STABILIZATION OF ANTACID FORMULATION WITHOUT SORBITOL.

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ABSTRACT

The aim of present study was to develop Stabilized Antacid formulation without using sorbitol base. Sedimentation, Redispersibility and caking were the major problem in the stabilization of the antacid formulation. It was very challenging to achieve Antacid formulation without using sorbitol. This challenge achieved by taking nine different (F1-F9) trails batches using Sodium alginate and Xanthan Gum (G). Formulation (F9) obtained from the above trial batches were selected on the basis of three months accelerated stability data.

Keywords: - Redispersibility, Sedimentation, Sodium alginate, Xanthan Gum.

1.1 INTRODUCTION

A Pharmaceutical suspension is a coarse dispersion in which internal phase is dispersed uniformly throughout the external phase. The internal phase consisting of insoluble solid particles having a specific range of size which is maintained uniformly throughout the suspending vehicle with aid of single or combination of suspending agent. The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non oral use. [1]

The suspension dosage form has long been used for poorly soluble active ingredients for various therapeutic indications. Development of stable suspensions over the shelf life of the drug product continues to be a challenge on many fronts.

A good understanding of the fundamentals of disperse systems is essential in the development of a suitable pharmaceutical suspension. The development of a suspension dosage form follows a very complicated path. The particle size distribution in the finished drug product dosage form is a critical parameter that significantly impacts the bioavailability and pharmacokinetics of the product. [2]

Sedimentation and suspension flows involve the mechanics, flow and transport properties of mixtures of fluids and solids, droplets or bubbles. Fundamental aspects of sedimentation and suspension flows include properties of suspensions and emulsions (rheology, particle size and shape, particle-particle interaction, surface characteristics, yield stress, concentration, viscosity),
individual particles (orientation and surfactants). [3]

Antacid are basic substances that neutralize gastric acid and raise pH of gastric contents. Antacid do not decrease acid production rather agents that raise the antral pH to > 4 evok reflex gastrin release, more acid is secreted specially in patients with hyperacidity and duodenal ulcer “acid rebound” occurs and gastric motility is increased. The potency of antacid is generally expressed in terms of its acid neutralizing capacity. The antacids most widely used are Sodium bicarbonate, Sodium hydroxide, Magnesium hydroxide.

Combinations of Mg2+ (rapidly reacting) and Al3+ (slowly reacting) hydroxides provide a relatively balanced and sustained neutralizing capacity and are preferred by most experts. Magaldrate is a hydroxymagnesium aluminate complex that is converted rapidly in gastric acid to Mg (OH) 2 and Al (OH) 3, which are absorbed poorly and thus provide a sustained antacid effect. Although fixed combinations of magnesium and aluminum theoretically counteract the adverse effects of each other on the bowel (Al3+ delays gastric emptying and may cause constipation, while Mg2+ exerts the opposite effects), such balance is not always achieved in practice.

Simethicone, a surfactant that may decrease foaming and hence esophageal reflux, is included in many antacid preparations. However, other fixed combinations that are marketed for “acid indigestion”, particularly those with aspirin, are potentially unsafe in patients predisposed to gastroduodenal ulcers and should not be used. [5]

2. MATERIAL AND METHODS

Aluminium hydroxide gel, Magnesium hydroxide, Dimethicone (Simethicone 100%) was obtained from Drugs & chemicals Pvt. Ltd. And Suneka Industries as a gift sample. Xanthan Gum (Germany) and Sodium Alginate were purchased from S.D. Fine chemicals limited, Mumbai. All the chemicals used were of analytical grades.

2.1. FORMULATION OF ORAL ANTACID SUSPENSION

A series of formulation were prepared as given in table 1 with various concentration of suspending agents and were evaluated for sedimentation volume and Redispersibility. Nine trails Were taken namely as F1 to F9 with different ratios of Xanthan Gum (Germany) and Sodium alginate. Trail with antibacterial effect of two different preservatives were also taken with Sodium methyl paraben and Sodium propyl paraben in F3 and F8 formulation and methyl paraben and propyl paraben in F1 to F2 and F8 formulation in which sodium saccharin was replaced by aspartame to improve the taste and stability.

Table 1: - Formula for Oral Antacid suspension.
## 2.2 PROCEDURE

Step no1: - Aluminium hydroxide was passed from the Mesh Size #40 and soaked into purified water for one hour.  
Step no 2: - Magnesium hydroxide was passed from the Mesh Size #40 and soaked into purified water for one hour.  
Step no 3: - Soak Xanthan gum (Germany) into hot purified water with continuous stirring until get smooth.  
Step no 4: - Soak Sodium alginate into hot purified water with continuous stirring until get smooth.
Step no 5: - Add Polysorbate 80 into hot purified water (30-35 degree), disperse aerosol into it and Simethicone separately one by one with continuous stirring.
Step no 6: - Add step no 5 into step no 3 with continuous stirring.
Step no 9: - Take small amount of water and dissolve Sodium methyl paraben, sodium propyl paraben and sodium saccharin one by one with constant stirring to get a clear solution in F3 to F9 formulation and in F8 formulation aspartame was dissolved in hot purified water maintain temperature at 70 degree and add into process with continuous stirring.
Step no 10: - Take small amount of hot water maintain temperature at 70-80 degree and dissolve methyl paraben, propyl paraben and sodium saccharin one by one with constant stirring to get a clear solution in F1 to F2 formulation.
Step no 11: - Add Step No 9/10 into step no 3 with continuous stirring.
Step no 7: - Add Half quantity of step no 4 into step no 1 and step no 2 with continuous stirring.
Step no 8: - Add step no 1 into step no 2 with continuous stirring.
Step no 12: - Add step no 2 into step no 3 with continuous stirring.
Step no 13: - Dissolve menthol in flavour and add into Step no 3 with continuous stirring.
Step no 14: - Dissolve Colour into purified water and add into Step no 3 with continuous stirring.
Step no 15: - Check the pH and maintain the pH with Potassium citrate within range (8-8.5)
Step no 16: - Volume was make up with purified water up to mark.
*In case of F1 and F2 formulation. All process are same instead of sodium alginate sorbitol was added into the batch.

3.0 EVALUATION OF DEVELOPED ORAL ANTACID SUSPENSION

3.1 Colour, odour and taste
All the developed batches of suspension were evaluated for organoleptic properties such as colour, odour and taste.

3.2 pH
pH of the suspension was determined by the use of Metler Toledo pH meter.

3.3 Viscosity
The viscosity of suspension was determined at ambient condition using DV III+, Brookfield Programmable Rheometer. In adapter 15ml of suspension was taken and the adapter is set over the viscometer by a stand such a way that spindle is completely immersed in the suspension. Spindle no. S0 was used to measure the viscosity of suspension.

3.4 Sedimentation Volume
Fifty ml each of suspension was taken in 50 ml stoppered graduated measuring cylinder. The suspension was dispersed thoroughly by moving upside down for three times. Later, the suspension was allowed to settle for three minutes and the volume of sediment was noted. This is the original volume of sediment (H0). The cylinder was kept undisturbed for 7 days. The volume of sediment read at 7 hr and every 24 hr for 7 days was considered as final volume of sediment (Hu).
Sedimentation Volume (F) = Hu/ Ho
The ultimate height of the solid phase after settling depends on the concentration of solid and the particle size. To obtain an acceptable suspension, F should be at least 0.9 for 1 h but a longer period was preferred for our purpose. Duplicates. Area was measured using developed HPLC method & Compared with standard and then % drug content was calculated as per the following formula.

3.5 Redispersibility

Fixed volume of each suspension (50 ml) was kept in stoppered cylinder which was stored at room temperature for 7 days. At regular interval, one stoppered cylinder was removed and moved upside down until there was no sediment at the bottom of the cylinder.

3.6 Assay of Oral Taste Masked Suspension

Suspension (5ml) was taken in 100 ml volumetric flask, 0.1 M HCl was added into it & sonicated it for 10 min. Volume was made up to 100 ml with 0.1 M HCl & filtered. Samples were prepared in duplicates. Area was measured using developed HPLC method & Compared with standard and then % drug content was calculated as per the following formula.

3.7 Accelerated stability study

F8 suspension was packed in 170 ml Pet bottle. The packed bottles were placed in stability chamber maintained at 40 ± 2 °C and 75 ± 5% RH for 3 month. Samples were collected at days 0, 30, 60 and 90. The analyses comprised chemical testing of quantifiable parameters, which could possibly change during storage, such as viscosity, pH, drug contents, sedimentation volume, Redispersibility, colour, taste, odour and drug release. [6]

4.0 RESULTS

4.1 EVALUATION OF DEVELOPED ANTACID SUSPENSION: -

Evaluation of Antacid was carried out for various parameters like confirmation of formation of complex, pH, odour, and taste, Viscosity, Sedimentation Volume, Redispersibility and assay.

### Table 2: Evaluation parameters of F1 to F9 Suspension

<table>
<thead>
<tr>
<th>Parameters</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
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<tbody>
<tr>
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<td>Light Pink</td>
<td>Light Pink</td>
<td>Light Pink</td>
<td>Light Pink</td>
<td>Light Pink</td>
<td>Light Pink</td>
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<td>Pink</td>
</tr>
<tr>
<td>Odour</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
</tr>
<tr>
<td>Taste</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
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<td>Sweet</td>
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<tr>
<td>pH</td>
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<td>08.47</td>
<td>08.37</td>
<td>08.55</td>
<td>08.00</td>
<td>08.10</td>
<td>08.68</td>
<td>08.17</td>
<td>08.50</td>
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</table>
### 4.2 ACCELERATED STABILITY STUDIES:

**Table 3: Accelerated Stability Studies.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Initials</th>
<th>1 Month</th>
<th>2 Month</th>
<th>3 Month</th>
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<tr>
<td>Colour</td>
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<td>No change</td>
<td>Slight change</td>
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<tr>
<td>Odour</td>
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<td>Peppermint</td>
<td>Peppermint</td>
<td>Peppermint</td>
</tr>
<tr>
<td>Taste</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
<td>Sweet</td>
</tr>
<tr>
<td>pH</td>
<td>08.50</td>
<td>08.40</td>
<td>08.45</td>
<td>08.45</td>
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<tr>
<td>Viscosity (CPS)</td>
<td>8471</td>
<td>8475</td>
<td>8470</td>
<td>8472</td>
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<tr>
<td>Sedimentation volume</td>
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<td>0.86</td>
<td>0.89</td>
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<tr>
<td>Redispersibility</td>
<td>++</td>
<td>++</td>
<td>+++</td>
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</table>
5.0 DISCUSSION

Formulation of oral stabilized form of antacid free of sorbitol was found to be optimized with the use of Xanthan Gum and alginate at 0.4% and 0.45% concentration respectively. F6 and F8 batches show satisfactory assay and sedimentation ratio result that it is fulfill the official requirement (To be comply with IP stated limits are between 90 to 110%) but physical properties of F6 suspension was not satisfactory. F2 was not easily redispersable and F3, F4, F5 Caking was observed. F1 having problem in the stability due to preservative used hence those batches were rejected. F8 was found to be stable in every aspect but fail to achieve result in taste because of the destability of the aspartame at a higher pH (8-8.5). F9 was found to be optimized batch as it showed complied assay result 99.6, 98.7, 99.5 in case of aluminium hydroxide, magnesium hydroxide, Simethicone respectively and was found to be easily redispersable even after seven days with no cake formation and sedimentation volume of 0.70 and also the stability was found up to mark.

6.0 CONCLUSION

The Antacid free of sorbitol final Batch (F9) prepared with Xanthan Gum (Conc. 0.4%) and Sodium alginate (Conc. 0.45%) showed the satisfactory result in every aspect of evaluation parameters and stability criteria in comparison with other formulation (F1-F8)

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7.0 REFERENCES


