EVALUATION OF THE SUSPENDING PROPERTIES OF A NEW PLANT GUM IN SULPHAMETOXAZOLE FORMULATIONS

John Oluwasogo AYORINDE* & Michael Ayodele ODENIYI
Department of Pharmaceutics and Industrial Pharmacy, University of Ibadan,
Ibadan, Nigeria
E-mail: *shogo205@yahoo.com

Abstract - Suspension dosage forms require the use of suspending agents in order to deliver a uniform dose of the active ingredient. The purpose of this study is to investigate the properties of a new plant gum as a cheap and effective natural polymer in the formulation of pharmaceutical suspensions. The gum obtained from the incised trunk of Cedrela odorata (family Meliaceae) was compared with hydroxypropylmethylcellulose and gelatin in Sulphamethoxazole suspension formulations at concentrations of 1.0 – 4.0% w/w. Assessment parameters were sedimentation volume, flow rate, viscosity and the effect of temperature on these parameters. The suspending characteristics of Cedrela gum compared well with that of hydroxypropylmethylcellulose in term of sedimentation volume, flow rate and viscosity and the natural gum could be used as a substitute in pharmaceutical suspensions.

Keywords: Cedrela gum, Rheological properties, Suspending agent

I. INTRODUCTION

Suspension dosage form is a preferred and widely accepted dosage forms for insoluble or poorly soluble drugs for various therapeutic applications [1]. The suspension dosage form has long been used for insoluble and poorly soluble drugs for making oral, topical and parenteral products. The suspension formulation is still very relevant in view of the fact that many of the recently discovered active pharmaceutical ingredients are quite hydrophobic with limited solubility.

One of the methods of enhancing the stability of suspensions is by increasing the viscosity of the dispersion medium [2]. This is achieved by the inclusion of suspending agents such as natural gums. Most suspending agents act as a suspending agent and also impart viscosity to the solution. Suspending agents form a film around particle and decrease interparticle attraction. A good suspension should have well developed thixotropy; at rest the solution is sufficiently viscous to prevent sedimentation and thus aggregation or caking of the particles and when agitated, the viscosity is reduced and provide good flow characteristic from the mouth of bottle.

The aim of the present work is to determine the rheological and stability properties of sulphamethoxazole suspension using Cedrela gum as a suspending agent. Cedrela gum is obtained from the incised trunk of Cedrela odorata (Meliaceae), a tree widely cultivated in the tropics. Sulphamethoxazole was chosen for this investigation because it is representative of practically insoluble drugs which would require a suspending agent in order to ensure uniform dosage when prepared as a liquid dosage form [6].

II. MATERIALS

The materials used were: Sulphamethoxazole (Qingdao Fraken International Trading Co., Ltd., Qingdao, China), Gelatin BP (Hopkins and Williams, Chadwell Health, Essex, UK), Hydroxypropylmethyl cellulose (Methocel K15M (Colorcon, England)), Cedrela gum powder. All other materials were of analytical grade.
III. METHODS

1. Gum extraction

Cedrella gum was obtained from the tree of *Cedrela odorata* and authenticated in Botany Department of University of Ibadan. It was purified using established methods [7]. The gum was hydrated in 0.5: 95.5 (v/v) CHCl₃/water mixture for 5 days with intermittent stirring; extraneous materials were removed by straining through a muslin cloth. The gum was precipitated from solution using absolute ethanol. The precipitated gum was filtered, washed with diethyl ether, and then dried in hot air oven at 40 °C for 18 h. The gum was pulverized using a laboratory blender and the size fraction < 170 µm was used.

2. Preparation of sulphamethoxazole suspension

Quantity (2g) of sulphamethoxazole was triturated in a mortar with 0.5g of Cedrela gum. Small portion of distilled water was added to the powder mix with constant stirring until a smooth paste was formed. The suspension was transferred to a 100ml glass measuring cylinder and the volume made up to 50ml with water, thus forming sulphamethoxazole suspension containing 1% Cedrela gum as suspending agent. The procedure was repeated using 2, 3 and 4%w/v of Cedrela gum. Similar sulphamethoxazole suspension formulations containing HPMC and Gelatin as suspending agents were prepared.

3. Suspension characteristics

Each suspension was stored at room temperature; observations were made for 7 days to determine the sedimentation volume, flow rate and viscosity.

Sedimentation volume (F)

The suspension sedimentation volume was determined using the following equation:

\[
F = \frac{V_u}{V_0} \times 100\%
\]

Where \(V_u\) is the ultimate volume and \(V_0\) is the initial volume of the suspension.

Flow rate (F)

The time taken for 10ml sample of suspension to flow through a 10ml pipette was determined and the flow rate calculated using the following equation:

\[
F = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (sec)}}
\]

Viscosity (η)

The viscosity of suspension samples was determined using the Brookfield Model – DV-11 + Pro viscometer (spindle 02), at 100 revolutions per minute. All determinations were carried out in at least triplicates and results obtained were expressed as the mean values.

Statistical analysis

Data were analyzed using t-test and ANOVA.

IV. RESULTS AND DISCUSSION

Sedimentation volume

The sedimentation volume increased with number of days of storage for both HPMC and gelatin with greater increase in gelatin (p<0.05), while for cedrela gum, the sedimentation volume was constant up to the fourth day of storage before a slight increase was observed on the 7th day (Table 1). This shows that cedrela gum possesses the ability to keep the gum suspended for a period of time longer than both HPMC and gelatin. Sedimentation volume was found to increase with concentration of suspending agent: this was true for between 1 and 3% cedrela gum after which a decreased volume was obtained. This suggests that cedrela gum has an optimum concentration of use as a suspending agent.

Table I: Values of flow rate (minutes) of suspension with different types and concentration of suspending agents (n=3)

<table>
<thead>
<tr>
<th>Suspending agent</th>
<th>Concentration (%w/v)</th>
<th>DAY 1</th>
<th>DAY 3</th>
<th>DAY 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin</td>
<td>1</td>
<td>6.715±0.064</td>
<td>6.500±0.003</td>
<td>6.460±0.028</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7.525±0.360</td>
<td>7.180±0.014</td>
<td>6.865±0.091</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>7.440±0.296</td>
<td>8.380±0.112</td>
<td>7.855±0.063</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>9.440±0.551</td>
<td>9.830±0.084</td>
<td>8.560±0.127</td>
</tr>
<tr>
<td>HPMC</td>
<td>1</td>
<td>7.015±0.035</td>
<td>6.930±0.028</td>
<td>6.930±0.042</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8.885±0.001</td>
<td>9.890±0.134</td>
<td>9.130±0.014</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>13.650±0.000</td>
<td>14.370±0.692</td>
<td>12.560±0.113</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>31.760±0.651</td>
<td>39.270±0.367</td>
<td>14.930±0.268</td>
</tr>
<tr>
<td>Gum</td>
<td>1</td>
<td>7.955±0.191</td>
<td>7.750±0.021</td>
<td>7.420±0.000</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8.530±0.212</td>
<td>8.945±0.502</td>
<td>8.780±0.028</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>11.200±0.098</td>
<td>11.480±0.410</td>
<td>10.865±0.049</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>15.450±0.417</td>
<td>13.715±0.346</td>
<td>14.280±0.042</td>
</tr>
</tbody>
</table>

Flow rate

Flow rate generally decreased with increasing days of storage and concentration of suspending agent. At 3%
concentration, the ranking was HPMC > Cedrela > gelatin (Fig 1.). There was significant difference in flow rate between gelatin and both HPMC and Cedrela gum whose flow rate was found to compare well. This suggests that the flow rate of cedrela gum is as pseudoplastic as that of HPMC and this is an indication of good re-dispersibility [8].

Figure 1: Representative plots of the effect of suspending agent (3%w/v) and time on the flow rate of Sulphamethoxazole suspensions

VISCOSITY

Viscosity of suspension decreased on storage and increased with concentration of suspendant. Suspension containing cedrela gum was found to be most viscous; the ranking was Cedrela gum > HPMC > gelatin. There was no significant difference in the viscosity of formulations containing HPMC and cedrela gum but significant difference exists for formulations containing gelatin. The viscosity of formulations containing cedrela gum also decreased significantly as the speed of shearing was increased from 50 to 100rpm. An ideal suspension should have a high viscosity at negligible shear (at shelf storage) and low viscosity at high shearing rate in order aid free flowing during agitation to facilitate easy pouring [9].

The results of flow rate and viscosity show the thixotropic (viscous) nature of cedrela gum while standing and pseudoplastic (fluid enough to flow) nature when disturbed.

Further, the effect of the temperature was investigated on the viscosity of the suspension formulations. For all concentration of suspending agent, viscosity decreases significantly as temperature was increased from 30° to 60° (Figure 2). This is attributable to the solubility of the drug increasing with temperature [10].

Figure 2: Representative plots of the effect of temperature on the viscosity of suspensions containing 3%w/v polymer

Temperature may affect the viscosity of a suspension by also modifying interfacial properties and thus inducing or reducing flocculation which increases viscosity. Temperature can also affect the viscosity of a system by increasing the Brownian movement. Also, temperature causes volume expansion in both the dispersion medium and the solid. However, liquid medium expands more than the solid and this leads to a decrease in volume fraction value and a decrease in viscosity [11].

V. CONCLUSION

A suspension of constant sedimentation volume was produced with Cedrela gum at concentration of 1-3% and the suspendability of the gum compared favourably with that of HPMC. Furthermore, a suspension of ideal characteristics of high viscosity at negligible shear (at storage) and low viscosity upon agitation was obtained with Cedrela gum and HPMC as suspending agents. This shows that cheap, locally sourced Cedrela gum could be substituted for synthetic and more expensive HPMC in the formulation of pharmaceutical suspensions.
REFERENCES


