“FORMULATION AND EVALUATION OF DICLOFENAC POTASSIUM SUSPENSIONS CONTAINING AN ANTACID”

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ABSTRACT
The present investigation is concerned with formulation and evaluation of diclofenac Potassium Suspension containing an antacid. Diclofenac potassium is a good Anti-inflammatory drug having a tendency to cause gastric acidity as a side effect. Hence an antacid was included in diclofenac sodium suspension, to counteract the side effect. Four formulations containing diclofenac potassium and aluminium hydroxide were prepared using xanthan gum. They were tested for assay, density, Ease of redispersibility, pH, dissolution rate, sedimentation parameters and taste. Formulation F4 containing xanthan gum as suspending agent was found be the best one with respect to physical stability and drug release. Hence an ideal suspension containing diclofenac potassium and aluminium hydroxide was formulated.

KEY WORDS: Oral suspension, Diclofenac potassium, Aluminum hydroxide, Xanthan gum.

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 through out 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.

**Classification**

**Based On General Classes**
1. Oral suspension
2. Externally applied suspension
3. Parenteral suspension

**Based On Proportion of Solid Particles**
1. Dilute suspension (2 to 10 % w/v solid)
2. Concentrated suspension (50 % w/v solid)

**Based on electrokinetic nature of solid particles**
1. Flocculated suspension
2. Deflocculated suspension

**Based on Size of solid particles**
1. Colloidal suspension (< 1 micron)
2. Coarse suspension (> 1 micron)
3. Nano suspension (10 nm)

**Advantages**
1. Pharmaceutical Suspension can improve chemical stability of certain drugs.
   E.g. Procaine penicillin G
2. Drug in suspension exhibits higher rate of bioavailability than other dosage forms.
3. Bioavailability is in following order,
   Solution > Suspension > Capsule > Compressed Tablet > Coated tablet
4. Duration and onset of action can be controlled.
   E.g. Protamine Zinc-Insulin suspension
5. Suspension can mask the unpleasant/ bitter taste of drug.
   E.g. Chloramphenicol.

**Disadvantages**
1. Physical stability, sedimentation and compaction can causes problems.
2. It is bulky, sufficient care must be taken during handling and transport.
3. It is difficult to formulate
4. Uniform and accurate dose can not be achieved unless suspension are packed in unit dosage form.

1.4. Features desired in pharmaceutical suspensions
1. The suspended particles should not settle rapidly and sediment produced, must be easily re-suspended by the use of moderate amount of shaking.
2. It should be easy to pour yet not watery and no grittiness.
3. It should have pleasing odour, colour and palatability.
4. Good syringeability.
5. It should be physically, chemically and microbiologically stable.
Parenteral/Ophthalmic suspension should be sterilizable.

Applications
1. Suspension is usually applicable for drug which is insoluble or poorly soluble. E.g. Prednisolone suspension
2. To prevent degradation of drug or to improve stability of drug. E.g. Oxytetracycline suspension
3. To mask the taste of bitter of unpleasant drug. E.g. Chloramphenicol palmitate suspension
4. Suspension of drug can be formulated for topical application e.g. Calamine lotion
5. Suspension can be formulated for parenteral application in order to control rate of drug absorption.
6. Vaccines as immunizing agent are often formulated as suspension. E.g. Cholera vaccine
7. X-ray contrast agents are also formulated as suspension. E.g. barium sulphate for examination of elementary tract.

Theory of Pharmaceutical Suspensions
Sedimentation behaviour: Sedimentation means settling of particle or floccules occur under gravitational force in liquid dosage form.

Theory of Sedimentation
Velocity of sedimentation expressed by Stoke's equation

\[ v_{sed} = \frac{d^2 (\rho_s - \rho_o) g}{18\eta_0} \]

Where, \( v_{sed} \) = sedimentation velocity in cm/sec
\( d \) = Diameter of particle
\[ r = \text{radius of particle} \]
\[ \rho_s = \text{density of dispersed phase} \]
\[ r_0 = \text{density of disperse media} \]
\[ g = \text{acceleration due to gravity} \]
\[ \eta_0 = \text{viscosity of disperse medium in poise} \]

**MATERIALS AND METHODS**

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Material</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac potassium</td>
<td>Gift sample from AARTI drugs Pvt Ltd</td>
</tr>
<tr>
<td>2</td>
<td>Xanthan gum</td>
<td>S D Fine-Chem Ltd</td>
</tr>
<tr>
<td>3</td>
<td>Alluminium hydroxide</td>
<td>S D Fine-Chem Ltd</td>
</tr>
<tr>
<td>4</td>
<td>Sodium benzoate</td>
<td>Merck Pvt Ltd</td>
</tr>
</tbody>
</table>

**Equipments used in the study**

**ANALYTICAL METHODS**

**Table 3.2: Equipment employed in the study**

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Equipment</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Digital Balance</td>
<td>Shimadzu</td>
</tr>
<tr>
<td>2</td>
<td>Electronic Balance</td>
<td>Shimadzu</td>
</tr>
<tr>
<td>3</td>
<td>UV Visible Spectrophotometer</td>
<td>Model-118 Systronics</td>
</tr>
<tr>
<td>4</td>
<td>Digital pH meter</td>
<td>ELICO LI 120</td>
</tr>
<tr>
<td>5</td>
<td>Specific gravity bottle</td>
<td>Jsgw</td>
</tr>
</tbody>
</table>

**Buffer Solution**

**Preparation of 6.8 pH phosphate buffer**

6.8g of potassium di hydrogen phosphate and 0.9g of sodium hydroxide were accurately weighed and taken into a 1000ml volumetric flask and made the volume up to the mark with distilled water.

**Spectrophotometric method**

A number of methods are reported in the literature for the estimation of diclofenac potassium. Spectrophotometric method was used for the estimation of diclofenac potassium at 276 nm in water.

**Standard Solution:** 100 mg of diclofenac potassium was dissolved in q.s water in a 100 ml volumetric flask (A), and the solution was made up to the mark with water. 10 ml of above solution was diluted to 100 ml with water. This standard solution had a concentration of 100 µg diclofenac potassium /ml, (B).
**Procedure**

The standard solution of diclofenac potassium (B) was suitably diluted with water to obtain a series of standard solutions containing 5, 10, 15, 20, 25 and 30 µg of diclofenac potassium per ml. The absorbance of the solutions was measured at 276 nm using Systronics Uv-Vis spectrophotometer. Water was used as a blank.

**3.4 Method of Preparation of suspensions**

Drug and all other excipients were weighed according to the formulae given in table 3.1. Suspensions are prepared by grinding (or) levigating the insoluble materials in the mortar to a smooth paste with a vehicle containing the wetting agent. All soluble ingredients are dissolved in same portion of the vehicle and added to the smooth paste to get slurry. The slurry is transformed to a graduated cylinder, the mortar is rinsed with successive portion of the vehicle. Add the vehicle containing the suspending agent (or) flocculating agent Make up the dispersion to the final volume. Thus suspension is prepared.

**RESULTS AND DISCUSSION**

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac Potassium (mg)</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>2</td>
<td>Aluminium Hydroxide (g)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Sodium Benzoate (mg)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>Xanthane gum (mg)</td>
<td>-</td>
<td>50</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>5</td>
<td>Distilled water (q.s) (ml)</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>
Evaluation Procedures for suspensions: The prepared suspensions were evaluated for assay, viscosity, density, and ease of redispersibility, pH, dissolution rate, sedimentation parameters and taste.

1. Assay
One ml of suspension was weighed and dissolved in 100 ml distilled water and the supernatant liquid taken & they are checked for their absorbance values.

2. Dissolution test
The dissolution rate testing of different diclofenac potassium formulations (table) was studied using USP XXII dissolution rate testing apparatus, (paddle type). The paddle was rotated at a speed of 50 rpm and the dissolution fluid (900 ml phosphate buffer solution) was maintained at a temperature of 37.50 ± 0.5 0C. At specific time intervals a 5 ml aliquot of dissolved medium was withdrawn and was replaced with fresh quantity of dissolution medium. The samples were suitably diluted with dissolution medium and assayed for diclofenac potassium content by measuring the absorbance at 276 nm using U.V Spectrophotometer. The percent of diclofenac potassium dissolved at various time intervals was calculated and plotted against time.

<table>
<thead>
<tr>
<th>Table3.7 : Dissolution Testing Conditions</th>
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<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Buffer</td>
</tr>
<tr>
<td>Temperature</td>
</tr>
<tr>
<td>Speed</td>
</tr>
<tr>
<td>Volume</td>
</tr>
</tbody>
</table>

3. pH test: A typical pH meter consists of a special measuring glass electrode connected to an electronic meter that measures and displays the pH readings of all suspensions.

4. Rheological method: It provides information about settling behavior. The arrangement of the vehicle and the particle structural features. Brookfield viscometer is used to study the viscosity of the suspension using spindle 63.

5. Sedimentation parameter: The suspension formulation (50 ml) was poured separately into 50 ml measuring cylinders and sedimentation volume was read after 1, 2, 3 and 7 days, and thereafter at weekly intervals for 12 weeks. Triplicate results were obtained for each formulation. Sedimentation volume was calculated according to the equation.
F = Vu/Vo
Where, F = sedimentation volume,
Vu = ultimate height of sediment
Vo = initial height of total suspension

6. Ease of redispersibility
The redispersibility of a suspension was evaluated qualitatively. The test consisted of manually shaking the cylinder after the sedimentation experiments were completed based on the time and the effort required to convert the sediment to homogenous suspension, the formulations were evaluated one inversion was considered as 100% easy to be redispersed. Every additional inversion decreased the percent ease of redispersibility by 5%.

7. Density: A specific gravity bottle was used to determine the density of the liquids. The specific gravity bottle is a glass flask with a close-fitting glass stopper with a capillary hole through it. The fine hole releases a top-filled pycnometer and allows for obtaining a given volume of measured and working liquid with accuracy. The weight of the empty pycnometer was noted. The pyconometer was then filled with the liquid until it overflowed. The outside of the bottle was cleaned until dry and the weight was recorded again. The difference in the weights was used for further calculations. This procedure was repeated to calculate the density of the polymeric solutions and the difference was recorded relative to the weight of the dispersion medium. The specific gravity could be determined relative to water.
The density was calculated using the following formula.
Density= weight (g)/volume (ml).

8. Evaluation of taste
Taste of drug was checked by time intensity method. For this purpose 6 human volunteers were selected. In this method a sample 5 ml was held in mouth for 60 seconds and volunteers were asked to evaluate the drug for taste. Bitterness levels were recorded at 2, 10 and 60 sec. The bitterness level was recorded against pure drug (5 ml) using a numerical scale (3– Strong Bitter, 2 – Moderate Bitter, 1 –Slight Bitter, X – Threshold Bitter, 0 – No Bitter). These volunteers were instructed not to swallow the suspensions, which were placed on the tongue. They were instructed to thoroughly gargle their mouth with distilled water after the completion of test.
CONCLUSION
The present investigation is concerned with formulation and evaluation of diclofenac Potassium Suspension containing antacid. Diclofenac potassium is a good Anti-inflammatory drug having a tendency to cause gastric acidity as a side effect. Hence an antacid was included in diclofenac Potassium suspension, to counteract the side effect.

Four formulations containing diclofenac potassium and aluminium hydroxide were prepared using polymer like xanthan gum. They were tested for assay, density, ease of redispersibility, pH, dissolution rate, sedimentation parameters and taste.

Formulation F4 containing xanthan gum as suspending agent was found to be the best one with respect to physical stability and drug release. Hence an ideal suspension containing diclofenac potassium and aluminium hydroxide was formulated.

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