IJPSR (2020), Volume 11, Issue 6 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 04 September 2019; received in revised form, 21 December 2019; accepted, 17 April 2020; published 01 June 2020

AN OLD ADAGE MANAGEMENT PERSPECTIVE FOR DANDRUFF

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Keywords:

Dandruff, Eiology, Pathogenesis, Zulamla

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ABSTRACT: Dandruff is a well-known and global consumer problem, characterized by flaking and scaling of the scalp, with itching and irritation. Although it is not a life-threatening disease, but it is directly related to individual self-esteem, confidence, and beauty. Approximately half of the population is suffering from dandruff and expending around billions of dollars, including hospital services and counter products. Despite its frequency, much controversy remains regarding the pathogenesis of dandruff. Many studies postulated that dandruff is caused by various microbial and non–microbial factors and interaction between them, such as Malassezia fungi, sebum secretion, and individual susceptibility. But some recent researches also claimed that dandruff is not only produced by fungi but there are some bacteria that also play a significant role in accelerating dandruff. The present treatment includes antifungal agents, no doubt, they have significant results but with lots of side effects and limitations. So, there's a need to formulate a cost-effective product that possesses anti-dandruff activity, and Zulamla (Hamdard Laboratory Patent Product) is used and is in the public domain from the last 35 years with no side effects. In this paper, dandruff etiology, pathogenesis, and pharmacological studies on Zulamla ingredients are discussed.

INTRODUCTION: Dandruff, also referred to as Pityriasis simplex / Pityriasiscapitis / Seborrheic dermatitis (confined to scalp) is a common dermatological problem that has existed since centuries. The word dandruff (dandriffe) is of Anglo-Saxon origin, a combination of 'tan' meaning 'tetter' and 'drof', meaning 'dirty' [1]. Dandruff is the persistent, relapsing inflammatory condition with the visual perception of individually distinguishable flakes on the scalp, in the hair, or on the clothing [2, 3].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(6).2557-65

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(6).2557-65

The development of dandruff is predicated on being determined by the colonization of yeast Malassezia furfur, sebum production, and individual susceptibility [4]. Both dandruff and seborrheic dermatitis are analogous as both affect the seborrheic glands of the body, having the same causative organism and etiology and respond to similar management and treatment; however, they only differ in magnitude, locality, and severity.

Dandruff is confined to scalp and has itching, flaking, redness of scalp with mild inflammation, while as Seborrheic dermatitis affects scalp as well as retro- auricular area, face, chest and back causing scaling, flaking, pruritis and inflammation [2, 5]. Several studies expose the fact that half of the population is suffering from dandruff [6]. It has a high socioeconomic impact. Prevalence is more in males than in females due to androgen hormones [7].

No residents in any geographical area would have passed through freely without being affected by dandruff at some stage in their life [1]. Together with counter products and hospital services, the total direct cost for treating dandruff was estimated to be $179 million, plus another $51 million indirect cost in the form of lost workdays [8]. Besides physical discomfort such as itching, dandruff is socially embarrassing and impacts negatively on patient's self-esteem. It has significant negative effects on a patient's quality of life (QOL) in the form of psychological distress and confidence [7].

Global treatment of dandruff comprises frequent use of shampoos and lotions containing azoles, namely, ketoconazole, fluconazole climbazole, keratolytic agents, salicylic acid, sulfur, zinc pyrithione, coal tar, steroid, selenium sulfide. however, all these treatment options are very costly, and the chances of recurrence are high. Usage of anti-dandruff shampoo for long duration results in dryness, itchy scalp and premature greying of hair [9]. And some of these agents may lead to some unwarranted effects like skin irritation from zinc pyrithione, the carcinogenic effect of coal tar when used in excess burning sensation by repetitive use of Salicylic acid and itching, rashes and allergy from ketoconazole [10, 11, 12].

Etiology of Dandruff: Based on recent evidences, dandruff depends on the sebaceous gland secretions, microfloral metabolism, and individual susceptibility, *etc*. that is on non-microbial and microbial factors [13].

Microbial Factors: The scalp has a biotic community of Staphylococcus spp., Propioni-bacterium spp, malassezia spp, and these are known components [14]. The density of these organisms varies from 103 to 105 organisms per mm square but during dandruff, malassezia increases by two times of its normal level [15]. malassezia is a leading cause of dandruff, and it is a monophyletic genus of fungi found in 7 billion human's skin [16] previously, referred to Pityrosporum ovale, or Pityrosporum orbiculare. In 1846, Eichstedt was the first who recognize the presence of this fungus on pityriasis versicolor.

But the role of Malassezia on dandruff was first studied in 1874 by McGinley *et al.,* and found that in normal subjects Malassezia species are 46%, in patients with dandruff is 74% and patients with seborrheic dermatitis is 83% [17]. For decades, Malassezia limited to two types of species, the lipid dependent Malassezia furfur, and the lipophilic Malassezia pachydermatis. But with advances in research, many other species of Malassezia came into light [18]. For many years, studies on dandruff predominantly focused on Malassezia species, out of 14 known cultured species, the most clinically significant species are M. restricta and M. Globosa and these two species are found to have more potential for the development of dandruff as compared to M. Furur [15, 19].

However, in this scalp biotic community, another microorganism community composed of anaerobic and aerobic bacteria such as Propionibacterium and staphylococcus. Disequilibrium in the proportion of these bacteria can lead to the formation of dandruff [20, 21]

Non Microbial Factors:

- Excessive sebum secretion
- Damage to scalp stratum corneum
- Individual susceptibility
- Dry scalp
- Excessive exposure to sunlight
- Frequent combing and over-shampooing
- Sensitivity to hair cosmetics
- Dirt and dust accumulation
- Other scalp conditions like psoriasis, eczema, *etc*.

But there is no sufficient evidence for above assumption [21, 22, 15]

Pathophysiology of Dandruff: A single square centimeter of the skin can be inhabited by one billion of microorganism and formed a complex community of skin microbiome [23]. Dandruff is a superficial disorder of the stratum corneum, and many evidences showed that the dandruff is dependent on three factors: Sebaceous gland activity, micro-floral metabolism and individual susceptibility [24, 25, 26, 20, 27, 28].

- **Sebaceous Gland Activity:** The function of sebum has been scandalous, but advances in analytical technology have made some progress. Human sebum is important for

barrier maintenance, epidermal development, protection, body odor, transporting antioxidants and production of pheromones [29]. However, some studies also showed its importance in hormonal signaling, epidermal differentiation, and protection from ultraviolet rays [30, 31]. Human sebum is a complex mixture of triglycerides, fatty acids, cholesterol, cholesterol esters, wax, squalene, and sterol esters [32]. When the sebum secretion occurs, the triglycerides and esters break down into diglycerides, monoglycerides, and free fatty acids by the microbes present on scalp. These free fatty acids play a key role in the initiation of irritants or itching. Simultaneously, the sebum provides a good habitat and nutrients for the development of fungi and bacteria [26, 20].

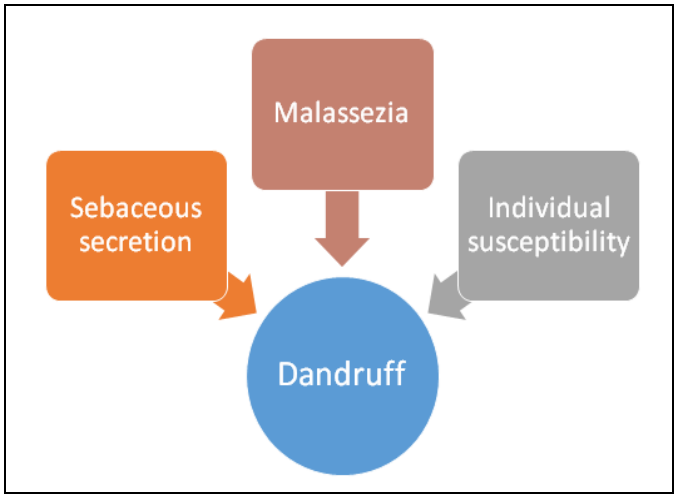

FIG. 1: INTERACTION BETWEEN SEBUM SECRETION, MALASSEZIA FUNGI AND INDIVIDUAL SUSCEPTIBILITY IN DEVELOPMENT OF DANDRUFF

- **Micro-floral Metabolism:** A number of studies prove the presence of microorganism on skin and their role on human body. But interestingly, the most famous fungi whose colonization begins immediately after birth is Malassezia and increases until 6-12 months of age. Recent metagenomic evidence suggests that, with age the skin colonization undergoes into variation and provides a protective effect over skin against dermatophytes [33, 34]. The non-microbial factors such as environ-mental conditions, gene induced variation, Lifestyle, hygiene, and immune system can lead to change in biotic community of microbes [35].

With the advanced molecular technique of terminal length polymorphism, Gemmer *et al.*, proved that the most prominent species on dandruff sufferers are M. globosa and M. restricta [36]. Malassezia is commonly found on sebum- rich areas of the body and degrade sebum, especially by lipases and produce free fatty acids [26]. The importance of fungal species in the development of dandruff is supported by the fact that treatment option available for dandruff has mainly antifungal property and these products have a significant effect on reduction of flaking and other symptoms [37].

- **Individual Susceptibility:** In 2005, a study on dandruff hypothesized that some people are susceptible to oleic acid, and some are not susceptible, so that the fatty acid metabolites of Malassezia, mainly oleic acid induces flaking on dandruff-susceptible patients [25]. This finding provides evidence of why some individual has dandruff or others not. Additionally, some other factors are also involved like immunodeficiency, nutritional disorders, drugs, and neuro-transmitter abnormalities [26].

- **Role of Bacteria in the Formation of Dandruff:** Clavaud *et al.*, studied that P. acnes and *S. epidermidis* were two bacterial species on dandruff and healthy scalp, and P. acnes is predominant in sebaceous rich areas. The study suggested that dandruff occurred not only due to the higher incidence of Malassezia but also due to the difference in balance between fungal and bacterial population in the scalp [38]. But in another study done by Xu *et al.*, suggested that P. acnes and S. epidermidis showed reciprocal inhibition with each other, which is concurrent to Clavaud *et al.*, study. The study found that Propionibacterium can secrete bacteriocins to suppress the growth of Staphylococcus, whereas Staphylococcus can mediate the fermentation of glycerol and inhibit the overgrowth of *Propioni-bacterium*. And the study concluded that the disequilibrium between both bacteria associated with the formation of dandruff [20].

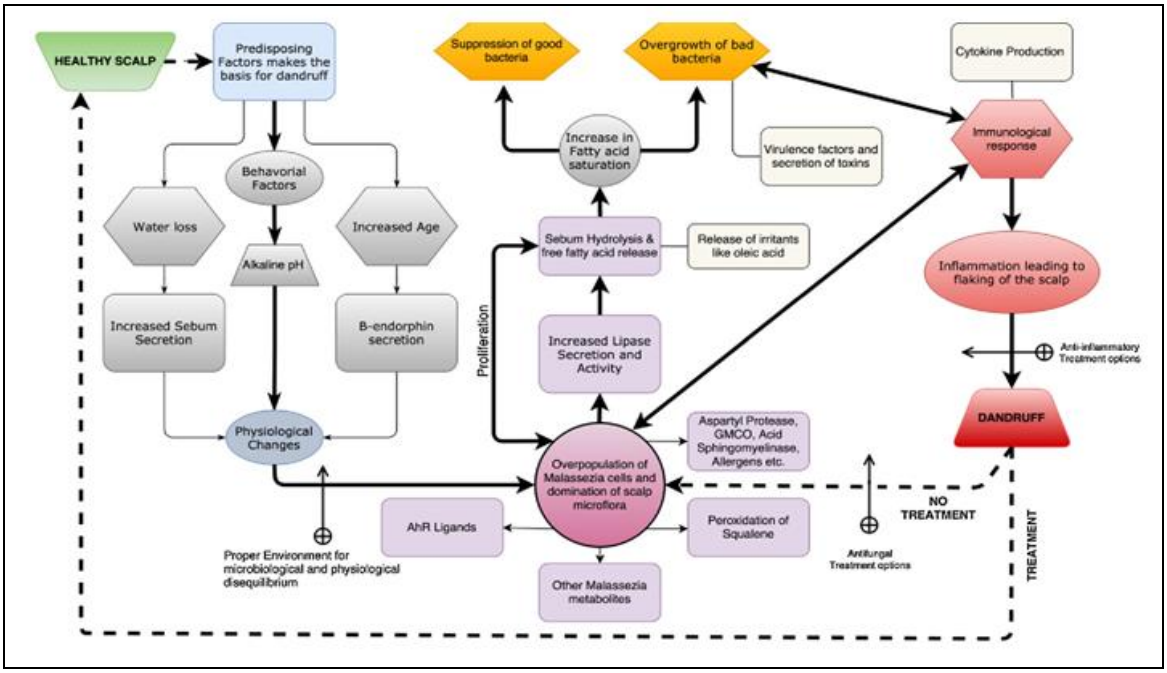

FIG. 2: MECHANISM OF DEVELOPMENT OF DANDRUFF

Management of Dandruff in Conventional Medicine: Therapeutic shampoo is a more convenient option for treating flakes and itching of the scalp. These products have the advantage over other topical formulation of cosmetics such as solutions, ointments, and foams.

The shampoos clean the scalp by emulsifying oily secretions and treat the underlying cause simultaneously. The shampoo applied for 5 to 10 min and then rinse for two to three times in a week for 4 weeks. There are many treatment options for managing dandruff through shampoos:

A. Keratolytic Shampoo: The pathogenesis of dandruff involves hyperproliferation, leading to the deregulation of keratinization and corneocytes clump together, appearing as large flakes of skin. Salicylic acid and sulfur are keratolytic agents which loosen the attachments of corneocytes by softening and dissolving and washed them.

- **Salicylic Acid:** It is a beta hydroxyl acid and keratolytic agent that is useful in removing scales [39]. Salicylic acid facilitates desquamation by solubilizing the intercellular cement that binds scales in the stratum corneum, thereby loosening the keratin.

- **Sulfur:** It is a yellow, nonmetallic element with both antimicrobial and keratolytic properties. The keratolytic effect is due to a reaction between the cysteine in keratinocytes and sulphur [40, 41].

B. Regulators of Keratinization:

- **Zinc:** Zinc act on stratum corneum and heals the scalp by normalizing epithelial and sebum production, and some studies also reveal that number of Malassezia organisms decreased on using Zinc pyrithione shampoo [42].

- **Tar:** Tar gels contain coal tar extract, and they have anti-proliferative and cytostatic effects that act on dandruff by dispersing the scales, which may reduce Malassezia colonization [43].

- **Steroids:** The pharmacokinetic properties of topical corticosteroids depend on the structure of the agent, the vehicle, and the skin onto which it is applied. Topical steroids have anti-proliferative and anti-inflammatory properties [44].

C. Antimicrobial Agents:

- **Selenium Sulfide:** It has anti-fungall properties and has a cytostatic effect on cells of stratum corneum. It is available in 1%, 2.25%, and 2.5% *etc.* Composition [45]

- **Imidazole Antifungal Agents:** Ketoconazole is an anti-fungal agent which acts by blocking

the biosynthesis of ergosterol, a derivative of fungal cell membrane. Ketoconazole is a broad-spectrum antimycotic agent, and it is a leading contender among all treatment options of dandruff. It is available on counter by 1%, 2%, 3% *etc.* [46]

- **Hydroypyridones:** It acts by interfering with the active transport of essential macro-molecules precursors, cell membrane integrity and respiratory cell processes of dermato-phytes and yeast such as Ciclopiroxolamine [46].

Management of Dandruff by Herbal Product-Zulamla:

Zulamal is a Powder Shampoo which Contains Ten Herbal Drug:

- *Emblica officinalis* L. (Aamla)
- *Terminalia chebula* Retz.(Halelasiyah)
- *Lawsonia inermis* L. (Berg Hina)
- *Acacia concinna* Mill. (Shikakai)
- *Mimusops elengi* L.(Post maulsari)
- *Nardostachys jatamansi* DC. (Balchar)
- *Rosa damascene* Mill. (Gulesurkh)
- *Santalum album* L. (Sandal safaid)
- *Acacia arabica* Mill. (Gondkeekar)
- *Brassica campestris* L. (Khali sarson)

1. *Emblica officinalis* L.

- **Antimicrobial Activity of *Emblica officinalis* L:** V. Anbukkarasi *et al.*, performed a study on *Emblica officinalis* and made zinc oxide and nanoparticles of methanolic extract of *Emblica officinalis* and showed that the combination of these act as a broad-spectrum antibacterial activity in six bacterial strains such as *B. subtilis*, *S. pneumonia*, S. epidermidis, *K. pneumonia*, *S. typhi* and *E. coli* [47]. S. Anbuselvi *et al.*, done study on *Emblica officinalis* seed extract by disc diffusion method against pathogenic organisms like *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeroginosa*, *Klebsella pneumonia*, *Aspergillus niger*, *Aspergillus fumigatus*, and *Candida tropicalis* and the extract showed maximum zone of inhibition against standard drug [48]. Naga *et al.* performed a comparative study between different plant extract and commercial available antidandruff shampoo. The study was done on fourteen plant extracts in which one was *Emblica officinalis* and the result was significant as compared to commercial antidandruff shampoo. *Emblica officinalis* showed antifungal activity against Malassezia [49]. Chandran *et al.*, formulated and evaluated an herbal antidandruff shampoo containing thirteen drugs in which *Emblica officinalis* was used as an aqueous decoction due to its antiseptic activity. Chandan *et al.*, mentioned *Emblica officinalis* an antidandruff agent [50]. Another study on herbal formulation named Herbello was done by Shah *et a*l., and the analysis of herb was carried out by inhibitory growth of *Malassezia furfur* through disc diffusion method. *Emblica officinalis* showed maximum inhibitory zone after Henna (*Lawsonia inermis*) [51].

2. *Terminalia chebula* Retz:

- **Antifungal Activity of *Terminalia chebula*:** Shinde *et al.*, studied antifungal activity of leaves of *Terminalia chebula* as aqueous, alcoholic and ethyl acetate extracts against five pathogenic fungi (*Aspergillus flavus*, *Aspergillus niger*, *Alternaria brassicicola*, A. alternate and Helminothosporium tetramera using paper disc method and found positive results [52]. Vonshak *et al.*, done a study on twenty-eight South Indian medicinal plants against six species of fungi (Trichophyton mentagropytes, *T. rubrum*, *T. soudanense*, *Candida albicans*, Torulopsis glabrata and *C. krusei*). An aqueous extract of *Terminalia chebula* showed an inhibitory effect on fungus [53].

3. *Lawsonia inermis* L:

- **Anti-dandruff Activity of *Lawsonia inermis* L:** Deviha *et al.*, conducted a study on anti-dandruff activity of ethanolic extract of leaves of *Evolvulus alsinoides*, *Lawsonia inermis* (Hina), *Azadirachta indica*, Hibiscus rosa-sinensis and *Murraya koenigii*. The leaves were collected, dried, and grinded into coarse powder and subjected to ethanolic extraction. And the dandruff samples were collected from scalp scrapping of subjects suffering from dandruff. The samples were inoculated on

Sabouraud's agar with olive oil and incubated for 7 days at 37 ºC. All the extracts showed a significant antifungal activity and the *Lawsonia inermis* (Hina) exhibited second maximum zone of inhibition [54].

4. *Acacia concinna* Mill:

- **Anti-dandruff Activity of *Acacia concinna*:** K. Jagajjanani Roa *et al.,* conducted a study on Acacia by using silver nanoparticles based green formulation in which the leaf extract of 40 and 13 nm sizes were used. The result showed significant fungi toxic property against *M. furfur* [55].

- **Anti-dermatophytic Activity of *Acacia concinna:*** Mansuang Wuthi-udomlert performed study on 35 isolates of dermato-phytes and each 20 isolates of *Candidia albicans, Cryptococcus neoformans* and *Penicillium marnaffei* by using ethanolic, chloroform, lyophilized and macerated extract of *Acacia concinna* and the study concluded that all the extract showed significant efficacy as an antifungal agent as compared to Ketoconazole [56]. Another anti-dermatophytic study was done by Natarajan on hexane, ethanolic, and ethyl acetate extracts of the pods of Acacia concinna against Microsporum nanum, *Epidermophyton floccosum*, *Trichophyton violaecum*, *Trichophyton mentagrophytes* and *Trichophyton rubrum*. The study was *in-vitro* and presented significant anti-dermophytic activity of Acacia [57].

5. *Mimusops elengi* L:

- **Antibacterial Activity of *Mimusops elengi*:** Ali *et al.,* performed in vitro study on bark, fruits, and leaves of *Mimusops elengi* with petroleum ether, ethyl acetate and methanol extracts against 7 pathogenic bacteria and 6 fungi by the standard disc diffusion method. The result showed antifungal activity [58].

6. *Nardostacys jatamansi* DC:

- **Anti-fungal Activity of *Nardostachys jatamansi* DC:** Mishra *et al.,* demonstrated antifungal activity against *Aspergillus flavus, Aspergillus niger* and *Fusarium oxysporum* and one more study on essential oil of Balchar indicate fungi static activity done by Sarbhoy *et al.* [59, 60]

7. *Rosa damascena* Mill:

- **Anti-microbial Activity of *Rosa damscena* Mill:** Shohayeb *et al.,* performed a study and petals were subjected to water, hexane, ethanol, and fractionated with ethyl acetate, butanol, and chloroform. The extracts were evaluated against eleven gram-positive, gram-negative, acid-fastt bacteria and three fungi. The study concluded that the extracts showed moderate broad-spectrum anti-microbial activity [61].

8. *Santalum album* L:

- **Anti-fungal Activity of *Santalum album* Linn:** Tabassum *et al.,* conducted a study on aqueous seeds extract of *Santalum album* Linn. and produced silver nitrate nanoparticles. The synthesized nano-particles were tested against antifungal and antibacterial activities using agar well diffusion method. The nanoparticles showed the inhibition of pathogens which cause superficial fungal infections like *C. albicans*, *T. rubrum* and *E. coli* and indicate potent antifungal activity compared with standard [62].

9. *Acacia arabica* Mill:

- **Antifungal Activity of *Acacia arabica* Mill:** F. Tissouras done a study on crude seeds oil of *Acacia arabica* and *Acacia raddiana* at various concentrations on *Aspergillus niger* and *Candida albicans* by two different methods that is broth dilution and diffusion in solid medium and the study showed positive result [63].

10. *Brassica campestris* L:

- **Anti-bacterial Activity of *Brassica campestris* L:** Agarwal *et al.,* conducted a study on five bacterial strains by disc diffusion method against ethanolic, petroleum ether, methanolic and ethyl acetate extracts of root,

stem, and leaves of *B. campestris* and found out effective antibacterial activity against *Staphylococcus aureus*, *Bacillus cereus*, *Pseudomoas aeroginosa*, *Escherichia coli* and *Staphylococcus epidermidis* [64].

CONCLUSION: Herbal drugs are used in various indigenous systems of medicine from ages as folk medicine. The literature survey reveals its diverse potent biological activities, which were proved through several *in-vitro* and *in-vivo* animal studies.

Emblica officinalis, *Lawsonia inermis*, *Acacia concinna etc.* has been used in washing hairs since centuries and now is scientifically proved to possess the anit-fungal, anti-dermatophytic, anti-dandruff activity and also do conditioning of hairs.

This experimental evidence and encouraging research results suggest that zulamla powder is safe and effective in Dandruff.

ACKNOWLEDGEMENT: This article has been prepared based on classical literature available and researches available online. We appreciate efforts of the authors in establishing such useful database.

CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

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How to cite this article:
Ahmed Y, Shakir SJ, Hashimi A, Binth MS and Jahangir U: An old adage management perspective for dandruff. Int J Pharm Sci & Res 2020; 11(6): 2557-65. doi: 10.13040/IJPSR.0975-8232.11(6).2557-65.