

A Comparison of Clinical Efficacy between a Basic Shampoo with Herbal Extracts Containing Climbazole and Its Similar Sample Containing Piroctone Olamine in the Treatment of Dandruff and Seborrheic Dermatitis

Hosein Rastegar, PhD¹
Hamidreza Ahmadi Ashtiani, PhD
Student²
Mohammad Baghaei, Pharm D³
Saeid Bokaei, PhD⁴
Amirhoushang Ehsani, MD⁵
Pedram Noormohammadpour, MD⁵
Sahar Azizahari, MD⁵
Ramin Khanmohammad⁶

1. Laboratory Research Centre of Food and Drug, Ministry of Health and Medical Educations, Islamic Republic of Iran
2. Department of Clinical Biochemistry, School of Medical Science, Tarbiat-e-Modarres University, Tehran, Iran and Biochemistry & Nutrition Department of Zanjan Medical University and Institute of Medicinal Plants, ACECR, Tehran, Iran
3. Research Unit of Pars Mehr Cerita company, Tehran, Iran.
4. Department of Epidemiology, Department of Food Hygiene, School of Veterinary Medicine, Tehran University, Tehran, Iran
5. Department of Dermatology, Razi Hospital of Dermatologic diseases, Tehran University of Medical Sciences, Tehran, Iran.
6. School of Medicine, Islamic Azad University of Medical sciences, Tehran, Iran

Corresponding Author:
Amirhoushang Ehsani MD
Department of Dermatology, Razi Hospital of Dermatologic diseases, Tehran University of Medical Sciences, Tehran, Iran.
ehsanih@sina.tums.ac.ir

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Introduction

Dandruff and seborrheic dermatitis are features of fungal involvement of the scalp and occur in nearly half of population in every gender and race¹. Dandruff is a non-inflammatory condition of scalp

Abstract

Background: Dandruff especially with itching and inflammation is a common complaint among patients in the clinic and its treatment is much challenging. Chemical anti fungal substances used in antidandruff shampoos are common treatments. The aim of this study was to compare the clinical efficacy of two of these anti dandruff substances, climbazole and piroctone olamine in the treatment of dandruff and seborrheic dermatitis in shampoos with herbal extracts.

Methods: One hundred and twenty men with scalp dandruff of the same severity, between 20-30 years old and in the same occupational condition in terms of sun exposure or environmental pollution were selected and divided randomly into two 60-subject groups. After each shampoo was applied 3 times a week for 5 weeks one in group 1 and the other in group 2, patients were assessed for existence of itching and redness of scalp and reduction in dandruff and results were compared between two groups.

Results: Itching and redness were completely cured in both groups after treatment. Dandruff was completely cured in 80% of patients and reduced in 20% of patients in climbazole group ($p < 0.001$), though completely cured in 55% of patients and reduced in 45% of patients in piroctone olamine group ($p < 0.001$). Climbazole was over piroctone olamine in reduction of dandruff with significant difference ($p < 0.01$).

Conclusion: Both shampoos containing climbazole or piroctone olamine beside herbal extracts are effective in the reduction of dandruff and relief of other seborrheic dermatitis symptoms but climbazole seems to be more effective than piroctone olamine in the treatment of dandruff. (*Iran J Dermatol 2009;12: 82-85*)

Keywords: dandruff, seborrheic dermatitis, climbazole, piroctone olamine, comparison

scaling and seborrheic dermatitis is an inflammatory condition of scalp with redness, itching and scaling². They both have three main etiologic factors ever known including malassezia fungi, sebaceous lipids and individual sensitivity³. Topical treatments for these two conditions are provided by the use of

substances such as zinc pyrithione, selenium sulphide, ketoconazole, piroctone olamine and climbazole ⁴⁻⁶.

Piroctone olamine and climbazole are widely used in the formulation of antidandruff shampoos, imported or produced inside country and no side-effects have been reported yet ⁷⁻¹³. There are no studies in publication that have compared the efficacy of these two substances in controlled conditions among human beings. Herbal extracts because of some special properties such as hair fortifying and anti hair loss effects in addition to their less side effects, lower costs and being more available are also now increasingly used in shampoos in Iran ¹⁴. There are few studies that have evaluated herbal extracts besides chemicals and there is no document dealing with cross reactions between them and their effects on clinical efficacy. In this study, we aimed to compare clinical efficacy of climbazole with piroctone olamine in the treatment of dandruff and seborrheic dermatitis in shampoos with herbal extracts.

Patients and Methods

A basic shampoo containing extracts of nettle, rosemary, chamomile, sage, peppermint and wheat germ was provided according to standards of shampoo in Iran, by the number of 3572 for normal hair having physical and chemical stability and a viscosity of about 12000 centipoise comprising by weight 14% active agent in pH=4 (9.1 percent anionic agent, 2.1% amphoteric agent and 2.8 percent nonionic), 13% sodium laureth sulfate 70, 7% cocoamido propyl baine 30, 4% cocoglucoside 40, 1.2% cocoamid dea 90 and other ingredients in table 1 ¹⁵. This mixture was the basic formulation wherein climbazole 65% offered by German Symrise company by the commercial name "Crinipan-AD" ¹⁶ and piroctone olamine 75% offered by Clarinet company by the commercial name "Octopirox" ¹⁶ were added each one separately to provide two new antidandruff products.

In this double blind clinical trial, 120 men with scalp dandruff of the same severity with or without inflammatory manifestations, between 20-30 years old and in the same occupational conditions in terms of exposure to sun or environmental pollution were selected and divided randomly into two 60-subject groups (group 1 and 2). These samples were selected among patients with dandruff or seborrheic dermatitis visited in 2 private clinics.

Existence or the absence of itching and redness beside dandruff and their severity was noted. The anti dandruff shampoo containing climbazole was

Table 1. Formulation of basic anti dandruff shampoo

Sodium laureth sulphate 70	13
Cocoamido propyl betaine 30	7
Cocoglucoside 40	4
Cocoamid dea 90	1.2
Propylen glycol	0.2
Rosemary glycolic extract	0.1
Nettle glycolic extract	0.1
Sage glycolic extract	0.1
Pepper mint glycolic extract	0.1
Chamomile glycolic extract	0.1
Wheat germ protein	0.2
Methy chloro isothiazolinon	0.1
Water	Up 100

Table 2. Grading of dandruff or seborrheic dermatitis

	redness	dandruff
No manifestation	No redness	No dandruff
mild	Faint pink color	Only scraped
moderate	Pink color	Obvious scaling
severe	Red color	Obvious sheets

used in group 1, three times per week and for a duration of 5 weeks and the shampoo containing piroctone olamine was used in group 2 with the same prescription ¹⁶. Each patient had to massage scalp with 7.5 ml of shampoo for 5 minutes, 10 minutes after hair had got wet in each time ¹⁷. At the end of treatment, each patient was assessed for existence of itching or redness and decrease in dandruff. Every assessment was done by 3 practitioners and according to the grading that was assigned before (Table 2). Both patients and observers were blind for applied drug (randomized double blind). Data were analyzed in SPSS-16 by paired t-test and chi square.

These two substances added to shampoos are approved by Ministry of Health and Medical Education of Islamic Republic of Iran and are widely used in Iranian shampoos. Formulation of basic shampoo was assigned according to standards of shampoo in Iran (number 3572) and were prescribed for patients who themselves wanted to receive treatment for their condition. Therefore, we met no ethical challenge.

Results

One hundred and twenty men with scalp dandruff, between 20-30 years old enrolled in this study.

In group 1 (applying climbazole shampoo) 21 patients had mild scalp redness, 24 patients had mild scalp itching and 9 had scalp itching of intermediate severity. After treatment, these two parameters were removed in all patients. Dandruff was completely cured in 80% of them while decreased in the remaining 20%. Effectiveness of this shampoo was statistically significant for all the parameters ($P < 0.001$). In group 2 (applying piroctone olamine shampoo), 15 patients had mild scalp redness, 27 patients had mild itching and 9 had itching of intermediate severity. After treatment, these two parameters were removed in all patients. Dandruff was cured completely in 55% of them while decreased in the remaining 45%. Effectiveness of this shampoo was statistically significant for all the parameters ($P < 0.001$).

Dandruff have shown a better cure by climbazole shampoo in compare with piroctone olamine shampoo with significant difference ($P=0.0063$)

Discussion

In this study, the effect of piroctone olamine and climbazole with extracts of nettle, chamomile, rosemary, sage, pepper mint and wheat germ was assessed. Benefit of these herbal extracts on the skin and hair is clear and are widely used in Iranian shampoos¹⁸. Piroctone olamine and climbazole are among substances with antidandruff effects and are also widely used in the formulation of shampoos with no significant or important side effects ever mentioned⁷⁻¹³. Azoles especially climbazole interfere with the fungal cell membrane permeability by inhibition of ergosterol synthesis that consequently leads to the leakage of cell contents and cell death. This agent influence 14- α demethylation of lanosterol that is catalyzed by a cytochrome p450 isozyme¹⁹. Climbazole also acts against *Pityrosporum Ovale*, one organism with pathogenic effects in dandruff and seborrheic dermatitis and can reduce dandruff, itching and redness of scalp¹¹. Antidandruff effect of piroctone olamine is urged by its cytostatic antibacterial and antifungal effects on scalp flora and *Malassezia Furfur*²⁰. This substance also results in reduction of hair loss and increase in hair thickness²¹. There has been no report of redness, scaling, itching, burn or irritation after application of piroctoneolamine^{9, 10, 12,13}. Shampoos and lotions containing climbazole have been well tolerated even after they have remained on skin for 48 hours. Testing 2 different hair tonics containing climbazole in rabbits also had shown no side effects⁷. Its ophthalmic side effects

have been transient redness and minor inflammation only after 5 minutes residence in the eyes. No important allergic reaction or severe ophthalmic involvement has been ever seen⁸. Plate incorporation test also revealed no mutagenic effect of climbazole²².

In this study, we did not find any adverse effects of either shampoo (containing climbazole vs piroctone olamine) in participants. This study shows that treatment by shampoos with herbal extracts containing climbazole or piroctone olamine makes significant reduction in dandruff with complete cure of itching and redness, though it offers climbazole over piroctone olamine in the reduction of dandruff with significant difference. As in climbazole group, of 60 patients with dandruff of intermediate severity, 48 (80%) were completely cured and 12 (20%) improved to mild severity in compare with piroctone olamine group that 33 patients (55%) of 60 were completely cured and 27 others (45%) improved to mild severity. This is confirmed by previous statements that believed antifungal agents such as azoles in preference to keratolytic and cytostatic agents for antidandruff effects, regarding to previous controlled and uncontrolled studies¹².

Our results in each group simulate those by two previous studies. Wigger Alberti et al, tested one shampoo containing 0.65% climbazole among 30 patients with seborrheic dermatitis and after 4 weeks of treatment, found receding of redness and itching in 80% of patients and reduction in the remaining 20%^{11,12}. Futterer in a control placebo trial after applying piroctone olamine 0.75% shampoo for 6 weeks achieved a reduction of dandruff symptoms in 54% of patients¹³. In a similar study, Rdtlisberger compared clinical efficacy of piroctone olamine 0.3% shampoo with 0.5% climbazole shampoo between two 10-patient groups (patients had different severities of dandruff in each group) and found no significant difference in therapeutic results of these two shampoos, though both had significant clinical antidandruff efficacy after they were applied 2 times a week for 5 weeks¹⁶. Our results may be more reliable first because of our larger sample size of 60 patients. To rationalize such discordance between these two studies, some obscure aspects should be cleared whether different formulations of basic shampoo can interfere with antidandruff effects of climbazole or piroctone olamine, persistency of shampoo on scalp is an important factor for augment of antidandruff effects and patients do exactly according to prescribed

method. It has been shown that antidandruff shampoos with lower percentage of climbazole but in lower pH of nearly 4-5.5 can remain for a longer duration on scalp that results in more clinical efficacy and decrease in shampoo price. In one study, climbazole 1% shampoo in pH=4 was significantly more effective than climbazole shampoo 1% in pH=7²³.

In conclusion, this study suggests that both shampoos containing climbazole or piroctone olamine beside herbal extracts are effective in the reduction of dandruff and relief of other seborrheic dermatitis symptoms, also demonstrate climbazole more effective than piroctone olamine in the treatment of dandruff.

Conflict of Interests

The authors have no conflict of interests in this article.

References

- Dawber P. Isolated dandruff. In: Bara R, Maibach HI (Eds). *Cosmetic Dermatology*. 1st ed. London: Martin Dunitz 1994;133-7.
- Pierard-Franchimont C, Xhaufaire-Uhoda E, Pierard GE. Revisiting dandruff. *Int J Cosmet Sci* 2006; 28:311-8.
- DeAngelis YM, Gemmer CM, Kaczvinsky JR, Kenneally DC, Schwartz JR, Dawson TL Jr. Three etiologic facets of dandruff and seborrheic dermatitis: malassezia fungi, sebaceous lipids, and individual sensitivity. *Investig Dermatol Symp Proc* 2005;10: 295-7.
- Guého E, Midgley G, Guillot J. The genus *Malassezia* with description of four new species. *Antonie van Leeuwenhoek* 1996;69:337-55.
- Gueho E, Leclerc MC, Hoog GS, Dupont B. Molecular taxonomy and epidemiology of *Blastomyces* and *Histoplasma* species. *Mycoses* 1997;40:69-81.
- Schmidt A. *Malassezia furfur*: a fungus belonging to the physiological skin flora and its relevance in skin disorders. *Cutis* 1997;59:21-4.
- Derma Consult GmbH- Gesellschaft zur Prüfung von Dermatika; Expertise: Examination of the Product "Crisan med" Concentration: 2% 8/5698/06/017 & "SP Antischuppenshampoo" Concentration: 10% 8/5906/06/003 by Human Patch test. Alfter, Germany: sponsored by Wella AG, Dermstadt; 1997.
- Bayer AG, Institut für Toxikologie. BAY e 6975-Lösung (0, 5%ig) - Prüfung auf Reizwirkung am Kaninchen. Pharma-Bericht-Nr. 5280. Wuppertal-Eberfeld; 1975.
- Schwartz, JR, Cardin CM, Dawson TL. Dandruff and seborrheic dermatitis. In: Schwartz, JR, Cardin CM, Dawson TL. *Textbook of Cosmetic Dermatology*, 3rd ed. Oxan, UK: Taylor & Francis. 2005;259-76.
- Bartalini P, Bilenchi R, Dina F. Anti-pityriasis activity of a line of products containing piroctone olamine. *G Ital Dermatol Venereol* 1987;122:11-9.
- Wigger-Alberti W, Kluge K, Elsner P. Clinical effectiveness and tolerance of climbazole containing dandruff shampoo in patients with seborrheic scalp eczema. *Praxis* 2001;90:1346-9.
- Adamski Z. The treatment of dannduff of the scalp. *Aesthetic Dermatol* 2006;2:49-56.
- Futterer E. Antidandruff hair tonic containing piroctone olamine. *Cosmetics and toiletries* 1988; 103:49-52.
- Nikbakht A, Kafi M. The history of traditional medicine and herbal plants in Iran. *Acta Horticulturae (ISHS)* 2004;790:255-8.
- Chao L. Simultaneous determination of four antidandruff agents including octopirox in shampoo products by reversed-phase liquid chromatography. *Int J Cosmet Sci* 2001;23:183-8.
- Rdthlisberger. R. Biochemist, Dermatological studies and efficacy testing, Cosmital SA, CH-Marly. Report on the comparative testing of octopirox and climbazole for antidandruff efficacy. Frankfurt; 1996 Sep 6. Report No: 45/72/94.
- Pierard-Franchimont C, Uhoda E, Loussouarn G, Saint-Leger D, Pierard GE. Effect of residence time on the efficacy of antidandruff shampoos. *Int J Cosmet Sci* 2003;25:267-71.
- Institut für experimentelle Dermatologie (IED) Universität Witten-Herdecke. test report. Epicutaneous Test for the analysis of the effects caused by Cosmetic Products to the skin of humans: Crisan med shampoo 8/5698/06/014-16 & Crisan Ultra Intensiv Shampoo 8/0282/06/01/377. Im Auftrag der Wella AG, Darmstadt ; 1997-8.
- Trevor AJ, Katzung BG. *Chemotherapy Drugs*. In: Trevor AJ, Katzung BG. *Katzung & Trevor Pharmacology Examination & Board Review*, 7th ed; Portland, OR:McGraw Hill 2005:361-485.
- Schmidt A. *Malassezia furfur*: a fungus belonging to the physiological skin flora and its relevance in skin disorders. *Cutis* 1997;59:21-4.
- Piérard-Franchimont C, Goffin V, Henry F, Uhoda I, Braham C, Piérard GE. Nudging hair shedding by antidandruff shampoos. A comparison of 1% ketoconazole, 1% piroctone olamine and 1% zinc pyrithione formulations. *Int J Cosmet Sci* 2002; 24:249-56.
- Pérez-Rivera AA, Hu T, Aardema MJ, Nash JF. Evaluation of the genotoxicity of the imidazole antifungal climbazole: Comparison to published results for other azole compounds. *Mutat Res* 2009; 672:27-39.
- Ryan J, Stansfield M. Low pH shampoo containing climbazole. 1988. England, United states Patent, Appl No:185, 583. Apr. 22.