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A REVIEW ON: FORMULATION AND EVALUATION OF METRONIDAZOLE SUSPENSION

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Abstract:

The present study aims to formulate and evaluate a metronidazole suspension using natural suspending agents as substitutes for synthetic ones. Metronidazole is an effective antiprotozoal and antibacterial drug that is commonly administered as an oral suspension to enhance patient compliance, particularly among pediatric and geriatric patients. In this work, natural polymers such as tragacanth gum, guar gum, and xanthan gum were employed as suspending agents owing to their biodegradability, biocompatibility, and low toxicity. The suspensions were prepared by dispersing metronidazole powder in aqueous solutions of these natural gums and subsequently evaluated for parameters including sedimentation volume, viscosity, redispersibility, pH, and drug content uniformity. The findings revealed that suspensions formulated with natural agents exhibited satisfactory stability and rheological properties comparable to those containing synthetic agents like sodium carboxymethyl cellulose (CMC). Among the tested formulations, xanthan gum demonstrated superior performance in terms of sedimentation stability and ease of redispersion. Additionally, the incorporation of acacia gum powder was found to further enhance the physical stability of the suspension as its concentration increased. Overall, natural suspending agents can serve as effective, eco-friendly, and economical alternatives for the preparation of metronidazole suspensions.

Key words:

Metronidazole suspension, Natural Suspending agents,Antiprotozoal, Antibacterial

Introduction:

Metronidazole suspension is an antibiotic formulation used for the treatment of infections caused by anaerobic bacteria and protozoa. It is commonly prescribed for conditions such as Amoebiasis (both intestinal and extra-intestinal), giardiasis (intestinal infections), Trichomoniasis (genital tract infections), and bacterial vaginosis (vaginal infections). The formulation is designed for oral administration and is available in different strengths to suit various therapeutic needs.

Pharmaceutical dosage forms generally contain several excipients in addition to the active drug, each serving a specific purpose in ensuring product stability and effectiveness. Among these, suspending agents play a crucial role in maintaining uniform dispersion of the drug particles. These agents can be classified into three main types: synthetic, semi-synthetic, and natural.

In this formulation, natural suspending agents such as acacia gum and tragacanth gum were utilized. These natural gums enhance the sedimentation volume, improve redispersibility, increase Pourability, and prevent the formation of compact sediments. By increasing the viscosity of the dispersion medium, they help retard the rate of particle settling and reduce agglomeration, thus maintaining the physical stability of the suspension.

Natural suspending agents offer several advantages over synthetic ones—they are non-toxic, biocompatible, chemically stable, eco-friendly, cost-effective, and readily available. Owing to these characteristics, they are widely preferred in pharmaceutical formulations. Oral suspensions are particularly suitable for pediatric and geriatric patients because they enable easy swallowing and flexible dose adjustment.

Metronidazole, an anti-infective agent with specific activity against various obligate anaerobes and protozoa, was selected as the model drug for this study due to its limited aqueous solubility (United States Pharmacopoeia, 2014; Stanley, 2003; Nash, 2001).

Important Points Regarding the Suspension

1. The suspension should preferably be administered after meals to minimize gastrointestinal discomfort.
2. The bottle must be shaken thoroughly before each dose to ensure uniform distribution of the drug.
3. It is essential to complete the entire prescribed course of therapy, even if clinical symptoms subside earlier, to prevent recurrence or resistance.
4. Alcohol consumption should be strictly avoided during treatment and for at least 48 hours after completion of therapy, as concomitant intake may cause adverse reactions such as nausea, vomiting, and headache.

Advantages of Suspension :

1. Ease of Administration: Suspensions are simple to administer and convenient for patients who require liquid dosage forms.

2.Suitable for All Age Groups: They are particularly appropriate for children, elderly individuals, and patients who experience difficulty swallowing tablets or capsules.

3. Accurate Dosage: They allow precise dose measurement and easy adjustment according to individual patient needs.

4. Rapid Absorption: The drug, being in a finely divided form, offers a larger surface area, leading to faster absorption and quicker onset of action.

5. Improved Palatability: The taste of unpleasant drugs can be masked effectively, enhancing patient compliance.

6. Maintenance of Therapeutic Levels: Suspensions can sustain uniform drug concentration in the systemic circulation for a longer duration.

Materials and Methods :

Materials

The following materials were used in the preparation of the metronidazole suspension: metronidazole powder, acacia gum, tragacanth powder, benzoic acid, double-strength chloroform water, raspberry syrup, and distilled water. All materials were of analytical grade. The formulation work was carried out in the Department of Medicinal Chemistry, Faculty of Pharmacy.

Method :

1.Preparation of CMC Mucilage

Ten milliliters of purified water were measured into a 100 mL beaker and gently warmed to approximately 60–70 °C (without boiling). About 0.5 g of carboxymethyl cellulose (CMC) was gradually sprinkled over the surface of the warm water with continuous stirring to prevent lump formation or agglomeration. Cold water was then added gradually with constant mixing until a smooth and uniform paste was obtained. The mixture was covered and allowed to stand for 10–15 minutes to ensure complete hydration, resulting in the formation of CMC mucilage.

2 .Preparation of Preservative and Sweetening Solution

In a separate beaker, 0.10 g of benzoic acid was dissolved in 5–10 mL of hot purified water and cooled to room temperature. To this solution, 60 mL of raspberry syrup and 10 mL of double-strength chloroform water were added and mixed thoroughly. A few drops of amaranth solution were incorporated to obtain a uniform light tint.

3.Dispersion of the Drug (Metronidazole)

Metronidazole powder (2.5 g) was finely triturated using a mortar and pestle. The powder was levigate with a small quantity of the prepared syrup from step 2 to form a smooth, air-free paste. The syrup acted as both a wetting agent and a taste-masking medium, providing good dispersion characteristics.

4.Formulation of the Suspension

The prepared CMC mucilage (step 1) was gradually incorporated into the metronidazole paste with continuous trituration to form a uniform slurry. Subsequently, the colored syrup-preservative-chloroform water mixture (step 2) was added slowly with constant mixing to maintain homogeneity. The mortar and beakers were rinsed with small volumes of purified water, and the rinsing was added to the main bulk. The final volume was made up to 100 mL with purified water and mixed thoroughly. A homogenizer or colloid mill was used to ensure complete dispersion and uniformity.

5. Packaging and Labeling

The prepared suspension was transferred into clean, sterile amber-colored bottles to protect it from light. The containers were properly labeled with necessary precautions, such as “Shake well before use.”

Evaluation Parameters

1.Determination of Sedimentation Volume

Twenty milliliters of each formulated suspension were transferred into 30 mL graduated cylinders in duplicate and kept undisturbed at room temperature for 45 days. The sedimentation volume was recorded at intervals of every five days. The sedimentation volume (F) was calculated using the formula:

F = \fra{V_u}{V_0}

Where:

V_0 = initial volume of the suspension

V_u = ultimate volume of the sediment

This parameter indicates the physical stability of the suspension and its ability to resist sedimentation over time.

2.Rheological Assessment

The flow behavior of each suspension was assessed by measuring the time required for 5 mL of the sample to flow from a 5 mL pipette, performed in duplicate. The flow rate was calculated using the formula:

\text{Flow Rate} = \frac{\text{Volume of pipette (mL)}}{\text{Flow time (s)}}

The shear rate was further determined using the equation:

\text{Shear Rate} = \frac{\text{Flow Rate (mL/s)}}{\text{Volume of Suspension}}

These measurements provided information about the viscosity and Pourability of the suspension.

3.pH Determination

The pH of each formulated metronidazole suspension was measured using a calibrated digital pH meter at 0, 10, 20, 30, and 40 days. The electrode of the pH meter was immersed in the suspension for 30 seconds before each reading was taken. The results reflected the stability of the suspension over time with respect to pH variation.

4.Redispersibility Test

Redispersibility was evaluated to determine the ease with which the sedimented particles could be re-dispersed upon shaking. Five milliliters of each suspension were transferred into four calibrated tubes and stored at room temperature for 5, 10, 15, 20, 25, 30, and 35 days. At the end of each storage period, the tubes were hand-shaken at a moderate and uniform rate of approximately 30 shakes. The ease of redispersion was visually observed and recorded.

5.Particle Size Analysis

The particle size distribution of metronidazole powder was determined using a sieve shaker. Sieves of decreasing aperture sizes (1000 µm to 90 µm) were arranged in descending order with a collection pan at the bottom. Ten grams of metronidazole powder were placed on the top sieve and shaken for five minutes. The quantity of powder retained on each sieve was weighed, and the mean particle diameter was calculated using standard particle size equations.

6.Viscosity Measurement

The viscosity of each suspension was determined using a Brookfield digital viscometer equipped with spindle number 2, operated at 60 revolutions per minute (rpm). Approximately 50 mL of the suspension was transferred into the viscometer beaker, and the measurement was carried out at room temperature. The instrument recorded the resistance to spindle rotation, indicating the viscosity of the sample. Each test was performed in triplicate, and the average value was reported.

7.Organoleptic Evaluation

Organoleptic characteristics such as color, odor, taste, and appearance were evaluated to assess the sensory acceptability of the suspension. These attributes are particularly important for ensuring patient compliance, especially in pediatric and geriatric formulations.

Conclusion

The study demonstrated that acacia gum, owing to its low cost, non-toxic nature, biocompatibility, and biodegradability, serves as an excellent natural alternative to conventional suspending agents. Among the various natural polymers investigated, formulations containing acacia gum exhibited superior suspendability and stability characteristics. Based on the evaluation parameters, acacia gum proved to be a highly effective excipient in the formulation of metronidazole suspensions. Its inherent viscosity and mucilage-forming ability also make it suitable for use as a thickening and stabilizing agent in pharmaceutical formulations. Furthermore, its versatility extends beyond pharmaceuticals, with potential applications in the food and cosmetic industries, even at relatively low concentrations.

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