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STABILISED SUSPENDING EFFICIENCY OF LAPONITE XLG AND SODIUM CARBOXYMETHYLCELLULOSE BLEND IN THE FORMULATION OF SULPHAMERAZINE SUSPENSION

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Abstract
Charged drugs like Sulphamerazine may make pseudoplastic/plastic materials become Newtonian and loose their suspending power. In this study, laponite XLG (laponite), a synthetic hectorite was employed as a protective colloid and viscosity stabilizer in a blend with sodium carboxymethylcellulose (SCMC), which exhibits high viscosity at low rates of shear and shear thinning characteristics. The viscosities and yield values of suitable concentrations (2%w/w SCMC, 4%w/w laponite, and a 1:1 ratio of 2%w/w laponite – SCMC blend) that yielded pseudoplastic/plastic properties were studied in the absence and presence of 1 - 4%w/w sulphamerazine. For this purpose, the rheograms of the systems were obtained by the use of a Haake rotoviscometer RV 12 utilizing a cup and rotor sensor system MV 1. In the absence of sulpamerazine, the blend had higher viscosity and yield value than either material alone, which were resistant to change in the presence of sulphamerazine. The blend was consequently very efficient in suspending sulphamerazine powder with no separation. Laponite changed from a pseudoplastic to a Newtonian fluid in the presence of sulphamerazine, but gave a flocculated suspension with a clear supernatant and a large sedimentation volume that was readily redispersed. SCMC on the other hand, allowed the sedimentation of sulphamerazine with low sedimentation volume and misty supernatant. The sediment was also difficult to redisperse, suggesting a deflocculated system. Laponite – SCMC blend could be a very useful and efficient suspending agent in the liquid formulation of difficult insoluble drugs, including magnesium trisilicate whose many marketed forms often show separation.

Keywords: *Laponite XLG,sodium; Carboxymethylcellulose and their blend; Suspending efficienc; Sulphamerazine suspension.*

INTRODUCTION

It is well known that systems of high viscosity may be obtained from most cellulose thickeners, but the yield values may be low due to the low interparticulate bonding (Newmann and Sansom, 1970). These authors similarly reported that systems of low viscosity and high yield value are readily formed from certain materials such as the swelling clays. As suggested by Mervine and Chase (1952), the ideal suspending agent should have a high viscosity at negligible shear, i.e. during shelf storage, and it should have a low viscosity at high shearing rates, i.e., it should be free-flowing during agitation, pouring and spreading. Pseudoplastic materials show these qualities (Martin et al, 1969; Rawlins, 1980). The static yield value

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is the minimum force necessary to initiate flow, and this together with the viscosity which controls sedimentation, can be obtained from the rheograms of the systems i.e. the plots of shear rate against shear stress.

Laponite XLG (laponite) acts as a thixotropic agent, protective colloid and viscosity stabilizer, while sodium carboxymethylcellulose (SCMC) can be used to increase the apparent viscosity of the system. By choosing the optimum ratio of the two, the overall level of thickeners may be reduced (Carless and Nixon, 1970). Laporte industries reported that a combination of laponite and SCMC is better than either material alone in paste production. They found that laponite-SCMC blends were twice as efficient as veegum-SCMC blends. Laponite is a synthetic swelling clay of the hectorite group and is similar to bentonite (Martindale extra Pharmacopoeia, 1982), however its synthesis is usually controlled and the product is free from the usual impurities normally present in any natural mineral (Newmann and Sansom, 1970). Laponite would therefore be suitable for formulating oral pharmaceuticals, but its use in such products has not been investigated before now.

MATERIALS AND METHODS

Materials: Sodium Carboxymethylcellulose 7MF (Hercules Ltd., London England), Laponite XLG food grade (Laporte Industries Limited, Cheshire England), Sulphamerazine powder B.P. (May & Baker Limited, Dagenham England).

Methods:

(a) Suspensions prepared: A series of 1 - 4%w/w sulpamerazine suspensions were prepared containing 2% SCMC, 4% laponite and 1:1 ratio of 2% SCMC – laponite blend. The sedimentation heights were represented as a percentage of the total suspension heights to give the sedimentation volumes.

(b) Measurement of rheological properties: Rheograms were obtained at 20^{o} C by the use of a Haake rotoviscometer RV 12 (Haake Mess-Technik GmbH u.Co., Kalsruhe Germany), using a cup and rotor sensor system MV 1. The test sample was placed into the annular space between the two concentric cylinders. The inner cylinder was made to rotate for 1 minute to a maximum shearing rate of 100rpm, and the torque was measured on an x – y – t recorder.

The viscosity was calculated according to the following equation:

$$\text{Viscosity} = \frac{S \times A}{n \times M}$$

Where S is the scale reading on the torque recording unit connected to the viscometer

n = the speed of rotation

A and M are calculation factors for MV 1 given in the Haake instrument manual as follows:

A (Pa/scale grad.) = 3.22

M (min/s) = 2.34

(c) The static yield value was determined as the point of intersection on the X-axis of the extrapolated ascending portion of the rheogram.

RESULTS

(i) In the absence of sulphamerazine, the viscosity and static yield value of SCMC - Laponite blend was seen to be higher than those of either material alone (Figure 1).

(ii) The blends also appear to be resistant to changes in the parameters measured in the presence of increasing concentrations of sulphamerazine (Figure 2).

(iii) The blend was very effective in preventing sedimentation, while SCMC and laponite allowed sedimentation which was more pronounced with SCMC (Figure 3).

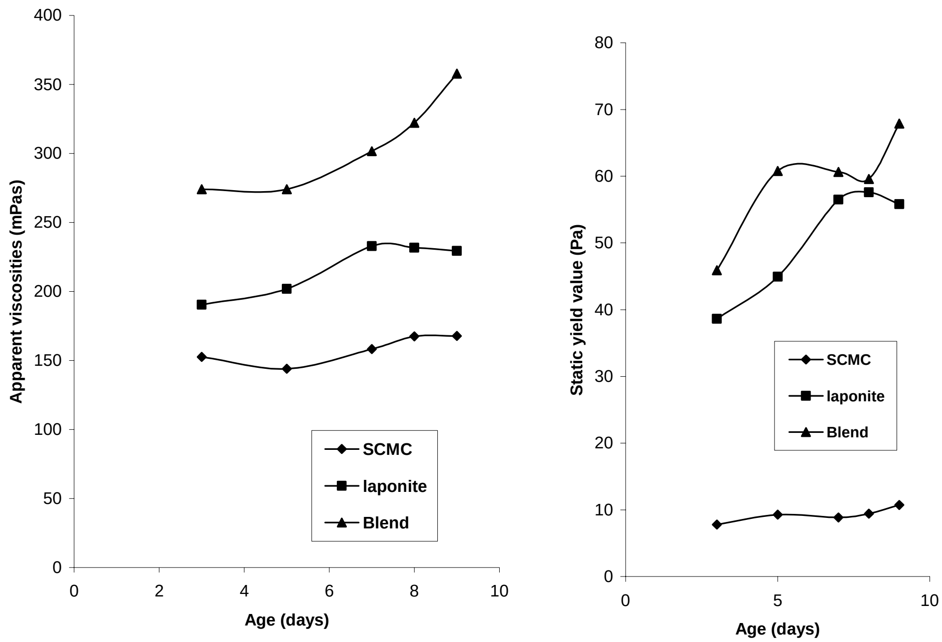

Figure 1: Effect of age on the apparent viscosities and static yield values of 2%w/w SCMC, 4%w/w Laponite, and their 1:1 (2%w/w) blend sheared for 1 min. at 20oC to a max. of 100rpm.

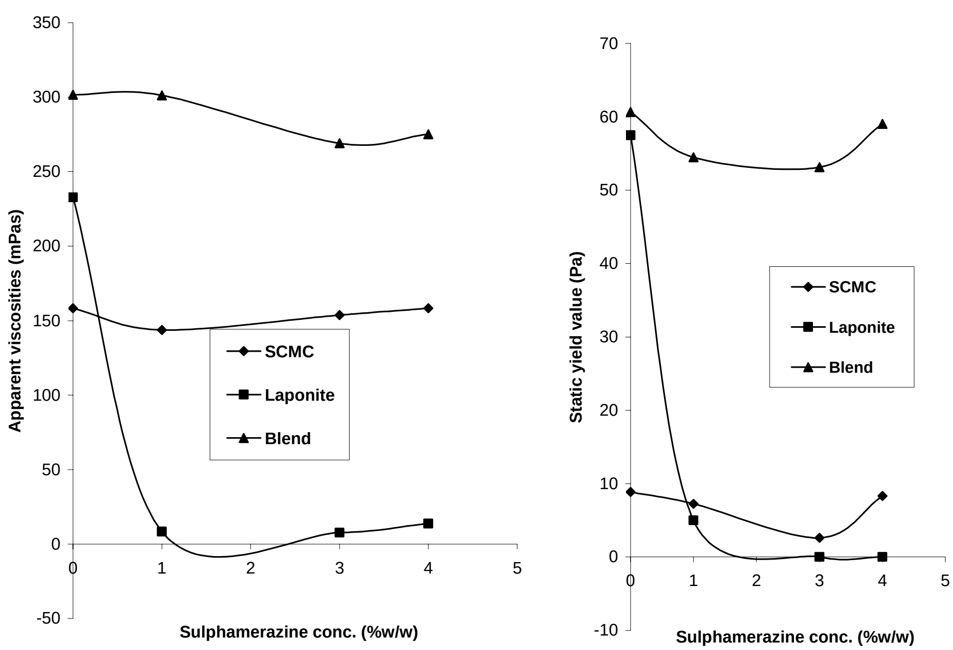

Figure 2: Effect of sulphamerazine concentration on apparent viscosities and static yield values of 7 day old 2%w/w SCMC, 4%w/w Laponite and their 1:1 (2%w/w) blend sheared for 1 min. at 20oC to a max. of 100rpm.

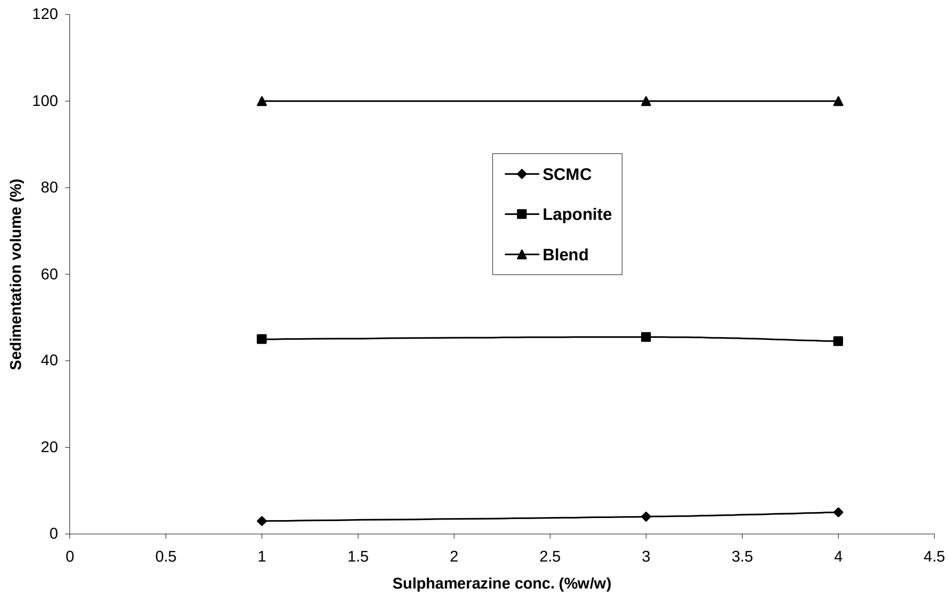

Figure 3: Sedimentation volumes after 7 days of different concentrations of sulphamerazine suspensions containing 2%w/w SCMC, 4% laponite and their 1:1 (2%w/w) blend.

DISCUSSION

The high viscosity of pseudoplastics at low rates of shear enables them to stabilize insoluble particles against rapid sedimentation, and their low viscosity at high shear (i.e shear thinning) enables easy pouring from the bottle. Sulphamerazine is a very poorly water soluble drug 1 in 6250 at 20^{o} C (Martindale extra Pharmacopoeia, 1982). It is also a crystalline powder which is charged due to the presence of benzene rings and electrophilic groups (Korolkovas, 1970). Sulphamerazine could therefore behave like a peptizing electrolyte and make pseudoplastic and plastic materials become Newtonian (Rawlins, 1980). All these would be expected to make the uniform dispersion of sulphamerazine difficult, and its choice in this study would demonstrate the suspending efficiency of SCMC, laponite and their blends.

(a) The rheology of the colloids in the absence of sulphamerazine

The slight increases in apparent viscosity and static yield value with age (Figure 1) are in agreement with the findings of Carless and Nixon (1970), who suggested that this may be due to slow swelling of individual particles allowing further particle to particle contact. Combining SCMC and laponite showed potentiation of rheological properties, resulting in the 2%w/w of the blend having higher viscosity and yield value than either 2%w/w SCMC or 4%w/w laponite. This would confer greater suspending power on the blend, and greater force would be needed to initiate flow.

(b) The rheology and sedimentation profiles of sulphamerazine suspensions formulated with the colloids

Figure 2, shows the effects of sulphamerazine on the rheology of the thickeners. The rheological properties of the blend were less affected than those of 2%w/w SCMC which in turn were less affected than those of 4%w/w laponite. The laponite was drastically affected and became Newtonian in the presence of sulphamerazine. However, the sulphamerazine suspensions containing laponite had high sedimentation heights, with clear supernatants, which were easily redispersed, suggesting flocculation. This could mean that the addition of negatively charged sulphamerazine to the inherently negatively charged laponite, would increase the charge density of laponite resulting in greater repulsion, consequently the system becomes more dispersed and viscosity drops. At the same time, the exchangeable cations of laponite (Newman and Sansom, 1970), are being transferred to the sulphamerazine. That way, the sulphamerazine gets more neutral and so is able to flocculate. For the SCMC-containing suspensions, the sedimentation height was low, the supernatant was misty and the sediment difficult to redisperse. This would indicate that the particles settled singly in a deflocculated state. Figure 2, shows that SCMC has a very low static yield value both in the presence and absence of sulphamerazine, thus would pour out easily and would also not prevent sedimentation.

The blend was thus much more resistant to the effects of sulphamerazine, and maintained its high viscosity and yield value (Figure 2). Thus sedimentation would be prevented much more efficiently by the blend than by SCMC or laponite alone at comparable concentration levels as seen in Figure 3. This is in agreement with the reports that laponite acts as a protective colloid and viscosity stabilizer, while cellulose ethers increase the apparent viscosity of a blend (Laporte laboratories handbook).

The laponite-SCMC blend would therefore be a very useful suspending agent in the liquid formulation of difficult insoluble drugs, including the practically insoluble magnesium trisilicate (Martindale extra Pharmacopoeia, 1982) whose many marketed forms often show separation.

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