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# DEVELOPMENT AND EVALUATION OF HERBO SYNTHETICGEL: A NOVEL TREATMENT FOR PSORIASIS

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**Keywords:**

Herbal gel, Cyclosporine, Aloe vera, *In-vitro,* psoriasis.

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**ABSTRACT: Background:** Psoriasis is an immune-mediated inflammatory disease characterized by excessive growth and abnormal differentiation of keratinocytes. **Objective:** In the present research work, an attempt has been made to formulate and evaluate gel containing cyclosporine, aloe vera and tree tea oil. **Methods:** The gel was prepared by a conventional method and evaluated for various parameters *viz.*, physical appearance, pH, drug content, viscosity, spreadability and *in-vitro* diffusion studies, *In-vitro* skin retention studies and stability studies. The prepared optimized gel was further compared with marketed formulation; all the formulations were good in appearance and had good homogeneity. **Results:** The optimized gel is shown spreadability co-efficient is 5.8 g cm/sec. The gel has shown 95 ± 0.32% releases in 6 h when evaluated for *in-vitro* diffusion studies. The biological evaluation of the optimized gel has shown 47.98 % drug activity, indicating good efficacy of the formulation against psoriasis. **Conclusion:** In conclusion, the prepared optimized gel has shown good spreading co-efficient and stability and can be effective for psoriasis as compared to available gel in the market.

**INTRODUCTION:** Psoriasis is a common inflammatory skin condition where the skin develops areas become thickly covered with silvery scales [1, 2]. Psoriasis occurs most commonly at the age of between 15 to 25 years and can affect both males and females. Noteworthy, fair people suffer more than black people. It is mainly occurring in a temperate climate. Psoriasis has a 1% incidence in India, whereas in the United States, it increases to 2-3% and in Northern Europe and Scandinavia, it is 1.5-3%. It is common in Japanese and rare in Chinese, West Africans, North American and Australians [3, 4]. Psoriasis is a life-long disease and the management and treatment of psoriasis are different depending on the severity of the disease [5]. The first line active treatment for psoriasis is the use of topical agents.

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The available therapies for topical treatment of psoriasis involve emollients, moisturizers, tars, enthralling, topical corticosteroids, vitamin A, vitamin D, and synthetic treatment corticosteroids, methotrexate, cyclosporine, immune modulators, and hydroxyurea [6]. The synthetic drugs used to treat it have various side effects like nausea, fatigue, liver damage, blood cell damage, kidney

problems, high blood pressure, high cholesterol level, bone marrow problems, and increased risk of skin cancer. Another option for treating psoriasis involves herbs that are free from side effects. The herbs *viz.* Aloe vera, Curcumin longa, Silybummarianum and various oils like tree tea oil, black seed oil, coconut oil, *etc.*, are reported to be used for psoriatic condition [7, 8, 9]. Cyclosporine is an immunosuppressant medication and natural product used in the treatment of psoriasis. Also, it is beneficial for many other dermatologic diseases such as psoriasis, lichen planus, behcet disease, atopic dermatitis, pyoderma gangrenous and epidermolysis bullosa acquisita.

The selective action of cyclosporine on helper T cells and its rapid therapeutic action and weak myelotoxicity are the key advantages in the treatment of many dermatologic diseases. Cyclosporines have more side effects when administrated orally. Therefore, the formulator suggests the use of cyclosporine as topical administration in case of psoriasis to be useful [10, 11, 12]. Aloe Vera, an herbal plant, a gel of which is widely used as a supplemental treatment for psoriasis. Aloe vera gels mostly consist of 98-99% water remaining more than 200 different components *viz.*, polysaccharides, vitamin, flavonoid, sterol, amino acid, *etc.*

These bioactive components result in beneficial effects of this herb in psoriasis [13, 14, 15]. Treatment of psoriasis, including topical agents, UV photometry, systemic agents, *etc*., can be used. Since the synthetic and herbal combination can be effective for psoriasis. So, topical treatment is mostly prescribed method in the case of psoriasis. The gel is semisolid, being either suspensions of small inorganic particles or large organic molecules interpenetrated with liquid. Moreover, a gel is a semisolid system of at least two interpenetrating phases: a gelling agent and a liquid. Gels that contain water are called hydrogels [16]. Thus it is hypothesized that the combination of cyclosporine and aloe vera will show synergistic action with dose reduction and efficacy against psoriasis will be enhanced. Therefore, in this research work, an attempt was made to formulate herbal gel containing Aloe vera along with Cyclosporine for the effective treatment of psoriasis.

**MATERIALS AND METHODS:** Drug (Cyclosporine) central Drug House (P) Ltd, New Delhi, Tea Tree oil, Carbopol 940 (1%w/v), methanol, propylene glycol, methylparaben, propylparaben, tri-ethanolamine were obtained from Research fine lab, Mumbai, Aloe vera from Herbal garden, Laureate Institute of Pharmacy and other ingredients used were of analytical grade.

**Extraction of Gel:** Aloe barbadensis Aloe vera (Aloe barbadensis Miller) leaves were collected in Nov-December 2018 in Kathog in the Jwalaji Region of Kangra. Specimens were collected and submitted for authentication to IHBT, Palampur. IHBT identified the sample as Aloebarbadensis. Samples were kept in a deep freezer at -40 ºC and were protected from light until further studies. The leaves used for extractions were pea-green in color, linear with spinal margins having spiral orientation. Leaves measured between 22 cm and 30 cm in length and were taken from 2-year old plants. All the leaves were washed with distilled water and then with chlorinated water (0.5% chlorine). Before slicing the leaf, spikes and margins were removed. Then the cortex was removed carefully from parenchyma using a sharp blade.

The cortex was carefully separated from the parenchyma using a scalpel-shaped knife. The gel wash was scraped off with the help of a knife and collected in the container. The clear, slightly yellowish gel so obtained was blended in a mixer for a minute and was collected in a container, stored in the freezer until further studies. The obtained gel was evaluated for the pH, acidity, and total antioxidant capacity determination. pH was determined in fresh samples using a pH meter. Acidity [17] of the aloe vera gel was determined by AOAC. potentiometric titration using 0.1 N NaOH (pH=8) using phenolphthalein as an indicator. An adequate amount (2g) of samples were placed in flasks, after which water was added to complete 50 mL. Results were expressed as a percentage of malic acid.

The total antioxidant capacity of aloe vera gel was determined by mixing an aliquot of 0.2 ml of sample solution (Two different concentrations) with 2 ml of reagent solution (0.6 M sulphuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate [18]. The test tubes were incubated at 95

°C for 10 min to complete the reaction. The absorbance was measured at 695 nm using a spectrophotometer against blank after cooling at RT. Ascorbic acid was used as a standard. A typical blank solution contained 2 ml of the reaction mixture, and the appropriate volume of the same solvent used for the samples/standard was incubated at 95 °C for 10 min, and the absorbance was measured at 695 nm. Increased absorbance of the reaction mixture indicated an increase in total antioxidant capacity. The Antioxidant Capacity was Estimated Using the Following Formula:

$$\text{Antioxidant effect (\%)} = [(\text{control absorbance} - \text{sample absorbance}) / (\text{control absorbance})] \times 100$$

**Formulation of Gel:** A different formulation of cyclosporine gel (G1 to G12) as shown in **Table 1** using 100 mg of cyclosporine was prepared using Carbopol and extracted fresh aloe vera in different concentrations. Carbopol 940 was soaked in the distilled water overnight. The next day, a properly swelled polymer is placed in the mortar, and glycerine and extracted aloe gel were added in it with continuous mixing using a pestle. Preservatives like methylparaben and propylparaben added to the mixture by continuous stirring. The drug was firstly dissolved in the methanol and then added to the mixture. The pH of the gel was adjusted by using triethanolamine. Prepared gel was left at room temperature and sonicated for 15 min to set and allow removing the air bubbles produced during mixing. Prepared cyclosporine gel was stored in an airtight container and evaluated for different parameters [19].

**TABLE 1: COMPOSITION OF ANTIPSORATIC GEL**

| S. no | Ingredients | G1 | G2 | G3 | G4 | G5 | G6 | G7 | G8 | G9 | G10 | G11 | G12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Cyclosporine (mg) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | Carbopol 940 (%) | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1.5 | 1.5 | 2 |
| 3 | Aloe vera (%) | 15 | 12 | 10 | 9 | 8 | 4 | 3 | 2 | 1 | 5 | 6 | 7 |
| 4 | Methanol (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 5 | Methylparaben (%) | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| 6 | Propylparaben (%) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| 7 | Xanthumgum (%) | 1 | 1 | 1.5 | - | - | 1 | 2 | 3 | - | 1 | 1.5 | 1 |
| 8 | Tea Tree oil (%) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9 | Propylene (ml) | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| 10 | Triethanolamine(ml) | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| 11 | Water(ml) | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |

Prepared gel was further evaluated for the following parameters:

**Homogeneity:** All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. The formulated gel was tested for its 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 a light microscope.

**Spreadability:** The spreadability of the prepared gel was evaluated using a fabricated spreadability apparatus. The apparatus was consisting of a wooden block, with a fixed glass slide and movable glass slide with one end tied to the weigh pan rolled on the pulley, which was at a horizontal level with a fixed slide. One gram of gel was poured onto the fixed glass slide, and the movable slide was placed on it. The weight (approx. 15 gm) was added to the weigh pan, and time was noted for complete removal of the moving slide from the fixed slide. Spread ability was measured using the given equation $S = m \times L/T$, where; S-Spread ability coefficient; m-Weight of gel in gm; L=Length of the slide; T= time taken (sec)

**Extrudability Study:** A good gel extrudes optimally from the gel with slight pressure applied. The extrude ability [20] of formulations from collapsible aluminium tubes was determined using a universal tube filling machine. Aluminium collapsible tubes filled with 10 g gels were held between two clamps. A tube was compressed, and the extrude ability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 sec.

**Measurement of pH:** The pH of gel formulations was determined by using a digital pH meter.

One gram of gel was 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.

**Drug Content:** 1g of gel formulation was taken and dissolved in 50 ml of phosphate buffer pH 5.5. The volumetric flask was kept for 2 h and shaken well in a shaker to mix it properly. The solution was passed through the filter paper and filtered. The drug content was measured spectro-photometrically at 216 nm for cyclosporine against corresponding gel concentration as blanks [21].

**Viscosity Study:** The measurement of viscosity of the prepared gel was done with a Brook field Viscometer. The gels were rotated at 20 and 30 rpm using spindle no. 64. At each speed, the corresponding dial reading was noted.

***In-vitro* Diffusion Studies:** *In-vitro* permeation studies of cyclosporine gel were performed through the goatskin using Franz diffusion cell assembly. Under sterile conditions, the shaven part of the goatskin was separated. The excised skin was washed with normal saline and subsequently used. The skin was on the diffusion assembly, keeping the stratum corneum towards the donor compartment. The receptor compartment consisted of 200 ml phosphate buffer pH 5.5, maintained at 37 °C. 1 ml sample was withdrawn at suitable time intervals and replaced immediately with an equal volume of fresh diffusion medium. The samples were analyzed spectrophotometrically at 216 nm against similarly treated blank after suitable dilution.

All experiments were performed in triplicate. The cumulative amount of cyclosporine permeated through goatskin was plotted as a function of time [22]. Data obtained from *in-vitro* release studies, various gel formulations were fitted to various kinetic equations such as zero-order, First order, Higuchi model, and Korsmeyer-Peppas model.

**Skin Retention Study:** Skin retention studies were carried out in order to analyze the content of the drug in the skin. At the end of the permeation experiments (after 24 h), the remaining formulation in the donor phase was scraped off the skin, and the exposed skin surface was rinsed with water and methanol to remove the excess drug from the surface. The skin was dried completely, and then a defined amount of methanol was added to the skin. The samples were vortexed for 10 min to extract the drug and stirred overnight. After that, the media was analyzed for the amount of drug retained in skin spectrophotometrically against similarly treated blank.

**Stability Study:** The prepared gel formulation was filled in the collapsible tubes and stored at ambient temperature (40 °C, 75 % RH). The gel formulation was evaluated for phase separation, color, viscosity, drug content, physical appearance, pH, and in vitro diffusion study after 3 months [23].

**Biological Evaluation:** The anti-psoriatic activity was carried out by using the mousetail model [24]. In this method, orthokeratosis is induced in the tail of the mouse, which generally has parakeratotic differentiation. In the present study, the same method was followed as described by Nupur P *et al.* 2014; the four groups of five albino mice each were treated once daily with saline solution, blank gel, marketed formulation, and optimized formulation G1. The formulations were applied once daily to the proximal half of the mouse tail for 4 weeks. Twenty- four hours after the last application of the formulation, the mice were killed by cervical dislocation. After that, the tail skin was cut by longitudinal dissection with a blade and stripped from the underlying cartilage.

The skin samples obtained were appropriately processed and stained with hematoxylin and eosin. The processed skins were examined microscopically for the presence of the granular layer in the scale regions and epidermal thickness. Induction of orthokeratosis in those parts of the adult mouse tail, which normally have a parakeratotic differentiation, was quantified, measuring the length of the granular layer (A) and the length of the scale (B). Ten sequential scales were examined for each skin section. The proportion, that is, A/B*100 represents the percent orthokeratosis per scale. An increase in the percentage of orthokeratotic regions will be called drug activity. It is calculated by using the formula:

DA = (Mean orthokeratosis of the treated group -Mean orthokeratosis of the control group) / (100 -Mean orthokeratosis of a controlled group) × 100

## RESULTS AND DISCUSSION:

**Extraction of Gel:** Gel obtained was clear, having a slight yellow color. The yield was calculated by keeping in view the weight of aloe vera leaves as 100%.

The cortex of leaf weighed about 36.13%, and the gel was about 52.7% of the total weight, while 11.17 % was loss during scrapping of gel. The pH in gel samples is slightly acidic, ranging from 4.5 to 5.5. The results indicate that Aloe vera plants under our conditions are able to buffer acidic pH. In this study, the acidity was measured as malic acid content as Aloe vera is a CAM plant. The relative malic acid content detected was 0.48 % (within the limits of IASC reported values 08% - 0.34%. Lower the values of pH more will be the stability of gel as it will be less susceptible to microbial contamination. The antioxidant capacity of the fresh gel was determined by the Phosphomolybdate assay method. The antioxidant effect was found to be 83.90 % and 86.56 % when used in two different concertations of 100 and 400 µg/ml, respectively, as shown in **Table 2.**

**TABLE 2: TOTAL ANTIOXIDANT CAPACITY OF EXTRACTED PECTIN**

| S. no | Solution | Concentration | Absorbance | Antioxidant effect (%) |
|---|---|---|---|---|
| 1 | Aloe vera Gel | 100 µg/ml | 0.161± 0.051 | 83.90 |
| | | 400 µg/ml | 0.524 ± 0.042 | 86.56 |
| 2 | Ascorbic acid | 100 µg/ml | 1.47 ± 0.018 | |
| | | 400 µg/ml | 3.901 ± 0.021 | |

Mean ± SD; (n=3)

**Evaluation of Gel:** The present research work was designed to develop gel containing synthetic and herbal ingredients for the effective treatment of psoriasis. The selected drug cyclosporine has low bioavailability and undergoes hepatic first-pass metabolism.

Moreover, it is more effective when applied topically. Hence the research work was designed in such a way that its application on the skin should enhance the efficacy of the drug on psoriasis, which is augmented with the addition of Aloe vera gel. The gel was prepared by the cold method.

The gel obtained was transparent in nature (G1-G19), whereas the gel formulation G10 -G12 was turbid that could be due to the increased concentration of the gelling agent.

The drug was subjected to systemic Pre formulation analysis followed by formulation and then its evaluation.

**TABLE 3: GEL WAS EVALUATED FOR DIFFERENT PARAMETERS AS FOLLOW**

| Formulation | Appearance | Homogeneity | Grittiness | Extrudability (%) | pH | Spreadibility (g.cm/sec) | Viscosity (cps) | Drug content (%) |
|---|---|---|---|---|---|---|---|---|
| G1 | Transparent | Good | No | 95.5 ± 0.12 | 5.4 ± 0.15 | 4.8 ± 0.93 | 1408 ± 15 | 96.3 ± 0.51 |
| G2 | Transparent | Good | No | 95.2 ± 0.12 | 5.6 ± 0.14 | 5.1 ± 0.85 | 1400 ± 14 | 98.9 ± 0.50 |
| G3 | Transparent | Good | No | 94.6 ± 0.12 | 5.3 ± 0.15 | 5.7 ± 0.92 | 1467 ± 16 | 96.7 ± 0.51 |
| G4 | Transparent | Good | No | 93.9 ± 0.11 | 5.5 ± 0.15 | 5.8 ± 0.94 | 1411 ± 15 | 97.4 ± 0.49 |
| G5 | Transparent | Good | No | 92.4 ± 0.11 | 5.9 ± 0.15 | 5.4 ± 1.71 | 1310 ± 09 | 97.6 ± 0.38 |
| G6 | Transparent | Average | No | 93.3 ± 0.11 | 5.9 ± 0.14 | 9.8 ± 1.84 | 1408 ± 11 | 98.2 ± 0.41 |
| G7 | Transparent | Good | No | 92.6 ± 0.12 | 6.1 ± 0.14 | 8.9 ± 0.99 | 1328 ± 12 | 96.2 ± 0.43 |
| G8 | Transparent | Good | No | 93.2 ± 0.13 | 6.7 ± 0.15 | 7.7 ± 0.87 | 1225 ± 11 | 96.4 ± 0.39 |
| G9 | Transparent | Average | Yes | 91.7 ± 0.11 | 5.9 ± 0.15 | 9.8 ± 1.92 | 1011 ± 08 | 96.7 ± 0.30 |
| G10 | Turbid | Average | Yes | 93.2 ± 0.12 | 6.5 ± 0.15 | 8.4 ± 1.78 | 1109 ± 12 | 97.3 ± 0.29 |
| G11 | Turbid | Poor | Yes | 90.1 ± 0.10 | 6.9 ± 0.15 | 7.7 ± 1.12 | 1209 ± 11 | 98.5 ± 0.50 |
| G12 | Turbid | Poor | Yes | 92.8 ± 0.12 | 5.9 ± 0.15 | 7.2 ± 0.98 | 1167 ± 13 | 97.1 ± 0.44 |

Mean ± SD; (n=3)

**Homogeneity & Grittiness:** All developed gels were homogenous in nature without any clumps. There were no foreign particles observed when seen under a light microscope. The G11 and G12 have shown poor homogeneity with lumps due to a higher concentration of gelling agents and difficulty in mixing.

**Spread Ability:** The prepared formulations showed good spreadability ranging from 4.8 ± 0.93 to 9.8 ± 1.92 g.cm/sec.

**Extrudability Study:** The extrude ability of all the formulations was found to be good in the range of 90.1 ± 0.104 to 95.5 ± 0.128 %.

**Measurement of pH:** The pH of gel formulations was found in the range of 5.3 ± 0.1526.9 ± 0.153, which is suitable for topical formulations.

**Drug Content:** The drug content of all the formulations was in the range of 96.2 ± 0.4398.9 ± 0.50 %, indicating the stability of the drug during formulation.

**Viscosity Study:** The viscosity of the gel formulations was determined and found in the range of 1011 ± 081408 ± 15 cps. Viscosity is an important parameter that is inversely proportional to the drug release from the gel. Therefore, the gel formulation should have optimum viscosity to get the maximum drug release. The appearance, homogeneity, grittiness, spreadability, extrude ability. pH, % drug content, and viscosity values were given in **Table 3.**

***In-vitro* Diffusion Studies:** Based on the results of the above studies, the formulation G1, G2, and marketed formulation were subjected to *in-vitro* permeation studies through the goatskin using Franz diffusion cell assembly.

The cumulative amount of cyclosporine permeated through goatskin was plotted as a function of time [20]. *In-vitro* diffusion studies from goatskin revealed that maximum drug release for G1, G2, and Marketed formulation is 48.13, 46.11, and 52.02 %, respectively, within 480 min as shown in **Table 4** and **Fig. 1.**

**TABLE 4: *IN-VITRO* DIFFUSION STUDY FOR FINAL FORMULATION G1 & G2 AND MARKETED FORMULATION BY USING GOATSKIN**

| S. no | Time(min) | %CPR | | |
|---|---|---|---|---|
| | | G1 | G2 | Marketed formulation |
| 1 | 10 | 0.72 ±0.050 | 0.56 ± 0.019 | 0.37 ± 0.021 |
| 2 | 20 | 1.17 ± 0.039 | 1.2 ± 0.041 | 0.98 ± 0.002 |
| 3 | 30 | 1.39 ± 0.042 | 1.19 ± 0.074 | 1.35 ± 0.007 |
| 4 | 60 | 2.75 ± 0.040 | 1.77 ± 0.083 | 1.99 ± 0.0068 |
| 5 | 120 | 9.43 ± 0.078 | 7.98 ± 0.0034 | 8.39 ± 0.012 |
| 6 | 180 | 12.18 ± 0.021 | 14.79 ± 0.001 | 17.30 ± 0.001 |
| 7 | 240 | 18.38 ± 0.011 | 18.24 ± 0.026 | 23.23 ± 0.004 |
| 8 | 300 | 23.5 ± 0.004 | 24.11 ± 0.031 | 28.30 ± 0.023 |
| 9 | 360 | 32.14 ± 0.041 | 31.05 ± 0.007 | 36.02 ± 0.004 |
| 10 | 420 | 39.61 ± 0.028 | 39.91 ± 0.001 | 47.02 ± 0.075 |
| 11 | 480 | 48.13 ± 0.016 | 46.11 ± 0.006 | 52.02 ± 0.068 |

Mean ± SD (n=3)

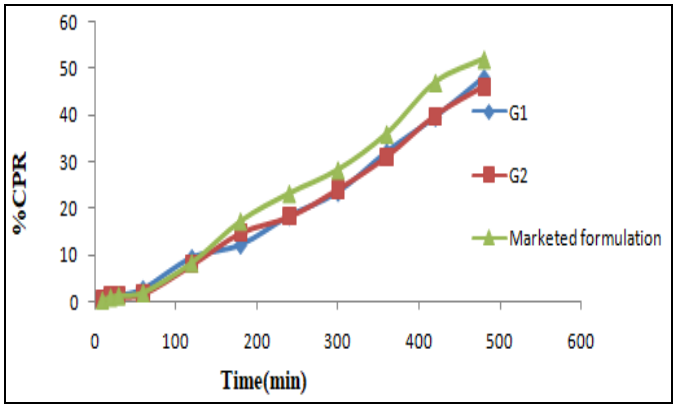


**FIG. 1: COMPARISON OF DRUG RELEASE PROFILE OF FINAL FORMULATIONS G1 & G2 AND MARKETED FORMULATION**

Data obtained from *in-vitro* release studies, G1, G2, and Marketed formulations were fitted to various kinetic equations such as zero order, first order, Higuchi model, and Korsmeyer-Peppas model as shown in **Table 5.**

**Skin Retention and Unreleased Drug From Gel:** The amount of cyclosporine retained in the skin in G1, G2, and Marketed formulation was 39 ± 2.28 µg/ml, 42 ± 3.01 µg/ml, and 20 ± 2.21 µg/ml respectively.

**Stability Study:** The stability of the selected formulation had been at ambient temperature (40 0C, 75 % RH) for 3 months. There were no significant changes in the viscosity and physical appearance of the gel after storing at different temperature conditions for three months **Table 6.**

**Biological Evaluation:** Based on *in-vitro* diffusion studies, G2 formulation was selected as an optimized formulation and subjected to biological evaluations. The Mouse tail model was used to study the antipsoriatic activity of optimized gel. Optimized gel G2 produced significant orthokeratosis when compared to the marketed

formulation. Parakeratotic condition is seen in the adult mouse tail, which is one of the hallmarks of psoriasis. The presence of the nucleus in control was more in number. Formulation G1 showed a decrease in the number of nucleus resulting in increased orthokeratotic activity. The Normal Saline, blank formulationand G2 formulation showed 12.10%, 22.08% and 54.28% orthokeratosis in mouse tail. The drug activity was found to be 47.98 %. Anti-psoriatic drug enhances the orthokeratotic cell differentiation in the epidermal scales. Orthokeratosis and drug activity in the mouse tail are shown in **Table 7** and **Fig. 2.**

**TABLE 5: ZERO ORDER, FIRST ORDER, HIGUCHI SQUARE ROOT AND KORSMEYER PEPPAS GRAPH FOR G1& G2 AND MARKETED FORMULATION**

| Formulation | Zero-order | | First-order | | Higuchi square root | | Korsmeyer Peppas | | Best fit model |
|---|---|---|---|---|---|---|---|---|---|
| Code | $R^2$ | Slope | $R^2$ | Slope | $R^2$ | Slope | $R^2$ | Slope | |
| G1 | 0.977 | 0.115 | 0.895 | 0.003 | 0.898 | 2.787 | 0.822 | 0.781 | Zero-order |
| G2 | 0.981 | 0.097 | 0.898 | 0.003 | 0.904 | 2.363 | 0.970 | 1.09 | Zero-order |
| Marketed formulation | 0.987 | 0.096 | 0.897 | 0.003 | 0.918 | 2.343 | 0.947 | 1.112 | Zero order |

**TABLE 6: STABILITY DATA OF DRUG LOADED GEL FORMULATIONS FOR G1 & G2**

| Parameters | Month 0 (G1) | Month 3 (G1) | Month 0 (G2) | Month 3 (G2) |
|---|---|---|---|---|
| Appearance | Transparent | Transparent | Transparent | Transparent |
| pH | 5.5 | 5.4 | 5.6 | 5.6 |
| Viscosity(cps) | 1408 | 1412 | 1400 | 1404 |
| Grittiness | Nil | Nil | Nil | Nil |
| Consistency | Good | Good | Good | Good |
| Drug content (%) | 96.3 ± 0.41 | 94.85 ± 0.48 | 98.9 ± 0.50 | 97.8 ± 0.45 |

Mean ± SD; (n=3)

**TABLE 7: PERCENT ORTHOKERATOSIS AND DRUG ACTIVITY**

| Group No | Formulation | Orthokeratosis (%) | Drug activity (%) |
|---|---|---|---|
| 1 | Saline solution | 12.10 ± 0.85 | 0 |
| 2 | Blank gel | 22.08 ± 1.05 | 11.35 |
| 3 | Optimized formulation G1 | 54.28 ± 1.23 | 47.98 |

Mean ± SD; (n=3)

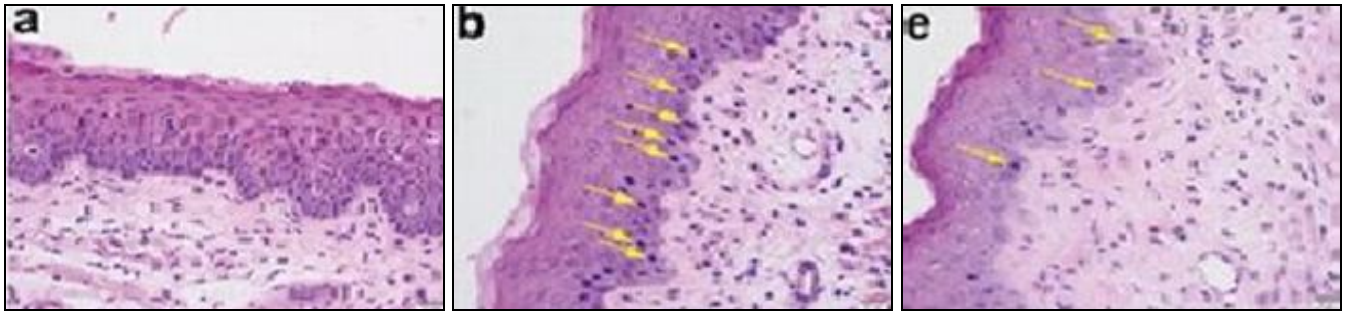


**FIG. 2: COMPARISON OF THE EFFECTS OF GEL ON MOUSE TAIL SKIN A) NORMAL SALINE B) BLANK GEL C) OPTIMIZED FORMULATION G2**

Anti-psoriatic drugs enhance orthokeratotic cell differentiation in the epidermal scales, which forms the basis of this method. AS indicated from skin retention studies that 50% of the drug is retained in the skin resulting in a better anti psoriatic activity which is further confirmed by enhanced orthokeratotioc activity of the drug.

**CONCLUSION:** The present research work was designed to develop gel containing synthetic and herbal ingredients for the effective treatment of psoriasis. The selected drug cyclosporine has low bioavailability and undergoes hepatic first-pass metabolism. Moreover, it is more effective when applied topically.

It was concluded that cyclosporine and aloe vera gel can be prepared successfully and show better activity when applied to psoriatic patients resulting in faster recovery and patient's compliance.

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**CONFLICTS OF INTEREST:** The authors have no conflict of interest.

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