Chapter 5 Pharmaceutical formulation and its evaluation

5.1 Introduction

Plants have been used in traditional medicine for several thousand years. Medicinal plants as a group comprise approximately 8000 species and account for about 50% of all the higher flowering plant species in India. The knowledge of medicinal plants has been accumulated in the course of many centuries based on different medicinal systems such as Ayurveda, Unani and Siddha. In a large number of countries, human population depends on medicinal plants for treating various illnesses as well as a source for livelihood. The World Health Organization (WHO) estimated that 80% of populations of developing countries rely on traditional medicines, mostly plant drugs, for their primary health care needs. Besides health care, herbs are also used for beautification of the body and for preparation of various cosmetics. In traditional system of medicine, many plants and herbal formulations are reported for hair growth promotion but lack of sound scientific backing and information limits their use (Rathi et al., 2009). The main problem associated with hair such fading, dandruff and shedding. On the basis of market and public survey carried out on crude drugs used presently for herbal hair oils gives us clue for selection of drugs for formulation of oil, cream and gel for hair growth promoting activity.

The preparation of any herbal cosmetics basically follows the same procedure as in the case of cosmetics. In preparation, suitable bioactive ingredients or their extracts are used along with requisite ingredients basically used for cosmetics. It requires selection of suitable emulsifying agent, appropriate ingredient composition and modified methodology to obtain desirable product of specified parameters. Association of botanicals and traditional cosmetic ingredients affects the finished products, which ultimately requires modifications in ingredient composition and formulation methods. The herbal cosmetics formulation is a sophisticated and sensitive technological profile because it retains the bioactivity of the botanicals during excessive processing and ascertains their availability after application on skin or hair. It is desirable that manufacturers should ensure the quality of products through systematic testing at their
level. Other parameters like organoleptic characteristics, pH, viscosity, stability towards light and refrigeration should also be evaluated.

5.2 Herbal hair oil

Hair is one of the vital parts of our body and it influences the overall appearance of the person. Hair care products are defined as those formulations which are used for cleansing, modifying the texture of hair, changing the color, giving life to the stressed hair, providing nourishment to the hair and giving the healthy appearance to the hair (Pande et al., 2011). There are two categories of hair care products; they are hair tonics and hair grooming aids. Hair oil which contains herbal drugs are called as hair tonics. These are formulated by herbal extracts in an oil base. Hair oils are the hair care formulations applied for treatment of hair disorders such as baldness, aggression of hair, discoloring of hair, hair falling, and dryness of hair etc (Nema, 2009). The nature of oil is non sticky and addition of perfumes enhances the fragrance and overall improves its popularity. Proper application of hair oil gives luster to hair, softening the hair, gives flowness to hair and more important gives cooling effect to brain. The most recognized hair care preparation is herbal hair oils, they moisturizes the scalp and also helpful in dry scalp and dry hairs. Herbal hair oil maintains normal functions of sebaceous gland as they supply normal essential elements for hair to naturally grow (Gautam, 2012).

Global status of herbal hair oil

According to World Health Organization (WHO) the global herbal market will grow $5 trillion by 2050. The News National from Nigeria Natural Medicine Development Agency (NNMDA) has projected hope that herbal market currently is $160 billion globally annually. Next to the China India is the largest producer of medicinal plants having greater than 40 % global diversity. Form the study on 'Herbal Industry Biz Potential', presently, the Indian herbal market is worth Rs 7,000 crore ($1.7 billion) and India exports herbal raw materials and medicines worth over Rs 3,600 crore ($902 million).
Preparation of herbal hair oil formulation

The herbs used in the present study for making herbal oil were dried, crushed and ethyl acetate fraction of ethanolic extract was taken. Coconut oil (Type I – based on vegetable oil) was used as base for preparation of oil formulation. The hair oil was prepared utilizing the ethyl acetate fraction of ethanolic extract mixed directly with boiled coconut oil with continuous stirring and heating until the drug had completely mixed in the coconut oil base. 1, 2, 3 % of drugs containing oils were prepared. Four hair oil formulations with EEEA 5 % (O1) and EEEA 10 % (O2) and EELN 5 % (O3) and EELN 10 % (O4) were prepared. Confirmatory test of oil as per Ayurvedic text, Agnipariksha and Vatipariksha were performed.

Evaluation of herbal oil preparation

The prepared oils were then subjected to physical and biological evaluation.

Physical evaluation

The prepared formulations were evaluated using standard methods of general characterization, physical and chemical evaluation including specific gravity, pH, viscosity, acid value, peroxide value and saponification value (Adhirajan et al., 2001).

Specific gravity

The specific gravity bottle was taken, rinsed it with distilled water, and dried in oven for 15 minutes, cooled, closed it with cap and weighed (a). The same specific gravity bottle was filled with the sample and closed it with cap and again weighed (b). The weight of sample per milliliter was determined by subtracting the weight (b - a).

pH

The pH of herbal hair oil was determined using pH meter.

Viscosity

The viscosity was determined using Ostwald’s viscometer.
Acid value

Preparation of 0.1 molar solution: 0.56 g KOH pellets was weighed and dissolved in 100 mL of distilled water and stirred continuously. The prepared 0.1 molar KOH solution was filled in the burette. Preparation of sample: 10 mL oil was measured and dissolved in 25 mL of ethanol and 25 mL of ether mixture and shaken. 1 mL of phenolphthalein solution was added and titrated with 0.1 molar KOH solution.

Peroxide value

5 g of the material was weighed accurately in a 250 ml glass stoppered conical flask and dissolved by shaking in 30 ml of a mixed solvent containing 3 parts by volume of glacial acetic acid and 2 parts by volume of chloroform. 0.5 ml of saturated potassium iodide solution was added and allowed to stand for exactly 1 minute with occasional shaking, then 30 ml of water was added and titrated with standard sodium thiosulphate solution. Thiosulphate solution was added until the colour of the titrated solution becomes light yellow. 1 ml of starch indicator solution was added and the titration was continued till the disappearance of the blue colour.

Saponification value

1 mL of oil was accurately weighed into a 250 mL of conical flask and 10 mL of ethanol: ether mixture (2: 1) was added. To this flask 25 mL of 0.5 N alcoholic KOH was added. The flask was kept for 30 min. and the flask was cooled. The cooled solution was titrated against 0.5 N HCl using phenolphthalein as indicator. Similarly the blank titration was performed without taking oil (sample). Amount of KOH in mg used was calculated.

Results

The results of general characteristic, physical and chemical evaluation are summarized in Table 5.1. All the parameters showed that they are within the limits of BIS (Bureau of Indian Standards). All the prepared formulations are colourless with pH 7.2 to 7.4. Specific gravity and refractive index of the prepared four oil formulations were 1.225 to 1.250 and 1.372 to 1.439 respectively. Viscosity values of the prepared oil
formulations were 112.1, 112.0, 111.8, 112.0 centipoise (cps) for O1, O2, O3 and O4 oil formulations.

**Table 5.1. Evaluation of parameters for herbal hair oil**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O1</td>
</tr>
<tr>
<td>Colour</td>
<td>Colourless</td>
</tr>
<tr>
<td>Odour</td>
<td>Pleasant odour</td>
</tr>
<tr>
<td>Appearance</td>
<td>Sediment and suspended matter free</td>
</tr>
<tr>
<td>pH</td>
<td>7.2</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.250</td>
</tr>
<tr>
<td>Refractive index</td>
<td>1.372</td>
</tr>
<tr>
<td>Viscosity (cps)</td>
<td>112.1</td>
</tr>
<tr>
<td>Acid value</td>
<td>0.82</td>
</tr>
<tr>
<td>Peroxide value (mE/1000 g)</td>
<td>6.0</td>
</tr>
<tr>
<td>Saponification value</td>
<td>248</td>
</tr>
<tr>
<td>Microbial count microorganism/gm</td>
<td>12</td>
</tr>
</tbody>
</table>
5.3 Creams

Creams are semisolid emulsion systems with opaque appearances, as contrasted with translucent ointments intended for application to the skin, hair or mucous membrane. Their consistency and rheologic character depend on whether the emulsion is water in oil or oil in water type and on the nature of the solids in the internal phase.

Preparation of cream formulation

An oil in water (O / W) emulsion - based cream (semisolid formulation) was formulated. The emulsifier (stearic acid) and other oil soluble components (white bees wax, stearyl alcohol, cetyl alcohol, mineral oil and ethyl acetate fraction of ethanolic extract of *Eclipta alba* or *Lippia nodiflora* were dissolved in the oil phase (Part A) and heated to 75° C. The preservatives and other water soluble components (methyl paraban, propyl paraban, triethanolamine, propylene glycol and water) were dissolved in the aqueous phase (Part B) and heated to 75° C. After heating, the aqueous phase was added in portions to the oil phase with continuous stirring until cooling of emulsifier took place (Johansson *et al.*, 2001 and Yongshan and Yimin, 1992). The formula for the cream is given in Table 2. Four different concentrations of herbal hair cream formulations were prepared using oil in water (O/W) emulsion based with EEEA 5 % (C1) and EEEA 10 % (C2) and EELN 5 % (C3) and EELN 10 % (C4).

Table 5. 2. Formula for cream

<table>
<thead>
<tr>
<th>PART A (Oily Phase)</th>
<th>% w/ w</th>
<th>PART B (Aqueous Phase)</th>
<th>% w/ w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredients % w/ w</td>
<td></td>
<td>Ingredients</td>
<td></td>
</tr>
<tr>
<td>Stearic acid</td>
<td>2.5 %</td>
<td>Propylene glycol</td>
<td>5.0 %</td>
</tr>
<tr>
<td>White bees wax</td>
<td>1.5 %</td>
<td>Triethanolamine</td>
<td>2.0 %</td>
</tr>
<tr>
<td>Stearyl alcohol</td>
<td>5.0 %</td>
<td>Methyl paraban</td>
<td>0.01 %</td>
</tr>
<tr>
<td>Cetyl alcohol</td>
<td>6.5 %</td>
<td>Propyl paraban</td>
<td>0.04 %</td>
</tr>
<tr>
<td>Mineral oil</td>
<td>5.0 %</td>
<td>Water</td>
<td>Upto 100 %</td>
</tr>
<tr>
<td>EEEA or EELN</td>
<td>EEEA (5.0 % or 10 %) or EELN (5.0 % or 10 %)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The herbal hair formulation was prepared using cream base incorporating all necessary ingredients along with the extracts of *E. alba* and *L. nodiflora*. Formulation was then evaluated for its physical properties.

**Evaluation of the cream**

The cream was then evaluated for the following physical parameters

**Formulation Properties**

The formulation properties of the cream were studied by visual appearance and characteristics.

**Presence of foreign particles/grittiness**

A small amount of cream was taken and spread on a glass slide free from grease and was observed against diffused light to check for presence of foreign particles.

**pH of the cream**

The pH of various formulations was determined by using digital pH meter. About 1 g of the cream was weighed and dissolved in 100 ml of distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values were calculated.

**Viscosity**

Viscosity of the formulation was determined by Brookfield Viscometer II + model using spindle no S – 64 at 20 rpm at a temperature of 25°C and the determinations were carried out in triplicate and the average of three readings was recorded.

**Determination of type of emulsion**

**Dilution test**

In this test the emulsion is diluted either with oil or water. If the emulsion is o/w type and it is diluted with water, it will remain stable as water is the dispersion medium but if it is diluted with oil, the emulsion will break as oil and water are not miscible with
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each other. Oil in water emulsion can easily be diluted with an aqueous solvent, whereas water in oil emulsion can be diluted with an oily liquid (Ashwini et al., 2014).

Dye solubility test

In this test an emulsion is mixed with a water soluble dye (amaranth) and observed under the microscope. If the continuous phase appears red, it means that the emulsion is o/w type as the water is in the external phase and the dye will dissolve in it to give color. If the scattered globules appear red and continuous phase colorless, then it is w/o type. Similarly, if an oil soluble dye (Scarlet red C or Sudan III) is added to an emulsion and the continuous phase appears red, then it is w/o emulsion (Ashwini et al., 2014).

Rheological behavioral of the cream

The rheological property was determined to know the flow behavior of formulation. The viscosity at different rpms was measured using Brookfield viscometer. The rheological behavior of the formulation was studied by taking 100 g of the cream in the beaker. The rate of shear was increased gradually from minimum to maximum and corresponding dial reading was noted; then, the rate of shear was decreased gradually to the lowest value and the dial reading was recorded. The graph was plotted between percent torque and viscosity to determine type of flow 13.

Partition coefficient of cream

The partition coefficient of drug between phosphate buffer solution (pH 7.4) and n-hexane was determined at (37\(^0\) C ± 0.2\(^0\) C). An excess amount i.e., 50 mg of cream was taken in a separating funnel containing 1:1 ratio of buffer 7.4 and hexane. It was placed on a water bath for 24 h. The solution was shaken occasionally. Then, both of them were separated and filtered through a 2 µ filter and the amount solubilized in each phase was determined by measuring the absorbance using UV spectrophotometer. Hexane has polarity zero. Hence it is chosen for the study of partition coefficient.
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Stability studies

**Globule size:** 1 mL of cream was diluted to 10 mL with glycerin. A few drops of this were transferred onto a glass slide and was focused in a microscope. By using eyepiece micrometer, the diameters of 200 particles were determined randomly.

**Phase separation:** The formulated cream was kept intact in a closed container at 25 - 30°C not exposed to light. Phase separation was observed carefully every 24 hrs for 30 days. Any change in phase separation was checked.

**Moisture absorption studies:** About 50 mg of cream was taken on a watch glass. A beaker was taken with full of water and was kept in a desiccator without adsorbents and allowed to get saturated. Watch glass with cream was introduced into the dessicator. It was left for 24 hrs.

**Shelf life:** The formulated product was stored in different temperature conditions like room temperature, 45°C and 55°C to accelerate degradation for 1 month. Samples were withdrawn periodically every week and observed for drug decomposition by taking the absorbance under UV spectrophotometer. From the concentrations, and the temperatures, the shelf life of the product can be estimated.

**Extrudability**

It is useful empirical test to measure the force required to extrude the material from a tube. The formulations were filled in standard caped collapsible tube and sealed. The tube was weighed and recorded. The tube was placed between two glass slides and was clamped. A 500 gm weight was placed over the glass slide and cap was opened. The amount of cream extruded were collected and weighed. The percent of cream extruded was calculated and grades were allotted (++++) Excellent, +++ Good, ++ Fair, + Poor).

**Spreadability**

Spreadability denotes the extent of area to which the formulation readily spreads on application to skin or hair. The bioavailability efficiency of a formulation also depends on its spreading value. The spreadability was expressed in terms of time in seconds taken by two slides to slip off from the cream, placed in between the slides, under certain load.
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Lesser the time taken for separation of the two slides, better the spreadability. Two glass slides of standard dimensions were taken. For this purpose, cream was applied in between two glass slides and they were pressed together to obtain a film of uniform thickness by placing 1000 gm weight for 5 minutes. Thereafter a weight (10 gm) was added to the pan and the top plate was subjected to pull with the help of string attached to the hook. The time in which the upper glass slide moves over the lower plate to cover a distance of 10 cm is noted. The spreadability (S) can be calculated using the formula (Ashwini et al., 2014).

\[ S = \frac{M \times L}{T} \]

where,

- **M** = Weight tied to upper slide
- **L** = Length of glass slide
- **T** = Time taken to separate the slides

**Results**

a. State - Semisolid

b. Color - light yellowish green (C1 and C2) and pale greenish colour (C3 and C4)

c. Odor - Characteristic

d. Appearance – Homogenous

The characteristics of cream in terms of appearance, pH, viscosity, spreadability, extrudability were analyzed by reported methods. The cream formulations prepared was found to be of a light yellowish green (C1 and C2 formulations) and pale greenish colour (C3 and C4 formulations) and all formulations had a pleasant odour. The results proved that the prepared formulations are also having the acceptable property. The pH of cream formulations was found in range of 6.8 to 7.0 which is acidic to neutral value (Table 5.3). It was found that the cream was homogenous, smooth, non – greasy film on the skin surface and consistent in nature and the cream was easily spreadable and moisturizes the skin surface of human volunteer.
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After observation it was found that cream did not leave greasy substances on skin surface after application. The viscosity of four cream formulations prepared was 26075, 26073, 26080 and 26071 centipoise (cps) for C1, C2, C3 and C4 cream formulations respectively. The cream was found to be of the o / w type emulsion by dilution and dye solubility test.

Table 5.3. Evaluation of herbal hair cream formulation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C1</td>
</tr>
<tr>
<td>Colour</td>
<td>Pale greenish white</td>
</tr>
<tr>
<td>Visual appearance</td>
<td>Smooth and consistent cream</td>
</tr>
<tr>
<td>Foreign particles</td>
<td>Free from foreign particles</td>
</tr>
<tr>
<td>Odour</td>
<td>Pleasant odour</td>
</tr>
<tr>
<td>pH</td>
<td>6.8</td>
</tr>
<tr>
<td>Viscosity (cps)</td>
<td>26075</td>
</tr>
<tr>
<td>Extrudability</td>
<td>Good</td>
</tr>
<tr>
<td>Spreadability</td>
<td>Easily spreadable</td>
</tr>
</tbody>
</table>
5.4 Gels

Gels are semisolid systems in which a liquid phase is constrained within a three dimensional polymeric matrix (consisting of natural or synthetic gums) in which a high degree of physical (or sometimes chemical) cross-linking has been introduced. The polymers used to prepare pharmaceutical gels include the natural gums tragacanth, pectin, carrageen, agar and alginic acid, synthetic and semisynthetic materials such as methyl cellulose, hydroxyethylcellulose, carboxymethylcellulose and the carbopols which are synthetic vinyl polymers with ionizable carboxyl groups. Gels are prepared by a fusion process or by procedure necessitated by the gelling characteristics of the gellant. Gels are a relatively newer class of dosage forms created by entrapment of larger amounts of aqueous hydro alcoholic liquids in a network of colloidal solid particles, which may consist of inorganic substance such as aluminium salts or organic polymers of natural or synthetic origins. Depending upon the nature of colloidal substance and the liquid in the formulation, the gel will range in the appearance from entirely clear to opaque. Most topical gels are prepared with organic polymers, such as carbopol940, which impart an aesthetically pleasing, clear sparkling appearance to the products and are usually washed of skin with water. The bulk of these semisolid preparations are applied to the skin, where they usually serve as vehicles for topically applied drugs, as emollients, or as protective or occlusive dressings.

Classification of gels

Gels may be classified either as two phases or single phase systems. The gels may consist of floccules small particles rather than large molecules as found in albumin hydroxide gel, bentonite magma and the magnesia magma and the gel structure in these two phase system is not always stable. Such gels may be thixotropic, forming semi-solids on standing and becoming liquids on agitation. On the other hand, a gel may consist of macro molecules existing as twisted matted strands. The units are often bound together by stronger types of vandervaal forces so as to form crystalline and amorphous regions throughout the entire system. Examples of such gels are tragacanth and carboxy methylcellulose. These gels are considered to be one phase systems. Gels may be classified as inorganic and organic. Most organic gels can be characterised as two-phase
systems. While organic gels belong to the class of single phase since the condensed matrix is dissolved in a liquid medium to form a homogenous gelatinous mixture.

**Properties of gels**

- Ideally, the gelling agent for pharmaceutical or cosmetic use should be inert, safe and non-reactive with other formulation components.
- The inclusion of a gelling agent in a formulation should provide a reasonable solid like nature during storage that can be broken easily when subjected to shear forces generated during shaking a bottle, squeezing a tube or during a topical application. The gel exhibit little viscosity change under the temperature variation of normal use and storage.
- Many gels, particularly those of a polysaccharide nature are susceptible to microbial degradation. Incorporation of suitable preservative may prevent contamination and subsequent loss of gel characteristics due to the microbial attack.
- A topical gel should not be tacky. Too high concentration of gel former or the use of an excessive molecular weight may produce gel difficult to dispense or apply.
- An ophthalmic gel must be sterile. The aim is to produce the suitable, elegant, economic gel product adequately suited for its intended use.

** Characteristics of gels**

**Swelling**

Gels can swell, absorbing liquid an increase in volume. Swelling can be looked on as the initial phase of dissolution. Solvent penetrates the gel matrix. Gel-gel interactions are replaced by gel- solvent interactions. Limited swelling is usually the result of some degree of cross linking in the gel matrix that the total dissolution. Such gel swells considerably when the solvent mixture possesses solubility parameters comparable to that of the gellant.
Syneresis

Many gel systems undergo a contraction upon standing and exude some fluid medium. The interstitial liquid is expressed, collected at the gel. This process is referred to as syneresis. Typically, syneresis has become more pronounced as the concentration of polymers decreases. The mechanism of concentration has been related to relaxation of elastic stresses developed during settings of the gel. The occurrence of syneresis indicates that the original gel was thermodynamically unstable.

Rheology

Solution of gelling agents and dispersions of flocculated solids are typically, pseudo plastic exhibiting a non-Newtonian flow behavior due to progressing breakdown of the structure of the system. The tenuous structure of inorganic particles dispersed in water is disrupted by an applied shear stress. As shear stress is increased, more and more inter-particulate associations are broken, exhibited as a greater tendency to flow. Similarly for macromolecules dispersed in a solvent, the applied shear stress is tending to align the molecule in the direction of stress. The molecules straighten out, becoming less entangled as shear increases, lessening the resistance to flow.

Structure

The rigidity of a gel arises from the presence of a network formed by the interlinking of particles of the gelling agents. The nature of the particle and the stress, straightening them out and lessening the resistance to flow.

Ageing

Colloidal systems usually exhibit spontaneous aggregation slowly. This process is referred to as ageing. In gels, ageing results in gradual formation of a denser network of the gelling agent.

Uses of gels

The use of gels and gelling agents are quite widespread, even in limiting our consideration to the pharmaceutical and cosmetic field only. Gels find use as delivery system for oral administration as gels proper or as capsules shells made from gelatin.
Gelling agents are useful as binder in tablet granulation, protective colloidal in suspensions, thickeners in oral liquids and suppository bases. Cosmetically, gels have been employed in a wide variety of products, including shampoos, fragrance products, skin and hair care preparations (Zatz and Kushla, 2005).

**Gel forming substances**

Many polymers are used to afford structural network that is necessary for the preparation of gel system. These are classified as follows

1. **Natural polymers**: Gelatin, Collagen, Alginate, Agar, Carrageenan, Tragacanth, Pectin, Xanthan gum, Guar gum, Cassia tora and Xanthin etc.,
2. **Semisynthetic polymers**: Methyl cellulose, Sodium carboxy methyl cellulose, Hydroxyl ethyl cellulose, Hydroxypropyl cellulose, Hydroxypropyl methyl cellulose.
3. **Synthetic polymers**: Carbopol 940, Carbopol 934, Carbopol 941, Poloxamer, Polyvinyl alcohol, Polyacrylamide, Polyethylene and its co – polymers
4. **Inorganic substances**: Bentonite, Aluminium hydroxide
5. **Colloidally dispersed solids**: Microcrystalline silica, Montmorrillonite clays, Colloidal cellulose.
7. **Other gelling agents**: Bees wax, Carnauba wax, Cetyl ester wax PEGs etc.,

In the present studies Carbopol 934 and sodium CMC are used as gelling agents.

**Method of preparation of gels**

Gels are normally in the industrial scale prepared under room temperature. However few of polymers need special treatment before processing. These gels can be prepared by following methods.

**Thermal effects**

Many hydrogen formers are more soluble in hot than cold water. The solubility of most lyophilic colloids is reduced on lowering of temperature so that cooling a concentrated hot solution will produce a gel. In contrast to this some materials such as
cellulose ether owe their water solubility to hydrogen bonding with water. Raising the temperature of these solutions will disrupt the hydrogen bonding and reduced solubility, which will cause gelation. Therefore this method cannot be adopted to prepare gels as a general method.

Example: Gelatin, agar, guar gum and cellulose derivatives.

**Flocculation**

Gelation is just produced by adding sufficient quantity of salt to precipitate to produce a gel state but insufficient to produce complete precipitation. It is necessary to ensure rapid mixing to avoid local high concentrations of precipitant. Solution of ethyl cellulose, polystyrene in benzene can gelled by rapid mixing with suitable amount of a non-solvent such as petroleum ether. The addition of salts to hydrophobic solution to bring about coagulation and gelation is rarely observed. The gels formed by flocculation are frequently thixotropic behavior. However, the addition of aluminum hydroxide betonite produces gels. As a general rule addition of about half of the amount electrolyte needed for complete preception is adequate.

**Chemical reaction**

In the preparation of gels by chemical reaction method interaction occur between the solute and solvent. For example aluminum hydroxide gels can be prepared by interaction in aqueous solution of an aluminum salts and sodium carbonate, an increased concentration of reactants will produce gel structures. Silica gel is another example and is produced by interaction of sodium silicate and acids in aqueous solution. Other examples that involve chemical reaction between PVA, cyanoacrylates with glycidol ether (Glycidol), toluene diisocyanates (TDI), methane diphenyl isocyanine (MDI) had cross – links with the polymeric chain (Niyaz et al., 2011).

**Selection and Optimization of gelling agent**

In order to optimize the concentration of gelling agent to achieve proper consistency of the gel formulations were prepared with different gel formers, Carboxy methylcellulose sodium and Carbopol 934 and different concentration of viscosity
enhancer *viz*, 0.5, 1.0, 1.5 and 2.0 % were tried and finally gel that showed good spreadability and consistency was selected for further herbal hair gel preparation.

**POLYMER PROFILE**

**Carbopol 934**

Carbopol / carbomer is a synthetic, high molecular weight, cross linked polymer of acrylic acid co polymerized ally sucrose or ally ethers of pentaerythrital.

**Chemical name**

Carboxy polymethylene.

**Description**

White colored, fluffy, acidic, hygroscopic powder with slight characteristic odour.

**Molecular weight**

3 × 10⁶

**Density (bulk)**

1.76 g / cm³

**Density (tapped)**

1.4 g / cm³

**Viscosity**

(0.5 % w/v aqueous dispersion).

**pH**

2.5 – 3.0 (1 % w/v aqueous dispersion)

**Solubility**

Soluble in water and after neutralization, in ethanol (95 %) and glycerin.

**Stability**

It is stable, through hygroscopic materials, and may be heated at temperature below 104° C for up to 2 hours without affecting their thickening efficiency. However exposing to excessive temperatures can results in dissociation and reduced stability. Complete decomposition occurs on heating for 30 minutes at 260° C.

**Safety**

Carbomer extensively used in non-parental medicines, particularly in topical liquids and semisolids preparations. It may also used in oral formulations. It is non-toxic and non-irritant, there is no evidence in human of hypersensitivity or allergic reaction to carbomer used topically.
Application: Mainly used in liquid or semisolid pharmaceutical formulation as suspending or viscosity increasing agents. It is used as a binder in tablet formulations in either direct compression or wet granulation processes. It is used as emulsifying agent in the preparation of o/w emulsion for external use. (Ainly et al., 1994).

POLYMER PROFILE

Sodium CMC: CMC is a cellulose ether, produced by reacting alkali cellulose with sodium monochloroacetate under rigidly controlled conditions. Prepared from cellulose by treatment with alkali and monochloro-acetic acid or its sodium salt.

Chemical Name: Cellulose, carboxymethyl ether, sodium salt

Chemical formula: \([\text{C}_6\text{H}_7\text{O}_2(\text{OH})_x(\text{OCH}_2\text{COONa})]\)

Description: White or slightly yellowish, almost odourless hygroscopic granules, powder or fine fibres

Molecular weight: \(3.1 \times 10^4\)

Density (bulk): \(0.75 \text{ g/cm}^3\)

Viscosity: (0.4 % w/v aqueous dispersion).

pH: 6.0 - 8.5 (1 in 100 soln)

Solubility: Yield viscous colloidal solution with water; insoluble in ethanol

Loss on drying: Not more than 12 % after drying

Safety: Carbomer extensively used in non-parental medicines, particularly in topical liquids and semisolids preparations. It may also used in oral formulations. It is non-toxic and non-irritant, there is no evidence in human of hypersensitivity or allergic reaction to carbomer used topically.

Application: Thickening agent, stabilizer, suspending agent
Preparation of base hair gel

- Measured quantity of methyl paraben, glycerine and weighed quantity of polyethylene glycol were dissolved in 35 ml of water in a beaker. Then it was stirred at high speed using mechanical stirrer.

- Then Carbopol 934 or sodium CMC and PVP were added slowly to the beaker containing above liquid while stirring.

- Then triethanolamine (gelling agents) was added slowly while stirring to attain gel structure.

- The gel was finally transferred to aluminium collapsible tubes and labelled accordingly. Different composition in base gel formulation is mentioned in Table 5.4.

Table 5.4. Different composition of base gel formulation

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Sodium CMC (g)</th>
<th>Carbopol 934 (g)</th>
<th>PVP (mg)</th>
<th>Methyl paraben sodium (mg)</th>
<th>Glycerine (ml)</th>
<th>PEG (ml)</th>
<th>Triethanolamine (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>-</td>
<td>0.5</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>0.6</td>
</tr>
<tr>
<td>G2</td>
<td>-</td>
<td>1.0</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>0.9</td>
</tr>
<tr>
<td>G3</td>
<td>-</td>
<td>1.5</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>1.2</td>
</tr>
<tr>
<td>G4</td>
<td>-</td>
<td>2.0</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>1.5</td>
</tr>
<tr>
<td>G5</td>
<td>0.5</td>
<td>-</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>0.6</td>
</tr>
<tr>
<td>G6</td>
<td>1.0</td>
<td>-</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>0.9</td>
</tr>
<tr>
<td>G7</td>
<td>1.5</td>
<td>-</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>1.2</td>
</tr>
<tr>
<td>G8</td>
<td>2.0</td>
<td>-</td>
<td>5</td>
<td>75</td>
<td>3</td>
<td>6.25</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Evaluation of base hair gel formulation

Physical appearance

The physical appearance was visually checked for the colour, appearance and the feel on application of prepared hair gel formulation was noted.

pH determination

The pH of all hair gel formulations were determined by using the digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. Electrodes were completely dipped into the hair gel formulations and pH was noted. The measurement of pH of each formulation was done in triplicate and average values were calculated.

Extrudability determination

The hair gel formulations were filled into collapsible metal tubes. The tubes were pressed to extrude the material and the extrudability of the formulations was checked. The extrudability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of gel in 10 seconds.

Viscosity determination

The viscosity of the prepared gel formulations was measured by Brook field viscometer model LV – DV-II+. The sufficient quantity of gel was filled in wide mouth jar separately. The height of the gel filled in the wide mouth jar should sufficiently allow dipping the spindle. The RPM of the spindle was adjusted to 2.5 RPM. The viscosities of the formulations were recorded.

Spreadability

It indicates the extent of area to which gel readily spreads on application to skin or affected part. The therapeutic potency of a formulation also depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel which is placed in between the slides under the direction of certain load.
Lesser the time taken for the separation of two slides, better the spreadability. It is calculated by using the formula

\[ S = \frac{M \times L}{T} \]

where,

\[ M = \text{Weight tied to upper slide} \]

\[ L = \text{Length of glass slide} \]

\[ T = \text{Time taken to separate the slides} \]

**Stability studies**

The stability studies were carried out for all the prepared gel formulations by freeze – thaw cycling. Here, by subjecting the formulations to a temperature of 4\(^\circ\) C for one month, then at 25\(^\circ\) C for one month and then 40\(^\circ\) C for one month and syneresis was observed. After this, the gel is exposed to ambient room temperature and liquid exudate separating is noted.

**Homogeneity**

After the gel formulations have been set in the container, all developed gels were tested for homogeneity by visual inspection. They were tested for their appearance and presence of any lumps, flocculates or aggregates.

**Grittiness**

All prepared gel formulations were evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation (Kaur *et al.*, 2010).

**Results**

**Optimization and selection of gel formulation**

One of the main ingredients of the gel formulation is the gelling agent. The concentration of viscosity enhancer or gel former is of immense value as a less concentration will lead to simple solution or lotion with very low consistency, while high
concentration may lead to formation of gels with high viscosity leading to non–uniform distribution of drug and problem with handling of gel formulation. Two different gel formers with various concentrations were tried in order to select the best gelling agent. Gels containing sodium CMC showed phase separation and are poor in consistency as indicated by spreadability and extrudability values, hence these gel formulations were rejected. Gels containing 0.5 % and 1 % of Carbopol 934 form a very thin gel that liquefies within 4 and 5 hours of preparation respectively. With 1.5 % Carbopol 934 gelling agent to some extent better gel was obtained but the problem of liquefaction after 28 hours was observed. Gel formulation containing 2 % of Carbopol 934 formed uniform and smooth gel that does not liquefy upon keeping long time.

The pH of the formulation was determined in order to be sure that the formulation can be used without the risk of irritancy to the skin. The pH was found to be 7.56 for G4 gel formulation which was very nearer to the neutral skin pH, thus the formulation G4 can be used without the risk of irritancy to the skin. This also indicated that the selected ingredients of the formulation did not alter the pH of the formulation (Table 5.5).

The spreadability of formulations was found to decrease with increasing the concentration of gelling agent. The value of spreadability for optimized gel was found to be 10.2 cm indicating that the gel is easily spreadable by small amount of shear. The results indicated that the formulation can be applied easily without being runoff. This promises that the formulation maintain a good wet contact time when applied to the site of application. According to the present study, 2 % of Carbopol 934 was selected as the optimized concentration of gelling agent and this gel formulation is used for further herbal hair gel preparations.
### Table 5.5. Evaluation of base hair gel formulation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G1</td>
</tr>
<tr>
<td>Feel of application</td>
<td>Smooth</td>
</tr>
<tr>
<td>Spreadability (g.cm/sec)</td>
<td>13.5</td>
</tr>
<tr>
<td>Consistency</td>
<td>Poor</td>
</tr>
<tr>
<td>pH</td>
<td>6.69</td>
</tr>
<tr>
<td>Viscosity (cps)</td>
<td>82,000</td>
</tr>
<tr>
<td>Extrudability</td>
<td>Good</td>
</tr>
</tbody>
</table>

### Preparation of herbal hair gel formulation

Herbal hair gel formulation was prepared with EEEA 5% (HG1) and EEEA 10% (HG2), EELN 5% (HG3), EELN 10% (HG4) and combination of EEEA (5%) and EELN (5%) (HG5) and pharmaceutical parameters were evaluated. Measured quantity of methyl paraben, glycerin and weighed quantity of polyethylene glycol were dissolved in about 35 ml of water in beaker. Then it was stirred at high speed using mechanical stirrer. Then carbopol 934 and PVP were added slowly to the beaker containing above liquid while stirring. Crushed menthol was incorporated slowly in above dispersion after smooth dispersion is obtained. Then triethanolamine (gelling agents) was added slowly while stirring to attain gel structure. The ethyl acetate soluble fraction of ethanolic extract of *Eclipta alba* and *Lippia nodiflora* was levigated using stainless steel spatula and porcelain slab. The gel was finally transferred in aluminium collapsible tube and labeled.
(Das et al., 2009). Different composition in preparing herbal hair gel is mentioned in Table 5. 6.

Table 5. 6. Formulae of herbal hair gel

<table>
<thead>
<tr>
<th>Formulation</th>
<th>HG1</th>
<th>HG2</th>
<th>HG3</th>
<th>HG4</th>
<th>HG5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbal Extract (g)</td>
<td>5 % of EEEA</td>
<td>10 % of EEEA</td>
<td>5 % of EELN</td>
<td>10 % of EELN</td>
<td>5 % of EEEA + 5 % of EELN</td>
</tr>
<tr>
<td>Carbopol 934 (g)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>PVP (mg)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Methyl paraben sodium (mg)</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Glycerine (ml)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PEG (ml)</td>
<td>6.25</td>
<td>6.25</td>
<td>6.25</td>
<td>6.25</td>
<td>6.25</td>
</tr>
<tr>
<td>Triethanolamine (ml)</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Evaluation of herbal hair gel formulations**

The physical appearance was visually checked for the colour, appearance and the feel on application of prepared herbal hair gel formulation were noted. And also other evaluation parameters like pH, viscosity, extrudability, spreadability, homogeneity and grittiness, feel of application, stability and consistency were evaluated as per the methods mentioned earlier in evaluation for base gel formulations. The results for the evaluation parameters of herbal hair gel are tabulated in Table 5. 7.
### Table 5.7: Evaluation parameters of herbal hair gel formulation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HG1</th>
<th>HG2</th>
<th>HG3</th>
<th>HG4</th>
<th>HG5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>Pale green colour</td>
<td>Pale green colour</td>
<td>Pale green colour</td>
<td>Pale green colour</td>
<td>Pale green colour</td>
</tr>
<tr>
<td>Appearance</td>
<td>Translucent</td>
<td>Translucent</td>
<td>Translucent</td>
<td>Translucent</td>
<td>Translucent</td>
</tr>
<tr>
<td>Odour</td>
<td>Pleasant odour</td>
<td>Pleasant odour</td>
<td>Pleasant odour</td>
<td>Pleasant odour</td>
<td>Pleasant odour</td>
</tr>
<tr>
<td>Spreadability</td>
<td>10.7</td>
<td>10.6</td>
<td>10.2</td>
<td>10.7</td>
<td>10.9</td>
</tr>
<tr>
<td>(g cm/sec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogeneity</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>Feel of application</td>
<td>Smooth</td>
<td>Smooth</td>
<td>Smooth</td>
<td>Smooth</td>
<td>Smooth</td>
</tr>
<tr>
<td>Consistency</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>pH</td>
<td>7.6</td>
<td>7.2</td>
<td>7.5</td>
<td>7.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Viscosity (cps)</td>
<td>1,52,000</td>
<td>1,51,065</td>
<td>1,52,070</td>
<td>1,52,013</td>
<td>1,52,075</td>
</tr>
<tr>
<td>Extrudability</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
</tr>
<tr>
<td>Stability</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
</tr>
</tbody>
</table>
From the physical evaluation the colour of prepared herbal hair gels was pale green in colour and appearance of gel was translucent and it was smooth on application. So it shows significant physical evaluation parameters. The subjective properties such as consistency were good and texture of prepared herbal hair gel was found to be smooth. The pH value of the prepared gel formulation was observed at room temperature and valued range at 7.2 to 7.6. As we go from epidermis to dermis, pH of the skin increases and attained the neutral value. So gel formulation having pH range 7.2 to 7.6 are desirable to skin since they do not interfere with the physiology of skin.

The prepared herbal gel formulations were subjected to accelerated stability testing. The prepared herbal gel was stored at 4°C, 25°C and 45°C in refrigeration, room temperature and oven for a period of 30 days to study effect of temperature and at different humidity condition. The physical parameters were evaluated during study period. The result of the study indicates that the preparation is physically stable at all temperatures tested.

Discussion

The usage of herbal cosmetics has been increased to many folds in personal care system and there is a great demand for the herbal cosmetics. Personal care industry is currently more concentrated on these herbal based cosmetics as now a days it is a fast growing segment with a vast scope of manifold expansion in coming years. The use of bioactive ingredients in cosmetics influence biological functions of skin and provide nutrients necessary for the healthy skin or hair. In general, botanicals provide different vitamins, antioxidants, various oils, essential oils, hydrocolloids, proteins, terpenoids and other bioactive molecules. There is tremendous scope to launch numerous herbal cosmetics using appropriate bioactive ingredients with suitable fatty oil, essential oils, proteins and additives. It is mandatory that adequate safety testing should be conducted according to existing rules and well documented along with the ingredients composition. Under current scenario, Indian market contribution is very less, which could be enhanced through systematic R & D efforts but it requires active collaboration amongst scientists, technologists, cosmetic industry and Government organization.
Conclusion

Topical formulations include oils, creams, ointments, pastes and gels out of which gels are getting more popular now a days because they are more stable and also can provide controlled release than other semisolid preparations. The gel formulation can provide better absorption characteristics and hence the bioavailability of drug. It also provides the better information regarding the formulation and evaluation parameters of the novel herbal gel for skin and hair care activity and to provide the better therapeutic effects to patient compliance (Kaur and Guleri, 2013).

Among the three formulations (oil, cream and gel) prepared, on the basis of pharmaceutical parameters gel formulation loaded with herbal extracts give the considerable results. Hence this herbal gel formulation was utilized for further pharmacological studies.
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