



# Formulation and Evaluation of lawsone Anti-dandruff Gel

<sup>1</sup>Koyte Yash Ranjit, <sup>2</sup>Sonwane Rahul Popat, <sup>3</sup>Unde Sushant Karbhari, <sup>4</sup>Wabale Sidhi Balasaheb, <sup>5</sup>Thange Apurva Bhanudas

<sup>1</sup>UG Scholar, <sup>2</sup>UG Scholar, <sup>3</sup>UG Scholar, <sup>4</sup>UG Scholar, <sup>5</sup>UG Scholar

Matoshri Miratai Aher College Of Pharmacy, Karjule Harya, Tal- Parner, Dist- Ahmednagar, Maharashtra

## ABSTRACT

Lawsonia is the principle colouring compound of Henna, Lawsonia inermis Linn. (Fam. Lythraceae). Henna has been used to treat skin infections such as tinea and it is known to have antibacterial and antifungal properties which have been attributed to naphthoquinones, including lawsone. Anti-dandruff activity of lawsone was determined on the pure culture of Malassezia Furfur at different concentration. Lawsonia showed good antidandruff activity. At present, there are number of antifungal agents use topical applications like clotrimazole, griseofulvin, itraconazole, fluconazole etc. Clotrimazole was used as a model drug. Clotrimazole is an imidazole derivative with a broad spectrum anti mycotic activity. It acts by inhibiting biosynthesis of ergosterol, an important component of fungal cell membranes. It is widely used for the treatment of local candidiasis, vaginal yeast infections; topical applications include fungal infections such as ring worm, athlete's foot and jock itch. Its action leads to increased membrane permeability and apparent disruption of enzyme systems bound to the membrane. The major drawback of this drug is its insolubility in water. The techniques generally employed to enhance the solubility of poorly water soluble drugs are, use of surface active agent, hydrates and solvates, polymorphism, complexation, solid dispersion. Among this solid dispersion is a unique technique used to increase solubility, dissolution and bioavailability of poorly water-soluble drugs. Conventional method for preparing solid dispersion includes solvent wetting method, physical mixture, complex formations, and solvent evaporation techniques. Creams, gels, ointments and pastes are some of the topical semisolid in use for many decades. The extensive studies on release properties have revealed that the active ingredients in gel based formulations are better percutaneously absorbed than cream or ointment bases.

**KEYWORDS:** Lawsonia, Dandruff, Gels

## INTRODUCTION

For several disorders the efficacies of many indigenous plants have been described by practitioners of medicinal plants. For treatment of various diseases and health conditions plant derived products have been used. Now days most used treatment are derived from plant sources. Henna is a tall shrub or small tree and its height is approximately 1.8 to 7.6m tall. The botanical name of the henna plant is Lawsonia inermis and its family is Lythraceae. Henna is also known as Mehendi, is an evergreen plant, henna having antibacterial, antifungal, antidiabetic, antifertility and immunomodulator activity. In this review we highlight or study on the antifungal and antibacterial activity of henna. The henna plant is widely cultivated as dye plant.



fig.1: henna plant benefits

Henna contains 2-hydroxy-1:4-naphthaquinone, 2-methoxy-3-methyl-1,4-naphthaquinone, and lawsone 1-1.4%. Henna is also used as cosmetic agents for nails, skin and dyeing hair. Henna is also used in the treatment of diseases such as spleen, pain, leprosy, edema, bronchitis, menstrual disorder, hemorrhoids, jaundice. It is also used as an antihemorrhagic agent and astringent. Henna plants have various benefits: 1. pain relief feature, 2. scabies treatment, 3. liver benefits, 4. effect on psychology, 5. headaches, 6. Acne and pimple, 7. infection, 8. Benefits to skin, 9. Benefits to hair, 10. Benefits to nails. For potential antimicrobial activity resistance of antibiotic exhibited by pathogenic microbial infectious agents, in folk medicine there is great interest to carry out screening of henna plants. The Etiology of Seborrheic Dermatitis remains unidentified, though many factors, including hormonal, have been implicated. This chronic inflammatory disorder is normally limited to areas where these sebaceous glands are present like head. In this condition of skin, the skin becomes crumbling. This type of dermatitis on scalp is harsh type of dandruff. When this type of dermatitis affects the scalp various people call it as dandruff. Seborrheic dermatitis occurs when in the neonatal period, it generally disappears by six to twelve months suggesting that it possibly is related to maternal hormone stimulation. Seborrheic dermatitis often affects people in post puberty. Further facts of hormonal influence is provided by research indicating that the human sebocyte responds to androgen stimulation. Although specific details remain unknown *Pityrosporum Ovale* is mainly found to take part in the demonstrating of the Seborrheic dermatitis. The migration rate of occupied skin by this organism may be lesser than of normal skin. Classified Common sites of dandruff distribution: The distribution is naturally symmetric and general sites of distribution are Hairy areas of head, Forehead, The external ear canals, Post auricular creases. It affects not just on the scalp but also affects the ears, eyebrows, side of nose, beard, and less commonly the central part of the chest. Dandruff is seen in all ages from baby to the elderly. In infancy scalp, "Cradle cap" is another term used for dandruff. Dandruff is commonly known as seborrheic dermatitis. Severe dandruff may be a very difficult and frustrating condition. Ongoing combination treatment of multiple shampoo, washes, cream and lotion may be required to treat resistance condition. Overall, dandruff treatment is safe and effective. The best shampoo choice includes zinc pyrithione, selenium sulphide, tar based shampoo. Prescriptions shampoo of dandruff such as ketoconazole have no over-the-counter brands. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Skin is one of the most readily accessible organs on human body for topical administration and is the main route of topical drug delivery system. It affords to maintain applied preparation intact for a prolonged time and this has resulted in its increasing use as a route of administration whether for local, regional or systemic effects. Topical anti-fungal are the agents, meant for topical use for fungal infection. Topical application of drug at the affected site offers potential advantage of delivering drug directly to the site of action. Local infection can be treated by application of products which form a transparent water vapour and air permeable film over the skin surfaces, from which drug releases continuously to the skin site and skin structure infection and the disease of the patient would be treated.

## HAIR ANATOMY

- Hair grows from hair follicles situated within the fatty layer of the scalp. Contrary to the popular belief that hair grows as single strands, hair follicles actually grow in groups of 1-4 hairs called "follicular units"
- At the base of each hair follicle is a hair bulb where the growth mechanism for producing hair occurs. Hair follicles get their nourishment from the blood vessels within the dermis. The cells divide and develop to produce the hair shaft.
- While the hair is still developing underneath the epidermis, it maintains a soft form. Once it pushes past the epidermis, its outside layer hardens into keratin.

## HAIR

In humans it is a special and cherished feature, especially, in females, but its main functions are in protection of the skin from mechanical insults and to facilitate home therapy, eyebrows and eyelashes, for example, stop things entering the eyes, while scalp hair prevents sunlight, cold, and physical damage to the head and neck.

## STRUCTURE OF HAIR

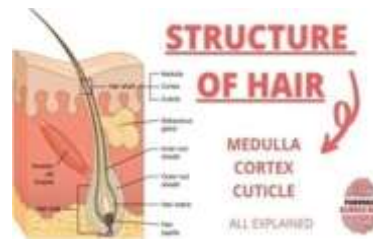


figure.2: structure of hair

A hair is composed of columns of dead, keratinized cells welded together. The shaft is a straight hair is rounded in cross-section, that of wavy hair is elliptical or kidney shaped. The root is the portion of the hair deep into the surface that penetrates into the dermis and sometimes into the subcutaneous layer. The shaft and root both consist of three concentric layers-

### Medulla

It is the central part of the shaft and is generally noticeable in thick hair. It is composed two or three rows of polyhedral cells containing pigment granules and air spaces.

### Cortex

It is located peripheral to the medulla and forms the major part of the shaft. It consists of elongated cells, containing pigment granules in dark hair while air in white hair

### Cuticle

It is a layer present in the outermost region of the hair. The cuticle has presence of thin heavily keratinized flat cells.

## HAIR PHYSIOLOGY:

- Anagen (growth phase): Most hair is growing at any given time. Each hair spends several years in this phase.
- Catagen (transitional phase): Over a few weeks, hair growth slows and the hair follicle shrinks.
- Telogen (resting phase): Over months, hair growth stops and the old hair detaches from the hair follicle. A new hair begins the growth phase, pushing the old hair out

## DANDRUFF

Dandruff (Hay et al., 1997) is a common scalp disorder affecting almost half of the population at the pre pubertal age and of any sex and ethnicity. Pityriasis simplex capillitii (commonly known as dandruff) is the shedding of dead skin cells from the scalp. The word dandruff is of Anglo Saxon origin, a combination of 'tan' meaning 'tetter' and 'drof' meaning dirty. Dandruff can be considered aesthetically displeasing and often causes itching. Dandruff is the result of a combination of factors. Some of these factors are well studied, whereas others have not been thoroughly investigated

## SEBORRHOEIC DERMATITIS

Flaking (Janniger et al., 1995) is a symptom of seborrheic dermatitis. Joseph bark notes that "redness and itching is actually seborrheic dermatitis and it frequently occurs around the folds of nose and the eyebrow areas, not just the scalp" (Zouboulis et al., 1998). Dry, thick, well defined lesions consisting of large, silvery scales may be traced to the less common psoriasis of the scalp (Schuab et al., 1999; Schechtman et al., 1995; Basset seguin et al., 1998)

## DANDRUFF COMPOSITION

Dandruff scale is a cluster of corneocytes, which have retained a large degree of cohesion with one another and detach as such from the surface of the stratum corneum. (Hay et al., 1997) The size and abundance of scales are heterogeneous from one site to another and overtime. Parakeratotic cells often make up part of dandruff. Their numbers are related to the severity of the clinical manifestations, which may also be influenced by seborrhea

## CAUSES

The most common cause of dandruff (Hay et al., 1997) is probably the fungus *Malassezia furfur* (previously known as *Pityrosporum ovale*) this fungus is a lipid dependent, dimorphic yeast like fungus occurring in human skin as an opportunistic pathogen and is responsible for many cutaneous diseases like dandruff, pityriasis versicolor, seborrheic dermatitis, tinea circinata etc. During dandruff, the levels of *Malassezia furfur* increase by 1.5 to 2 times its normal level (Cowley et al., 1990). Dandruff is sometimes caused by frequent exposure to extreme heat and cold. The severity of dandruff may fluctuate with season as it often worsens in winter. Other causative factors include family history, food allergies, excessive perspiration, use of alkaline soaps and stress. Even the season of the year can contribute to the problem, cold, dry winters are notorious for bringing on dandruff. Dandruff can also be aggravated by exposure to dust, UV light/harsh shampoos and hair dyes. The cause of dandruff

is un defined. Now there are so many experts who think that the dandruff is not caused by the poor cleanliness .Persons who are highly sensitive to yeast havinghigh improbability of having dandruff. That's why we can say that the yeast may play an important part in causing dandruff. Malassezia is a type of fungi and its sensitive people who get dandruff find that it gets lost during the warmer season and higher in cold. UV light from the sun interacts with the yeast. Several say, that during winter skin becomes dried due to coldair and hot area temperature, that causes dandruff more liable. Fungi Malassezia is generally present on everyone's scalp. Normally, this fungus does not show any problem. Though, it can grow un control. It nourished by the oils and by the hair follicles secretion. When occurs, the scalp can become irritated and produces extra skin cells. After that the extra skin cell side andfall off. Then they mix with the oil of the hair and scalp, and turn into a flaky scale which we can say as dandruff.

### SEBORRHEIC DERMATITIS:

Person who suffers from seborrhoea dermatitis are more sensitive to dandruff. Seborrhoea dermatitis affects various areas of the skin include the back of the ears, the breastbone, eyebrows ,and the sides of the nose, not only on the scalp. The patient who suffers with this disease will have red, greasy, itchy, irritates skin covered with flaky white scales.Disease conditions: People with psoriasis, eczema and some other skin disorders have a tendency to getdandruff much more often than other people. Adults with Parkinson's disease and some other neurological disease are more prone to having dandruff and seborrhoea dermatitis. Patients who having heart disease and they recover from heart attack having dandruff more than the other persons.

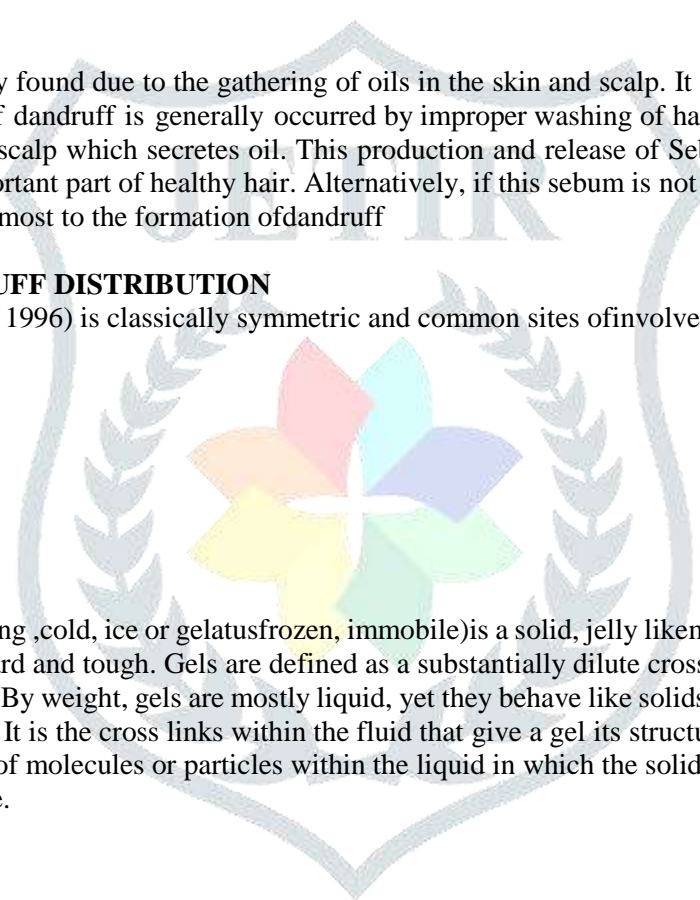
### OIL-RELATED DANDRUFF:

This kind of dandruff is commonly found due to the gathering of oils in the skin and scalp. It may result because of irregular cleanliness practices. This type of dandruff is generally occurred by improper washing of hair and not enough shampooing. Sebaceous glands are foundin the scalp which secretes oil. This production and release of Sebum oil is a natural incident in human beings and it make an important part of healthy hair. Alternatively, if this sebum is not cleared regularly, it can binned with dead skin and dirt which foremost to the formation of dandruff

### COMMON SITES OF DANDRUFF DISTRIBUTION

The distribution (Thomas P, et al., 1996) is classically symmetric and common sites of involvement are as follows:

- ❖ Hairy areas of head.
- ❖ Eyebrows and eyelashes.
- ❖ Beard.
- ❖ Fore head.
- ❖ The external ear canals.
- ❖ Post auricular creases



### GELS

A gel (from the Latin Gelu-freezing ,cold, ice or gelatusfrozen, immobile)is a solid, jelly likematerial that can have properties ranging from soft and weak to hard and tough. Gels are defined as a substantially dilute cross-linked system, which exhibits no flow when in the steady-state. By weight, gels are mostly liquid, yet they behave like solids due to three dimensional cross linked network within the liquid. It is the cross links within the fluid that give a gel its structure and contribute to stickiness. In this way gels are a dispersion of molecules or particles within the liquid in which the solid is the discontinuous phase and the liquid is the continuous phase.

#### Types of gels

##### 1. Controlled release gels-

These gels were formed in simulated tear fluid at concentrations of polymer as low as 0.1% and it was shown that sodium was the most important gel-promoting ion in vivo.

##### 2. Organogels

Organogels are affected by the presence of additives such as the hydrophilic surfactant, polysorbate 20, which improve gel stability.

##### 3. Extended release gels

It is a controlled release technology consists of an agglomerated, hydrophilic complex that, when compressed, forms a controlled-release matrix. It consisting of xanthan and locust bean gums (two polysaccharides) combined with dextrose surrounds a drug core. In the presence of water, interactions between the matrix components form a tight gel while the inner core remains unwetted.

##### 4. Amphiphilic gels

Amphiphilic gels can prepared by mixing the solid gelator like sorbitan monostearate or sorbitan monopalmitate and the liquid phase like liquid sorbitan esters or polysorbate and heating them at 60°C to form a clear isotropic sol phase, and cooling the sol phase to form an opaque semisolid at room temperature.

### 5. Hydrophilic gels

Hydrophilic gels are composed of the internal phase made of a polymer producing a coherent three-dimensional net-like structure, which fixes the liquid vehicle as the external phase. Intermolecular forces bind the molecules of the solvent to a polymeric net, thus decreasing the mobility of these molecules and producing a structured system with increased viscosity.

### 6. Non-aqueous gels

Ethylcellulose was successfully formulated as a nonaqueous gel with propylene glycol dicaprylate/dicaprate. The novel nonaqueous gel exhibited rheological profiles corresponding to a physically cross-linked three dimensional gel network, with suitable mechanical characteristics for use as a vehicle for topical drug delivery. Molecular conformation of the solvent was found to influence the molecular interactions associated with formation of ethylcellulose gel networks.

### 7. Bio-adhesive gels

Bioadhesive gels were formulated for nasal delivery of insulin. A nasal perfusion test was carried out to study the toxicity of four absorption enhancers like saponin, sodium deoxycholate, ethylenediamine tetra-acetic acid (EDTA) and lecithin.

### 8. Thermosensitive sol-gel reversible hydrogel

They are polymeric solutions which undergo reversible sol to gel transformation under the influence of environmental conditions like temperature and pH which results in in situ hydrogel formation.

### 9. Complexation gels

The goal of oral insulin delivery devices is to protect the sensitive drug from proteolytic degradation in the stomach and upper portion of the small intestine. The insulin remained in the gel and was protected from proteolytic degradation. In the basic and neutral environments of the intestine, the complexes dissociated which resulted in rapid gel swelling and insulin release.

### 10. Hydrogel

Hydrogels are gel systems in which water is immobilised by insoluble polymer. The elements of hydrogels are water and a polymeric substance that is hydrophilic, but not water soluble. When exposed to water, the dry polymer swells and absorbs liquid.

## PROPERTIES OF GELS

Various Properties of Gels are Following:

- A. Physical properties
- B. Physiological properties
- C. Application properties
- D. Hydrophilic properties
- E. Rheological properties

#### A. Physical Properties

- Smooth texture
- Elegant in appearance
- Non dehydrating
- Transparent and translucent
- Non greasy
- Semi solid in nature

#### B. Physiological Properties

- Non irritating
- Do not alter membrane / skin functioning
- Miscible with skin secretion
- Have low sensitization index

#### C. Application Properties :

- Easily applicable with efficient drug release.
- High aqueous washability.

#### D. Hydrophilic Properties :

The water absorbing capacity of oleaginous and water-in-oil bases may be expressed in terms of the water number, defined in 1935 by Casparis and Meyer as the maximum quantity of water that is held (partly emulsified) by 100g of a base at 20°C

C. The test consists of adding increments of water to the melted base and triturating until the mixture has cooled. When no more water is absorbed, the product is placed in a refrigerator for several hours, removed, and allowed to come to room temperature. The material is then rubbed on slab until water no longer exudes, and finally, the amount of water remaining in the base is determined.

### E. Rheological Properties :

Gels exhibit different rheological properties. Do not flow at low shear stresses but undergo reversible deformation like elastic solids. When a characteristic shear stress, called the yield value or yield stress, is exceeded, they flow like liquids. Yield stresses usually are caused by structural networks extending throughout an entire system. To break such a network requires stress produce no flow but only elastic deformation. When the yield stress is exceeded, the network is partly ruptured and flow occurs<sup>28</sup>.

### Advantages

- Gels are used to achieve optimal cutaneous and percutaneous drug delivery.
- They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH.
- Gels are having property to avoid enzymatic activity and drug interaction with food and drinks.
- They can substitute for oral administration of medication when the route is unsuitable.
- They can avoid the first pass effect, that is, the initial pass of drug substance through the human body.
- They avoid systemic and portal circulation following gastrointestinal absorption.

### Disadvantages

- Gels have possibility of allergenic reactions.
- Enzyme in epidermis may denature the drugs of gels.
- Drugs of larger particle size do not absorb through the skin.
- They have poor permeability of some drugs through the skin.
- Selection of area to be examined carefully during application of gels.
- Gels which are used for the introduction into body cavity or the eyes should be sterilized.
- They may cause application side reactions.

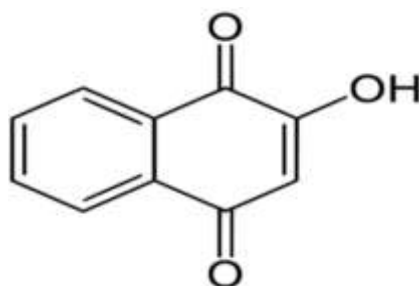
## AIM AND OBJECTIVE

**AIM-** Formulation and Evaluation of lawsone Anti-dandruff Gel.

### OBJECTIVE-

1. The purpose of the study is to formulate Gel.
  2. To prevent the dandruff and their infections.
  3. The formulation contains the lawsone which helps to reduce dandruff and fungal infection.
- Evaluation of Gel.

## DRUGS PROFILE



**Drug name -** Lawsone

**Chemical formula -** C<sub>10</sub>H<sub>6</sub>O<sub>3</sub>

**Molecular weight-** 174.15g/mol

**Description-** Lawsone is 1,4-Naphthoquinone carrying a hydroxy function at C-2. It is obtained from the leaves of Lawsonia inermis. It has a role as a protective agent and an antifungal agent. It is an automer of a naphthalene-1,2,4-trione.

**Indication-**

Lawsone is used to dye wool and silk in orange shade. The dye has also long been used by the people, especially the ladies of India and the middle Eastern countries for tinting finger nails and the palms of their hands a reddish-brown, dyeing the hair and eyebrows and for other forms of personal adornment

**ADVANTAGES:**

There are many advantages of henna that are following:

**Relief from headache :**

Apply henna paste on forehead which helps in alleviating the headache and relaxes your muscles.

**Treats Skin Issues:**

Henna plant has antifungal and anti-bacterial properties which also helps in soothing burns, eczema and other fungal infection.

**MATERIALS & METHODS****METHODS-****Preparation of gel**

Measured quantity of methylparaben, polyethylene glycol and glycerin were dissolved in 10ml of water in beaker and were stirred at high speed using mechanical stirrer. Then carbopol 940 was added slowly to the above beaker while stirring and it was allowed to hydrate for 2 hr (Phase I). Lawsone was dissolved in propylene glycol (Phase II) and then the Phase II solution was added slowly to the Phase I and stirred for 5 min. The final weight was adjusted to 20gm by adding sufficient amount of water with stirring. Finally, Triethanolamine was added slowly while stirring till it attain neutralized gel structure. The details of formulations are shown in Table .

**Evaluation of Gel:****1. Physical evaluation:**

Physical parameters such as color, appearance and consistency were checked visually.

**2. pH of formulation:**

The pH of the formulated gel was determined using digital pH meter . The electrode was immersed in the gel and readings were recorded from pH meter.

**3. Lawsone content:**

Accurately weighed quantity of gel (100 mg) was dissolved 10 ml methanol, filtered and lawsone content was determined by analysing spectrophotometrically at 452nm.

**4. Viscosity study:**

The viscosity of prepared gel was measured by using Brookfield viscometer using a spindle No.63 at 100 rpm. Gel (50 g) was kept in 50 ml beaker which was set till spindle groove was dipped and dial reading was measured after three minutes. From the obtained reading, viscosity was calculated

**5. Spreadability:**

The weighed quantity of gel (about 0.5g) was sandwiched between two glass slides. 100 g of weight was placed on the slides. The weight was placed for specific period of time for 10min. Then weight was removed and diameter of the spread circle was measured at different points.

Spreadability was calculated by using formula .

$$S = (M \times L)/T$$

Where,

S is spreadability, M is weight placed on the slide, L is diameter of circle in cm and T is Time in Sec.

**RESULT**

Table.1: formula of gel

Ingredients	L1	L2	L3	L4	L5	L6
Lawsone (mg)	20	20	20	20	20	20
Carbopol 940 (g)	0.5	1	1.5	2	2.5	3
Propylene glycol (ml)	3	3	3	3	3	3
Polyethylene glycol- 400(ml)	4	4	4	4	4	4
Glycerin (ml)	0.6	0.6	0.6	0.6	0.6	0.6
Methyl paraben (g)	0.04	0.04	0.04	0.04	0.04	0.04
Triethanolamine (ml)	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s
Dist. Water (ml)	20	20	20	20	20	20

**Preparation and Evaluation of gel:**

The prepared gel formulations were orange transparent coloured, homogenous, and without air bubbles. All the formulations showed a pH in between 6-7 which is appropriate to prevent skin irritation. The spreadability of formulated gel was decreased as the concentration of gelling agent increased. Formulation L1 to L3 shows satisfactory spreadability. All formulations showed an increased viscosity as the concentration of the gelling agent was increased. By taking viscosity, spreadability and pH in consideration of the formulation the L2 was taken as the optimized batch

**Determination of lawsone Content in gel formulations:**

The content of lawsone was greater than 91% for all formulations, showing that the drug was distributed uniformly.

table .2: determination of lawsone content gel

Sr. No	Formulation	pH	Viscosity (cps)	Appearance	Spreadability	Lawsone content
1	L1	6.8	55675	Transparent	1.09	91%
2	L2	7.2	51989	Transparent	1.02	94%
3	L3	6.9	56753	Transparent	0.77	95%
4	L4	6.4	57891	Transparent	0.5	91%
5	L5	6.9	58131	Transparent	0.51	94%
6	L6	6.5	58419	Transparent	0.45	92%

**Anti-dandruff activity of formulation:**

Formulation L2 batch was subjected to determination of anti-dandruff activity. Antidandruff activity of the lawsone gel was compared with the clotrimazole gel prepared by using the same base of gel. Anti-dandruff activity was determined by measuring the zone of inhibition. The formulations L2 batch shows good zone of inhibition with compared to clotrimazole gel as shown in table

Table .3: Antidandruff activity of formulation

Formulation	Concentration (mg/ml)	Zone of Inhibition (mm)
Lawsone gel (L2)	1mg/ml	22.6±0.14
Clotrimazole Gel	1mg/ml	27.7±0.26

**CONCLUSION**

Considering some drawbacks of synthetic drugs, lawsone a chief chemical constituent of Hennawas evaluated for its antidandruff activity and further formulated into a gel formulation. Anti-dandruff activity of lawsone was determined on the pure culture of Malassezia Furfurat different concentration. Lawsone showed good antidandruff activity. Lawsone gel was prepared by using carbopol 940 as a polymer in varying concentration from 0.5g-3g. After preparation of formulation the formulation were evaluated for drug content, viscosity and spreadability. In-vitro diffusion of lawsone hair gel was performed in phosphate buffer 5.0. Formulation batch L2 showed 94.20% cumulative percentage drug release up to 6 hr. Same formulations were evaluated for the zone of inhibition for their anti-dandruff activity against Malassezia Furfur. The formulations L2 batch shows good zone of inhibition with compared to clotrimazole gel.

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