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NEW PARADIGM OF DRUG COMBINATION FORMULATION FOR PSOARIASIS THERAPY AND ITS SUPERIORITY COMPARED BY STANDARD THERAPY

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Abstract
Background: Psoriasis is a chronic inflammatory skin disease characterized by persistent itching and a high rate of recurrence. Until now, the primary issue with these two diseases has been their inability to respond to therapy; thus, it is critical to develop an appropriate combination therapy for these two diseases. Due to the fact that psoriasis patients experience alternating periods of remission and exacerbation, dermatologists should tailor psoriasis treatment to the severity of the disease at the time it manifests, with the goal of extending remission and improving quality of life. Thus, it is critical to achieve maximum treatment efficiency in order to prolong the period of remission and improve quality of life. Method: This study is a study comparing the effectiveness of a new treatment therapy using a combination therapy of 0.05% Clobetasol with 3% liquor carbonis detergent and 2% salicylic acid compared to standard therapy, namely 0.05% Clobetasol. This study is a restrospective cohort therapy at the Indra Clinic. The samples of this study were all cases of psoariasis of the skin at Indra's clinic in the 2016-2017 period that met the inclusion criteria. The independent variable of this study was the drug formulation with the dependent variable in the form of clinical improvement and the appearance of side effects. Results: The cure rate was 86,2 percent for the 29 respondents who received the combination formulation, compared to 54,5 percent for the 22 respondents who received standard therapy containing Clobetasol 0.05 percent (p : 0,028). There were no statistically significant differences in adverse events between the two intervention groups.
Conclusion: Innovative drug formulations (clobetasol 0.05% with 3% liquor carbonis detergent and 2% salicylic acid) for psoariasis are proven to be more effective and superior than standard therapies

Keywords: clobetasol; liquor carbonis detergens; salicylic acid; psoriasis

INTRODUCTION

Psoriasis is a chronic inflammatory condition of the skin that is characterized by well-defined erythematous plaques that are rough, layered, and silvery white in color. This disease is chronic and recurrent, with the patient experiencing periods of remission and exacerbation on a regular basis. Psoriasis is the most common autoimmune disease, characterized by an abnormal activation of the cellular immune system [1–6]

Psoriasis prevalence varies significantly between countries, ranging from 0.09 percent to 11.43 percent, making it a serious global problem affecting at least 100 million people. Around 10% – 25% of patients develop psoriatic arthritis, which causes joint pain and swelling. Psoriasis can affect both men and women of any age and frequently recurs. [7,8]

Psoriasis affects between 2% and 3% of the world's population, with men and women having an equal chance of developing it. The Asian race has a relatively low prevalence of psoriasis, estimated to be around 0.4 percent. There is a significant difference in the prevalence of psoriasis between African Americans and white

Americans, according to studies (1.3 percent vs. 2.5 percent). Psoriasis is uncommon in children under the age of ten, peaking between the ages of fifteen and thirty. From January to December 2009, data on patient visits to the Dermatology and Venereology Polyclinic of Sanglah General Hospital in Denpasar revealed 156 new cases of psoriasis from 10,856 visits (1.4 percent). [5,9–12]

Due to the possibility of developing psoriatic arthritis and a variety of other systemic diseases, psoriasis can result in significant morbidity. Around 10% – 30% of patients with psoriasis are at risk of developing psoriatic arthritis. Along with an increased risk of morbidity, patients with severe psoriasis faced an increased risk of mortality, with men dying 3.5 years earlier and women 4.4 years earlier than healthy subjects. Longitudinal studies indicate that spontaneous remission occurs with varying frequency in approximately one-third of psoriasis patients. [4,5,13,14]

Psoriasis management is complicated by a variety of factors that contribute to and influence the severity of the disease. It is critical to avoid triggers for this condition, which include physical trauma, infection, stress, seasonal and climate changes, beta blocker use, chloroquine use, alcohol use, and smoking. Due to the fact that psoriasis patients experience alternating periods of remission and exacerbation, dermatologists should tailor psoriasis treatment to the severity of the disease at the time it manifests, with the goal of extending remission and improving quality of life. [15–18]

Due to the critical nature of treatment efficiency in extending the duration of remission and improving quality of life, a new treatment formulation is required to accomplish this goal. The purpose of this study is to evaluate the efficacy of a new treatment regimen that contains 0.05 percent clobetasol, 3% liquor carbonis detergent, and 2% salicylic acid, and to compare it to standard therapy, which contains 0.05 percent clobetasol.

METHOD AND MATERIAL

This study was a retrospective cohort study that analyzed the comparisons between 2 treatment formulations. The population of this study were all cases of psoariasis on the skin at Indra's clinic in the period 2016-2017. The research sample is part of the study population that meets the inclusion criteria. The inclusion criteria in this study were a minimum age of 12 years and a diagnosis of psoariasis of the skin by a Dermatologist. The exclusion criteria in this study were incomplete medical record data or there was a history of allergy to drug content. The minimum sample size required is 20 samples for each treatment formulation group (type 1 error is 5% and type 2 error is 20%). The sampling method used was non random purposive sampling. The procedure of this study is to look at all patient medical record data from 2016 to 2017 and look for data on the diagnosis of psoariasis in the skin and the therapy given. The independent variable of this study was a treatment formulation for psoariasis in the skin in the form of clobetasol 0.05%, or a combination of 0.05% Clobetasol with 3% liquor carbonis detergent and 2% salicylic acid topically. The dependent variables in this study were treatment success (improved or not), side effects during treatment, and post-treatment symptoms. Analysis of research data is divided into two, namely descriptive data analysis and analytic data analysis. Descriptive data analysis includes the proportion (%) for the type of qualitative data and the distribution of centralized data (mean, SD, median, minimum, maximum). Analytical data

analysis used the comparative test for unpaired categorical data in the form of the Peason Chi Square test, Chi Square with Yates Correction, or Fisher Exact in accordance with the applicable data provisions for each statistical test.

RESULT

This study enrolled 51 individuals who had skin psoariasis. There were 29 respondents who received clobetasol formulation therapy (0.05 percent clobetasol with 3% liquor carbonis detergent and 2% salicylic acid) and 22 respondents who received standard clobetasol therapy. Table 1 summarizes the demographic characteristics of each group of patients.

Table 1. Demographic Characteristics of Respondents

Variable	Treatment		p-value
	Clobetasol Formulation N : 29 responden	Clobetasol 0,05% N : 22 responden	
Age	36,72 (17,7)	35,82 (20,4)	> 0,05
Sex • Male • Female	 15 (51,7%) 14 (48,3%)	 12 (54,5%) 10 (45,5%)	> 0,05

The therapy was administered for one week before being re-examined at the subsequent visit. The cure rate was 86,2 percent for the 29 respondents who received a combination formulation containing 0.05 percent clobetasol, 3 percent liquor carbonis detergent, and 2% salicylic acid, compared to 22 respondents who received standard therapy containing 0.05 percent clobetasol. obtained a 54,5 percent cure rate. The Chi Square with Yates Correction statistical test revealed a difference in the degree of clinical improvement between psoariasis and formulation therapy when compared to standard therapy (p-value: 0.028).

Table 2. Therapeutic Effectiveness between 2 Treatment Regimens

Parametric	Clinically after 1 week		p-value
	Remission in <1 week	Remission in > 1 week	
Combination of 0.05% clobetasol with 3% liquor carbonis detergent and 2% salicylic acid	25 (86,2%)	4 (13,8%)	0,028
The standard regimen of 0.05% Clobetasol	12 (54,5%)	10 (45,5%)	

The assessment of adverse effects was conducted using two drug formulations. It was discovered that side effects consisted solely of persistent itching and redness during drug use. The Fisher Exact test revealed no statistically significant difference

in adverse events between the two intervention groups.

Table 3. Side effects between the 2 Treatment Regimens

Variable	Drug Formulation		p-value
	Clobetasol Formulation N : 29 responden	**Clobetasol 0,05% N : 22 responden**	
Side effects			
• Persistent itching	2 (6,9%)	3 (13,6%)	> 0,05
• Redness	4 (13,8%)	5 (22,7%)	> 0,05
• Skuama	-	-	-
• Hyperpigmentation	-	-	-
• Hypopigmentation	12 (41,4%)	13 (59%)	> 0,05

DISCUSSION

Psoriasis is a chronic, multisystem inflammatory disease characterized by abnormal skin differentiation and hyperproliferation as a result of immune system dysfunction. The skin becomes hyperresponsive during the course of the disease due to a failure to regulate the immune response and the formation of reactive memory cells that continuously recruit inflammatory mediators. Hyperplasia and hyperkeratosis occur as a result of chronic inflammation, resulting in the thickening of the skin and the formation of scales. This is a chronic disease that has a remission-exacerbation cycle and occasionally does not respond to therapy. Environmental, genetic, and immunological factors all have an effect on psoriasis. The elbows, knees, scalp, back, groin, and glans penis are frequently affected by red, scaly patches. Extracutaneous manifestations of psoriasis include nail involvement and psoriatic arthritis. Psoriasis severity is generally quantified using the Psoriatic Area and Severity Index (PASI) score or the Physicians' Global Assessment (PGA).[1,19–24]

Psoriasis treatment is determined by its severity. The management of this disease is based on manipulating the immune system to reduce its activity and restore normal functioning. The first line of treatment for mild-moderate psoriasis is topical agents. The primary goals of therapy are symptom suppression and long-term disease severity modulation. Additionally, this topical therapy aims to improve overall quality of life with few side effects. The combination of corticosteroids and Liquor Carbonis Detergent has a favorable therapeutic response, and the availability of stain- and odor-reducing preparations has reintroduced this therapy into use. Additionally, it is known that anthralin, tazotrene, salicylic acid, phenol, and calcipotriene are effective when combined with corticosteroids. Retinoids, methotrexate, cyclosporine, 6-thioguanine, azathioprine, and hydroxyurea are used to treat severe cases. UVA and UVB phototherapy are also known to be effective.[1,25,26]

Different formulations of topical steroids have varying potencies. Its efficacy is proportional to the degree of steroid molecule penetration into the skin, which is influenced by the chemical structure of the steroid used. The dosage form and the state of the skin also have an effect on the drug's

absorption. In children, low-potency steroids should be used. In adults, steroids should be of low to moderate potency. Clobetasol is a powerful anabolic steroid. It is typically used at a concentration of 0.05 percent in the treatment of skin diseases. Clobetasol is an anti-inflammatory agent that is used to treat a variety of skin conditions.[27–31]

Liquor Carbonis Detergent is derived from the primary condensation of coal. This preparation is believed to work by inhibiting DNA synthesis and keratinocyte proliferation. The topical detergent Liquor Carbonis acts as a keratolytic, antiacanthotic, photosensitizer, vasoconstrictor, antipruritic, and antimicrobial. In comparison to corticosteroids, this medication is effective for long-term management of mild to moderate psoriasis with fewer side effects and a lower risk of recurrence.[32–34]

Keratolytics are recommended as adjuvant therapy in psoriasis of mild to severe severity. The main goals of keratolytic use are hydration of the stratum corneum, desquamation of the skin, reducing itching, increasing penetration of topical drugs and phototherapy. Salicylic Acid (2-Hydroxybenzoic Acid / Orthohydrobenzoic Acid) is a member of the hydroxy acid group. Salicylic Acid can be extracted naturally or synthesized chemically. Topical salicylic acid functions as a keratolytic, comedilytic, reduces sebum production, antihyperplastic, desmolytic, antimicrobial and anesthetic. Salicylic acid as a keratolytic has been widely researched and used. At concentrations of 5% and above, this preparation has a rapid and deep keratolytic effect that causes desquamation. The underlying mechanism is that salicylic acid reduces the intercellular cohesion between corneocytes by dissolving the intercellular material and decreasing the pH of the stratum corneum, resulting in increased hydration and softening.[35–39]

Based on a case study conducted by Frankel et al. entitled "Coal tar 2% foam in combination with a superpotent corticosteroid foam for plaque psoriasis: case report and clinical implications, as well as published in J Clin Aesthet Dermatol, a combination of Liquor Carbonis Detergent 2% with Clobetasol 0.05% gives good results. in psoriasis patients. The study by Jacobi et al. with the title "Keratolytics and emollients and their role in the therapy of psoriasis: a systematic review", and published in Dermatol Ther (Heidelb, suggests salicylic acid administration reduces the severity of psoriasis with a rapid onset. Corticosteroid administration is accompanied by a liquor carbonis detergent and / or salicylic acid was also suggested in the studies of Brakeley, et al, Zhu et al, and Khandpur et al for use in the treatment of psoariasis.[39–43]

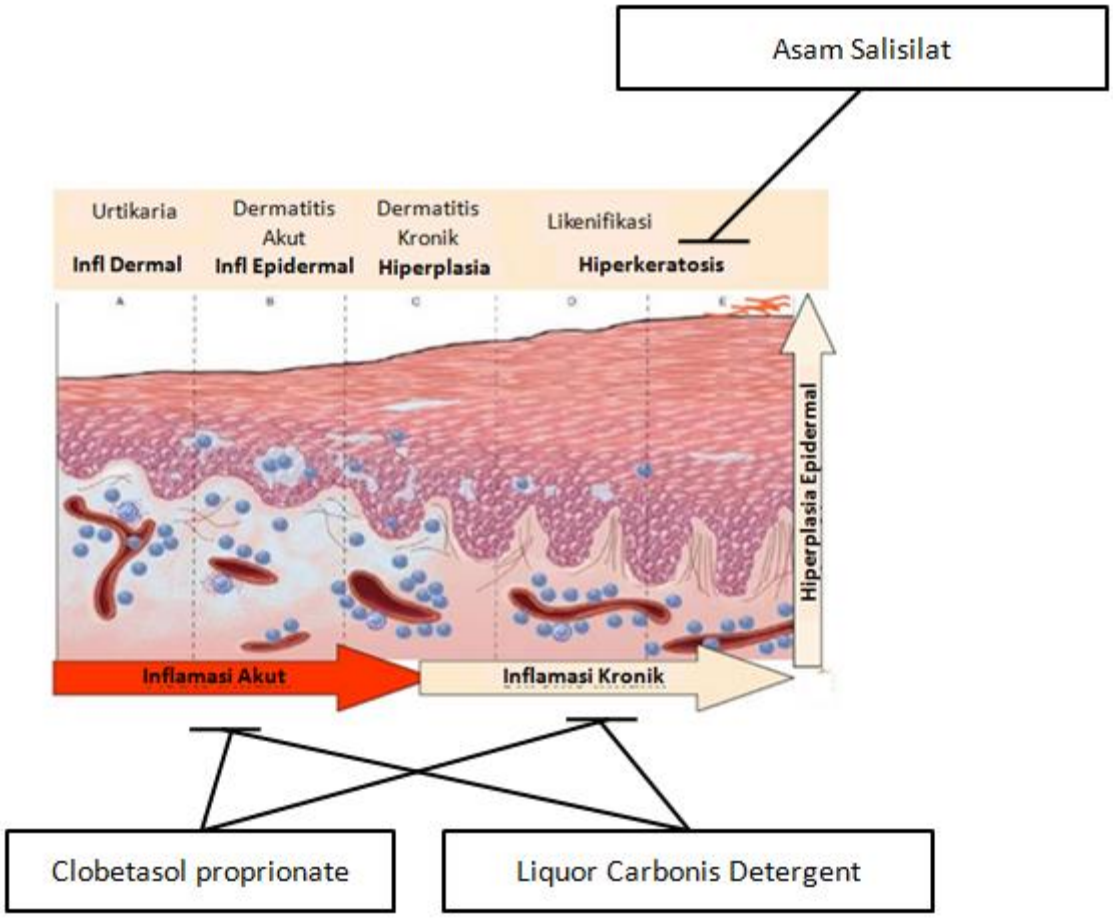

Figure 1. Mechanism of keratolytic and anti-inflammatory action in psoriasis

Effects of Clobetasol, Liquor Carbonis Detergent, and Salicylic Acid according to the pathogenesis of psoriasis. Psoriasis is based on the pathogenesis of chronic inflammation of the skin. (A) Urticaria is a response to acute inflammation that appears first due to inflammation of the dermis. (B) In acute dermatitis the inflammation continues on the epidermal layer. (C) If the dermatitis is chronic, there will be hyperplasia of the epidermal layer. (D) Over time hyperkeratosis occurs so that scales (E) appear on the skin as seen on lichenification. In the skin, Clobetasol propionate and Liquor Carbonis Detergent work by inhibiting inflammation so as to decide the course of the disease that leads to hyperplasia and hyperkeratosis. Salicylic Acid acts as a keratolytic which eventually removes the excess scales due to hyperkeratosis. Through the combination of the three, the thickening and scales on the skin surface will gradually disappear.[1,19–24]

Ointments and serums are prepared in accordance with the standard for dermatological drug preparations. A combined psoriasis ointment is prepared by mixing 500 grams of Vaseline Album with Clobetasol 0.05–1.5 percent, Liquor Carbonis Detergent 3-5 percent, and Salicylic Acid 2–5%. Natrosol 20%, Clobetasol 0.05–1.5%, Liquor Carbonis Detergent 3-5%, and Salicylic Acid 2–5% are used in the serum. The mixture is diluted to a concentration of 100 percent aqua. The ointment and serum preparations are placed in a container designed for this purpose. Instructions for use, indications, contraindications, and adverse effects are included on the container.

Serum is intended for use on areas that are excessively hairy. Ointments can be used on hairy or non-hairy skin, but they will feel sticky when applied to hairy areas. By preparing these two types of preparations, maximum therapy can be delivered to the entire surface of the affected skin.

CONCLUSION

The innovative therapy of a 0.05 percent Clobetasol mixture with 3% liquor carbonis detergent and 2% salicylic acid has been shown to provide a greater level of clinical improvement than standard Clobetasol therapy. The cure rate was 86,2 percent in the group receiving 0.05 percent Clobetasol mixed formulation innovation therapy combined with 3 percent liquor carbonis detergent and 2 percent salicylic acid, compared to 54,5 percent in the group receiving standard therapy containing 0.05 percent Clobetasol. There were significant differences between the two therapy groups, but there were no significant differences in side effects.

REFERENCE

1. Rendon A, Schäkel K. Psoriasis Pathogenesis and Treatment. Int J Mol Sci [Internet]. 2019 Mar 23;20(6):1475. Available from: https://www.mdpi.com/1422-0067/20/6/1475
2. Korman NJ. Management of psoriasis as a systemic disease: what is the evidence? Br J Dermatol [Internet]. 2020 Apr 15;182(4):840–8. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/bjd.18245
3. Monteleone G, Pallone F, MacDonald TT, Chimenti S, Costanzo A. Psoriasis: from pathogenesis to novel therapeutic approaches. Clin Sci [Internet]. 2011 Jan 1;120(1):1–11. Available from: https://portlandpress.com/clinsci/article/120/1/1/68785/Psoriasis-from-pathogenesis-to-novel-therapeutic
4. Krueger JG. Psoriasis pathophysiology: current concepts of pathogenesis. Ann Rheum Dis [Internet]. 2005 Mar 1;64(suppl_2):ii30–6. Available from: https://ard.bmj.com/lookup/doi/10.1136/ard.2004.031120
5. Gudjonsson JE, Elder JT. Psoriasis: epidemiology. Clin Dermatol [Internet]. 2007 Nov;25(6):535–46. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0738081X07001514
6. Mak RKH, Hundhausen C, Nestle FO. Progress in Understanding the Immunopathogenesis of Psoriasis. Actas Dermosifiliogr [Internet]. 2009 Dec;100:2–13. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0001731009733721
7. Cox NH. Fitzpatrick's Dermatology in General Medicine. Br J Dermatol. 2004;
8. World Health Organization. Global Report on Psoriasis. Glob Rep Psoriasis [Internet]. 2016;978(70):1–26. Available from: http://www.who.int/about/licensing/copyright_form/index.html%0Ahttp://www.who.int/about/licensing/
9. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. International Journal of Molecular Sciences. 2019.
10. Bakshi H, Nagpal M, Singh M, Dhingra GA, Aggarwal G. Treatment of Psoriasis: A Comprehensive Review of Entire Therapies. Curr Drug Saf. 2020;
11. Unissa R, Kumar PM, Pasha M, Begum S, Maheswari B. Psoriasis: A Comprehensive Review. Asian J Res

Pharm Sci. 2019;

12. Coimbra S, Santos-Silva A. Biomarkers of psoriasis severity and therapy monitoring. World J Dermatology [Internet]. 2014;3(2):15. Available from: http://www.wjgnet.com/2218-6190/full/v3/i2/15.htm

13. Amin M, Lee E, Tsai T, Wu J. Psoriasis and Co-morbidity. Acta Derm Venereol [Internet]. 2020;100(3):81–7. Available from: http://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3387

14. Lønnberg AS, Skov L. Co-morbidity in psoriasis: mechanisms and implications for treatment. Expert Rev Clin Immunol [Internet]. 2017 Jan 2;13(1):27–34. Available from: https://www.tandfonline.com/doi/full/10.1080/1744666X.2016.1213631

15. Lee EB, Wu KK, Lee MP, Bhutani T, Wu JJ. Psoriasis risk factors and triggers. Cutis [Internet]. 2018 Nov;102(5S):18–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30566552

16. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk Factors for the Development of Psoriasis. Int J Mol Sci [Internet]. 2019 Sep 5;20(18):4347. Available from: https://www.mdpi.com/1422-0067/20/18/4347

17. Xhaja A, Shkodrani E, Frangaj S, Kuneshka L, Vasili E. An Epidemiological Study on Trigger Factors and Quality of Life in Psoriatic Patients. Mater Socio Medica [Internet]. 2014;26(3):168. Available from: http://www.scopemed.org/fulltextpdf.php?mno=162669

18. Huerta C, Rivero E, Rodríguez LAG. Incidence and Risk Factors for Psoriasis in the General Population. Arch Dermatol [Internet]. 2007 Dec 1;143(12). Available from: http://archderm.jamanetwork.com/article.aspx?doi=10.1001/archderm.143.12.1559

19. Ogawa E, Sato Y, Minagawa A, Okuyama R. Pathogenesis of psoriasis and development of treatment. J Dermatol [Internet]. 2018 Mar;45(3):264–72. Available from: http://doi.wiley.com/10.1111/1346-8138.14139

20. Hugh JM, Weinberg JM. Update on the pathophysiology of psoriasis. Cutis [Internet]. 2018 Nov;102(5S):6–12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30566550

21. Talamonti M, Galluzzo M, Bernardini N, Caldarola G, Persechino S, Cantoresi F, et al. Psoriasis Area and Severity Index response in moderate-severe psoriatic patients switched to adalimumab: results from the OPPSA study. J Eur Acad Dermatology Venereol [Internet]. 2018 Oct;32(10):1737–44. Available from: http://doi.wiley.com/10.1111/jdv.15077

22. Carrera CG, Dapavo P, Malagoli P, Naldi L, Arancio L, Gaiani F, et al. PACE study: real-life Psoriasis Area and Severity Index (PASI) 100 response with biological agents in moderate-severe psoriasis. J Dermatolog Treat [Internet]. 2018 Jul 4;29(5):481–6. Available from: https://www.tandfonline.com/doi/full/10.1080/09546634.2017.1395805

23. Pascoe VL, Enamandram M, Corey KC, Cheng CE, Javorsky EJ, Sung SM, et al. Using the Physician Global Assessment in a Clinical Setting to Measure and Track Patient Outcomes.

JAMA Dermatology [Internet]. 2015 Apr 1;151(4):375. Available from: http://archderm.jamanetwork.com/article.aspx?doi=10.1001/jamadermatol.2014.3513

24. Chessa E, Piga M, Floris A, Devilliers H, Cauli A, Arnaud L. Use of Physician Global Assessment in systemic lupus erythematosus: a systematic review of its psychometric properties. Rheumatology [Internet]. 2020 Dec 1;59(12):3622–32. Available from: https://academic.oup.com/rheumatology/article/59/12/3622/5891911

25. Bakshi H, Nagpal M, Singh M, Dhingra GA, Aggarwal G. Treatment of Psoriasis: A Comprehensive Review of Entire Therapies. Curr Drug Saf [Internet]. 2020 Jun 20;15(2):82–104. Available from: http://www.eurekaselect.com/178694/article

26. Golbari NM, Porter ML, Kimball AB. Current guidelines for psoriasis treatment: a work in progress. Cutis [Internet]. 2018 Mar;101(3S):10–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29718028

27. Pels R, Sterry W, Lademann J. Clobetasol propionate - Where, when, why? Drugs of Today [Internet]. 2008;44(7):547. Available from: http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=4&p_RefId=1122221&p_IsPs=N

28. Warino L, Balkrishnan R, Feldman SR. Clobetasol propionate for psoriasis: are ointments really more potent? J Drugs Dermatol [Internet]. 2006 Jun;5(6):527–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16774104

29. Gottlieb AB, Ford RO, Spellman MC. The Efficacy and Tolerability of Clobetasol Propionate Foam 0.05% in the Treatment of Mild to Moderate Plaque-type Psoriasis of Nonscalp Regions. J Cutan Med Surg Inc Med Surg Dermatology [Internet]. 2003 Jul 1;7(3):185–92. Available from: http://link.springer.com/10.1007/s10227-002-0114-5

30. Feldman SR, Yentzer BA. Topical Clobetasol Propionate in the Treatment of Psoriasis. Am J Clin Dermatol [Internet]. 2009 Dec;10(6):397–406. Available from: http://link.springer.com/10.2165/11311020-000000000-00000

31. Olsen EA, Cornell RC. Topical clobetasol-17-propionate: Review of its clinical efficacy and safety. J Am Acad Dermatol [Internet]. 1986 Aug;15(2):246–55. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0190962286701643

32. KANZLER MH, GORSULOWSKY DC. Efficacy of topical 5% liquor carbonis detergens vs. its emollient base in the treatment of psoriasis. Br J Dermatol [Internet]. 1993 Sep;129(3):310–4. Available from: http://doi.wiley.com/10.1111/j.1365-2133.1993.tb11852.x

33. MERK H, RUMPF M, BOLSEN K, WIRTH G, GOERZ G. Inducibility of arylhydrocarbon-hydroxylase activity in human hair follicles by topical application of liquor carbonis detergens (coal tar). Br J Dermatol [Internet]. 1984 Sep;111(3):279–84. Available from: http://doi.wiley.com/10.1111/j.1365-2133.1984.tb04724.x

34. Thawornchaisit P, Harncharoen K. A comparative study of tar and betamethasone valerate in chronic plaque psoriasis: a study in Thailand. J

Med Assoc Thai [Internet]. 2007 Oct;90(10):1997–2002. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18041415

35. Arif T. Salicylic acid as a peeling agent: a comprehensive review. Clin Cosmet Investig Dermatol [Internet]. 2015 Aug;455. Available from: http://www.dovepress.com/salicylic-acid-as-a-peeling-agent-a-comprehensive-review-peer-reviewed-article-CCID

36. Lebwohl M. The role of salicylic acid in the treatment of psoriasis. Int J Dermatol [Internet]. 1999 Jan;38(1):16–24. Available from: http://doi.wiley.com/10.1046/j.1365-4362.1999.00500.x

37. Torsekar R, Gautam M. Topical therapies in psoriasis. Indian Dermatol Online J [Internet]. 2017;8(4):235. Available from: http://www.idoj.in/text.asp?2017/8/4/235/209622

38. de Mare S, Calis N, den Hartog G, van Erp PEJ, van de Kerkhof PCM. The Relevance of Salicylic Acid in the Treatment of Plaque Psoriasis with Dithranol Creams. Skin Pharmacol Physiol [Internet]. 1988;1(4):259–64. Available from: https://www.karger.com/Article/FullText/210784

39. Jacobi A, Mayer A, Augustin M. Keratolytics and Emollients and Their Role in the Therapy of Psoriasis: a Systematic Review. Dermatol Ther (Heidelb) [Internet]. 2015 Mar 21;5(1):1–18. Available from: http://link.springer.com/10.1007/s13555-015-0068-3

40. Frankel AJ, Zeichner JA, Del Rosso JQ. Coal tar 2% foam in combination with a superpotent corticosteroid foam for plaque psoriasis: case report and clinical implications. J Clin Aesthet Dermatol [Internet]. 2010 Oct;3(10):42–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20967195

41. Gooderham M, Blakely K. Management of scalp psoriasis: current perspectives. Psoriasis Targets Ther [Internet]. 2016 Mar;33. Available from: https://www.dovepress.com/management-of-scalp-psoriasis-current-perspectives-peer-reviewed-article-PTT

42. Zhu TH, Nakamura M, Farahnik B, Abrouk M, Singh RK, Lee KM, et al. The Patient's Guide to Psoriasis Treatment. Part 4: Goeckerman Therapy. Dermatol Ther (Heidelb) [Internet]. 2016 Sep 29;6(3):333–9. Available from: http://link.springer.com/10.1007/s13555-016-0132-7

43. Khandpur S, Sahni K. An open label prospective randomized trial to compare the efficacy of coal tar-salicylic acid ointment versus calcipotriol/betamethasone dipropionate ointment in the treatment of limited chronic plaque psoriasis. Indian J Dermatol [Internet]. 2014;59(6):579. Available from: http://www.e-ijd.org/text.asp?2014/59/6/579/143523