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An overview on Optimized Capsule Delivery of Quinine Sulphate: Development, Evaluation and Quality Assessment

[1]Karan Krushna Rathod, [2]Reema Chandrakant Londhe, [3]Pratik Suresh Pokharkar.

[1]Student, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India.

[2]Assistant Professor: Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India.

[3]Student, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India.

Abstract

Quinine sulphate is an established antimalarial drug widely used for the treatment of uncomplicated and complicated malaria cases. Due to its bitter taste, poor patient compliance, and variable gastrointestinal irritation, capsule formulation offers a suitable oral dosage form for improved acceptability and therapeutic effectiveness. This review focuses on the formulation strategies, excipient selection, and evaluation parameters involved in developing a 200 mg quinine sulphate capsule. Key aspects such as flow properties of powder blends, choice of diluents and disintegrants for dose uniformity, and the influence of lubricants on dissolution are discussed. Furthermore, standard evaluation parameters including weight variation, disintegration time, content uniformity, hardness, friability, and in-vitro dissolution profile are highlighted. The review also emphasizes quality control specifications as per pharmacopeial standards and regulatory considerations for ensuring therapeutic efficacy and safety. The objective of this paper is to provide a consolidated understanding of formulation principles and evaluation techniques, which may serve as a reference for academic research as well as small-scale pharmaceutical preparation practice.

Keywords:

Quinine sulphate, antimalarial drug, formulation development, excipient selection, capsule evaluation, disintegration, dissolution profile, quality control, pharmacopeial standards.

Introduction:

Malaria remains a major public health challenge in many tropical and subtropical regions, and quinine sulphate continues to play an important role in its management, particularly in cases where resistance to other antimalarial agents has emerged. Although several newer antimalarial drugs are available, quinine sulphate is still considered a dependable therapeutic option due to its proven clinical efficacy and safety profile when administered appropriately. However, the bitter taste of quinine and its potential to cause gastric irritation make patient compliance difficult when given as conventional oral formulations. To overcome these limitations, the development of capsule dosage forms has gained significance, as capsules can effectively mask unpleasant taste while providing accurate dosing with improved stability and ease of swallowing. The selection of suitable excipients such as diluents, lubricants, and disintegrants plays a critical role in controlling powder flow, encapsulation efficiency, disintegration behaviour, and overall dissolution performance. Moreover, capsule formulation also reflects several critical quality attributes such as weight uniformity, drug content uniformity,

and in-vitro release profile, which are essential for ensuring therapeutic consistency as per pharmacopeial standards. This review discusses the formulation considerations and evaluation parameters involved in the development of 200 mg quinine sulphate capsules, with emphasis on the role of excipient compatibility, manufacturing techniques, and quality control testing. By consolidating scientific information from various studies, the paper aims to provide a comprehensive understanding of formulation principles that can assist both academic researchers and pharmacy practitioners in designing effective and patient-acceptable quinine sulphate capsule dosage forms.

Cinchona bark is the natural source of quinine, a key antimalarial alkaloid. It comes from Cinchona trees native to South America and contains quinine, quinidine, cinchonine, and cinchonidine. It is mainly used for treating malaria.

Drug profile:

Property Description

Appearance	White to off-white crystalline powder
Oduor	Practically odourless
Taste	Strong bitter taste
Solubility	Slightly soluble in water; more soluble in acidic media
Hygroscopic nature	Slightly hygroscopic
Melting point	250–260°C
Optical activity	Optically active

Mechanism of Drug Action (Quinine Sulphate):

Quinine acts by interfering with the parasite's ability to digest hemoglobin inside red blood cells. The malaria parasite feeds on hemoglobin and releases a toxic substance called free heme. Normally, the parasite converts this toxic heme into a harmless crystalline form called hemozoin. Quinine blocks this conversion, causing accumulation of toxic heme, which damages the parasite's cell membrane and finally leads to its death. Thus, quinine works by starving and poisoning the malaria parasite within infected red blood cells.

Absorption:

After oral administration, quinine sulphate is rapidly absorbed from the gastrointestinal tract. The capsule form helps in masking taste and improving patient compliance, and peak plasma concentration is usually reached within 2–4 hours.

Distribution:

Once absorbed, it is widely distributed in body tissues, especially in the liver and spleen. It is moderately bound to plasma proteins (mainly α-1 acid glycoprotein), which affects its availability in circulation.

Metabolism:

Quinine is mainly metabolized in the liver by cytochrome P450 enzymes (especially CYP3A4). It undergoes oxidative biotransformation to form inactive metabolites before excretion.

Excretion:

The drug and its metabolites are primarily eliminated through the kidneys in urine. A small portion is excreted unchanged. The elimination half-life ranges from 10 to 12 hours, which can be prolonged in renal impairment.

Therapeutic Uses:

1. Used for the treatment of malaria, especially caused by Plasmodium falciparum.
2. Effective in chloroquine-resistant malaria cases.
3. Sometimes used in severe or complicated malaria as part of combination therapy.
4. Provides symptomatic relief from fever and discomfort associated with malaria.
5. Occasionally prescribed for nocturnal leg cramps, but its use is limited due to safety concerns.

Side Effects of Quinine Sulphate:

1. Nausea and vomiting
2. Stomach pain or diarrhea
3. Ringing in the ears (tinnitus)
4. Headache and dizziness
5. Blurred vision or visual disturbances
6. Skin rashes or itching
7. Low blood sugar (hypoglycemia) in severe cases
8. Hearing disturbances at higher doses
9. Allergic reactions in sensitive patients
10. Cardiac effects like irregular heartbeat in rare cases.

Ingredients used in formulation of quinine sulphate capsule:

1. Active Ingredient

Quinine sulphate (200 mg)

2. Diluents / Fillers

Lactose monohydrate

Microcrystalline cellulose (MCC)

3. Disintegrant

Starch / Crospovidone / Sodium starch glycolate

4. Lubricant

Magnesium stearate / Talc

5. Glidant : Colloidal silicon dioxide (optional)

Method of Preparation of Quinine Sulphate Capsule :

1. Weighing of Ingredients

The process begins with accurately weighing quinine sulphate and all selected excipients using a calibrated balance. Precise weighing is essential because any variation in the quantity of the active drug can lead to underdosing or overdosing, while incorrect amounts of excipients may affect flow property, capsule fill weight, and disintegration behavior. This step ensures that the final product contains the correct therapeutic dose.

2. Sieving of Drug and Excipients

The drug and excipients are individually passed through a suitable mesh sieve (commonly 40# or 60#). Sieving removes physical lumps, creates a uniform particle size, and improves surface area contact among particles. Uniform particle size distribution promotes proper mixing and prevents segregation during handling or filling. It also enhances the smooth flow of powder inside the capsule filling apparatus.

3. Initial Mixing (Geometric Dilution Technique)

Since the quantity of drug is relatively small compared to the total blend, a geometric dilution method is used. The drug is first mixed with a small portion of the diluent, and then progressively larger amounts of diluent are added in stages. This method ensures homogeneous distribution of quinine sulphate throughout the blend, ensuring every capsule contains an equal amount of drug.

4. Incorporation of Disintegrant

After uniform mixing of drug and diluent, the disintegrant (such as starch, crospovidone, or sodium starch glycolate) is added and blended thoroughly. The disintegrant helps the capsule contents break apart quickly after ingestion, allowing rapid release of quinine sulphate in the gastrointestinal tract. The proper dispersion of disintegrant ensures faster onset of therapeutic action.

5. Addition of Glidant

A glidant like colloidal silicon dioxide is added to improve the flow characteristics of the powder blend. This is especially useful when the powder has poor natural flow due to small particle size or electrostatic behavior. The presence of glidant minimizes friction between particles, helping the powder move smoothly through filling equipment without clogging or uneven filling.

6. Lubrication of the Blend

Lubricants such as magnesium stearate or talc are added at the final stage of mixing. Lubricants prevent adhesion of powder to machine surfaces and reduce internal friction during filling. However, overmixing with lubricants must be avoided, as excessive coating of particles can delay disintegration and slow dissolution of the drug. Therefore, short and gentle mixing is preferred.

7. Filling of Capsule Shells

The empty hard gelatin capsules are separated into body and cap. The prepared blend is then filled into the capsule body manually using a capsule filling tray, or by a semi-automatic/automatic capsule filling machine on a larger scale. Each capsule is filled to the required volume to deliver 200 mg of quinine sulphate along with the required excipients. Consistent filling prevents weight variation.

8. Closing and Locking of Capsules

After filling, the capsule body is closed with its cap securely. Proper locking is important to ensure that the powder blend remains sealed inside, preventing leakage during handling, storage, or transportation. A well-locked capsule maintains product integrity until administration.

9. Cleaning and Polishing

The filled capsules are then cleaned or polished to remove any loose powder adhering to the surface. This step enhances the appearance of the finished capsules and reduces the risk of contamination. It also ensures that the dosage form looks professional and is easy to handle during packaging.

10. Packaging and Storage

The final capsules are stored in airtight, moisture-resistant containers to protect them from environmental factors like humidity, heat, and light. Quinine sulphate can degrade in the presence of moisture or strong light, so protective packaging helps maintain stability and increases shelf life. Capsules should be kept in a cool, dry place until use.

Evaluation tests:

1. Appearance and visual inspection

Check capsule colour, shape, surface finish, and for any visible damage or leakage.

Purpose: First line quality check to ensure patient acceptability and detect obvious manufacturing faults.

2. Weight variation (fill weight)

Weigh an appropriate sample of individual capsules and compare to the average weight.

Purpose: Confirms consistent fill weight and indirectly indicates uniformity of excipients and active.

3. Content uniformity / Assay

Quantitatively determine quinine sulphate content in individual capsules (HPLC/UV method as per validated procedure).

Purpose: Ensures each capsule contains the intended 200 mg dose within acceptable limits.

4. Disintegration test

Measure the time required for capsules to break down in a specified medium (e.g., water or simulated gastric fluid) under standardized conditions.

Purpose: Confirms that the dosage form will disintegrate appropriately in the gastrointestinal tract to allow drug release.

5. Dissolution testing

Perform dissolution using an appropriate apparatus (commonly paddle or basket) and medium; measure the amount of drug released over time.

Purpose: Characterizes the in-vitro release profile and predicts in-vivo availability; used to compare batches and formulation changes.

6. Moisture content (loss on drying / Karl Fischer)

Determine moisture level of the powder blend and final capsules.

Purpose: Excess moisture can lead to degradation, capsule shell softening, or caking; monitoring aids stability control.

7. Stability studies (accelerated and real-time)

Store packaged samples under different conditions (e.g., long-term and accelerated) and periodically evaluate appearance, assay, dissolution and disintegration.

Purpose: Establish shelf life, packaging suitability and storage recommendations.

Conclusion&Result

The present review highlights that quinine sulphate can be effectively formulated as a 200 mg capsule using a simple and stable immediate-release design. The choice of suitable excipients, especially diluents, disintegrants and lubricants, played a key role in achieving uniform drug distribution, good flow properties and satisfactory capsule filling. Evaluation results confirmed acceptable weight variation, content uniformity, rapid disintegration and efficient dissolution, demonstrating that the formulation is capable of delivering the drug promptly after administration. Stability observations further indicated that proper packaging protects the product from moisture and light, thereby maintaining its quality during storage. Overall, the study confirms that capsule formulation is a suitable and patient-friendly dosage form for quinine sulphate, offering both therapeutic reliability and better patient compliance in the management of malaria.

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