# Evaluation of anti-dandruff activity and safety of polyherbal hair oil : An open pilot clinical trial

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## ABSTRACT

*Dandruff is a common disorder affecting the scalp and can be an embarrassing condition. Currently available treatment options have certain limitations, either due to poor efficacies or due to compliance issues. Furthermore, these drugs are unable to prevent recurrence, which is common troublesome clinical problem. This study was planned to evaluate the clinical efficacy and safety of "Anti-Dandruff Hair Oil" in the management of dandruff.*

*This study was an open, non-comparative, non-randomized, phase III clinical trial, conducted as per the ethical guidelines of Declaration of Helsinki and was approved by Institutional Ethics Committee. Twenty-five patients of both sexes, from the age group of 20-45 years, who were clinically diagnosed as suffering from mild to moderate dandruff, and who were willing to give informed consent were enrolled in the study. Patients with severe hair fall due to endocrine disorders, patients with scanty hair and those with severe scalp skin infection were excluded from the study. All enrolled patients underwent a thorough clinical examination, with special emphasis on local scalp skin examination. All patients were advised to apply 10 ml of "Anti-Dandruff Hair Oil", twice daily for a period of 2 weeks with gentle massage to the entire scalp and were advised to leave the "Anti-Dandruff Hair Oil" on the scalp for a contact period of minimum 3-4 hours after application. All patients were followed for a period of 2 weeks. Clinical assessment of scalp lesions was done objectively and also subjectively. Thorough scalp examination was done after the completion of 1 week and at the end of the study. The severity of the dandruff symptom was recorded on a score scale and patients, with help of a linear analogue scale, did the subjective assessment. The predefined primary efficacy endpoints were rapid clinical improvement and symptomatic control of dandruff. The predefined secondary safety endpoints for short- and long-term were assessed by incidence of adverse events and patient compliance to the therapy. All adverse events reported or observed by patients were recorded with information about severity, date of onset, duration and action taken regarding the study drug. Statistical analysis was done according to intention-to-treat principles. The minimum level of significance was fixed at 99% confidence limit and a 2-sided p value of $<0.0001$ was considered significant.*

*A total 25 patients were enrolled in the study. There was a highly significant reduction ($p<0.001$) in the mean score for itching and white scales at the end of 2 weeks. In subjective evaluation, majority of patients experienced remarkable overall improvement. There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent. Therefore, it may be concluded that, "Anti-Dandruff Hair Oil" is effective and safe in the management of dandruff.*

**ABBREVIATIONS**
IL : interleukin
γ-IFN : gamma-interferon

## INTRODUCTION

Dandruff is a common disorder affecting the scalp and can be an embarrassing condition. The worldwide incidence of dandruff is around 5%. Dandruff mostly occurs after puberty (between ages of 20 and 30 years) and affects males more than females.[1]

Dandruff (also referred as "Pityriasis simplex") is characterized by scaling of the scalp, which may be associated with seborrhea[2] and is considered as the precursor of seborrheic dermatitis.[3] The yeast, *Pityrosporum ovale* is implicated as the contributing organism in the etiology of dandruff, due to its lipase activity (which releases proinflammatory free fatty-acids) and its ability to activate the alternative complement pathway.[4]

Currently available treatment options in the management of dandruff include therapeutic use of zinc pyrithione, salicylic acid, imidazole derivatives, glycolic acid, steroids, sulphur and tar derivatives. However, these agents have certain limitations, either due to poor efficacies or due to compliance issues. Furthermore, these drugs are unable to prevent recurrence, which is a common troublesome clinical problem.

"Anti-Dandruff Hair Oil" is a polyherbal formulation indicated for dandruff. "Anti-Dandruff Hair Oil" contains the extracts of *Hibiscus rosa-sinensis, Centella asiatica, Eclipta alba, Emblica officinalis* and *Terminalia bellirica*. This study was planned to evaluate the clinical efficacy and safety of "Anti-Dandruff Hair Oil" in the management of dandruff.

### Aim of the study

This pilot study was planned to evaluate the clinical efficacy and safety (short- and long-term) of "Anti-Dandruff Hair Oil" in the management of dandruff.

### Study design

This pilot study was an open, non-comparative, non-randomized, phase III clinical trial, conducted at the Department of Dermatology of St. John's Medical College and Hospital, Bangalore, as per the ethical guidelines of Declaration of Helsinki, from January to February 2001. The study protocol, case report forms (CRFs), regulatory clearance documents, product related information and informed consent form (in Kannada and English) were submitted to the Institutional Ethics Committee and were approved by the same.

### Materials and methods

#### Inclusion criteria

Twenty-five patients of both sexes, from the age group of 20-45 years, who were clinically diagnosed as suffering from mild to moderate dandruff, and who were willing to give informed consent were enrolled in the study.

#### Exclusion criteria

Patients with severe hair fall due to endocrine disorders, patients with scanty hair and those patients with severe scalp skin infection were excluded from the study.

#### Study procedures

All enrolled patients underwent a through clinical examination, with special emphasis on local scalp skin examination. All patients were advised to apply 10 ml of "Anti-Dandruff Hair Oil", twice daily for a period of 2 weeks with gentle massage to the entire scalp and were advised to leave the "Anti-Dandruff Hair Oil" on the scalp for a contact period of minimum 3-4 hours after application. Patients were told to restrict themselves to the "Anti-Dandruff Hair Oil" as the only treatment for their dandruff and resort to no other active treatment intervention during the study period was allowed.

**Follow-up and assessment**
All patients were followed for a period of 2 weeks and at each follow-up visit, they were asked about the frequency of the application of Anti-Dandruff Hair Oil on a provided to them calendar in order to check the compliance to the treatment. Clinical assessment of scalp lesions was done objectively (by doctor) and also subjectively (by patient). Thorough scalp examination was done after completion of 1 week and at the end of the study. The severity of the dandruff symptoms (itching, white scales and hair fall) was recorded on a score scale from 0 to 3 (0=Nil, 1=Mild, 2=Moderate and 3=Severe). Patients, with help of a linear analogue scale did the subjective assessment and the extreme ends of a linear analogue scale were predefined as "no improvement" and "total cure" from dandruff.

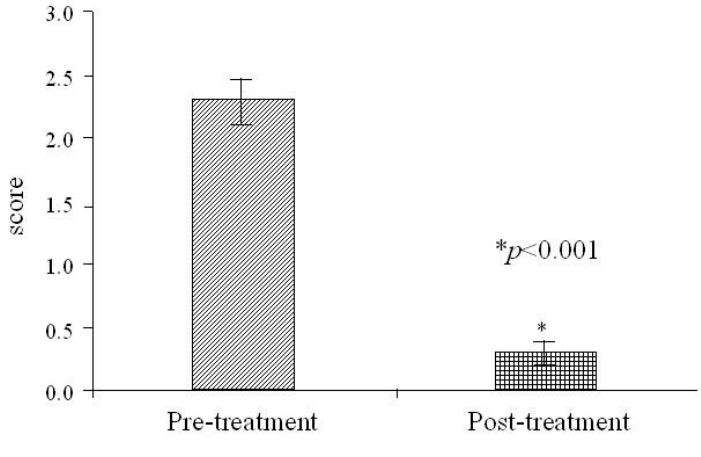
**Primary and secondary endpoints**
The predefined primary efficacy endpoints were rapid clinical improvement and symptomatic control of the dandruff. The predefined secondary safety endpoints for short- and long-term were assessed by incidence of adverse events and patient compliance to the therapy.

**Adverse events**
All adverse events reported or observed by patients were recorded with information about severity, date of onset, duration and action taken regarding the study drug. Relation of adverse events to study medication were predefined as "Unrelated" (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), "Possible" (follows a known response pattern to the suspected drug, but could have been produced by the patients clinical state or other modes of therapy administered to the patient), and "Probable" (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state).

Patients were allowed to voluntarily withdraw from the study if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance was not regarded as treatment failure and reasons for non-compliance were noted.

**Statistical analysis**
Statistical analysis was done according to intention-to-treat principles. The changes in various parameters from baseline values and the values after 2 weeks were evaluated by "Paired '*t*' Test". The minimum level of significance was fixed at 99% confidence limit and a 2-sided *p* value of <0.0001 was considered significant.

**Figure 1: Improvement in the mean score for scalp itching with Anti-Dandruff Hair Oil**

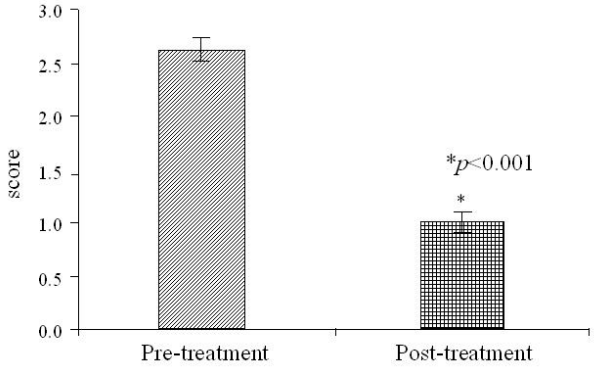



**RESULTS**
A total of 25 patients (11 males and 14 females) were enrolled in the study. There was a highly significant reduction ($p<0.001$) in the mean score for the itching from 2.2857 ± 0.184 to 0.2857 ± 0.10 at the end of 2 weeks (Figure 1). Similarly, there was significant ($p<0.001$) reduction in the mean score for white scales from 2.6190 ± 0.1085 to 1.00 ± 0.097, at the end of 2 weeks (Figure 2).

In subjective evaluation, majority of patients 22/25 (88%) experienced remarkable overall improvement and the mean overall subjective improvement score was 78.25% as assessed on the linear analogue scale

There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent.

**Figure 2: Improvement in the mean score for scalp white scales with Anti-Dandruff Hair Oil**




## DISCUSSION

Dandruff, which is visible desquamation of scalp is the mildest manifestation of seborrheic dermatitis and caused by *P. ovale* combined with multiple host factors[5]. The age of onset suggests that an androgenic influence may be responsible, when the level of sebaceous activity is at its peak. Dandruff is commonly aggravated by changes in humidity, trauma (scratching), season and emotional stress. Dandruff may improve in summer (as ultraviolet rays from sunlight counteracts *P. ovale*) and may get worse in winter. Pityrosporum organisms are linked to T-cell depression, increased sebum levels and an activation of the alternative complement pathway.

Clinically, the greyish white flakes of skin are often very visible on the hair and shoulders. The other commonly associated symptoms of dandruff are itching with scalp soreness. Seborrheic eczema is a more severe form of dandruff that also affects the skin around the eyebrows, nose, ears, face and forehead, and the scales are yellowish greasy with inflamed skin. The severity of dandruff varies from mild dandruff to exfoliative erythroderma. The differential diagnosis of dandruff includes conditions such as eczema, atopic dermatitis, candidiasis, contact dermatitis, dermatomyositis, drug eruptions, drug-induced photosensitivity, impetigo, lichen simplex, chronicus lupus erythematosus, nummular dermatitis, pemphigus, pityriasis rosea, tinea capitis, xerotic eczema, and vitamin B and/or zinc deficiency.

The aim of treatment is to reduce the level of the *Pityrosporum ovale* on the scalp, and the goals of therapy are to reduce morbidity and prevent complications. A variety of topical compounds with antipityrosporal activity are useful in treating dandruff. Imidazoles, selenium sulphide, zinc pyrithione, coal tar and salicylic acid are the common drugs used for the treatment of dandruff, either alone or in combination.[6] But, with the available therapies, the problem of complete symptomatic control and clinical cure are not addressed and dandruff usually recurs on the stoppage of the treatment.[7]

This study observed a significant reduction in the mean scores of itching and white scales and subjective evaluation revealed remarkable improvement. The excellent antidandruff action of "Anti-Dandruff Hair Oil" might have been due to the synergistic antifungal, anti-inflammatory and local immunostimulatory actions of its ingredients.

*In vitro* studies have demonstrated fungicidal activity of *Hibiscus rosa-sinensis* and the minimum inhibitory concentration for *P. ovale* was between 500 and 1000 µg/ml.[8] Adhirajan et al. reported that *Hibiscus rosa-sinensis* has potency for hair follicle activation and hair growth, based on *in vivo* and *in vitro* methods.[9]

The principle ingredients of *Emblica officinalis* are tannoids (emblicanin A and B, punigluconin, and pedunculagin).[10] The active ingredients of *Eclipta alba* are triterpenoid glucosides (daucosterol, stigmasterol-3-O-glucoside and ecliptasaponin C).[11] Wang et al. isolated S3A, a RG-I pectin, the active ingredient from *Centella asiatica.*[12]

Anti-Dandruff Hair Oil has potent antioxidant activity. *Emblica officinalis* has potent antioxidant efficacy attributable to the presence of flavonoids.[13] Khanom et al. demonstrated the strong superoxide-scavenging activity of *Emblica officinalis.*[14] Sai Ram et al. observed that, *Emblica officinalis* significantly inhibited free radical production and restored the anti-oxidant status.[15] In another study Sai Ram et al. reported enhanced cell survival, decreased free radical production and higher anti-oxidant levels by *Emblica officinalis.*[16] Ganju et al. observed that *Emblica officinalis* decreases the induction of nitric oxide synthase.[17] Jayashree et al. documented that *Centella asiatica* significantly increased the antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase) and antioxidants (glutathione and ascorbic acid).[18]

Anti-Dandruff Hair Oil has potent anti-inflammatory activity. Sai Ram et al. observed that *Emblica officinalis* significantly inhibited the interleukin and gamma-interferon production.[15] *Eclipta alba* has potent anti-inflammatory[19] and analgesic activities.[20]

Anti-Dandruff Hair Oil has potent immunostimulatory activity. Sai Ram et al. observed that *Emblica officinalis* significantly relieved the immunosuppressive effects.[15] Wang et al. observed that derivatives of *Centella asiatica* had immuno-stimulating activities.[12]. Jayathirtha et al. assessed the immunomodulatory activity of *Centella asiatica* using carbon clearance, antibody titer and cyclophosphamide immunosuppression parameters.[21]

*Centella asiatica* was demonstrated as clinically beneficial in hyperproliferative skin disorders like psoriasis.[22] *Centella asiatica* is known to accelerate wound healing by increasing remodeling of the collagen matrix in the wound and by stimulating glycosaminoglycan synthesis.[23] Shukla et al. observed that *Centella asiatica* increases hydroxyproline, tensile strength, collagen content and better epithelization, thereby facilitates healing.[24] Enhanced healing activity of *Centella asiatica* has been attributed to increased collagen formation and angiogenesis and it appears that it enhances antioxidant levels at an initial stage of healing, which may be an important contributory factor in the healing properties.[25] Suguna et al. studied the effects of oral and topical administration of *Centella asiatica* on dermal wound healing. The *Centella asiatica* increased the cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, protein and collagen content of granulation tissues. Quicker and better maturation and crosslinking of collagen was observed as indicated by the high stability of acid-soluble collagen and increase in aldehyde content and tensile strength. *Centella asiatica* treated wounds were found to epithelialize faster and the rate of wound contraction was higher, as compared to control wounds. The results show that *Centella asiatica* produces different actions on the various phases of wound repair.[26]

## CONCLUSION

Dandruff is a common disorder affecting the scalp and can be an embarrassing condition. Currently available treatment options in the management of dandruff have certain limitations, either due to poor efficacies or due to compliance issues. Furthermore, these drugs are unable to prevent recurrence, which is the common troublesome clinical problem. “Anti-Dandruff Hair Oil” is a polyherbal formulation indicated for dandruff. “Anti-Dandruff Hair Oil” contains extracts of *Hibiscus rosa-sinensis, Centella asiatica, Eclipta alba, Emblica officinalis* and *Terminalia bellirica*. This study was planned to evaluate the clinical efficacy and safety of “Anti-Dandruff Hair Oil” in the management of dandruff.

This pilot study observed a significant reduction in the mean scores of itching and white scales and subjective evaluation revealed remarkable improvement. The excellent antidandruff action of "Anti-Dandruff Hair Oil" might have been due to the synergistic antifungal, anti-inflammatory and local immunostimulatory actions of its ingredients. There were no clinically significant adverse reactions, either reported or observed, during the entire study period and overall compliance to the treatment was excellent. Therefore, it may be concluded that, "Anti-Dandruff Hair Oil" is effective and safe in the management of dandruff.

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**References**

1. Shimer A, Nathansohn N, Kaplan B, Weiss G, Newman N, Trau H. Treatment of scalp seborrheic dermatitis and psoriasis with an ointment of 40% urea and 1% bifonazole. *Int. J. Dermatol.* 2000; 39: 521-538.

2. Dawber RPR, Dide, Berker and Fennella Wojnarowska. *Disorders of Hair*. Champion RH, Burton JL, DA Burns DA and Breatnach SM (Editors), Rook/Wilkinson/Eblinng Textbook of Dermatology, 6th Edition, 1998: 4: pp. 2941-2942.

3. Burton JL, Holden CA. 1998. *Eczema, Lichenification and Prurigo*. Champion RH, Burton JL, DA Burns DA and Breatnach SM (Editors), Rook/Wilkinson/Eblinng Textbook of Dermatology, 6th Edition, 1998; 1: 638-642.

4. Shuster S. The etiology of dandruff and the mode of action of therapeutic agents. *Br. J. Dermatol.* 1984; 111: 235-242.

5. McGrath J, Murphy GM. The control of seborrhoeic dermatitis and dandruff by antipityrosporal drugs. *Drugs* 1991; 41: 178-184.

6. Faergemann J, Jones JC, Hettler O, Loria Y. 1996. *Pityrosporum ovale* (Malassezia furfur) as the causative agent of seborrhoeic dertmatitis: New treatment options. *Br. J. Dermatol.* 1996; 134 (Suppl. 46): 12-15.
7. Phadke V, Pimpley A, *et al.* In: A combination of 2% ketoconazole plus 1% zinc pyrithione is more effective than 2% ketoconazole alone in the treatment of dandruff. Abstract presented at the 28th National conference of the Indian Association of Dermatologists, Venereologist, and Leprologists, Bangalore, India. 2000; January 27th –30th.
8. Krishnamurthy JR, Ranganathan S. Antipityrosporum ovale activity of a herbal drug combination of *Wrightia Tinctoria* and *Hibiscus Rosa-sinensis Ind. J. Dermatol.* 45(3): 125-126.
9. Adhirajan N, Ravi Kumar T, Shanmugasundaram N, Babu M. *In vivo* and *in vitro* evaluation of hair growth potential of *Hibiscus rosa-sinensis* Linn. *J. Ethnopharmacol*. 2003; 88(2-3): 235-239.
10. Bhattacharya A, Ghosal S, Bhattacharya SK. Anti-oxidant activity of tannoid principles of *Emblica officinalis* (Amla) in chronic stress induced changes in rat brain. *Indian J. Exp. Biol*. 2000; 38(9): 877-880.
11. Zhang M, Chen Y. Chemical constituents of *Eclipta alba* (L.) Hassk. *Zhongguo Zhong Yao Za Zhi*. 1996; 21(8): 480-481, 510.
12. Wang XS, Dong Q, Zuo JP, Fang JN. Structure and potential immunological activity of a pectin from *Centella asiatica* (L.) Urban. *Carbohydr. Res*. 2003; 338(22): 2393-2402.

13. Anila L, Vijayalakshmi NR. Flavonoids from *Emblica officinalis* and *Mangifera indica*-effectiveness for dyslipidemia. *J. Ethnopharmacol.* 2002; 79(1): 81-87.
14. Khanom F, Kayahara H, Tadasa K. Superoxide-scavenging and prolyl endopeptidase inhibitory activities of Bangladeshi indigenous medicinal plants. *Biosci. Biotechnol. Biochem*. 2000; 64(4): 837-840.
15. Sai Ram M, Neetu D, Yogesh B, Anju B, Dipti P, Pauline T, *et al.* Cytoprotective and immunomodulating properties of Amla (*Emblica officinalis*) on lymphocytes: an *in vitro* study. *J. Ethnopharmacol*. 2002; 81(1): 5-10.
16. Sai Ram M, Neetu D, Deepti P, Vandana M, Ilavazhagan G, Kumar D, *et al.* Cytoprotective activity of Amla (*Emblica officinalis*) against chromium (VI) induced oxidative injury in murine macrophages. *Phytother. Res*. 2003; 17(4): 430-433.
17. Ganju L, Karan D, Chanda S, Srivastava KK, Sawhney RC, Selvamurthy W. Immunomodulatory effects of agents of plant origin. *Biomed. Pharmacother*. 2003; 57(7): 296-300.
18. Jayashree G, Kurup Muraleedhara G, Sudarslal S, Jacob VB. Anti-oxidant activity of *Centella asiatica* on lymphoma-bearing mice. *Fitoterapia* 2003; 74(5): 431-434.
19. Ferreira AA, Bezerra GA, Matos FJ, Viana GS. Antinociceptive, anti-inflammatory and bronchodilator activities of Brazilian medicinal plants containing coumarin: A comparative study. *J. Ethnopharmacol*. 2000; 70(2): 151-159.
20. Sawant M, Isaac JC, Narayanan S. Analgesic studies on total alkaloids and alcohol extracts of *Eclipta alba* (Linn.) Hassk. *Phytother. Res*. 2004; 18(2): 111-113.
21. Jayathirtha MG, Mishra SH. Preliminary immunomodulatory activities of methanol extracts of *Eclipta alba* and *Centella asiatica*. *Phytomedicine* 2004; 11(4): 361-365.
22. Sampson JH, Raman A, Karlsen G, Navsaria H, Leigh IM. *In vitro* keratinocyte antiproliferant effect of *Centella asiatica* extract and triterpenoid saponins. *Phytomedicine* 2001; 8(3): 230-235.
23. Maquart FX, Chastang F, Simeon A, Birembaut P, Gillery P, Wegrowski Y. Triterpenes from *Centella asiatica* stimulates extracellular matrix accumulation in rat experimental wounds. *Eur. J. Dermatol*. 1999; 9(4): 289-296.
24. Shukla A, Rasik AM, Jain GK, Shankar R, Kulshrestha DK, Dhawan BN. *In vitro* and *in vivo* wound healing activity of asiaticoside isolated from *Centella asiatica*. *J. Ethnopharmacol*. 1999; 65(1): 1-11.
25. Shukla A, Rasik AM, Dhawan BN. Asiaticoside-induced elevation of anti-oxidant levels in healing wounds. *Phytother. Res*. 1999; 13(1): 50-54.
26. Suguna L, Sivakumar P, Chandrakasan G. Effects of *Centella asiatica* extract on dermal wound healing in rats. *Indian J. Exp. Biol*. 1996; 34(12): 1208-1211.

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