

FORMULATION AND EVALUATION OF MINOXIDIL GEL IN COMBINATION WITH ALOE VERA FOR TOPICAL APPLICATION FOR THE TREATMENT OF ALOPECIA

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ABSTRACT: Minoxidil as topical solution in aqueous vehicle in treatment of alopecia offers limited contact time with scalp. Hence, there is a need for a suitable topical drug delivery system which would increase the contact time leading to increase in local drug concentration of therapeutic effect. The main objective of these study was to formulate, characterize and evaluation minoxidil gel in combination with different extract for enhanced topical drug delivery. Formulations were prepared by using carbopol 940, HPMC, as viscosity enhancing agents. And Aloe vera used as soothing agent, natural polymer, hair growth promoter. The formulations were evaluated by appearance, gelation, measurement of pH, spreadability and skin irritation tests were done. A stable minoxidil gel formulation is prepared by using aloe vera, carbopol 940, HPMC, propylene glycol, triethanolamine, ethanol used in the treatment of alopecia. The developed formulations were stable, non-irritant to albino rats.

Keywords: HPMC, Carbopol 940, Minoxidil, Anti-Alopecia, Aloe vera, Albino rats.

I. INTRODUCTION

Topical drug delivery system is one of the system is one of the effective ancient method is used till now. Topical administration is the favoured route for local delivery of therapeutic agents due to its convenience and affordability. The specific challenge of designing therapeutic system is to achieve an optimal concentration of a certain drug at its site of action for an appropriate duration.

Gels are substantially dilute cross-linked system which exhibits no flow when in steady state. They consist of two component semi solid systems rich in liquid. Gels have become a premier material used for drug delivery formulations due to its biocomparability, network structure and molecular stability of the incorporated bioactive agents. Gels are used in topically, gels are basically used in topically, gels are having property to avoid enzymatic activity and drug interaction with food and drinks. They can substitute for oral administration when route is unsuitable.

Alopecia areata is a recurrent, genetic, immune mediated diseases that affects 2.1% of population including children and adults, characterized as patches of hair loss of scalp. Although the etiology of alopecia areata is purely understood, but the number of factors such as genetics, stress, diet, hormones, vaccination etc. Determined the physical and biochemical status of the immune system and hair follicles. It is also known that T-lymphocyte play an important role in alopecia areata is filtrating against the hair fall leading to abrupt conversion from anagen to telogen phases.

MINOXIDIL is a pyrimidine N-oxide that is pyrimidine-2,4-diamine 3-oxide substituted by a piperidin-1-yl group at position 6. It has a role as a vasodilator agent and antihypertensive agent. Minoxidil is a common medication prescribed for treating hair loss related problems. It provides remarkable benefits to patients with hair disorders.¹

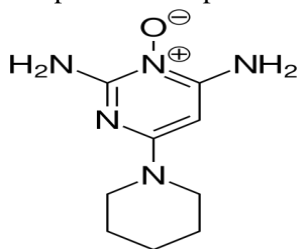


Fig.1. Minoxidil

Minoxidil is a powerful vasodilator, i.e. direct relaxation of arteriolar smooth muscle with little effect on venous capacitance. Minoxidil is the only FDA approved topical medication with proven efficacy for the treatment of androgenic alopecia. Alopecia is characterized by round or oval patches of non – scarring hair loss. It is believed that it only causes scalp hair loss that may be partial or complete, but sometimes it may progress to cause total body hair loss.

Introduction to Aloe vera:

Scientific name: *Aloe barbadensis miller*.

Family: Liliaceae

Genus: Aloe

Chemical constituents: Aloin, catechin, Anthraquinone.

Aloe vera is a cactus like plant, which has been used by mankind as a mankind for a thousand of years in folk medicine for therapeutic uses specially on skin. Aloe vera gel is cooling and soothing when applied to the skin, which is why it's sometimes used to treat burns and skin wounds. Seborrheic dermatitis is the clinical term for the condition we call dandruff. The symptoms of an itchy scalp and flaking skin under the hair can be treated with aloe vera. The fatty acids found in the aloe plant have anti-inflammatory properties which helps in the scalp inflammation caused by dandruffs. Aloe vera cleanses the hair shaft and remove the extra shaft efficiently without damaging the hair strands. Aloe vera contains vitamins A, C, and E, all three of these vitamins contribute to cell turnover, promoting healthy cell growth and shiny hair, in Aloe vera gel there is also vitamin B₁₂ is present which helps in preventing hair fall.^[3,4]

Anthraquinones	Saccharides	Vitamins	Enzymes	Low molecular weight substances
aloe-emodin aloetic acid anthranol barbaloin isoberbaloin emodin ester of cinnamic acid	cellulose glucose mannose aldopentose acemannan acylyted glycomannan glactogalacturan	A B ₁ B ₂ B ₆ B ₁₂ C β-carotene choline folic acid α-tocopherol	amylase carboxypeptidase catalase lipase oxidase	arachidonic acid cholesterol gibberellin lignin salicylic acid β-sitosterol steroids triglycerides uric acid

Table: Main ingredients of aloe vera.

II. MATERIALS AND METHODS:

MATERIALS

Minoxidil was collected from Sincorpo Laboratories, Hyderabad. Carbopol 940 was collected from **NP CHEM-Mumbai**, Propylene glycol was collected from **VIRAT LABS Mumbai**, Ethanol, Triethanolamine, HPMC were collected from **VENKATESWARA SCIENTIFIC TRADERS**, Distilled water collected from **Nalanda College of Pharmacy lab**.

INSTRUMENTS

ELITE ISO 9001:2006 (Magnetic stirrer), **INFRA DIGI IR-501** (digital pH meter), **WARMEX** (Water bath), **CITIZEN BALANCE BL- 220H** (Electronic weighing balance).

METHODS

Preparation of minoxidil gel: Accurately weighed amount 50 mg of minoxidil was dissolved in solvent mixture (ethanol, propylene glycol and water). Then the required quantity of polymers added to the solutions with the constant stirring on a magnetic stirrer at 900-1000 rpm for 15 mins. Later the speed was reduced to avoid air entrapment. The pH of above method was adjusted to 7.4 with triethanolamine. The solution is finally gelled by adding Carbopol 940, carefully with constant stirring. After stirring, the beaker contain gel was allowed to stand in a waterbath 25°C for 30 mins.

Preparation of aloe vera containing minoxidil gel: Extraction of aloe vera gel the thick and pleasant leaves of the aloe vera plant collected from medicinal garden of Nalanda College of Pharmacy. The leaves of aloe vera are spliced together, washed with water and a medium chlorine solution, then temporarily chopped to remove the aloe vera, and the sticky jam is removed from the center of leaves of the aloe vera plant. Extract was triturated by using mortar and pestle. Extract was mixed with minoxidil, propylene glycol and ethanol mixed and stirred at 1000 rpm for 30 minutes and it was gelled by adding Carbopol 940 at water bath at 25°C for 30 minutes.

Ingredients	F1	F2	F3	F4	F5
Carbopol 940	30 mg	-	30mg	-	50 mg
Propylene glycol	5 ml	5 ml	5 ml	5 ml	5 ml
Ethanol	3 ml	3 ml	3 ml	3 ml	3 ml
HPMC	600 mg	-	-	400 mg	200 mg
Triethanolamine	1 ml	1 ml	1 ml	1 ml	1 ml
Water	2 ml	2 ml	2 ml	2 ml	2 ml
Minoxidil	50 mg	-	50mg	50mg	50 mg
Aloe vera	-	2 gm	2 gm	2 gm	3 gm

Table 1: Formulation table.

II. EVALUATION TESTS

Homogeneity: All developed gels are tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

Grittiness: All the formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom particular matter and from grittiness as desired for any topical preparation.

Skin irritation test: The Albino rats of 200 g were used for this test. The intact skin was used for this study. Rat hair was removed a day before the experiment. The animals were divided into three groups, each group contains 4 rats. The gel containing drug were used on test animals. One piece of cotton wool was dipped in the gel and was placed on the back (right side). After 3 days of examination, red spots were found on the skin, considered as erythema.

Drug content: To ensure uniform formulation of the gel, it was sampled from the different locations in the mixer and assayed for the drug content. Drug content of the gels was determined by dissolving an accurately weighed quantity of gel (about 1 gm) in about 100 ml of pH 6.8-phosphate buffer.

Spreadability test:

During the experiment, a test sample of a certain mass is placed on a glass plate, which is covered on top with another plate with an attached wooden block. A weight is placed on the upper plate for a while. After this, the weight is removed, a weighting agent is attached to the wooden block and the time that is needed for the upper plate to completely separate from the lower plate is measured.

Spreadability can be measured by this formula: $S = M \cdot L / t$

Where, S- Sample for spreadability, M- wt. tied to upper slide (g), L- glass plates length (cm), t- time taken to separate.

III. RESULT AND DISSCUSSION

Gel formulations were prepared with an intension of increasing the contact time of the drug with the scalp region so that minoxidil is released in a prolonged manner for a extended period of time. Carbopol, HPMC, Aloe vera used as gelling agents. The solvent system consisting of propylene glycol: water: ethanol has been proved to be a good system to deliver minoxidil topically.

The in-vitro drug release profiles of the formulations in phosphate buffer pH 7.4 show differences depending on their composition. From the data obtained from evaluation parameters. It is evident that formulations F₁, F₅ were found to be satisfactory in all the aspects among them the most preferred is the formulation F₅ as the Carbopol, HPMC, aloe vera were used as gelling agents, hence in the present study is a combination of natural polymer (aloe vera) were used in the preparation of topical gel. Among all combinations F₅ found to be all the

evaluation parameters and also in terms of least side effects as the natural polymer used is aloe vera.

Spreadability of the formulations are measured through the equation $S=M*L/t$

Where, S- Sample for spreadability, M- wt. tied to upper slide (g), L- glass plates length (cm), t- time taken to separate.

Spread ability coefficient of Gel Formulations:

Sl. No	Formulation code	M (gm)	L (cm)	T (sec)	S=M*L/t
1.	F ₁	5	5	3.85	6.49
2.	F ₂	5	5	3.4	7.35
3.	F ₃	5	5	0.2	125
3	F ₄	5	5	6	4.16
5.	F₅	5	5	2.35	10.63

Table 2: spreadability test.

Comparing with all the formulations F₅ shows the best result, while F₃ & F₄, didn't get the proper gel in nature.

Formulation code	Drug content (%)	Homogeneity	Spreadability	Skin irritation
F ₁	96.34	Homogenous	6.49	Erythema
F ₂	-	Homogenous	7.35	No irritation found.
F ₃	94.93	Slightly homogenous	125	Does not applied on albino rat.
F ₄	95.93	Homogenous	4.16	Does not applied on albino rat.
F ₅	97.50	Homogenous	10.63	No irritation found.

Table 3: Table of evaluation tests.

IV. CONCLUSION

The present study aimed to formulate & evaluate minoxidil loaded aloe vera gel. Minoxidil loaded aloe vera gel was successfully formulated & evaluated. From this study it can be concluded that it is possible to design minoxidil loaded aloe vera gel for the treatment of alopecia that have more moisturizing properties is due to the presence of aloe vera & it also imparts the nutritional support to the system, it also minimizes the side effect associated with Minoxidil, which indicates that the proposed formulation can be an excellent therapy for the treatment of alopecia with less side effects & better efficacy.

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