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A REVIEW ON FORMULATION AND EVALUATION OF QUININE SULPHATE SUSPENSION

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ABSTRACT

Quinine sulphate is an antimalarial drug and is very much effective against resistant strains of Plasmodium falciparum, where other antimalarials like chloroquine, sulphadoxine-pyrimethamine are ineffective. But, it is a very bitter drug and taste should be masked to formulate it in a palatable form. So in the work undertaken, an attempt was made to mask the taste, by complexation technique using ion-exchange resins and to formulate into a suspension.The products were evaluated for bitterness, drug content, particle size, viscosity, sedimentation time and volume, redispersibility and drug release and also subjected to stability studies. Of the different resins, lndion 234 was found to be the most suitable one. The release studies showed complete drug release within 20 min. Stability studies indicated no appreciable changes in the above mentioned parameters for 3 months.

KEYWORDS:

Quinine Sulphate ,Suspension Formulation ,Antimalarial Suspension,Pharmaceutical Suspensions, Taste Masking.

INTRODUCTION:

Quinine sulphate is a well-established antimalarial drug used to treat malaria, particularly for _Plasmodium falciparum_ infections. Formulating it as a suspension offers several advantages, especially for pediatric and geriatric patients who may have difficulty swallowing tablets.

KEY POINTS

1. Dosage Form: Quinine sulphate suspension is a liquid dosage form where the drug is dispersed in a suitable vehicle.

2.Therapeutic Use: Effective against malaria, a life-threatening disease prevalent in tropical regions.

3. Formulation Challenges:

Taste Masking: Quinine sulphate has a bitter taste, necessitating the use of sweeteners and flavors.

Physical Stability: Suspending agents like xanthan gum or carboxymethylcellulose are used to prevent sedimentation and ensure uniform dosing.

Preservation: Preservatives are added to prevent microbial growth in the aqueous vehicle.

CHEMICAL STRUCTURE AND PROPERTIES

Quinine sulphate is a salt form of quinine, an alkaloid derived from the bark of the _Cinchona_ tree. Its chemical properties are crucial for understanding its formulation and therapeutic use.

CHEMICAL STRUCTURE

Chemical Formula: $C_{20}H_{24}N_2O_2 \cdot H_2SO_4$ (quinine sulphate dihydrate: $C_{20}H_{24}N_2O_2 \cdot H_2SO_4 \cdot 2H_2O$)

Structure: Quinine sulphate consists of quinine (a quinoline methanol compound) and sulphuric acid.

PHYSICAL PROPERTIES:

1. Appearance: White, crystalline powder.

2. Solubility:

- Slightly soluble in water.
- More soluble in acidic solutions.

3.Melting Point: Decomposes at around 235°C.

4.pH: Solutions are slightly acidic.

CHEMICAL PROPERTIES:

1. Alkaloid Nature: Quinine is a weak base, forming salts with acids like sulphuric acid.

2. Stability

Light Sensitivity: Quinine sulphate is sensitive to light, which can lead to degradation.

pH-Dependent Stability: More stable in acidic pH.

PHARMACOLOGICAL PROPERTIES:

1. Antimalarial Activity: Effective against _Plasmodium_ species.

2. Mechanism: Interferes with the parasite's heme detoxification process**.**

USE IN FORMULATION

Particle Size: Important for dissolution rate and bioavailability.

Solubility: Limited solubility in water necessitates careful formulation to ensure uniform dispersion.

MECHANISM OF ACTION:

Quinine sulphate suspension works by delivering the antimalarial drug quinine sulphate to the bloodstream, where it targets the malaria parasite within red blood cells.

KEY STEPS

1. Ingestion and Absorption: The suspension is ingested orally, and quinine sulphate is absorbed into the bloodstream.

2. Distribution to Red Blood Cells: Quinine sulphate is distributed throughout the body, accumulating in infected red blood cells containing the malaria parasite.

3. Action on Parasite: Quinine sulphate interferes with the parasite's heme detoxification process, leading to the accumulation of toxic heme, which damages the parasite and ultimately leads to its death.

4. Elimination of Parasite: The dead parasites are then cleared from the bloodstream, reducing the parasite load and alleviating symptoms.

BENEFITS OF SUSPENSION FORMULATION

Rapid Onset: The suspension formulation can provide a faster onset of action compared to solid dosage forms.

Dose Flexibility: The suspension allows for adjustable dosing, making it suitable for pediatric and geriatric patients.

Improved Compliance: The palatable formulation improves patient compliance, especially in pediatric patients.

USES:

1. Malaria Treatment

- Uncomplicated Malaria: Effective against _Plasmodium falciparum_, _P. vivax_, _P. ovale_, and _P. malariae_ infections.

-Severe Malaria: Used in critical cases where rapid treatment is essential.

2. Pediatric Use

- Suitable for children who have difficulty swallowing tablets or capsules.

- Allows for precise dosing adjustments based on weight and age.

3. Geriatric Use

- Provides a convenient dosage form for elderly patients with swallowing difficulties.

4. Emergency Situations

- Useful in areas where malaria is endemic and rapid treatment is required.

5. Alternative to Other Antimalarials

- Used when other antimalarial drugs are not suitable due to resistance or side effects.

MATERIALS:

Quinine Sulphate powder , carboxymethyl Cellulose,methyl paraben, propyl paraben,mannitol, raspberry syrup , glycerine, distilled water .

METHOD OF PREPARATION:

Formulation of Quinine Sulphate Suspension (60 ml)

Formula (for 60 ml)

1. Quinine Sulphate: 300 mg (1% w/v)
2. *Suspending Agent (Xanthan Gum)*: 0.3 g (0.5% w/v)
3. Sweetening Agent (Sucrose): 6 g (10% w/v)
4. Preservative (Methylparaben): 0.06 g (0.1% w/v)
5. Flavoring Agent: q.s. (as needed)
6. Purified Water: q.s. to 60 ml

PROCEDURE

1. Weigh Ingredients: Accurately weigh quinine sulphate, xanthan gum, sucrose, and methylparaben.
2. Prepare Suspending Agent: Disperse xanthan gum in a small amount of hot purified water (e.g., 10 ml) with stirring to form a uniform dispersion. Let it cool.
3. Dissolve Sucrose: Dissolve sucrose in a portion of purified water (e.g., 20 ml) with gentle heating if necessary.
4. Mix Quinine Sulphate: Gradually add quinine sulphate to the cooled xanthan gum dispersion and mix well.
5. Combine Mixtures: Add the sucrose solution to the quinine sulphate mixture and mix uniformly.
6. Add Preservative: Dissolve methylparaben in a small amount of purified water and add it to the mixture.
7. Add Flavor: Add flavoring agent as needed and mix well.
8. Make Up Volume: Add purified water to make up the final volume to 60 ml and mix thoroughly.
9. Homogenize: Use a homogenizer or stirrer to ensure uniform particle size and distribution.
10. Fill and Label: Fill the suspension into suitable containers and label according to regulatory requirements.

EVALUATION PARAMETERS:

1.Physical Characteristics

i) Visual Appearance: The suspension should exhibit uniform color and consistency without signs of aggregation.

ii) pH Measurement: pH determines both drug stability and palatability; measured using a calibrated pH meter.

iii) Viscosity: Determined with a Brookfield viscometer to evaluate flow behavior and pourability.

Iv)Sedimentation Volume: Assessed using the formula

$F = Vs / Vt$

Where:

F = Sedimentation volume

Vs = Volume of sediment

Vt = Total volume of suspension

V) Redispersibility: The ease of re-dispersing settled particles after shaking is tested to ensure homogeneity upon administration.

2. Chemical Characteristics

i) Assay: The content of quinine Sulphate should remain within the specified limits to confirm dose uniformity.

ii)Impurity Profile: The presence of degradation or by-products must be minimal to maintain safety and efficacy.

iii)Stability Testing: Conducted under different storage conditions to assess the chemical and physical integrity of the suspension.

3. Pharmacotechnical Parameters

i)Dissolution Profile: Determines the release rate of albendazole, directly influencing its bioavailability.

ii)Particle Size Analysis: Uniform particle distribution prevents rapid sedimentation and ensures dose accuracy.

iii)Zeta Potential: Evaluated to predict electrostatic stability; a higher zeta potential suggests better dispersion stability.

FUTURE ASPECTS:

Quinine sulphate suspension has a promising future in the pharmaceutical industry, particularly in the treatment of malaria and other diseases.

- Increased Adoption in Malaria Treatment: Quinine sulphate suspension is expected to continue playing a vital role in treating malaria, especially in regions where resistance to other antimalarial drugs is a concern.

- Sustainable Production Methods: Advances in biotechnology and synthetic biology may lead to more efficient and environmentally friendly production methods, reducing costs and increasing accessibility.

- New Formulations and Delivery Systems: Researchers are exploring novel formulations and delivery systems, such as sustained-release tablets and nanoparticles, to improve patient compliance and reduce side effects.

- Expanded Therapeutic Applications: Quinine sulphate may be investigated for its potential use in treating other conditions, such as antiviral infections, muscle pain, and restless legs syndrome.

- Growing Demand in Emerging Markets: The quinine sulphate market is expected to grow steadily, driven by increasing demand in malaria-endemic countries and emerging markets.

CONCLUSIONS:

The formulation of quinine sulphate suspension is a valuable approach for delivering this antimalarial drug, particularly for patients who have difficulty swallowing tablets or require flexible dosing. By carefully selecting excipients and optimizing the formulation, it is possible to create a stable and effective suspension that provides consistent therapeutic benefits.

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