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ASSESSMENT OF PHARMACEUTICAL QUALITY PARAMETERS OF PRIMAQUINE TABLET FOR THE TREATMENT OF MALARIA

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1.ABSTRACT

Malaria is a life-threatening vector-borne parasitic disease caused by Plasmodium species and transmitted through the bite of infected Anopheles mosquitoes. Primaquine phosphate is an important antimalarial drug used for the radical cure of Plasmodium vivax infections. The present work focuses on the pre formulation studies, formulation, and evaluation of primaquine phosphate tablets prepared by direct compression method. Physicochemical properties, compatibility studies, and optical characterisation of the drug were studied. Tablets were evaluated using pharmacopoeial tests including hardness, friability, weight variation, disintegration, dissolution, assay, and stability studies. The results demonstrated that the prepared formulation complied with standard quality control parameters and showed satisfactory performance. This study highlights the importance of systematic pre formulation and evaluation in developing effective and stable primaquine phosphate tablet formulations.

2.KEYWORDS: Malaria, Primaquine Phosphate, Pre formulation Studies, Direct Compression, Tablet Evaluation, Stability Studies, Storage.

3.INTRODUCTION

It is an endemic vector-borne parasitic disease caused by protozoan parasites of the genus *Plasmodium* in tropical and subtropical regions worldwide. *Plasmodium* consists of over 200 species, infecting mammals, birds, and reptiles, and malaria parasites generally tend to be host-specific. *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale*, and *Plasmodium knowlesi* are the five known species of the genus *Plasmodium* that causes malaria in humans.

Among them, *P. falciparum* is the most pathogenic species that accounts for 60–70% deaths. Malaria parasite completes its life cycle in two different hosts; invertebrate-*Anopheles* mosquitoes, and vertebrate-humans.[1]

SYMPTOMS

The most common early symptoms of malaria are fever, headache and chills. Symptoms usually start within 10–15 days of getting bitten by an infected mosquito. Symptoms may be mild for some people, especially for those who have had a malaria infection before. Some types of malaria can cause severe illness and death. Infants, children under 5 years, pregnant women, travellers and people with HIV or AIDS are at higher risk. Severe symptoms include:

1)extreme tiredness and fatigue

2)impaired consciousness

3)multiple convulsions

4)difficulty breathing

5)dark or bloody urine

6)jaundice (yellowing of the eyes and skin)

7)abnormal bleeding.[2]

ETIOLOGY

Protozoan parasites of the genus Plasmodium originate from photosynthetic protozoa named Dinoflagellates. About 200 different species of protozoa have been identified so far and among them, at least 13 species are known to be pathogenic to humans. Five of the parasites namely P. falciparum, P. vivax, P. malariae, P. ovale (P. ovale curtisi and P. ovale wallikeri), and P. knowlesi are well-known etiologies of malaria in humans.

In Africa, the most prevalent and pathogenic species is P. falciparum. However, malaria infection from most malaria-endemic regions of Africa shows the presence of multiple sympatric species and co-infection within an individual human host or mosquito vector. P. malariae is the species most commonly found in sympatry with P. falciparum in malaria-endemic regions of Africa.

In each endemic area, malaria is transmitted by a specific set of Anopheles species. So far, more than 400 different species of Anopheles mosquitoes have been identified. But only 30 of them are known to transmit malaria. All vectors of malaria undergo the bite between dusk and dawn.

Stability is observed in the distribution pattern of the mosquito species in malaria-endemic regions of the African continent. The complete disappearance of a given vector species from a region is unusual and when the non-indigenous vector is introduced to the area, it is a serious public health concern since it is known to result in devastating epidemics. Indigenous vectors are hard to eradicate with known vector eradication activities.[3]

LIFE CYCLE OF MALARIA

The life cycle of the malaria parasite is a complex process involving an Anopheles mosquito and a vertebrate host. The first stage of the infection is the entrance of the sporozoites in mosquito saliva into the skin and bloodstream of the human host and then, it invades hepatocytes to undergo asexual replication. During this phase (hepatic or pre-erythrocytic phase) the rupture of infected hepatocytes results in the release of thousands of merozoites. In the case of P. vivax and P. ovale infections, some form dormant hypnozoites which remain within hepatocytes for periods of several months, and even as long as 4 years, before developing and multiplying to initiate a new episode of erythrocytic infection.

The erythrocytic infection involves the interaction of the merozoites with the red blood cells (RBC). The merozoites head orients and adjoin with the erythrocytes membrane by deforming the surface host cell. Then, through parasite-induced re organization of the erythrocyte cytoskeleton, the parasite enters the erythrocyte to undergo the second asexual reproduction. While younger erythrocytes are targeted favorably by P. vivax and P. ovale, erythrocytes of any age are invaded by P. falciparum and P. knowlesi. In contrast, P. malariae prefers senescent erythrocytes. After invading RBC, merozoites reproduce into trophozoites and then into schizonts which erupt from the erythrocytes to release merozoites and re invade new RBCs and continue the asexual replication cycle.

The sexual reproduction cycle of malaria starts when a portion of trophozoites matures to male and female sexual progeny or gametocytes. The transmission of the malaria parasite from the mammalian host to the mosquito is mediated by these gametocytes. During the bite of an anopheles mosquito, the matured gametocytes will be taken to the mid gut of the mosquito. Inside the mid gut, gametocytes get converted into fertile gametes and the next stage involves the conversion of zygotes into ookinetes which are motile and invasive. The ookinetes in turn get converted into oocysts in the mid gut basal lamina. The oocyst then matures releasing sporozoites, which migrate to the salivary gland of the mosquito. The parasite is transmitted to another mammalian host through an infected mosquito bite.

PATHOPHYSIOLOGY OF MALARIA

Malaria pathophysiology differs between uncomplicated and severe disease. In uncomplicated malaria, fever results from the rupture of infected red blood cells and the release of merozoites, which stimulate macrophages to produce pro-inflammatory cytokines, especially TNF-α. The fever pattern varies by species: Plasmodium vivax and Plasmodium ovale cause tertian fever (every 48 hours), Plasmodium malariae causes quartan fever (every 72 hours), while Plasmodium falciparum typically produces an irregular fever pattern. Severe malaria is mainly due to cytoadherence, where infected red blood cells bind to vascular endothelium. In P. falciparum, the virulence factor PfEMP1 forms surface "knobs" that mediate adhesion to endothelial receptors, leading to sequestration of infected cells in deep microvasculature. This process contributes to complications such as cerebral malaria. In addition, rosetting (binding of infected to uninfected red blood cells) impairs microcirculation and causes tissue hypoxia. Parasite toxins such as glycosyl phosphatidy linositol (GPI) further stimulate excessive cytokine production, resulting in high fever, endothelial activation, nitric oxide release, tissue damage, and suppression of bone marrow function.[4]

ANTI-MALARIAL AGENTS

Antimalarial medications are a type of antiparasitic chemical agent, often naturally derived, that can be used to treat or prevent malaria. Effective anti-malarial drug treatment reduces malaria transmission. This alone can reduce the incidence and prevalence of malaria, although the effects are greater in areas of low transmission where a greater proportion of the infectious reservoir is symptomatic and receives anti-malarial treatment.[5]

CLASSIFICATION

a. Cinchona Alkaloids:

e.g. Quinine, quinidine

b. 4- Aminoquinolines:

e.g. Chloroquine, amodiaquine.piperaquine

c. 8- Aminoquinolines:

e.g. Primaquine, Pamaquine

d. Quinoline-Methanol:

e.g. Mefloquine

e. Naphthaquinone:

e.g. Atovaqoune

f. Pyrimidines:

e.g. Pyrimithamine, Trimethoprim

g. Sulphones:

e.g. Dapsone, Sulfamethopyrazine

h. Biguanides:

e.g. Proguanil, Chloroproguanil

i. Sesquiterpine Lactone:

e.g. Artemisinin, Artemether

k. Antibiotics:

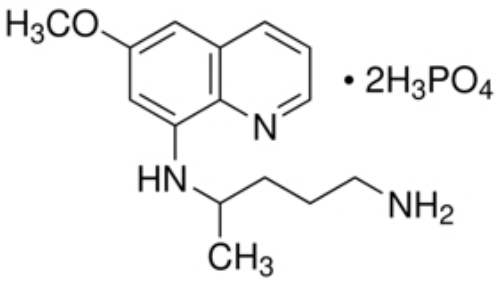
e.g. Tetracycline, doxycycline, clindamycin [6]

PRIMAQUINE PHOSPHATE

Primaquine is an antimalarial drug of the 8- aminoquinoline class. Currently it is the only medication used for radical cure of *Plasmodium vivax* infection. Unfortunately, its use is not without risk. Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency have an increased susceptibility to haemolysis when given primaquine. This potentially fatal clinical syndrome can be avoided if patients are tested for G6PD deficiency and adequately informed before being treated. It is available in the form of oral tablets. [7]

Molecular Formula: $C_{15}H_{21}N_3O \cdot 2H_3PO_4$

Molecular Weight: 259.353 g/ mol



MECHANISM OF ACTION

The mechanism of action of the 8-amino quinolines is unknown, it is known that primaquine can generate reactive oxygen species via an autoxidation of the 8-amino quinoline group with the formation of radical anion. As a result, cell destructive oxidants, such as hydrogen peroxide, super oxide, and hydroxyl radical can be formed.[8]

4.METHODS AND MATERIALS

PRE FORMULATION STUDIES

It is defined as an investigation of physical & chemical properties of drug substance alone and when combined with excipient. Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterised with the goal of designing optimum drug delivery system. [9]

CLASSIFICATION OF PRE-FORMULATION STUDIES OF PRIMAQUINE PHOSPHATE

1) PHYSICOCHEMICAL PROPERTIES:

a) Organoleptic Properties

b) Solubility

c) pka

d) pH

e) Partition coefficient

f) Melting point

2) OPTICAL PROPERTIES:

a) UV-VIS Spectroscopy (λ-Max)

3) COMPATIBILITY STUDIES:

a) Fourier Transmission Infra-Red Spectroscopy(FTIR)

1) PHYSIOCHEMICAL PROPERTIES

a) organoleptic properties:[10]

Organoleptic properties are the sensory characteristics specifically color, odor, taste etc., that are perceived by human senses (sight, smell, taste, touch, and sometimes hearing).

PROPERTIES	DESCRIPTION
Appearance	Orange to Reddish-orange crystalline powder
Taste	Bitter taste
Odour	Odourless
Physical Nature	Crystalline solid

b) solubility:

Solubility, the phenomenon of dissolution of solute in solvent to give a homogenous system, is one of the important parameters to achieve desired concentration of drug in systemic circulation for desired pharmacological response.[11]

Procedure: Solubility data of primaquine were generated by performing solubility studies of the API using the standard shake-flask method in water and compendial buffers of pH 1.0, 1.2, 4.5, 6.8, and 7.5 at 37°C. The experimental studies were carried out according to the Biopharmaceutical Classification System (BCS) guidelines for the determination of API solubility. Around 30mg of primaquine phosphate was added to 3mL of the buffer medium.

According to the pharmacopoeial standards, primaquine is described to be "soluble" in water. A solubility of 66.67mg/mL in water and an intrinsic solubility (–log *S*o) of 2.77± 0.03 at 25°C have been reported. The pH of a 10mg/mL solution was found to be acidic with a pH range of 2.5–3.5.[12]

c) pka:

pka The acid dissociation constant (pKa) is an index of the extent of ionization of a drug at different pH values, and is therefore, an important parameter that reflects Optimization.

pka (Quinoline Ring Nitrogen): 3.2

pka (Terminal aliphatic amine Group): 10.4

d) pH:

pH (potential of hydrogen) is a logarithmic scale from 0 to 14 measuring the acidity or alkalinity of an aqueous solution. A pH of 7 is neutral (e.g., pure water), less than 7 is acidic (higher H^+ concentration), and greater than 7 is alkaline/basic.

The pH of a 10 mg/mL solution was found to be acidic with a pH range of 2.5–3.5.

e) partition coefficient:

When a material is placed in an environment consisting of organic and aqueous phase, it gets distributed into two phases. The relative quantities that get distributed are expressed in the form of ratio known as partition co-efficient.

$$\text{Partition coefficient } (P) = \frac{\text{Concentration of drug in organic phase}}{\text{Concentration of drug in aqueous phase}}$$

Procedure: The partition coefficient of Primaquine between n-octanol & water was determined by slight modification of "Shake Flask Method", at room temperature. Excess amount of API was added in 10ml mixture of n-Octanol and water (1:1). The system was prepared in triplicate and was shaken gently in the separating funnel for 24 hours for achieving equilibrium. Then the two phases were separated and the concentration of API in both phases was determined by UV spectroscopy and partition coefficient was calculated using the equation.[13]

The partition coefficient was found to be 2.2[13]

f) melting point:

The melting point of a solid substance is the temperature at which it changes from a solid state to a liquid state. Experiment Measure Melting Point is a method for measuring the melting points of 'Samples' using the capillary method. The capillary method is a common technique used in laboratories for measuring the melting point of a substance. This method involves placing a small amount of the solid sample into a thin capillary tube and observing the temperature range over which the substance transitions from a solid to a liquid state. [14]

The melting point was found to be < 25 °C [14]

2) OPTICAL PROPERTIES

λ-max:

The analytical technique measures the amount of monochromatic light absorbed by colorless substances in the near UV (200–400 nm) range. The processes required to ascertain the "identity, strength, quality, and purity" of such chemicals are included in the pharmaceutical analysis. It also covers the examination of raw materials and intermediates used in the pharmaceutical production process. [15]

Procedure: To prepare a spectrophotometer sample, it is essential to begin with a suitable specimen that is homogeneous and free from contaminants. Next, prepare the appropriate medium, dissolve and filter to remove any particulates. Additionally, prepare a standard solution to construct a calibration curve. Preparation before measurement: Confirm that the spectrophotometer is in normal working condition for calibration to ensure measurement accuracy. Measure the sample according to the established steps and record the measurement values. Finally, Analyze the measurement results and calculate the sample concentration.[16]

3)COMPATIBILITY STUDIES

Drug-excipient compatibility study is a very much important stage of formulation development of drug products in combination with excipients. It's a significant phase of the pre-formulation study. Drug product not only contains active pharmaceutical ingredient (API) but it's a combination of different forms of excipients. it's important to study the physical and chemical interaction between API and excipient. . [17]

FOURIER TRANSMISSION INFRA-RED SPECTROSCOPY(FTIR)

FT-IR may be used to identify unidentified elements, assess the quality or consistency of a sample, and count the number of ingredients in a combination. Utilizing potassium bromide (KBr) powder, and FT-IR spectra of medication samples was obtained from 400 to 4000 cm−1. The sample (Drug: KBr-5:95) was put into a sample holder before their infrared absorption spectra were taken. Therefore, FT-IR spectra have been investigated for the qualitative identification of drug sample. The drug's infrared spectrum was then measured and contrasted with the industry norm. [18]

PHARMACOKINETIC PROPERTIES OF PRIMAQUINE PHOSPHATE

- **Absorption:** Primaquine is readily and completely absorbed from the GI tract after oral administration.
- **Peak Plasma concentration:** Achieved within 2–3 h of administration.

Distribution: Primaquine is extensively distributed into the tissues and has a mean apparent volume of distribution (Vd) ranging from 200 to 300 L.

- **Metabolism:** CYP1A2 along with CYP2D6 were identified as the main cytochrome P450 isoforms catalyzing the metabolism of primaquine.
- **Elimination Half-life:** lies between 3-8 hrs.
- **Excretion:** Primaquine is predominantly cleared by nonrenal elimination, with only about 1%–4% unchanged drug being excreted in the urine over 24 h.[12]

FORMULATION OF TABLETS

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or moulding methods.

According to the Indian Pharmacopoeia, Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents

ADVANTAGES

- They are easy to carry.
- They are easy to swallow.
- They are attractive in appearance.
- Unpleasant taste can be masked by sugar coating
- An accurate amount of medicament, even if very small, can be incorporated.

DISADVANTAGES

- Difficult to swallow in case of children and unconscious patients.
- Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character.
- Bitter tasting drugs, objectionable odour, or drugs sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression or the tablets may require coating. [19]

TYPES OF FORMULATION OF TABLETS

1. Direct Compression Method.
2. Wet Granulation Method.
3. Dry Granulation Method.

DIRECT COMPRESSION METHOD

Direct compression is the preferred method if powder blend has adequate flow, compactibility, and cohesion with low segregation potential. This is the simplest process that involves the least extent of material handling. Direct compression involves simply mixing the required ingredients and compressing them into tablets on the press. [20]

- Milling
- Weighing
- Sieving
- Blending
- Compression

WET GRANULATION METHOD

Wet granulation is most used process of granulation in pharmaceutical industry during tablet manufacturing. The formulation of granules also helps to reduce segregation and improve the content uniformity of the final product.[21]

Mixing of API (active pharmaceutical ingredient) And excipient

↓

Preparing a damp mass using binder solution

↓

Screening – granulation and drying

↓

Sizing this granulation by dry screening

↓

Lubricant and compression.

DRY GRANULATION METHOD

Dry granulation,is a pharmaceutical manufacturing process used to create granules from powders without the use of a liquid binder or solvent. It's especially beneficial when dealing with moisture-sensitive or heat-sensitive materials.

Material Preparation: Blending of the active pharmaceutical ingredient (API) and excipients to form a homogeneous powder mixture.

Compaction: The powder mixture is then fed into a compaction unit. Here, it's compressed between two counter-rotating rollers. The compression forms compacted ribbons of the material.

Milling: The compacted ribbons are passed through a milling system. This step breaks the ribbons into granules of the desired size.

Final Blend: The granules are then blended with other excipients if needed to create the final tablet formulation.[22]

FORMULATION OF PRIMAQUINE PHOSPHATE TABLET

The marketed Primaquine phosphate Tablet is routinely prepared by Direct compression method, other method are used only in specific situations.

FORMULATION CHART [23]

INGREDIENTS	FORMULA
PRIMAQUINE PHOSPHATE	15 mg
CARNAUBA WAX	0.1-58 mg
LACTOSE, UNSPECIFIED FORM	60-90 mg
MAGNESIUM STEARATE	0.75-3 mg
POLYETHYLENE GLYCOL 400	3-7.5 mg

POLYSORBATE 80	0.1-2 mg
FERRIC OXIDE RED	qs
TALC	1.5-7.5 mgmg
TITANIUM DIOXIDE	qs
HYPROMELLOSE 2910	3-7.5 mgmg
STARCH, CORN	7.5-15 mg

EQUIPMENT

- Analytical balance
- sieve/mill
- V-blender
- tablet press
- film-coater
- de-duster
- packaging machine.

PROCEDURE

i. Sieve API and excipients through appropriate mesh (e.g., #30–#40) to break lumps and ensure uniform particle size.

ii. Pre-blend the API with diluent and superdisintegrant in a tumble blender for an empirically determined time (e.g., 5–10 minutes at lab scale) to ensure uniform distribution. (Use validated blending time to avoid segregation.)

iii. Add glidant (colloidal silica) and blend briefly (1–2 minutes).

iv. Add lubricant (magnesium stearate) last and blend gently for a short time (e.g., 1–2 minutes) to avoid over-lubrication which reduces tablet hardness and dissolution.

v. Compression: Compress the blend using appropriate tooling to target tablet weight and hardness. Monitor tablet weight, thickness and hardness during compression. Adjust compression force to obtain desired hardness.

vi. In-process checks: Check weight variation (20 tablets), hardness (10 tablets), friability (sample), and disintegration (3 tablets) at regular intervals. [24]

EVALUATION OF TABLET

The compendia, such as the United States Pharmacopeia (USP), and the regulatory bodies, such as the United States Food and Drug Administration (FDA), in addition to historic

product-development experience, inform the desired quality attributes of the tablets. Tablets are usually tested for the following characteristics:[25]

TYPES OF EVALUATION

►PHYSICAL EVALUATION

- Appearance
- size and shape
- Hardness test
- weight variation test
- Friability Test
- Thickness Test

►CHEMICAL EVALUATION

- Assay
- content uniformity Test

►PHARMACEUTICAL EVALUATION

- Dissolution Test
- Disintegration Test

PHYSICAL EVALUATION

►APPEARANCE

Appearance is the first most required quality for the acceptance of tablet. General elegance and its identity play a major role for the consumer acceptance. Acceptance of the appearance of batches of the tablet has been done based on the measurement of the following factors like size, color, shape, presence or absence of odor, taste etc.

►SIZE AND SHAPE

Size and shape of a tablet has been determined by its thickness. Size and shape of table plays an important role in its patient compliance as the size of the tablet increases it is not much easier for its administration. Micrometer is the devise which is used to determine the thickness of a tablet. It can be acceptable if the batch falls within the ±5% of standard deviation.[26]

►HARDNESS TEST

Hardness Test is the most important feature for assessing tablet in the study it was found that Tablet passed the test of tablet crushing strength or hardness both these brand have acceptable crushing strength of Between 5Kg/Cm^2 to 10kg/ Cm^2This test done from Pfizer Test machine [27]

►WEIGHT VARIATION TEST

20 Tablets of all the batches were collected randomly during compression and weight of individual tablet was carried out. Limit: Weight of all individual tablets should be in the limit of Average wt ± 7.5%. Average weight was carried out by calculating the total wt. of 20 tablets (individually weighed) and dividing this value by 20.

►FRIABILITY TEST

Roche friabilator is the equipment which is used for the determination of friability. It is expressed in percentage. Note down the initial weight of the tablets individually (W initial). Tablets are placed ina plastic chamber which revolves at 25 rpm and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (W final) and observe any weight difference before tablet and after the friabilator processing .Limits: loss in weight less than 0.5 to 1% of the initial weight of the tablet should be considered as acceptable limits. Percentage of friability is calculated as:

F={(W initial)- (W final)/ (W initial)}×100. [28]

►THICKNESS TEST

The most commonly used instrument to measure tablet thickness is the vernier calliper.

The vernier calliper gives reading in millimetres and it is available both in digital display and manual reading.

To measure the tablet thickness simply place the tablet in between the jaws and slide the scale jaw to press the tablet against the stationary jaw.

The reading on the display is noted and it is the actual thickness of the tablet. [29]

CHEMICAL EVALUATION

►ASSAY OF TABLET

This test measures the exact amount of active drug in the tablet. It ensures the tablet contains the same amount of medicine as stated on the label.

Principle: Measures the actual amount of active pharmaceutical ingredient (API).

Procedure:

- Prepare sample and standard solutions.
- Analyze using titration, spectrophotometry, or HPLC.
- Calculate API content. [30]

►CONTENT UNIFORMITY TEST

Initially weigh the tablet and then powder it. Now the powdered tablet is transferred into a 100 ml volumetric flask and adds 0.1 N HCl up to mark. Now filter the solution and discard first few ml of filtrate. Take 10 ml of filtrate should be taken into a 50 ml volumetric flask and add 0.1 N HCl up to the mark and analysed spectrophotometrically at 274 nm and 234.5 nm. The concentration of the content of the drug (µg/ml) was calculated by using the standard calibration curve of the respective drug.

Drug content is calculated by using the below formula:

Concentration of the drug in (µg/ml) × 100 × 50/10 × 1000 [27]

PHARMACEUTICAL EVALUATION

►DISINTEGRATION TEST

Disintegration of tablets is evaluated to ensure that the tablet dissolves or breaks apart into smaller particles or granules on contact with water under agitation. This allows the DS to dissolve from its primary particles, being fully available for dissolution and absorption from the GI tract. Tablet dis-integration is evaluated in a standardized apparatus that subjects six tablets to a defined mechanical stress in individual reciprocating cylinders in a suitable aqueous medium at 37°C, to reflect the conditions on oral inges-tion. The time it takes for the last of six tablets to disintegrate into smaller particles and disappear from the reciprocating cylinders is called disintegration time. The disintegration media required varies depending on the type of tablets to be tested. The disintegration time is generally not more than 15 min for IR tablets.The disintegration test is used as a control for tablets intended to be admin-istered by mouth, but not for the tablets intended to be chewable and SR.[25]

►DISSOLUTION TEST

As drug absorption and physiological availability depend on having the DS in the dissolved state at the site of absorption, dissolution, also termed drug release, is an important property of tablets. The rate and extent of dissolution of a drug are tested *in vitro* by a suitable dissolution test. Dissolution is used as both a quality control tool to ensure batch-to-batch and

tablet-to-tablet uniformity in drug-release characteristics of the tab-lets and sometimes also as a tool for *in vitro–in vivo* correlation (IVIVC) of drug release (*in vitro*) and drug absorption (*in vivo*). Dissolution test provides a means of control in ensuring that a given tablet formulation is similar with respect to the rate and extent of drug release as the batch of tablets

STABILITY STUDIES OF TABLET

Stability studies of pharmaceutical products may be expressed as the time during which the pharmaceutical products retain its physical, chemical, microbiological, pharmacokinetic properties and characteristics throughout the shelf life from the time of manufacture. Shelf life of the product can be defined as the substance reduces to 90% of its original concentration. Shelf life is a technical term used to denote the stability of the product and it is expressed as expiry date. Expiration varies for each pharmaceutical preparations.

IMPORTANCE OF STABILITY STUDIES

Product instability of active drug may lead to under medication due to the lowering of the drug in dosage form.

- During the decomposition of the drug or product it may lead to toxic products.
- During the marketing from one place to another during the transportation the drug has the compatibility to change its physical properties.
- Instability may be due to changing in physical appearance through the principles of kinetics are used in predicting the stability of drug.

TYPES OF STABILITY STUDIES ON DRUG SUBSTANCES

A comprehensive pharmacopoeial protocol (USP) prescribes the criteria for acceptable levels of physical, chemical, microbiological, therapeutic and toxicological stability studies.

Physical stability

The original physical properties such as appearance, colour, dissolution, palatability, suspendability are retained. The physical stability may affect the uniformity and release rate, hence it is important for the efficacy and safety of the product.

Chemical stability

It is the tendency to resist its change or decomposition due to the reactions that occur due to air, atmosphere, temperature, etc.

Microbiological stability

The microbiological stability of the drugs is the tendency to resistance to the sterility and

microbial growth. The antimicrobial agents used in the preparation retain the effectiveness within specified limits. This microbiological instability could be hazardous to the sterile drug product.

Therapeutic stability

The therapeutic effect (Drug Action) remains unchanged.

Toxicological stability

Toxicological stability has no significant increase in the toxicity occurs.

STABILITY TESTING METHODS

Stability testing is a procedure performed for all the pharmaceutical products at various stages of the product development. In the early stages, the stability testing is performed by the accelerated stability studies which mainly are performed at high temperature\ humidity.

TYPES OF STABILITY TESTING

- Long-Time stability testing - 25^{O}C/60% RH or 30^{O}C/65%RH for 12 months
- Intermediate stability Testing – 30±2^{O}C and 65±5% RH for 6 months
- Accelerated Stability Testing - 40^{O}C/75% RH for 6 months[31]

PACKAGING,STORAGE,LABELLING

PACKAGING

Packaging in the pharmaceutical industry varies from drug to drug and normally there are three levels of packaging commonly referred to as the primary, secondary, and tertiary packaging.

1. Primary packaging system is the material that first envelops the product and holds it i.e., those package components and subcomponents that actually come in contact with the product, or those that may have a direct effect on the product shelf-life e.g., ampoules and vials, prefilled syringes, IV containers, blister packs, etc.

2. Secondary packaging system is outside the primary packaging and used to group primary packages together e.g., cartons, boxes, shipping containers, injection trays, etc.

3. Tertiary packaging system is used for bulk handling and shipping e.g., barrel, container, edge protectors, etc.

TYPES OF PACKAGING MACHINE

- Strip Packing Machine

 Blister Packaging Machines

 Aluminium foil packaging machine

 Fill & Sealing Machine

TYPES OF PACKAGING

►STRIP PACKAGING

Strip packaging is a method in which drugs, whether in tablet or capsule form, are enclosed in a continuous strip of flexible material. The strip is usually made of plastic or aluminum and protects the drugs from elements, ensuring their high efficacy.

►BLISTER PACKAGING

Blister packaging consists of a pre-formed plastic cavity or blister bonded to a lidding material that contains single-unit doses. The product is easy to see, and you can also ensure proper protection from heat and moisture.

►BOTTLE PACKAGING

Bottles are often made of glass and plastic (polyethylene or polypropylene) and are used to securely hold tablets and capsules. They can also feature childproof safety mechanisms and are amber-colored to protect light-sensitive medications from degradation or other chemical reactions.[32]

LABELLING

LABEL - label means a display of written, printed or graphic matter upon immediate container or the wrapper of a drug package.

TYPES OF LABEL

►MANUFACTURER LABEL

A label which contains drug information for the use of medical practitioners, pharmacists, or nurses supplied by the manufacturer, packer, or distributor of the drug (FDA).

LEGAL REQUIREMENTS OF A MANUFACTURER LABEL

- The name of preparation
- Strength and dosage form
- Quantity
- Instructions for the use
- Precautions & warnings
- Registration number

- Batch number
- Manufacturing & Expiry date
- Price
- The name and address of pharmaceutical industry

►DISPENSING LABEL

Dispensing label is defined as the label used for dispensing, bearing the name and address of the supplier, the nature of the medicine and any other prescribed directions, the name of patient and the date of dispensing.[33]

STORAGE

Primaquine phosphate Tablets are supplied as pink, convex, discoid, film-coated tablets of 26.3 mg (= 15 mg base), printed with a "W" and "P97" on one side.

Available in bottles of 100 tablets.

Store at 25° C (77° F); excursions permitted to 15° C – 30° C (59° F – 86° F) [see USP Controlled Room Temperature]

It can be exposed to temperatures between 59 F and 86 F (15 C and 30 C) for shorter periods of time, such as when transporting it.

Dispense in tight, light-resistant container as defined in the USP/NF.[34]

6.RESULT AND DISCUSSION

Results:

The physicochemical properties of primaquine phosphate were found to be suitable for tablet formulation with good solubility. UV analysis confirmed the λmax and linear calibration, while FTIR studies showed no drug–excipient interaction. The tablets made by direct compression were of uniform weight, thickness and appearance. The hardness and friability were within limits, disintegration was rapid and dissolution showed satisfactory drug release.

Assay and content uniformity complied with pharmacopoeia standards. Stability studies did not show any significant changes under storage conditions.

DISCUSSION

The drug properties made it suitable for direct compression. The evaluation parameters revealed that the tablets complied with the quality standards of immediate release dosage forms. The fast drug release and stable profile indicate the effectiveness of formulation for the treatment of malaria.

7.CONCLUSION

The study successfully formulated and evaluated primaquine phosphate tablets using direct compression method.

Preformulation studies guided the selection of suitable excipients and method.

The prepared tablets satisfied all quality control parameters and remained stable under different storage conditions.

This formulation can be effectively used for the treatment and radical cure of malaria.

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9.REFERENCE

1. Fikadu M, Ashenafi E. Malaria: An overview. *Malaria Journal*. 2023;16:333947.
2. World Health Organization. Malaria. 2024. Available from: https://www.who.int
3. Buchanan HD, Goodman CD, McFadden GI. Roles of the apicoplast across the life cycles of rodent and human malaria parasites. *J Eukaryot Microbiol*. 2022;69(6).
4. Tuteja R. Malaria—an overview. *FEBS J*. 2007;274(18):4670–4679.
5. White NJ. The role of anti-malarial drugs in eliminating malaria. *Malar J*. 2008;7(S1).
6. Tripathi KD. *Essentials of Medical Pharmacology*. 7th ed. New Delhi: Jaypee Brothers Medical Publishers; 2013. p. 816–817.
7. Recht J, Ashley E, White N. Safety of 8-aminoquinoline antimalarial medicines. 2014.
8. Camarda G, Jirawatcharadech P, Priestley RS, Saif A, March S, Wong MHL, et al. Antimalarial activity of primaquine operates via a two-step biochemical relay. *Nat Commun*. 2019;10(1):1–9.

9. Boreddy S. Preformulation. 2026. Available from: https://www.slideshare.net
10. Primaquine diphosphate: Comprehensive profile. *Profiles Drug Subst Excip Relat Methodol*. 2005;153–208.
11. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: importance and enhancement techniques. *ISRN Pharm*. 2012;2012:195727.
12. Nair A, Abrahamsson B, Barends DM, Groot DW, Kopp S, Polli JE, et al. Biowaiver monographs for immediate-release solid oral dosage forms: primaquine phosphate. *J Pharm Sci*. 2012;101(3):936–945.
13. OECD. Test No.107: Partition coefficient (n-octanol/water): shake flask method. OECD Guidelines; 1995.
14. Experiment measure melting point documentation. 2024. Available from: https://www.emeraldcloudlab.com
15. Shabbir SW, Chauhan S. A review on use of ultraviolet spectroscopy. *Innovare J Med Sci*. 2024;12(4):5–11.
16. Zhang X, Li Y, Kumar P, Singh R. Ultraviolet-visible spectroscopic analysis of pharmaceutical compounds. *Adv Pharm Anal*. 2025;12:23761.
17. Shinde DV. Drug-excipient compatibility study. 2020. Available from: https://veeprho.com
18. Sharma P, Tailang M. Primaquine-loaded transdermal patch for treating malaria. *Future J Pharm Sci*. 2022;8:43.
19. Ubhe T, et al. A brief overview on tablet and its types. 2020;1:21–31.
20. Leveraging direct compression technology to improve tableting efficiency. 2021. Available from: https://www.americanpharmaceuticalreview.com
21. Zarekar SG, Raykar SD, Zende GS, Puranik AK, Ingle SJ. A review on the wet granulation technique. *World J Biol Pharm Health Sci*. 2024;20(2):113–124.
22. Understanding dry granulation in pharmaceutical manufacturing. 2023. Available from: https://kevin.in
23. DailyMed. Primaquine phosphate tablet, film coated. 2026. Available from: https://dailymed.nlm.nih.gov
24. Ashwini M, Barde C, Akshay M, Gadhari R. Formulation and development of immediate-release tablet of chloroquine. Available from: https://ijirt.org
25. Evaluation of tablets. Available from: https://www.pharmacy180.com
26. Kushwaha N, Jain A, Jain PK, Khare B, Jat YS. Overview on formulation and evaluation aspects of tablets. *Asian J Dent Health Sci*. 2022;2(4):35–39.

27. Jadhav B, Dhas R, Shaikh ST. Evaluation of the general marketed tablet. *Int J Pharm Sci*. 2024;2(2):176–183.
28. Prashar D. Formulation and evaluation aspects of tablets—an overview. 2012. Available from: https://www.academia.edu
29. Ahmad S. Thickness test for tablets. 2022. Available from: https://www.pharmainform.com
30. Coffie A. Standard pharmacopoeial tests performed on tablets. 2025.
31. Aashigari S, Ramya G, Sneha S, Vykuntam U, Potnuri N. Stability studies of pharmaceutical products. *World J Pharm Res*. 2019;8:479–492.
32. Types of tablet packing machines. Available from: https://www.lfatabletpresses.com
33. Hameed K. Pharmaceutical labelling. 2015. Available from: https://www.slideshare.net
34. Primaquine phosphate tablets, USP. 2026. Available from: https://www.accessdata.fda.gov