

Chemical Agents for Dandruff Control

SITARAMDIXIT

Applications Manager (Fragrances), Bush Boake Allen India Ltd., Mumbai.

It is mandatory and has been a regular practice for surgeons and nurses in an operating table, workers in pharmaceutical and food industries, and chefs while cooking, to wear caps. Do you know why it is so? This is because it is universally accepted that bacteria and fungi are disseminated from human hair. Surprised? Yes, it is true. Human hair harbours many organisms; notably pathogenic bacteria's like *Staphylococcus Aureus*, *Escherichia Coli*, *Streptococcus Viridons*, Fungi, and Yeast's that can cause unwanted disorders to an individual.

Dandruff is one such irritating problem affecting as many as 40% of men and women over the age of thirty. Dandruff is not infectious and so in the true sense cannot be considered as a disease. It is very common among adults and is not usually found in early childhood or the pre-puberty years. It confirms our premise that it is, probably due to an individual's hormonal secretion or body constitution. Some researchers believe that metabolic activity, improper diet, stress; allergic inflammatory reactions brought by pharmaceutical products or topical cosmetic applications may be responsible for causing dandruff.

We know that skin is composed of two main layers, the "Epidermis", and the "Dermis". The Epidermis is the most superficial layer, composed of stratified squamous epithelium. From the outside inward, the stratified epithelium is divided into five layers. "Stratum Corneum" is the most superficially placed cells without nuclei that are keratinised, with indistinct cell outlines. This layer is thickest at the soles and the palms and very thin at the lips. Hairs' nails, etc., are outgrowths of this layer. "Stratum Lucidum" is a thin, slightly transparent layer 3 to 5 cells deep and placed below the "Stratum Corneum" very similar to it with indistinct cell outline without nuclei. "Stratum Granulosum" consisting of 3 to 5 layers of flattened polyhedral cells is followed by "Stratum Spinosum" that is also made up of polyhedral cells of variable thickness. The surface of these cells is covered with minute spines, that interdigitate with similar spines of adjacent cells. These cytoplasmic protrusions are also called as the "Prickle Cells". The branches of two cells do not have cytoplasmic continuity but are attached to by well-developed cytoplasmic nodes or desmosomes. These cells are basophilic supported by a network of cytoplasmic fibrils. Star shaped branched cells capable of DNA synthesis, also called as "cells of Langerhans" is scattered irregularly throughout this skin layer. "Stratum Germinativum" (Stratum Malpighii), composed of a single layer, of columnar epithelium, having transverse, thin, short, cytoplasmic process on its basal lamina, anchors the epithelium to the lower dermis. These cells with oblong nuclei,

with cuboidal to columnar cell's structure are placed perpendicular to the basement membrane, and produce newer cells to replace those above by the process of "mitosis." The Epidermis of the scalp gets affected when an individual is afflicted by dandruff.

Dandruff is very easy to diagnose. It presents a scaly condition of the scalp leading to skin scales easily visible on the hair and often falling on one's shoulders. Shedding of human skin is a natural process, however in case of dandruff the very fine and almost invisible scales, clump together to form abundant visible silver grey scales. It is often associated with some itching but with very little or no sign of inflammation. Scales may be either dry or greasy, covered with a film of sebum. Studies have revealed that dandruff results from a scalp skin disorder. Dandruff that is not directly related to hair chemistry is conspicuously absent in bald males.

Severe dandruff when ignored often leads to a condition called "Seborrheic dermatitis". In this condition the scalp has, red sharply outlined marginated lesions covered with greasy scales. The underlying skin is usually moist and red with definite signs of inflammation. Sometimes it extends beyond the area of scalp and includes, the forehead, back of the neck and behind ears. It is commonly seen in the external auditory canal, which can later become secondarily infected with bacteria.

Seborrheic dermatitis implies that it is a disorder of the sebum producing Sebaceous glands. Surprisingly, sometimes there is no abnormality of sebum or sebaceous glands. Therefore, why seborrheic dermatitis is caused, one has no clue. However, it occurs predominantly in sebum producing areas and varies with times of high androgenic or seborrheic activity. Seborrheic dermatitis is six times more prevalent in males than females again confirming an androgenic hormonal connection. "Cradle Cap", is the infantile form of seborrheic dermatitis. It is largely self-limiting and is usually due to excess circulation of androgens in the blood stream.

The clinical and histological difference between seborrheic dermatitis and dandruff are disputed by various researchers. The non-inflammatory scaly scalp disorder considered as dandruff, falls within the preview of the cosmetic and toiletries field. Severe seborrheic dermatitis ideally falls in the clinical field. Severe seborrheic dermatitis sometimes can be confused with psoriasis, fungal intertrigo, contact dermatitis, or eczema and localised lesions or may resemble

tinea capitis, which require treatment from a medical practitioner and a dermatologist.

The exact cause of dandruff is still not very clear and established theories are disputed by many authors. However, it is generally accepted that the primary cause of dandruff is fungal. Fungi are any major group of saprophytic and parasitic lower plants that lack chlorophyll. They usually have little or no mycelium and reproduce by budding. It is now believed that dandruff is caused by fungus named pityrosporum ovale. pityrosporum ovale reacts with the scalp lipids and decomposes them to free fatty acids and lipo peroxides. Free fatty acids and lipo peroxides causes skin irritation leading to mitosis and increase in keratinocytes which further results in the formation of silvery grey scales causing dandruff.

Individuals affected by dandruff have a thinner incoherently formed stratum corneum. Scales are formed due to rapid turnover of epidermal cells of the scalp. The loose scales thus formed are shed leading to visible signs of dandruff on the scalp hair and shoulder. Complete eradication of fungus pityrosporum ovale from the scalp does not eliminate dandruff. Similarly, dandruff is not always found in persons having the fungus pityrosporum ovale. Therefore, the cause of dandruff is still an enigma. However, these organisms are certainly found in larger numbers in persons affected by dandruff than those not affected by it. It is not known whether pityrosporum ovale just takes advantage of a more suitable environment and perhaps only help in aggravating the problem or otherwise. However, severity of the symptoms is directly related to the quantity of pityrosporum ovale in the total microflora count of the scalp with

- * 46% in normal unaffected individuals.
- * 74% in persons with dandruff.
- * 83% in those with scalp seborrheic.

Dry dandruff normally caused by external topical agents, like soaps, shampoos, hair lotions and creams, etc., can be alleviated by eliminating the use of these products. Greasy dandruff can be often alleviated by regular washing, massaging, maintaining good scalp hygiene, and applying suitable anti-dandruff agents. Varieties of chemicals have been used in the treatment of greasy dandruff.

Shampoos containing coal tar either alone or along with sodium salt of sulphosuccinate of the undecylene alkalimides was first found to reduce dandruff. Constant research led to the discovery of other chemical actives that are effective in dandruff control. Many chemical agents reported to be effective in controlling dandruff, namely phenols, cationic germicides like 5% cetavlon solution, trichloromethyl mercapto derivatives, 2.5% solution of tellurium oxide, etc., are nowadays commercially not widely used.

Sulphur, resorcinol, salicylic acid, selenium disulphide, ketoconazole, zinc - pyridine - 2 thiol oxide, zinc pyrithione, octopirox, climbazole, etc., are some anti-dandruff agents that are used nowadays in commercial applications to control dandruff.

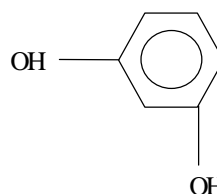
Sulphur (S = 32.06)

Precipitated sulphur, sublimed sulphur, and washed sulphur are three elemental forms of sulphur that are used in product applications. Precipitated sulphur also called as "Milk of Sulphur" is obtained by boiling sulphur with calcium hydroxide or lime and precipitating the filtered solution with hydrochloric acid. Precipitated sulphur that contains polythionic acids is the most effective form of sulphur for dandruff control.

Precipitated sulphur is a fine pale greyish or greenish yellow amorphous or microcrystalline powder. It is practically odourless, tasteless and free from dirt. Precipitated sulphur is insoluble in water and alcohol. It is soluble in hot aqueous solution of alkali hydroxides with the formation of polysulphides and thiosulphates. Precipitated sulphur is sparingly soluble in anhydrous lanolin, at 45 degrees centigrade and in olive oil.

Precipitated sulphur is a good antiseptic and parasiticide for external use. Sulphur is usually used in combination with lime, resorcinol, salicylic acid for making preparations like lotions, pastes, creams, ointments, etc. Though precipitated sulphur is, an effective treatment for dandruff control, certain precautions is mandatory during its usage. The skin should be cleaned thoroughly before applying the lotion or cream in the affected portion of the scalp. Only small amount of the product should be rubbed very gently into the roots of the hair. It should not be applied to broken or inflamed skin or come in contact with eyes. Prolonged usage should also be avoided and application of the product stopped if excessive dryness or irritation of skin occurs.

Resorcinol (Benzene 1, 3 diol, $C_6H_6O_2 = 110.1$)



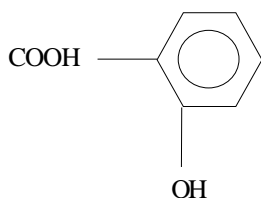
Resorcinol has good antipruritic exfoliative and keratolytic properties. It is a colourless needle shaped crystalline powder with a characteristic odour and a sweet taste. Resorcinol has a melting point of 109 - 111 degrees centigrade and becomes pink when exposed to air and light. It is soluble in water and alcohol, glycerol, fixed oils and ether. Products containing resorcinol at 2% levels is used in dandruff control. Resorcinol along with sulphur is an effective anti-dandruff agent.

Resorcinol should not be used over large raw skin surface particularly in high concentration. Prolonged usage of resorcinol based application products on raw surface results in Myxoedema (dry skin, hair loss, loss of mental and physical vigour) and so should be avoided.

The hair should be thoroughly washed and rinsed of all traces of soap or alkali before application of the product containing resorcinol. In presence of soap or alkali, resorcinol may discolour hair slightly.

The scalp skin should be cleaned thoroughly and the product applied sparingly. It should not be applied to broken or inflamed skin or come in contact with eyes. Prolonged usage should also be avoided and application of the product stopped if excessive dryness or irritation of skin occurs.

Salicylic Acid (2 Hydroxy Benzoic Acid, $C_7H_6O_3 = 138.1$)



Salicylic acid is found in the form of esters in several plants. It is found notably in wintergreen leaves and bark of sweet birch. Salicylic acid is an odourless, needle like crystal or crystalline powder having a melting point of 157 to 159 degrees centigrade. It is soluble in water, alcohol, ether and in solutions of ammonium acetate, borax, sodium phosphate, potassium, and sodium citrate. It is incompatible with iron salts and with oxidising substances.

Salicylic acid is a keratolytic substance, having bacteriostatic and fungicidal properties. It is used externally in lotions and ointments or creams for the treatment of dandruff and other fungal infections of skin. Salicylic acid preparations in combination with, coaltar, mercuric chloride, benzoic acid, sulphur, or zinc oxide is normally preferred for treatment of dandruff. Preparation in the form of lotion, collodion, paste, or cream is rubbed gently into the affected area and roots of the hair and allowed to dry for freedom from dandruff. However, care should be taken to avoid using the product in broken or inflamed skin or to be exposed to eyes. Prolonged usage should also be avoided and application of the product discontinued if excessive dryness or irritation of skin occurs.

Selenium disulphide ($SeS_2 = 143.1$)

Selenium disulphide is a very effective compound due to its good cytostatic ability to lower the corneocyte quantity thereby controlling dandruff. Selenium disulphide is a bright orange to

reddish orange powder with a faint odour of hydrogen sulphide. It is prepared either by the action of selenious acid and hydrogen sulphide or by the fusion of sulphur and selenium. Selenium disulphide is insoluble in water and in organic solvents. Selenium disulphide is applied as an either cream or lotion to the scalp to control dandruff. A 2.5% suspension of selenium disulphide in a medium containing, a buffer, detergent, and dispersing agent is suitable for this purpose.

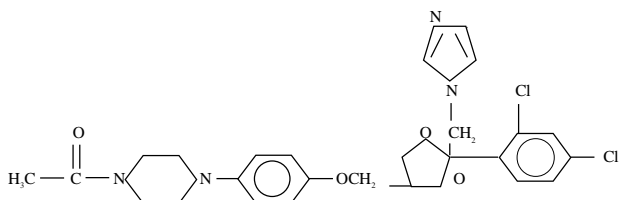
The hair is first thoroughly washed with soap and rinsed. 5 to 10 ml of the application is then applied to the scalp together with a little warm water to produce lather. The lather is then gently rubbed into the roots of the hair and left for 2 to 3 minutes. The lather is rinsed out and a second application done so that the scalp area having dandruff is exposed to at least 5 minutes to the action of selenium disulphide. The hair is then thoroughly rinsed and all traces of selenium disulphide suspension are removed. If this is not done then yellow or orange discoloration of hair may take place. The application is normally used twice a week and then gradually reduced as the dandruff get under control. It is to be noted here that repeated use of the product can lead to hair loss.

Selenium disulphide is very highly toxic. It is believed to be a carcinogen. However, it is absorbed only in trace quantities through scalp skin and so suitable in dandruff control. Selenium disulphide should not be used in areas that are inflamed or has broken skin. Extreme care is to be taken so that selenium disulphide does not enter the eyes. It should not be applied to skin around the eyes to avoid cutaneous absorption. Hands and fingernails should be carefully washed and rinsed after using the application.

Although selenium disulphide is very effective in controlling dandruff products made, is dark brown in colour, unattractive, cosmetically unappealing, and unpleasant to use. Due to its toxic nature, products having Selenium disulphide as an active are considered more to be an ethical or pharmaceutical product to be used under medical supervision.

Sulphur, resorcinol, salicylic acid, selenium disulphide are all very effective anti-dandruff agents for use in controlling dandruff. However, they have their disadvantages of them having to be used only after carefully following the mandatory precautions of usage. Commercial products are available in the market but due to the cumbersome usage conditions, they are used only in severe cases of dandruff, when over the counter cosmetic products. Commercial preparations for the treatment of dandruff and seborrheic dermatitis of the scalp generally include the use of a shampoo a post shampoos rinse or a hair dressing containing one or more of the active ingredient available.

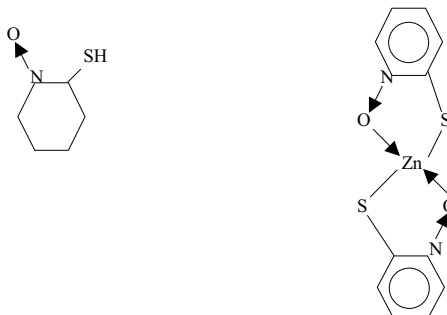
Ketoconazole (Cis - 1 - Acetyl - 4 - {4 - [(2 - (2, 4 dichlorophenyl) - 2 - (1H - imidazol - 1 - yl methyl) - 1, 3 - dioxalan - 4 - yl] methoxyphenyl } piperazine,
 $C_{26}H_{28}Cl_2N_4O_4 = 531.44$



Ketoconazole is crystalline in nature having a melting point of 146 degree centigrade. It is a very effective anti-dandruff agent. Ketoconazole as a raw material is not easily available commercially, being protected by patent laws. A 2% ketoconazole in shampoo base is marketed for dandruff treatment. Use of shampoo formulation 2 to 3 times a week is effective in treating dandruff. Regular usage once a week can prevent recurrence after the initial cure has been effected. In order to maximise the antifungal effect of ketoconazole the shampoo is left on the scalp for atleast five minutes.

Pyrithione

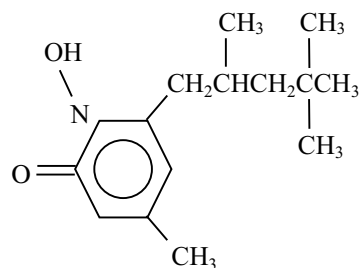
(1 Hydroxy -2 (1H) - pyridinethione, 2- pyridinethiol 1 Oxide; 2 Mercaptopyridine 1- Oxide) Omadine;
 $C_5H_5NOS = 127.18$



The pyridines - N - oxides also known as cyclic thiohydroxamic acids or pyridinethions are highly active antibacterial and antifungal agents. The zinc derivative $C_{10}H_8N_2O_2S_2Zn$, zinc pyrithione, zinc pyridinethione, bis (2 - pyridylthio) zinc 1, 1' - dioxide, bis - (1 - hydroxy - 2 - (1H) - pyridinethionato - O, S) zinc; zinc omadine is a safe agent for incorporation into shampoos at 2% levels. It is a very good anti dandruff agent but acts more slowly than selenium disulphide. It does not penetrate the skin and supposedly not produce toxic reactions when used with normal precautions. However, in some cases it has been found to cause irritation of scalp that can be countered by addition of conditioning agent's like stearyl dimethylamine oxide as claimed. Dimer $C_{10}H_8N_2O_2S_2$, dipyrithione, 2, 2' - dithiobis pyridine 1,1 - dioxide, OMDS, omadine disulphide is another derivative also as a fungicide.

Piroctone

1 Hydroxy - 4 - methyl - 6- (2, 4, 4 trimethylpentyl) - 2 (1H) - pyridinone; $C_{14}H_{23}NO_2 = 237.34$

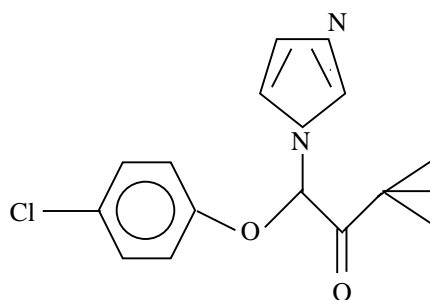


Piroctone a derivative of pyridone is another chemical used as an anti-dandruff agent. It is crystalline product having a melting point of 108 degree centigrade. The ethanolamine salt (1:1), $C_{16}H_{30}N_2O_3$ Octopirox is also an effective anti-dandruff agent for use in shampoo applications. It claimed to be slightly superior to zinc pyrithione.

Climbazole, 1 - (4 Chlorophenoxy) - 1 - (Imidazol - 1-ly) 3 - 3 - dimethyl - 2 - Butanone; $C_{15}H_{17}Cl_2N_2O_2 = 292.8$

Climbazole belonging to theazole class of antimycotics is also being used in dandruff treatment. It is an off white to greyish non-hygroscopic crystalline powder with a characteristic odour. It is stable to heat, light and metal ions.

Climbazole is insoluble in water but is soluble in ethanol, benzyl alcohol, fragrance oils, phenoxyethanol and surfactants like cocoamide DEA, propyl betaine, etc. Climbazole is a safe agent for use both in leave on and wash off application products.



Dandruff is chronic relapsing problem caused by fungi, that is probably a normal inhabitant of the scalp, but becomes pathogenic when present in high numbers. The management of the problem is likely to be a long time affair. Dandruff even though is a significant problem and we can reasonably assume that individuals can make correct diagnosis all by themselves. Dandruff is essentially a self-treatment condition and it is important that effective treatment should be available easily over the counter to the affected persons.