions, adhesives, coatings, water treatment.

A pharmaceutical suspension, like other disperse systems, is thermodynamically unstable. Therefore, it necessary to include in the dosage form, a stabilizer or suspending agent which reduces the rate of settling and permits easy of redispersion of any settled particulate matter. The main advantage of using GG in suspension it was low cost, easy availability and capacity to form viscous solution and gels at low concentration [2]. While Xanthan gum (XG) is an anionic microbial polysaccharides and it was proved to have good and superior performance in stabilizing suspensions as it form gel like network structure on standing by intermolecular interaction but easily broken and flow when applied shearing [3].

This study is aim to valuate Gar gum stability in suspension in different temperature level and taking Xanthan gum for comparison.

MATERIAL AND METHOD

The materials used in this study include Metronidazole Benzoate (fine powder) donated by WAFRA PHARMA company, polyethylene glycol, propylene glycol, disodium hydrogen orthophosphate, sodium dihydrogen phosphate, methyl and propyl paraben, fine powder xanthan gum (donated by GMC) and fine powder guar gum (donated by Arabic Gum company). The instruments were used include Mixer, pH meter (HANNA instrument), Myr viscometer and Sanyo incubators.

Preparation of Metronidazole Benzoate suspension

Formulated Metronidazole Benzoate suspensions containing different concentration of guar gum as following: 0.1%, 0.3%, 0.5% and 0.7% and for those containing xanthan gum the different concentration range from 0.2%, 0.4%, 0.6% to 0.8%. The remaining excipients included in the formulations consisted of preservatives, wetting agent and co-solvent. Then suspending agents, were kept at constant levels in all formulations in order to study the effects of the suspending agents alone as in table1 and the formulation process was followed the same general method [4].

Table1: the formula of Metronidazole Benzoate suspension [4].

Formula composition	Quantity %	Unit dose formula (per 5 ml)
Metronidazole Benzoate	4.07% w/v	200mg
Methyl Paraben	0.18% w/v	9 mg
Propyl Paraben	0.02% w/v	1 mg
Sucrose	30% v/v	1000.5 mg
Saccharin sodium	0.15% w/v	7.5 mg
Sodium phosphate monobasic	0.86% w/v	43.1 mg
Sodium phosphate dibasic	0.54% w/v	27 mg
PEG 600	15% v/v	0.75 ml
Propylen Glycol	3% v/v	0.15 ml
Suspending agents	Different Concentrations	-
Distilled water	-	Add to 5ml

Determination of the suspensions properties

Sedimentation volume and re-suspendability

The formulated suspensions were placed in the measuring cylinders (100ml), stopper with rubber and foil and were putted on vibration free surface. Then, the sediment volume was measured on the first hour, 2nd hour, one day, two day, 1week, 2 weeks, 4weeks and thereafter monthly for eight months. The re-dispersibility test was done using 100ml by measuring cylinder after the sedimentation test was done. The formulated suspensions were shaken manually by hand at 180° movement.

The cake sediment layer formations were evaluated quantitatively based on the number of shaking required to convert the sediment to uniformly dispersed suspension, more than 10 times the cake or sediment layer formations were consider as (+) (Mahmud et al., 2009) [5].

Viscosity

The different concentrations were put separately into 100 ml beaker appropriate enough to immerse the spindle groove in the fluid. The speed of rotation was varied (200, 100, 60, 50, 30 RPM) to determine its effect on the viscosity values at temperatures of 30°C, 40°C and 50°C in the first month of storage and the last month of storage [6].

RESULTS AND DISCUSSION:

Sedimentation volume results

The results of sedimentation in different temperatures degrees were shown in Figure 1- 6.

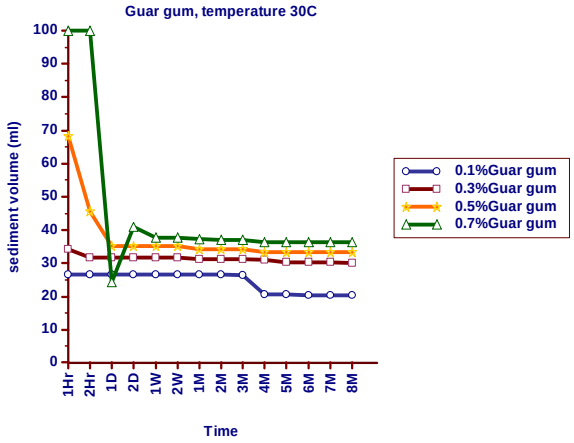

Figure1: the sedimentation volume (ml) of formulated M.B. suspensions containing guar gum at a temperature of 30°C.

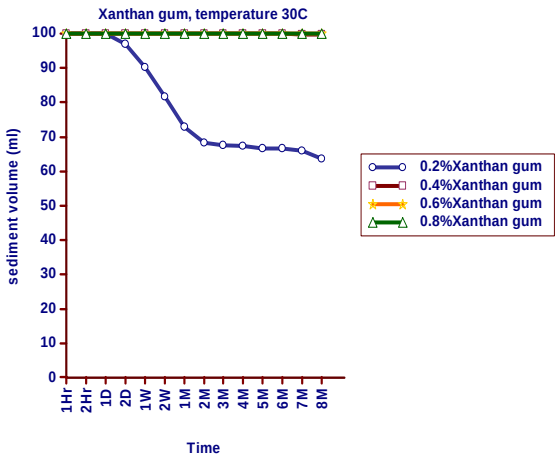

Figure 2: the sedimentation volume (ml) of formulated M.B. suspensions containing Xanthan gum at a temperature of 30°C.

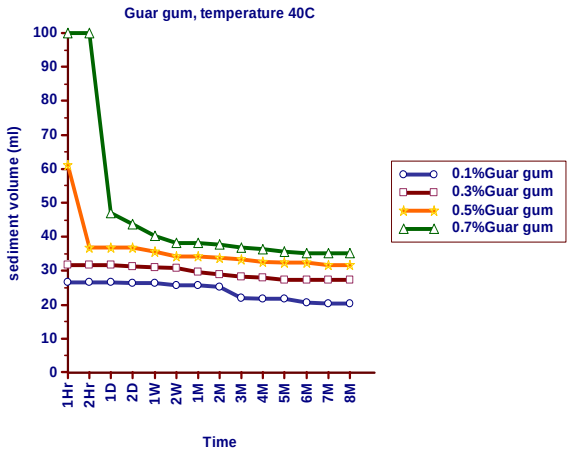

Figure3: the sedimentation volume (ml) of formulated M.B. suspensions containing guar gum at a temperature of 40°C.

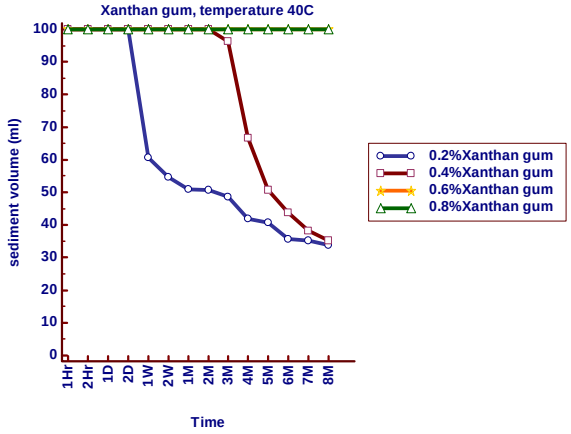

Figure4: sedimentation volume (ml) of formulated M.B. suspensions containing Xanthan gum at a temperature of 40°C.

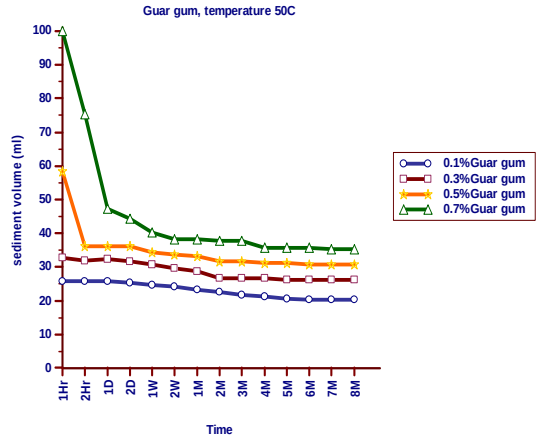

Figure5: the sedimentation volume (ml) of formulated M.B. suspensions containing guar gum at a temperature of 50°C.

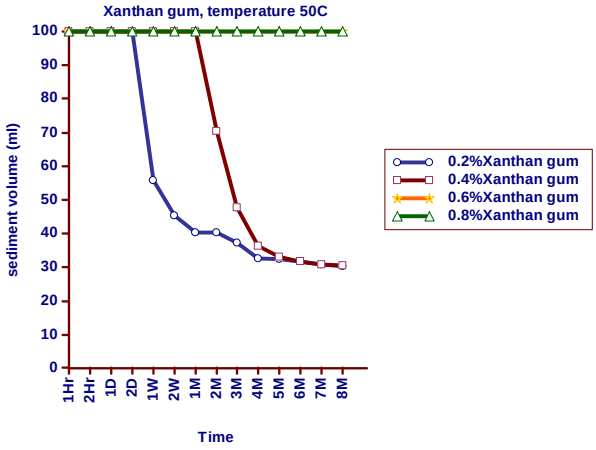

Figure6: the sedimentation volume (ml) of formulated M.B. suspensions containing Xanthan gum at a temperature of 50°C.

Regarding, homogenous behavior the suspensions that containing Xanthan gum (XG) in concentration (0.4%, 0.6% and 0.8%) were found to be homogenous throughout the storage period. Formulated suspension containing 0.2% XG was homogenous for one week. So the formulated suspensions containing XG had larger sedimentation volume compared to those containing guar gum Table 2. Moreover, XG made gel network like structure and highly extended due to repulsion from the charged groups on the side chain in a solution, while guar gum tended to self associate due to absence of the charged group [7].

While sedimentation properties at 40°C and 50°C temperatures of GG were found different GG, that might be due to the effect of temperature on viscosity or shifting pH of the suspensions from neutral point that affecting the compatibility between water and guar molecules and as consequence viscosity decrease [8].

Re-suspend ability results

The results of re-suspend ability were shown in Table 2.

Table 2: Number of shaking to make homogenous suspension at temperature 30°C:

Concentration	Mean SD	Cake sediment formation
0.1%GG	2.3 ± 0.6	-
0.3%GG	2.7 ± 0.6	-
0.5%GG	2.3 ± 0.6	-
0.7%GG	2.7 ± 0.6	-
0.2%XG	3.7 ± 0.6	-
0.4%XG	1.7 ± 0.6	-
0.6%XG	0.7 ± 0.6	Homogenous
0.8%XG	Not shaken	Homogenous

Viscosity results

The results of viscosity ability were shown in Figures (7-12).

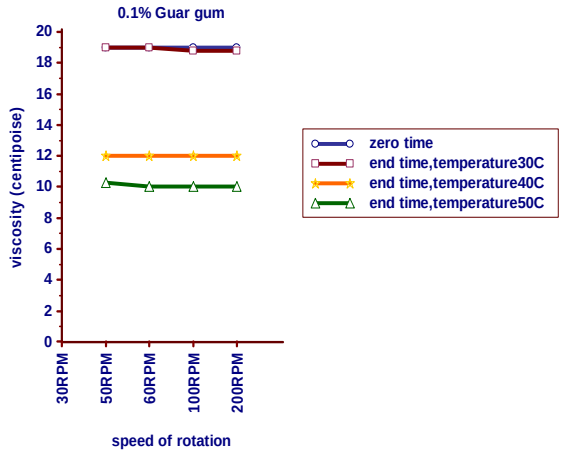

Figure 7: The viscosity in centipoise of formulated M.B. suspension containing 0.1% guar gum against speed of rotation (RPM).

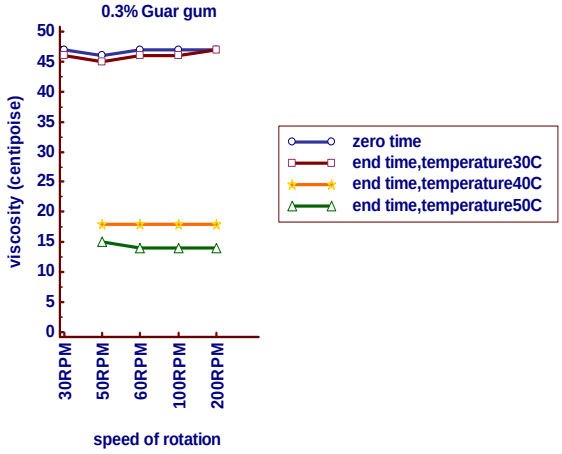

Figure 8: The viscosity in centipoise of formulated M.B. suspension containing 0.3% guar gum against speed of rotation (RPM).

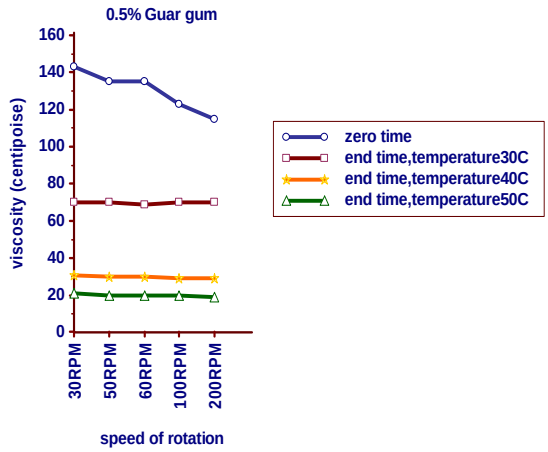

Figure 9: the viscosity (centipoise) of formulated M.B. suspension containing 0.5% guar gum against speed of rotation (RPM) at temperatures of 30°C, 40°C and 50°C.

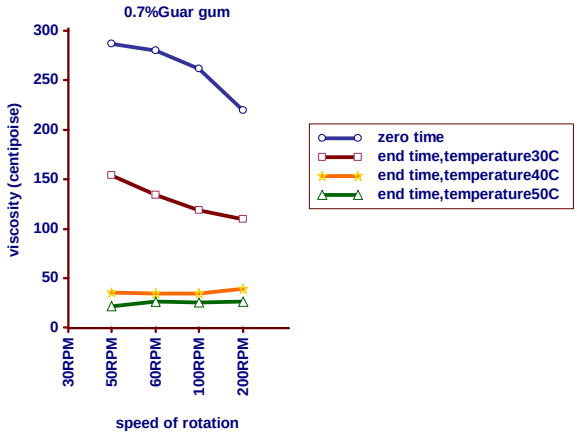

Figure 10: the viscosity (centipoise) of formulated M.B. suspension containing 0.7% guar gum against speed of rotation (RPM) at temperature of 30°C, 40°C and 50°C.

Figure 11: the viscosity (centipoise) of formulated M.B. suspension containing 0.2% Xanthan gum against speed of rotation (RPM) at temperatures of 30°C, 40°C and 50°C.

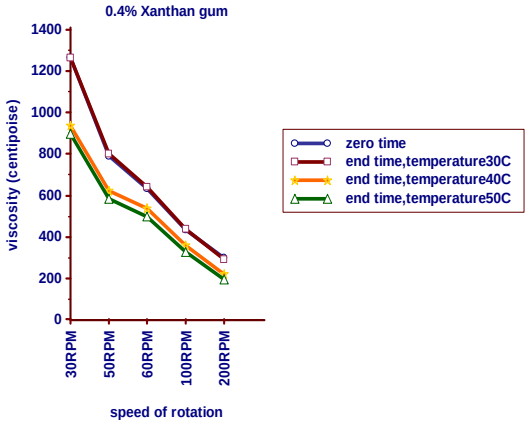

Figure12: the viscosity (centipoise) of formulated M.B. suspension containing 0.4% Xanthan gum against speed of rotation(RPM) at temperatures of 30°C, 40°C and 50°C.

The results revealed that formulated suspension containing 0.8% XG was too viscous and this might be due to high entanglement density and the intermolecular interaction of high concentrated XG [9].

Moreover, the formulated suspensions containing 0.1%, 0.3% Guar gum formed cake sediment at temperature of 40°C, this might be due to reduction in viscosity and less self association between GG molecules in these lower concentrations to retard the sedimentation [10 and 11]. In the mean time, all formulated suspensions containing GG and 0.2% XG formed cake sediment at a temperature 50°C. Also, there were less viscous to resist the sedimentation of the particles due to effect of the temperature on viscosity. Thus, the formulated suspensions containing 0.4%, 0.6% Xanthan gum had high viscosity enough to resist the sedimentation and re-suspended easily at temperature of 40°C and 50°C.

Regarding Newtonian flow the results found that formulated suspensions which containing 0.1% and 0.3% Guar gum showed Newtonian flow properties, while the formulated suspension containing 0.5% GG showed slight Non Newtonian (pseudoplastic flow) at zero time and disappeared or became Newtonian at the end of the storage period and at temperatures

above 30°C; as shown in Figure 9. This might be due to destruction of the network structure of polymer molecules or reduction in the conformation of self- association of the molecules which indicated by thermal induced change in consistency or bacterial induced degradation [11]. On the other hand, the formulated suspensions containing 0.7% GG showed non-Newtonian flow at first and the end time of storage, but at temperatures of 40°C and 50°C the non-Newtonian behavior changed to Newtonian behavior at end time as shown in Figure 10. This might be due to degradation or thermal induced change in self association of GG molecules [12]. While formulated suspensions containing different concentrations of XG concentrations showed non-Newtonian behavior at end time of storage and at temperatures of 40°C and 50°C. The slight reduction in viscosity of the formulated suspensions containing Xanthan gum at temperatures of 40°C and 50°C might be due to effect of thermal motion or changed the conformation of the XG as shown in Figures 9 – 10.

CONCLUSION

In view of these properties, GG might be considered as weak suspending agent when comparing with XG as it showed less aesthetic appearance as it had high sedimentation volume. Also the flow behavior of the GG in solution was Newtonian behavior except for 0.7% GG that showed Non-Newtonian behavior. This flow behavior was not stable at temperatures of 40°C and 50°C, as the Newtonian flow was disappeared. So GG is better to have synergist action with other suspending agents and also GG is might be better to modifying chemically to improve its physical and chemical properties.

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