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# Formulation Development and Evaluation of Novel Poly-Herbal Anti-Acne Gel

**Sharma Mayank[1]*, Rathore Vikas [2]**

**[1]School of Pharmacy, Devi Ahilya University, Indore, (M.P)**
**[2]Department of Pharmaceutical Technology, Noida Institute of Engineering and Technology, Greater Noida, (U. P),India.**

***Corres.author: mayank2306@gmail.com**

**Abstract:** Herbal remedies are more acceptable in the view that they are safe with fewer side effects than the synthetic ones. Herbal formulations have more demanded in the market. The present work deals with the Development and Evaluation of Novel Poly-Herbal Anti-Acne Formulation containing hydro-alcoholic extract of neem leaves,(Azadirachta indica), extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil. Although various anti acne herbal formulations for acne are available in the market, we propose to make use of hydro-alcoholic extract of neem (Azadirachta indica) leaves ,extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil. The plants have been reported in the literature having good anti-microbial, anti-oxidant and anti-inflammatory activity. Various formulation batches i.e., F1 to F19 were prepared using different gelling agents like carbopol 934, carbopol 940 and HPMC K4M in varied concentrations. Prepared formulations (F1 to F19) were evaluated for various parameters like colour, appearance, consistency, washability, pH, spreadability along with antimicrobial efficacy study. Optimized formulation was compared with the marketed preparation. Amongst all the formulation studied batch F4 was found optimum for all the parameter. It is a very good attempt to establish the herbal gel containing hydro-alcoholic extract of neem leaves (Azadirachta indica) extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil .
**Key words:** Poly-Herbal Anti-Acne Formulation, Ocimum Sanctum (OS), neem (Azadirachta indica), Aloe vera powder, tea tree oil.

## Introduction

Acne vulgaris is an extremely common disorder of skin (pilocebaceous unit) that affects virtually all individuals at least once during life. The incidence of acne peaks at teenage, but substantial numbers of men and women between 20-30 years of age are also affected by the disorder. [1] Acne may be classified as comedonal, papular, pustular, cystic, and nodular. Comedonal acne is non-inflammatory and divided into two types: whiteheads and blackheads. White heads (closed comedo) present as fresh or white colored, raised bumps whereas blackhead (open comedo) present as open pores containing dark colored skin roughage consisting of melanin, sebum, and follicular cells. Papules appear as red, solid, elevated lesions often less than 5 mm in diameter. Pustules are circumscribed skin elevations containing purulent material.Cysts and nodules are solid, elevated lesions involving deeper dermal and subcutaneous tissue. Cysts are less than 5 mm in diameter whereas nodules exceed 5 mm.

The pathogenesis of acne involves multiple physiological factors. These include follicular hyper proliferation; increased sebum production due to higher androgen levels and colonization of organism, *Propionibacterium*

*acnes* [2]. Novel concepts have emerged to help better understand its pathogenesis; these include variations in target cell sensitivity, biological markers, neuro-endocrine, genetic, and environmental factors. Plenty of herbal as well as synthetic ingredients are reported to have remarkable beneficial effect on acne vulgaris. [3, 4, 5] They may have different mechanisms like, (a)Control sebum secretion, (b)Antibiotics which inhibit *Propioni bacterium acne, the* main causative organism of acne, (c) Keratolytic which removes the keratin layer and prevents the trapping of sebum under the skin, (d) Anti-inflammatory which prevents the worsening of condition due to inflammation or redness etc.

Numbers of formulations are available in the market with variety of active pharmaceutical ingredients for the treatment of acne. Topical formulations, available in the market are as follows: Gel, Cream, Lotion, Face wash or cleansers, Face pack or mask. Neem (*Azadirachta indica, Meliaceae*) neem leaves, extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil are reported to have very beneficial effect on acne due to anti-microbial, anti-inflammatory and anti-oxidant activities of different chemical constituents. [1, 3, 4]

## Methods

### Preparation of Extracts [6]

Leaves of neem were cut into small pieces. Leaves of ocimum santum were crushed to make powder. Desired quantities of herbal drugs were weighed and were individually added to the conical flask containing five times volume of 1:1 water-ethanol mixture. Contents were allowed to boil on water bath under reflux condition for about 30 min. Contents were filtered out and residues were again boiled with five times volume of 1:1 water-ethanol mixture on water bath under reflux condition for about 15 min. Contents were filtered out and filtrates were combined. Filtrate was allowed to evaporate in evaporating pan until the desired concentration of the extract was obtained.

### Development of Formulation

Various formulation batches were prepared according to the Table 1. [7, 8] The desired concentration of gelling agents were weighed accurately and dispersed in hot purified water (not more than 60°C; 50 % weight of the batch size) with moderate stirring, avoiding air entrapment and allowed to soak overnight. Desired quantity of methyl paraben was dissolved in remaining amount of water by gentle heating. Desired quantity of polyethylene glycol 4000, propylene glycol and herbal extracts were added to the above mixture. This was finally mixed with previously soaked gel formulation. Triethanolamine was added at last to adjust the pH. Prepared formulations were filled in a suitable container and labeled accordingly.

## Evaluation of Formulations

### Physical evaluation

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

### Washability

Formulations were applied on the skin and then ease and extent of washing with water were checked manually.

**pH:** [8]

pH of 1% aqueous solution of the formulation was measured by using a calibrated digital pH meter at constant temperature.

**Table 1: Composition of developed Formulations**
Quantity taken per 100 gm gel ( in grams)

| Ingredients | F 1 | F 2 | F 3 | F 4 | F 5 | F 6 | F 7 | F 8 | F 9 | F 10 | F 11 | F 12 | F 13 | F 14 | F 15 | F 16 | F 17 | F 18 | F 19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Neem | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | - | - | - | - | - | - | - | - | - | 2.5 |
| Ocimum Santum | - | - | - | - | - | - | - | - | - | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 2.5 |
| Aloevera | - | - | - | 0.5 | 1.0 | 1.5 | 0.5 | - | - | 0.5 | 1.0 | 1.5 | - | - | - | - | - | - | - |
| Tea Tree Oil | - | - | - | 0.5 | 1.0 | 1.5 | - | - | - | - | - | - | 0.5 | 1.0 | 1.5 | - | - | - | - |
| Carbopol | 0.5 | 1.0 | 1.5 | - | - | - | - | - | - | 0.5 | 1.0 | 1.5 | - | - | - | - | - | - | - |
| Hpmc(934) | - | - | - | 0.5 | 1.0 | 1.5 | - | - | - | - | - | - | 0.5 | 1.0 | 1.5 | - | - | - | 0.5 |
| Hpmc(940) | - | - | - | - | - | - | 3.0 | 3.5 | 4.0 | - | - | - | - | - | - | 3.0 | 3.5 | 4.0 | - |
| Peg 4000 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |
| Propylene Glycol | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 | 15.0 |
| Mathyl Paraben | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Tea | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S |
| Purified Water | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S |

**Spreadability:** [8]

Spreadability was determined by an apparatus suggested by Multimer et al [9] fabricated in-house. The apparatus consist of a wooden block with a fixed glass slide andmovable glass slide with one end tied to weight pan rolled on the pulley, which was in horizontal level with fixed slide. The spreadability of the formulated gel was measured on the basis of 'Slip and Drag' characteristics of gel. An excess of gel (about 2g) under study was placed on this ground slide. The gel was then sandwiched between two slides. One kg weight was placed on the top of the two slides for 5 min to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull off 50 gm. (M) with the help of string attached to the hook and the time (T, in seconds) required by the top slide to move a distance (L) of 7.5 cm be noted. A shorter interval indicated better spreadability. Spreadability (S) was calculated using the following formula:

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

**Microbial assay** [9, 10, 11]

The antibacterial activities of different formulations were determined by modified agar well diffusion method. In this method, nutrient agar plates were seeded with 0.2 ml of 24 h broth culture of S. *aureus*. The agar plates were allowed to solidify. A sterile 8 mm borer was used to cut wells of equidistance in each of plates. 0.5 ml of formulations, herbal extracts and marketed clindamycin gel were introduced into the wells at randomly. The plates were incubated at 37$^{o}$C for 24 hours. The antibacterial activities were evaluated by measuring the zones of inhibition (in mm). The results of evaluation are displayed in Table 2. Formulation F2-F5, F8, F11-F14, F17 and F19 had semisolid consistency. All the formulations were found homogenous, easily washable. All the formulations had very slightly alkaline pH which were compatible with normal skin physiology.

**Table 2: Evaluation of Formulations**

| Formulation/ Batch (Code) | Colour | Consistency | Washability | pH | Spreadability (gm-cm/sec) | Zone Of Inhibition (mm |
|---|---|---|---|---|---|---|
| Marketed | Colorless | Semi-solid | Good | 7.05 | 27.71619 | 10 |
| Neem extract | Green | - | - | - | - | 8 |
| Ocimum sanctum extract | Green | - | - | - | - | 5 |
| Aloevera gel | Colorless | - | - | - | - | 4 |
| Tea tree oil | Clear with yellow tinge | - | - | - | - | 5 |
| F1 | Green | Fluid | Good | 7.38 | 186.5672 | 7 |
| F2 | Green | Semi-solid | Good | 7.43 | 11.31563 | 5 |
| F3 | Green | Semi-solid | Good | 7.01 | 3.74925 | 4 |
| F4 | Green | Semi-solid | Good | 7.98 | 62.5 | 6 |
| F5 | Green | Semi-solid | Good | 7.05 | 3.949447 | 5 |
| F6 | Green | Stiff | Good | 7.05 | 3.022975 | 5 |
| F7 | Green | Fluid | Good | 7.15 | 50.81301 | 5 |
| F8 | Green | Semi-solid | Good | 7.90 | 13.01631 | 3 |
| F9 | Green | Stiff | Good | 7.11 | 2.345803 | 2 |
| F10 | Yellowish green | Fluid | Good | 7.13 | 168.1614 | 3 |
| F11 | Yellowish green | Semi-solid | Good | 7.15 | 10.71123 | 2 |
| F12 | Green | Semi-solid | Good | 7.05 | 3.640423 | 2 |
| F13 | Green | Semi-solid | Good | 7.93 | 51.86722 | 3 |
| F14 | Green | Semi-solid | Good | 7.89 | 4.032692 | 3 |
| F15 | Green | Stiff | Good | 7.10 | 2.907878 | 2 |
| F16 | Green | Fluid | Good | 7.12 | 53.87931 | 3 |
| F17 | Green | Semi-solid | Good | 7.48 | 12.36807 | 2 |
| F18 | Green | Stiff | Good | 7.64 | 2.458372 | 1 |
| F19 | Green | Semi-solid | Good | 7.30 | 62.5 | 5 |

## Discussion

Amongst all the formulations F4, F7, F13, F16 and F19 had very optimum spreadability. All the formulations showed considerable zone of microbial inhibition. Herbal extract and formulation of neem showed comparatively more antimicrobial activity than formulation prepared with nutmeg. F1 and F4 showed better antibacterial activity.

## Conclusions

Natural remedies are more acceptable in the belief that they are safer with fewer side effects than the synthetic ones. Herbal formulations have growing demand in the world market. It is a very good attempt to establish the herbal gel containing hydro-alcoholic extract of neem leaves (*Azadirachta indica*) neem leaves, extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil. This study revealed that the developed single herbal formulation F4 consisting neem leaves,(Azadirachta indica), extract from leaves of Ocimum Sanctum (OS), Aloe vera powder &tea tree oil was comparatively better than other formulation.

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