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## FORMULATION & EVALUATION OF KETOCONAZOLE SHAMPOO

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### ABSTRACT

Shampoo is a hair care product that is used for cleansing of hair and nourishing them and making them protective against outer environment. It removes oil, dirt, dandruff and other particles. So basically ketoconazole shampoo helps for the treatment of dandruff and fungus in the scalp which is also called as seborrheic dermatitis. So we have made 1 formulation and compared with the marketed formulation danfree shampoo which is marketed by cipla. With comparison with that product our product shows similar results obtained by marketed product. So we can say our product got satisfactory results and also we have compared the results obtained with available parameters, Basically the ketoconazole shampoo we examined by checking its PH, viscosity, appearance, foam ability and foam stability, surface tension measurement, stability studies, Wetting time, percentage of solid content etc. and the shampoo has been formulated using ingredients like ketoconazole [API], PVP, Sodium metabisulfite, Sodium lauryl sulphate, Stearic acid, Methyl cellulose, EDTA, sodium hydroxide, amaranth color and water. more specifically the product we formulated is sulphate free.

**Keywords:** Introduction, Ketoconazole Study, Formulation, Evaluation Test, Result.

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### I. INTRODUCTION

Shampoo is a hair care product used for cleansing of hair, removing dirt, making them strong and nourishing they are applied on the scalp and should be rinsed out after sometime. It is in the form of a viscous liquid. Hair is a key component of human beauty. Throughout the beginning of time, people have used herbs for cleansing, beautifying, and controlling hair. Use of synthetic substances has increased over time, but people are now becoming more aware of their serious negative effects, including eye and scalp irritation, hair loss, and dryness of the hair. Some areas drew people to use herbal products since they are safer, less expensive, and have few negative effects. This in turn increased customer demand. Most popular hair care product is shampoo. It can be used to clean the hair and scalp of dirt, dandruff, previously applied hair styling product residue, and environmental pollutants<sup>1</sup>. It comes in viscous liquid form. Hair cleansers, often known as shampoos, are used not only to clean the hair but also to add gloss, keep the hair manageable and oily, and occasionally get rid of dandruff. The most prevalent dermatological skin concern relating to the scalp, dandruff is a non-inflammatory, chronic disorder that is evident by an enormous range of scalp tissue being impacted<sup>3</sup>. Although the primary cause of dandruff cannot be seen clearly, there are other contributing causes, including an oily scalp and poor hygiene that might result in a fungal infection and it appears more often if the hair is not washed for a week. Dandruff is known to be controlled by fungistatic ingredients in anti-dandruff shampoos. *Malassezia furfur* is a typical lipophilic, saprophytic yeast that grows on the face, scalp, and upper trunk of humans. This unicellular fungus known as tinea versicolor, seborrheic dermatitis, folliculitis, and atopic dermatitis is linked to several skin conditions that primarily affect the top layers of the skin<sup>4</sup>. A severe condition of the stratum corneum of the scalp, dandruff is characterized by hyperproliferative cells that cause swelling, itching, and redness. Seborrheic dermatitis has a similar clinical appearance and symptoms but is more severe. Lipophilic yeast *Malassezia furfur* absorbs Free Fatty Acids (FFAs) from sebaceous triglycerides, which causes the symptoms to appear. The stratum corneum is breached by the FFAs, which also cause trans-epidermal water loss that is ascribed to dandruff. The use of topical antifungal medications or other items is a part of treating dandruff. Recurrences are common, thus prophylaxis with skin and hair treatments is necessary to maintain healthy skin and a youthful appearance. Today's market offers a variety of anti-dandruff shampoos, including synthetic, herbal, medicated, and non-medicated shampoos. The most well-known herbal anti-dandruff shampoos are those that give the idea of being purer, safer, and more effective. Since no surfactants are used during the preparation of herbal anti-dandruff shampoos, they are free from side effects, have good stability, and are less toxic than synthetic shampoo<sup>6</sup>. Surfactants found in synthetic shampoo have the potential to cause major side effects like scalp itchiness, hair loss, drying of hair, greying of hair, split ends, and eye irritation. Due to their

negligible negative effects and low cost, herbal cosmetics are attracting large populations for these reasons<sup>7</sup>. Herbal shampoo is viewed as an alternative to synthetic shampoo, however, creating cosmetics from entirely natural ingredients is challenging. the manufacture of shampoo frequently uses a variety of medicinal plants, many of which have been identified in the literature to have positive benefits on hair.

Be simple or plain shampoo, antibacterial or anti-dandruff shampoo, or nutritional shampoo including vitamins, amino acids, and proteins hydrolysate, depending on the nature of the contents<sup>8</sup>. Plant products can be employed in a variety of forms, including powdered form, crude form, returned extracts, or derivative forms<sup>9</sup>. Developing herbal anti-dandruff shampoo from a single natural component that is milder and safer than synthetic therapies while still competing favorably with their foaming, detergency, and solid content is rather difficult. To combat dandruff, wash our hair, and work as a conditioning agent without harming or damaging our hair; we thought about creating a pure herbal anti-dandruff shampoo Dandruff is a common scalp disorder affecting almost half of the population at the pre- pubertal age and of any gender and ethnicity. No population in any geographical region would have passed through freely without being affected by dandruff at some stage in their life. The word dandruff (dandruff, dandriffe) is of Anglo-Saxon origin, a combination of 'tan' meaning 'tetter' and 'drof meaning 'dirty'. Dandruff affects aesthetic value and often causes itching. It has been well established that keratinocytes play a key role in the expression and generation of immunological reactions during dandruff formation. The severity of dandruff may fluctuate Dandruff is a common scalp condition that occurs when dead skin is shed, producing irritating white flakes and possibly an itchy scalp. Ordinarily, dandruff results from excessive drying of skin and over. Any substance which destroys or prevents the growth of fungi. It is one of the antibiotic groups. There are several classes of antifungal drugs: Polyenes, which cause an increase in fungal cell wall permeability leading to its death. Examples: amphotericin B, natamycin, nystatin. Azoles, which act either by inhibiting the synthesis of ergosterol, a component of fungal cell wall or by causing direct wall damage. Examples: clotrimazole, econazole, fluconazole, itraconazole, ketoconazole, miconazole. Pyrimidines, which interfere with the normal function of fungal cells. Example: flucytosine. Syn antimycotic agent,

## II. CLASSIFICATION OF SHAMPOO

### 1. Based on Appearance

Powder shampoo, Liquid shampoo or lotion shampoo, Gel shampoo or Solid shampoo, Oil shampoo, Cream shampoo.

### 2. Based on Use or Function

Conditioning shampoo, Antidandruff shampoo, Therapeutic shampoo Balancing shampoo, Baby shampoo [ 2- 4]

Dandruff is a skin condition that mainly affects the scalp. Symptoms include flaking and sometimes mild itchiness. A more severe form of the condition, which includes inflammation of the skin, is known as seborrhoeic dermatitis.<sup>[5]</sup>

## III. FACTORS THAT CAUSES DANDRUFF

### 1. Skin oil, commonly referred to as sebum or sebaceous secretions

### 2. The metabolic by-products of skin micro-organisms (most specifically Malassezia yeasts)

### 3. Individual susceptibility and allergy sensitivity

#### 1. Scalp conditions

#### 2. Yeast overgrowth

#### 3. Less shampooing

#### 4. Underlying medical conditions

#### 5. Allergy<sup>[6]</sup>.

An antifungal medication, also known as an antimycotic medication, is a pharmaceutical fungicide or fungistatic used to treat and prevent mycosis such as athlete's foot, ringworm, candidiasis, serious systemic infections such as cryptococcal meningitis, and others.

Ketoconazole is antifungal of azole group, it is a imidazole derivative of antifungal agent<sup>[7]</sup>

**DESCRIPTION**

Ketoconazole Shampoo, 2% is a red-orange liquid for topical application, containing the broad spectrum synthetic antifungal agent ketoconazole in a concentration of 2% in an aqueous suspension. It also contains: coconut fatty acid diethanolamide, disodium laureth sulfosuccinate, FD & C Red No. 40, hydrochloric acid, imidurea, laurdimonium hydroxypropyl hydrolyzed collagen, PEG-120 methyl glucose dioleate, purified water, sodium chloride, sodium hydroxide, and sodium lauryl ether sulfate. Ketoconazole is cis-1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy] phenyl]piperazine and has the following structural formula:

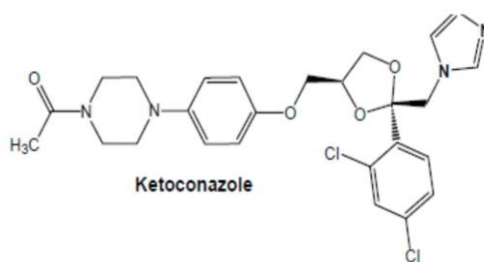


Figure 1

**IV. AIM & OBJECTIVE**

To develop a Ketoconazole Herbal Shampoo that combines the antifungal efficacy of ketoconazole with the natural benefits of herbal extracts for hair and scalp health.

Objectives:

1. Formulation Development:

- Identify and select suitable herbal extracts known for their scalp-nourishing and antimicrobial properties, such as aloe vera, tea tree oil, neem,
- Optimize the formulation to ensure compatibility and stability of ketoconazole with herbal extracts in a
- Achieve an appealing fragrance and aesthetic appearance while maintaining therapeutic efficacy.

2. Evaluation :

- Conduct in vitro studies to assess the antifungal activity of the shampoo against fungal strains commonly associated with scalp conditions like dandruff and seborrheic dermatitis.

3. Safety and Compatibility Testing:

- Evaluate the compatibility of the shampoo with different hair types and assess any potential side effects or allergic reactions.

4. Formulation Optimization:

- Fine-tune the formulation based on feedback from clinical trials and user studies to enhance efficacy and user satisfaction
- Ensure the shampoo is easy to rinse off, leaves hair manageable, and does not cause scalp dryness or irritation.

By focusing on these aims and objectives, the formulation and evaluation of the Ketoconazole is done

• **Need of Study**

Studying the formulation and evaluation of ketoconazole shampoo is important for several reasons:

1. **Therapeutic Efficacy:** Understanding how different formulations affect the therapeutic efficacy of ketoconazole is crucial. This includes studying factors like ketoconazole concentration, pH balance, and the presence of other active ingredients that can enhance its antifungal properties.
2. **Safety and Tolerability:** Evaluating the formulation helps ensure that the shampoo is safe for use on the scalp and doesn't cause irritation or other adverse effects. This involves testing for skin irritation, sensitization, and overall dermatological safety.

3. Stability: Shampoo formulations must be stable over time to maintain their efficacy and appearance. Stability studies are necessary to determine the shelf life and storage conditions required for the product.

4. Consumer Acceptance: Formulation studies often include consumer testing to assess factors like fragrance, texture, and ease of use, which can impact user satisfaction and compliance.

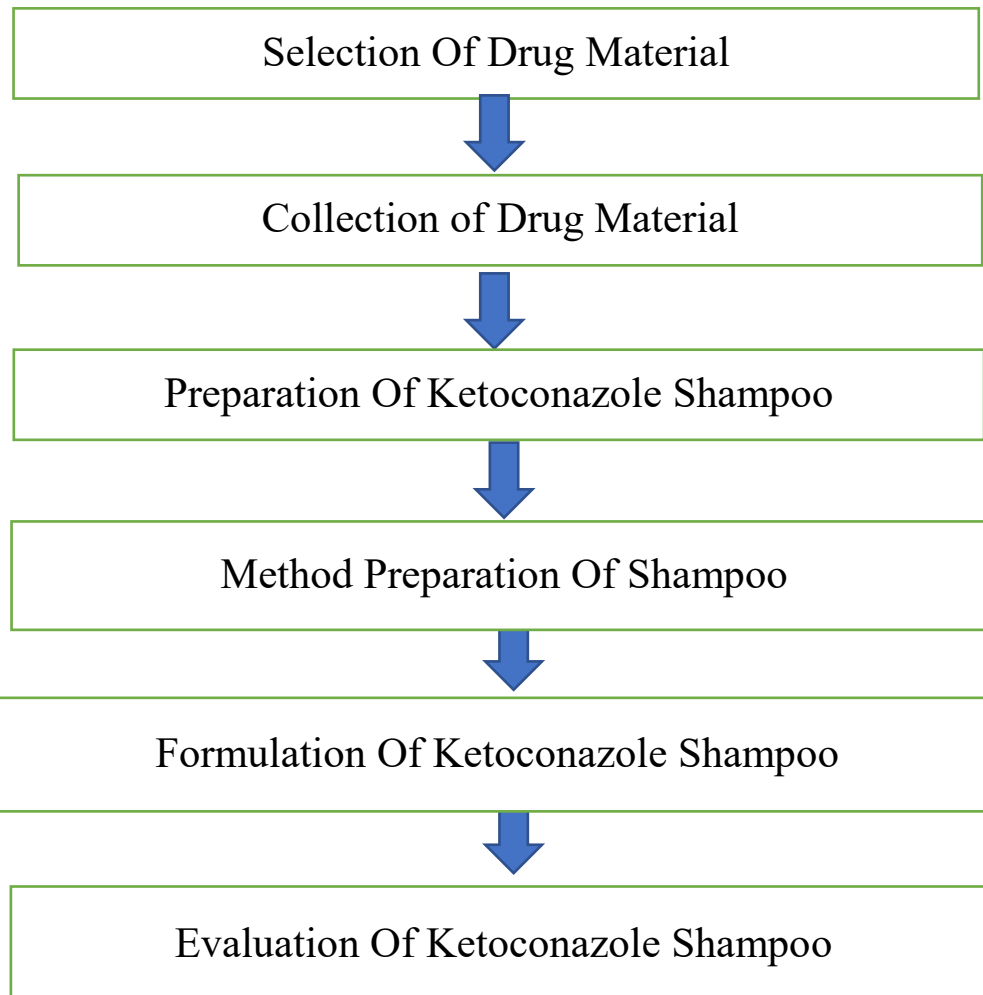
5. Comparative Studies: Comparing different formulations allows researchers to identify the optimal combination of ingredients and properties that maximize ketoconazole's effectiveness against fungal infections like dandruff (seborrheic dermatitis).

6. Regulatory Compliance: Formulation studies ensure that the shampoo meets regulatory standards for pharmaceutical or cosmetic products, depending on the intended use and claims made.

Overall, thorough study and evaluation of ketoconazole shampoo formulations are essential to develop a product that is effective, safe, stable, and well-received by consumers.

- **Plan of Work**

Creating a plan of work for formulating and evaluating a Ketoconazole Herbal Shampoo involves several key steps to ensure systematic development and thorough evaluation. Here's a structured



- **Formulation**

Materials used:

Digital balance [ Wensar weighing scales Ltd] ,

Humidity chamber[Humidity chamber],

Brookfield viscometer [Brookfield] . [8]

## V. METHOD

Firstly methyl cellulose to be taken which is used as a thickener and heating them by mixing it with deionised water , then it should be mixed with sodium lauryl sulphate stearic acid with the above solution. Then to the above solution sodium meta bisulfide were added ,finally API Ketoconazole drug is mixed with above prepared solution, then the solution were allowed to cool for sometime at room temperature ,after that remaining ingredients i.e., EDTA, PVP, Fragnance, colourant were added. To balance the P<sup>H</sup> sodium hydroxide was added, finally water was added to make upto 100ml.

**Table 1:** Formulation composition of respective ketoconazole shampoo

INGREDIENTS	F1	M1
Ketoconazole	1gm	COMOPARISIO N WITH THE MARKETED FORMULATION
PVP	5g	
Sodium metabisulfite	0.1g	
Sodium lauryl sulphate	40g	
Stearic acid	1.25g	
Methyl cellulose	0.9g	DANFREE SHAMPOO MARKETED BY CIPLA
EDTA	0.1g	
Sodium hydroxide	0.5g	
Rose water	1ml	
Amaranth colour	0.3ml	
Water	Qs	

### • Evaluation

#### EVALUATION OF KETOCONAZOLE SHAMPOO

##### 1. ORGANOLEPTIC PROPERTIES:

- i) colour: pink
- ii) Fragrance: sweet
- iii) Clarity: No greedy particle present
- iv) Physical appearance :No aggregates

##### 2. P<sup>H</sup> DETERMINATION:

The ph of formulated anti-dandruff shampoo was determined using ph paper. Required amount of shampoo was added to 10ml of distilled water in this solution PH paper was dipped and colour change was noted<sup>[9]</sup>

##### 3. DETERMINATION OF PERCENT OF SOLIDS:

Clean dry evaporating dish were taken & 4gms of shampoo was added ,& then dish was kept on hot plate to evaporate the liquid solution. after that solid contents were weighed & percent of solid were calculated A good shampoo will be between 20 -30% solids <sup>[9]</sup>

##### 4. DIRT DISPERSION:

2 drops of shampoo were added to the test tube which was containing 10ml of distilled water, to this 1 drop of indian ink were added & shaken for ten times. Amount of ink in the foam was noted Shampoo that causes the ink to concentrate in the foam is considered as of poor quality, the dirt should stay in water. The amount of ink in the foam was indicated by the rubric such as none, moderate, light or heavy<sup>[9]</sup>

##### 5. FOAM ABILITY & FOAM STABILITY:

Foam ability was determined using cylinder shake method. Briefly, 50 mL of the 1% commercial or formulated shampoo solution was placed into a 250 mL graduated cylinder; it was covered with one hand and shaken 10

times. The total volume of the foam content after 1 min of shaking was recorded. Foam stability was evaluated by recording the foam volume after 1 min and 4 min of shake test<sup>(9)</sup>

5. VISCOSITY MEASUREMENT:

Viscosity was measured by using Brookfield visometer<sup>9)</sup>

6. SURFACE TENSION MEASUREMENT:

It is measured using stalagnometer, 10% (10ml of shampoo in 100ml of distilled water) of shampoo solution was prepared thoroughly cleaned the stalagnometer with chronic acid & purified water (because surface tension is highly affected with grease & other lubricants)

Data was calculated by the following equation<sup>(9)</sup>

$$R_2 = \frac{(W_3 - W_1) n_1}{(W_2 - W_1) n_2} \times R_1$$

Where,

W1=Weight of empty beaker

W2=Weight of beaker with distilled water

W3=Weight of beaker with shampoo solution

n1= number of drops of distilled water

n2= number of drops of shampoo solution

R1= surface tension of distilled water

R2= surface tension of shampoo solution

7. WETTING TIME DETERMINATION:

The canvas paper was cut into 1-inch diameter discs having an average weight of 0.44g. The smooth surface of disc was placed on the surface of 1% shampoo solution & the stop watch started. The time required for the disc to begin to sink was noted as wetting time.<sup>(9)</sup>

8. STABILITY STUDIES:

Stability studies is performed to check physical & chemical integrity of the formulation. The thermal stability of the formulated product studied by placing them in glass tubes in humidity chamber at accelerated 40 +/- 2°C/60 +/- 5%Rh, at room temperature 25 +/- 2°C/75 +/- 5%Rh. the sample kept for stability was evaluated for their appearance, physical stability for a period of 1 month. <sup>(10)</sup>

**VI. RESULT AND DISCUSSION**

VALUES OF FORMULATED PRODUCT

1 Organoleptic properties

<i>Colour</i>	<i>Odour</i>	<i>Appearance</i>
Pink	Sweet	No aggregates

VALUES OF MARKETED PRODUCT

1 Organoleptic properties

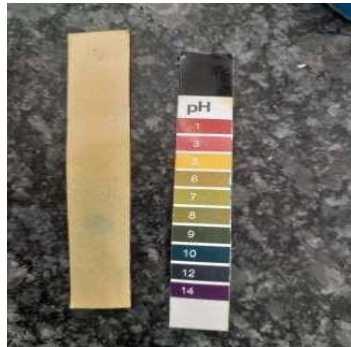
<i>S.no</i>	<i>Parameter</i>	<i>Drug</i>
1	Colour	White
2	Odour	Sweet
3	Clarity	No greedy particles were present



2. Ph Determination

**Table 3:** pH of Ketoconazole shampoo

F1	M1
6.5 ± 0.2	5.5 ± 0.2



3. DETERMINATION OF PERCENT OF SOLIDS

**Table 4:** determination of percent of solids

F1	M1
22 %	21 %

Distilled water to which 1 drop of indian ink was added. Amount of ink in the foam was noted as none. In formulated and marketed product none of them shows dirt.

5 Viscosity measurement:

The viscosity evaluated for the prepared formulation was found to be 30,750cps

6. FOAM ABILITY & FOAM STABILITY:



It is determined by using cylinder shake method

**Table 5:** Foam ability and stability

F1	M1
70ml after 1mins	108ml after 1mins

7. SURFACE TENSION MEASUREMENT

**Table 6:** surface tension measurement

F1	M1
5.01dynes/cm	4.273dynes/cm

8. WETTING TIME DETERMINATION

**Table 7:** Wetting Time Determination

F1	M1
30 Secs	45secs



9. Solubility studies of ketoconazole :

**Table 8:** Solubility of ketoconazole drug

Solvent	Solubility
Water	Slightly soluble
Ethanol	Soluble
Dimethyl formamide(DMF).	Soluble

10. STABILITY STUDIES:

**Table 9:** stability studies

S.no	Duration	PH		Visual appearance		Wetting time(secs)		Foam ability	
		25±2°C/ 65±5% RH	40± 2°C/75% +5%RH	25±2°C/ 65±5% RH	40± 2°C/75%+ -5%RH	25±2°C/ 65±5% RH	40± 2°C/75% +5%RH	25±2°C /65±5% RH	40± 2°C/75% +5%RH
1	1days	6.5	6.4	No visual changes	No visual changes	32secs	30secs	68ml after 1min	65ml after 1min
2	30days	6.3	6.3	No visual changes	No visual changes	28secs	31secs	72ml after 1min	70ml after 1min

The selected formulation was stored at 25±2°C/65±5%RH, 40±2°C/75%±5%RH, for a period of 1 month. The sample kept for stability was evaluated for PH, visual appearance, foam ability & stability wetting time. All the parameters were found to be within limits after 1 month. Discussion- The topical ketoconazole shampoo and conditioner was formulated using different ingredients such as Sodium metabisulfite, Sodium lauryl sulphate, Stearic acid, Methylcellulose, EDTA, Sodium hydroxide, Rosewater, Amaranth colour, Water & pvp was added as a conditioner. Stability studies were performed. The excipients along with the pure drug was found to be compatible when evaluated. Finally ketoconazole shampoo and conditioner were evaluated for PH, Dirt dispersion, percent of solid content, surface tension, foam ability & stability.

**VII. CONCLUSION**

Ketoconazole is azole group of drug used for treating fungal drug and treat dandruff caused by fungus. 1 formulations were prepared and characterization of formulation were carried out and compared with marketed (danfree) shampoo and shows similar results.

The PH values for ketoconazole shampoo formulation was found to be 8.5

The percent of solids contents was found to be 22% foam ability & foam stability was determined i.e., 70ml after and wetting time was observed as 30secs and Stability studies were carried out for a period of 1 month & it shows no significance changes in the characteristics of ketoconazole formulation.

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