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The Effect of Electrolyte Concentration and Polymer Content on the Rheological Behavior of Magnesium Hydroxide Suspension

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Authors' contributions

This work was carried out in collaboration between all authors. Author EM designed the study. Author SH wrote the manuscript and analysis the experiment. Author AS statistical analysis. Author MM performed the experiment. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: Magnesium hydroxide (Mg $(OH)_2$) is an alkaline compound that is used as an anti-acid and laxative agent. The objective of the study was to find the effect of electrolyte concentration and polymers on the rheological behavior of Mg $(OH)_2$ suspension.

Place and Duration of Study: Department of Pharmaceutics, Faculty of Pharmacy and Nanotechnology Research Center Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Methodology: To evaluate the effect of structural vehicle, some suspending agents such as carboxymethyl cellulose (CMC), polyvinyl pyrrolidone (PVP), tragacanth and magnesium aluminum silicate (Veegum) alone or in combination were utilized. NaCl (0.01 and 0.05 wt/vol %) was employed as flocculating agents. Physical stability parameters such as sedimentation volume, and the ease of redispersion of the

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suspensions were evaluated. After incorporation of structural vehicles, the rheological properties of formulations were also studied to find out their rheological behavior.

Results: The results showed that the combination of suspending agents had the most physical stability and pseudoplastic behavior with some degree of thixotropy. NaCl as flocculating agent (0.01 wt/vol %) in formulations containing tragacanth and CMC improved the rheological behavior of suspensions and sedimentation volume, while the presence of PVP could not affect these properties.

Conclusion: The results showed that viscosity and thixotropy measurement are a reliable factor to study suspension stability.

Keywords: Suspension; rheology; thixotropy; magnesium hydroxide.

1. INTRODUCTION

A suspension is a dispersed system in which the internal phase consists of solid particles and the external phase is a liquid vehicle. Suspensions are best conventional dosage forms of drugs with slow dissolution rate and show patient compliance [1]. A suspension should be uniform and any sedimentation which occurs during storage should be easily redispersed on agitation. Controlled flocculation and rheologic modification of suspensions are important factors in their preparation [2]. Rheological study of suspensions provides valuable information for efficient utilization, transport and handling of materials in industrial applications [3].

The thixotropy and hysteresis loop are some of the main rheological phenomena. With pseudoplastic systems, the down curve is frequently displaced to the left of the up curve. This phenomenon, known as thixotropy, can be defined as an isothermal and comparatively slow recovery, on standing of a material, which has lost its consistency through shearing [4,5]. The area surrounded between ascending and descending curves that is called hysteresis loop, can give information about the structure breakdown and rebuilding [5,6,7]. Controlled flocculation and rheologic modification are important factors in preparation of suspensions. Flocculated suspensions settle rapidly to form large, loose and easily dispersible sediments [2]. Non-Newtonian polymers are utilized in many industries including food, textile, pharmaceutical and cosmetics. They are employed in suspensions as structural vehicles and exhibit non-Newtonian (plastic or pseudoplastic) flow with some degree of thixotropy. Various types of polymers are used as rheology control agents such as CMC, methylcellulose, NaCMC, PVP, xanthan gum, chitosan [6, 8, 9, 10], poloxamer [11], tragacanth [12] and Veegum [13].

The aim of the study was to investigate the effect of electrolyte concentration and polymers on the rheological behavior of Mg $(OH)_2$ suspension.

2. MATERIALS AND METHODS

Magnesium hydroxide, tragacanth, Veegum, sodium lauryl sulfate (SLS), carboxy methyl cellulose (CMC), polyvinyl pyrrolidone (PVP) and sodium chloride were purchased from Merck, Germany.

2.1 Preparation of Suspensions

Factorial design was used for formulation. SLS (0.1 wt. %) was used as wetting agents. Magnesium hydroxide (170 mesh and 16 wt. %) was used to prepare suspensions using Veegum (1 wt %), CMC (0.5, 0.8 and 1 wt. %), PVP (0.2 and 0.5 wt.%) and tragacanth (0.5 and 1 wt.%) alone and their different combinations as structural vehicles (Table 1).

At the first, polymers were distributed in the water and after completely dispersion, were added to the powder of $Mg(OH)_2$. Sodium chloride (0.01and 0.05 wt. %) was added as flocculating agent. The physical stability and rheological properties of the formulations were then evaluated.

Table 1. Composition of different formulation of magnesium hydroxide (16%) suspensions

Formulation	Tragacanth (wt/vol %)	CMC (wt/vol %)	Veegum (wt/vol %)	PVP (wt/vol %)	NaCl (wt/vol %)
F_1	0.5	0	0	0	0
F_2	1	0	0	0	0
F_3	0	0.5	0	0	0
F_4	0	1	0	0	0
F_5	0	0	1	0	0
F_6	0	0	0	0.5	0
F_7	0.5	0.5	0	0	0
F_8	0	0.8	0	0.2	0
F_9	0	0	0.8	0.2	0
F_{10}	0.5	0.5	0	0	0.01
F_{11}	0.5	0.5	0	0	0.05
F_{12}	0	0.8	0	0.2	0.01
F_{13}	0	0.8	0	0.2	0.05

2.2 Physical Stability

After preparation, sedimentation volume (F) of the suspensions was measured daily and the heights of sediments were recorded when there was no change in 3 consecutive readings. In order to evaluate the ease of redispersion**,** the suspension samples were rotated periodically at 180 degree.The number of revolutions (n) was recorded when the suspension restored to homogeneity [14]. After the volume of sediment was unchanged, the degree of flocculation was calculated as $\beta = F/F_\infty$, where β is the degree of flocculation, and F and F_∞ are sediment volume of flocculated and deflocculated suspensions, respectively. Microscopic image of magnesium hydroxide suspensions that were stored two months at room temperature was examined by optical microscope (Olympus, R4, Japan).

2.3 Rheological Assessment

The rheological behavior of magnesium hydroxide suspensions in different formulations was determined using a Brookfield viscometer (RVDV-I+Digital with No. 2 spindle). The viscosity of samples was determined at 0.5, 1, 2, 2.5, 4, 5, 10, 20, 50 and 100 rpm after 1 min rotation at room temperature. The results were plotted as rheograms and their rheological behaviors were determined by fitting on the corresponding Newtonian equation (Eq. 1).

$$\tau^N = \eta'\delta \quad (1)$$

where τ is shear stress, δ and η' are shear rate and viscosity coefficient, respectively, and N is an indicator for defining the type of flow. Since the viscosity of pseudoplastic substance decreases with increasing rate of shear, apparent viscosity of the formulations at 20 rpm of shear rate was obtained from the slope of the tangent to the curve at that point. The area of the hysteresis loop of the rheograms was calculated from the difference between the areas under the up curve and the down curve by using the trapezoidal rule [5, 6, 7].

3. RESULTS AND DISCUSSION

According to the results shown in Table 2, the suspensions containing individual suspending agents showed low sedimentation volume indicating poor stability. On the other hand, the combination of suspending agents showed higher sedimentation volume and stability.

Table 2. The value of sedimentation volume (F) and ease of redispersion (n) for magnesium hydroxide suspension in different formulations (mean ± SD n=4)

Formulation	F (%)	n	β
F_1	22 ± 1.6	9 ± 1.1	0.33
F_2	28.5 ± 1.3	11 ± .87	0.43
F_3	5.3 ± 0.66	24 ± 1.2	0.08
F_4	74 ± 0.79	27 ± 1.8	1.13
F_5	51 ± 0.66	>50	0.78
F_6	23 ± 1.3	18 ± 1.3	0.35
F_7	86 ± 1.5	6 ±1.1	1.32
F_8	76 ±1.7	20 ± 1.4	1.16
F_9	54 ± 1.8	>50	0.83
F_{10}	96 ± 1.1	7 ± 1.3	1.47
F_{11}	96 ± 1.3	9 ± 1.5	1.47
F_{12}	72 ± 1.3	7 ±1.6	1.10
F_{13}	56 ± 15	8 ± 1.2	0.86

The values of N as an indicator for defining the type of flow for different formulations are presented in Table 3. In Newtonian fluids, shear stress and shear rate are directly proportional (N =1), so the rheogram will be a straight line, while in non-Newtonian fluids (N >1), there is not a direct relationship between them [15]. According to the values of N, all formulations showed pseudoplastic behavior. The important parameter for predicting flow behavior of liquid dispersion is the areas of hysteresis loop, which are shown in Table 3. Evaluation of hysteresis area revealed that all of the formulations except formulations F_3, F_5, F_6 and F_{11} were thixotropic. It is generally accepted that greater the hysteresis area, stronger the thixotropic property and a good suspension should have a relatively high pseudoplastic behavior with some degree of thixotropy [16].

By increasing the concentration of tragacanth from 0.5 to 1%, the sedimentation volume and ease of redispersion values improved significantly (P=.0001 and P=.001, respectively). Also, the value of apparent viscosity and hysteresis loop was increased (P=.001). Increasing the concentration of tragacanth may lead to formation of loose networks that need more time for structural rebuilding.

Table 3. Indicator for defining the type of rheological behavior (*N*), hysteresis loop and pseudoplastic viscosity at 20 rpm (η_{20}) in different formulations

Formulation	**N**	**Hysteresis loop** (dyne.cm/min)	η_{20} **(CP)**
F_1	1.72	198	11.40 ± 0.76
F_2	1.93	261	76.1± 0.9
F_3	1.18	*	19.7± 0.8
F_4	1.56	117	191.8 ± 0.8
F_5	1.37	*	9.56 ± 0.72
F_6	1.69	*	0.38 ± 0.08
F_7	1.63	306	141.4 ±1.8
F_8	1.42	270	94.3 ±0.8
F_9	1.61	49	0.19 ±0.03
F_{10}	2.02	243	77.6 ± 2.2
F_{11}	4.86	*	143 ± 2.6
F_{12}	1.25	234	88 ± 1.4
F_{13}	1.24	117	46.9 ± 0.8

**: No Hysteresis loop*

CMC at concentration of 0.5% did not show thixotropic behavior and the value of apparent viscosity was 19.7 ± 0.8 cP, while increasing the concentration to 1% induced thixotropy and increased the value of apparent viscosity (191.8 ± 0.8 cP) and a recognizable hysteresis loop was observed. It is suggested that as same as tragacanth, increasing the concentration of CMC may cause constitution of large loose networks that while crumbled, need more time for structural rebuilding.

Veegum (1%) had the highest value of n in comparison with the other suspending agents (n>50). It may be due to formation of house of cards structure that could not be easily dispersed. PVP (0.5%) had the lowest apparent viscosity (0.38 ± 0.08 cp) and no hysteresis loop and proper rheological behavior was observed. According to the results, PVP and Veegum (formulation F_5 and F_6) alone could not be employed as suspending agent.Microscopic image of magnesium hydroxide suspensions in a formulation containing Veegum is shown in Fig. 1.

The value of F for tragacanth (0.5 wt/vol %) was 22 ± 1.6%, while in combination with CMC (0.5 wt/vol %), the sedimentation volume increased (86 ± 1.5 %) (*P*=.001). Furthermore, combination of CMC and tragacanth (formulation F_7) improved thixtropy behavior and the value of hysteresis loop (306 dyne.cm/min) and apparent viscosity (141± 1.8 cp) were significantly different from when these polymer were used individually (*P*=.001). It is suggested that attachment of CMC and tragacanth may hinder the formation of bridge between particles and prevent their coagglumeration, so when the structure of suspension destroys, more time is necessary for rebuilding their structure; thus, the hysteresis loop increases.

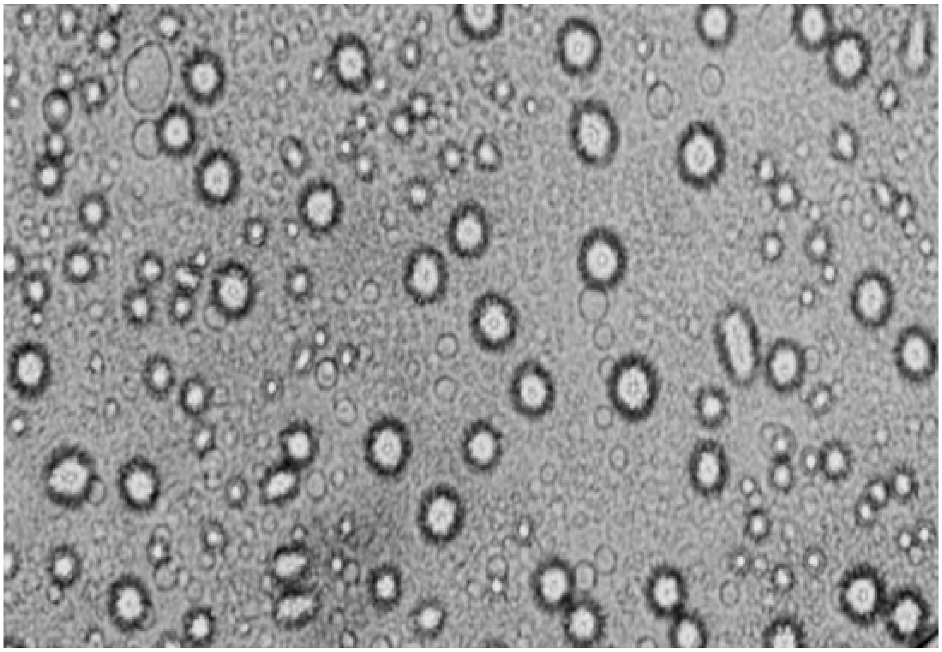

Fig. 1. Microscopic image of magnesium hydroxide suspensions in a formulation containing Veegum (1%) (x 40)

According to the results (Table 2 and 3), in formulation F_8, the value of F, n, apparent viscosity and hysteresis loop showed significant different with formulation F_9 (*P* =.001). Regarding the results, CMC can improve the property of PVP better than Veegun. Although the value of viscosity and hysteresis loop in formulation F_7 and F_8 without NaCl were high; nevertheless, stability flocculation was not observed. Therefore, sodium chloride was added as flocculating agent. Flocculating agents are added to reduce the electrical forces of repulsion between particles and to allow forming the flocks in order to prevent cake formation [8].

Regarding to the results, presence of NaCl (0.01 wt/vol %) in formulation F_{10} decreased the apparent viscosity (77.6±2.2) and hysterias loop (243 dyne.cm/min) in comparison with formulation F_7 (without NaCl) (Figs. 2a and 2b). It is believed that when electrolytes were added to the suspensions as flocculating, by reducing surface charge and zeta potential, they reduce repulsion forces, the phenomenon that causes rapid structural restoration of suspensions after shear. In formulation F_{11} with high concentration of NaCl (0.05 wt/vol %), the apparent viscosity of suspension increased (143±2.6), but there was no thixotropic behavior. According to the results, NaCl at high concentration (0.05 wt/vol %), in formulation containing tragacanth and CMC did not allow the recovery of the rheological properties of the initial suspensions. However, sedimentation volume in formulation F_{10} and F_{11} increased (96 ±1.1% and 96 ± 1.1%, respectively) by adding NaCl (0.01 and 0.05%), in comparison with formulation F_7 (86±1.5%) that was free of NaCl.

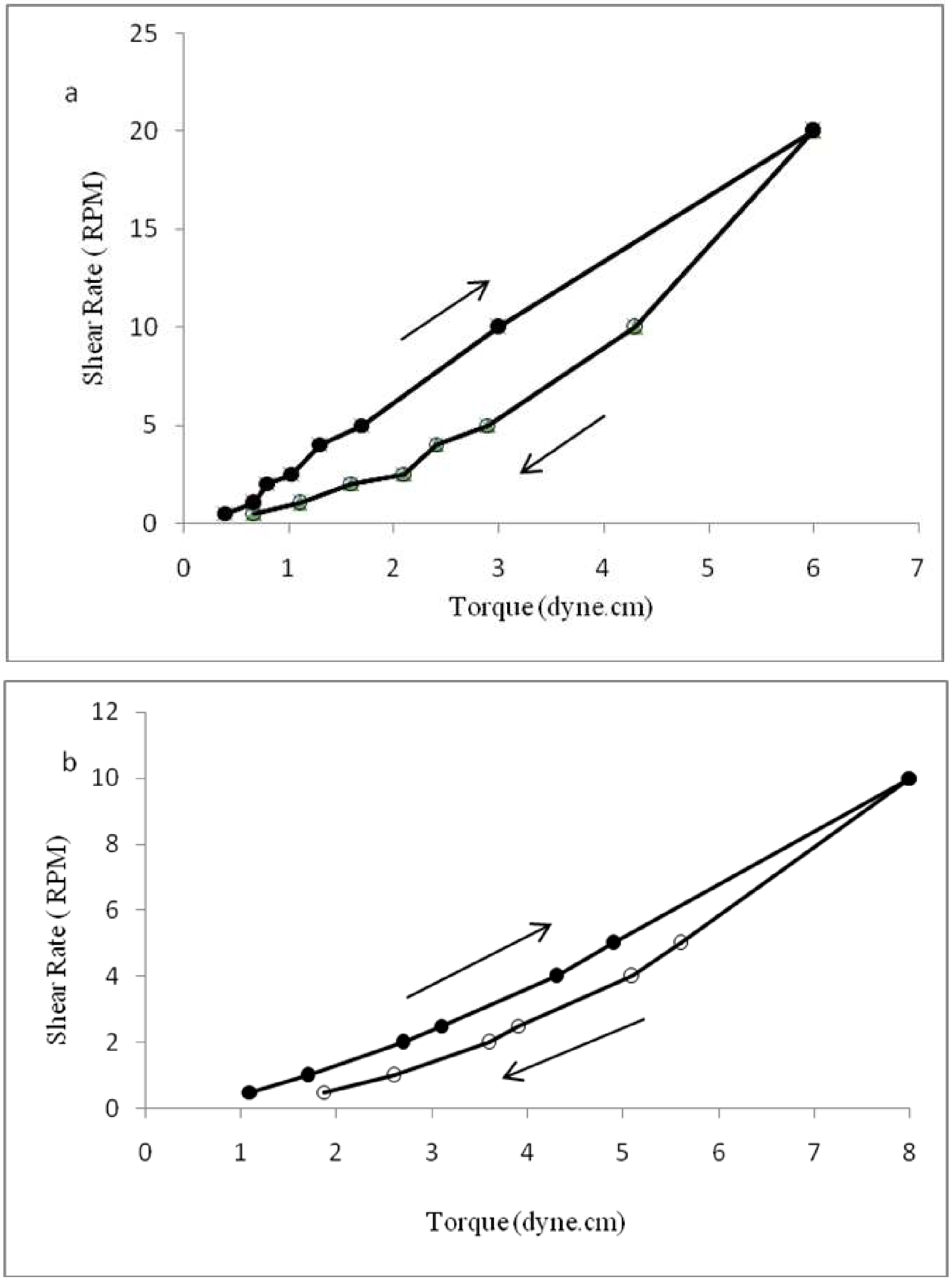

Fig. 2. Rheograms and thixotropy of magnesium hydroxide suspensions in a formulation a) F_7 and b) F_{10}

In formulations F_{12} and F_{13}, in presence of PVP (instead of tragacanth), by adding NaCl (0.01 and 0.05 wt/vol %), the value of apparent viscosity (88±1.4 and 46.9±0.8 cp, respectively) and hysterias loop (234 and 117, respectively) reduced. In addition, NaCl could not considerably affect on the sedimentation volume.

4. CONCLUSION

According to the results, the combination of the suspending agents in comparison their individual application improved suspension characteristics. Rheological studies showed all formulation had pseudoplastic behavior. When NaCl (0.01%) as flocculating agent in formulation containing tragacanth and CMC was added to improve the rheological behavior of suspension and sedimentation volume, but the presence of PVP instead of tragacanth could not improve these properties. In conclusion, tragacanth can be employed as suspending agents when the NaCl is selected as flocculating agents in preparation of suspension.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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