

Effect of Zinc Pyrithione in Dandruff

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ABSTRACT

Dandruff is a common scalp condition to be associated with microbes *Malassezia restricta*. Zinc pyrithione has been used as an ingredient for anti-dandruff treatments. The mechanism of Zinc Pyrithione has been analysis in several contains ; however , a non-pathogenic model yeast , such as *Saccharomyces cerevisiae* was most often used .The goal of the present study was to understand that, how Zinc Pyrithione inhibits the growth of *Malassezia restricta* .we investigated the cellular metal content and pharmacological profile of Zinc pyrithion treatment against *Malassezia restricta* cells. Dramatically cellular zinc level and a small cellular copper levels is increased by zinc pyrithione.Farther , Zinc pyrithione inhibits the Fe-S cluster synthesis in *M.restricta* these is shows by transcriptome analysis .we also observed that significantly treatment of Zinc Pyrithione reduced the secretion of lipases, whose activities contribute on the survival and virulence of *M.restricta* on human skin (scalp). An observation of these study is that inhibitory mechanism are associated with action of Zinc Pyrithione against *M.restricta* is an increase the zinc cellular level of the skin , inhibits the mitochondrial function and a decrease the level of lipase expression.The growth of yeast can be inhibit by the Zinc Pyrithione, hance the factor cousing dandruff. Zinc Pyrithione is used in various hair and skin care products.such as shampoos, lotion, shops facewash etc.Its is clinically proved that Zinc pyrithione is over the counter drug. it should be topically not for systemically.

Key words: *Malassezia restricta*, virulence, cluster, *Saccharomyces cerevisiae*, lipases

I. INTRODUCTION

Dandruff occurs, when small bits of dry skin are shed from the scalp. these flakes in hair and our shoulder. dandruff may make our scalp itchy,too. It's a problem, but it is not as simple as it seems.

Dandruff is actually quite tricky to define because it overlaps with seborrheic dermatitis,

condition of chronic form of eczema and other skin condition that lead to a scaly scalp. it is caused by dry skin,or the buildup of oil .skin condition like seborrheic dermatitis, seborrheic dermatitis (SD) and dandruff are very common dermatological problems that affect the seborrheic areas of the body. They are considered the as same basic situation shearing many features and responding to similar treatment, differing only in locality and severity. dandruff is restricted to the scalp and involves itchy,flaking skin without visible inflammation sd affect the scalp as well as face,retro-auricular area and the upper chest, causing flaking,scaling,inflammation and pruritus and can have marked erythema.flaking in SD and dandruff is usually white to yellowish and might be oily or dry.

This is estimated that SD and dandruff combine affect half of the adult population. despite such high prevalence, the etiology is not well understood various intrinsic and environmental factors ,such as sebaceous secretion , skin surface fungal colonization , individual susceptibility, and interaction between these factor ,all contribute to the pathogenesis. There are also contrary finding about the ability of *Malassezia* to assimilate unsaturated fatty acid for growth,which hasimplication for elucidating the specific pathway underlying SD pathogenesis. further for more, while *Malassezia* yeast.Genetic, pathophysiology and strategies for better treatment. SD and dandruff is a very common dermatological disorder in India and worldwide. It is also associated with psychiatric disease,neurological disease, Parkinson's disease tardive dyskinesia, mood dipression, mental strass,traumatic brain injury , epilepsy, hepatitis c virus facial nerve palsy, pinal cord injury,and patient having congenital disorder such as down syndrome .moreover , dermatitis of face may also developed in patient treated for psoriasis and UV therapy. Approximately 50% of population in worldwide affected from dandruff and seborrheic dermatitis generally adult.

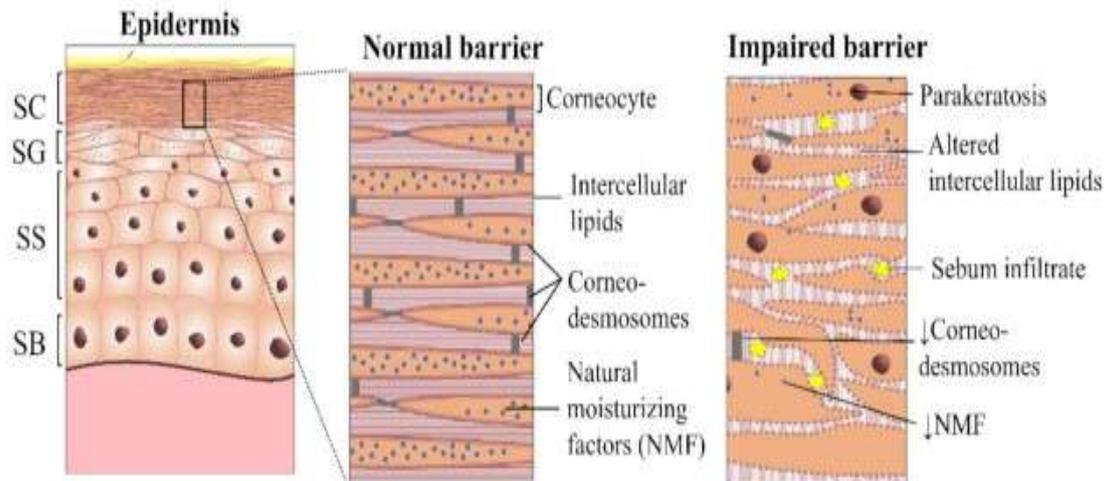


Fig.1 : Epidermal structure highlighting key features of the normal stratum corneum (SC) barrier and impaired barrier in seborrheic dermatitis. Proliferation of keratinocytes occurs exclusively from the stratum basale (SB). As these cells progressively travel upwards differentiation occurs in the stratum spinosum (SS) and granulosum (SG), resulting in the cornified cells of the SC, which are continuously shed from the skin surface by the process of desquamation.

Dandruff: Dandruff is Spread out flaking on the scalp and hair that is light, white to yellow in color and free of erythema. lacking to a little itching. may extend to the eyebrows, hairline, and retroauricular region.

SD in infants scalp Cradle Cap: The most typical. Within three months after birth, reddish-yellow plaques covered in thick, oily scales appeared on the vertex.

Face/Retro-auricular area Salmon-colored plaques that are erythematous, flaky, and appear on the forehead, eyebrows, eyelids, nasolabial folds, or retro-auricular regions.

SD in adult scalp Alopecia may take several forms, from mild desquamation to honey-colored crusts stuck to the scalp and hair. May continue into the forehead as the scaly, erythematous "corona seborrheica."eyebrows, glabella, nasolabial folds, and forehead. May disperse to cheeks and malar areas in the dispersion of butterflies.

Scaling between the lashes on the eyelids is yellowish. may result in honey-colored crusts on the free edge of blepharitis.

Activity of sebaceous gland

Humans have sebaceous glands (SGs) all over their skin, with the exception of their palms and soles. Abnormalities in lipid composition may potentially contribute to the development of SD, most likely by creating an environment that is conducive to *Malassezia* growth, as sebum

production is highest on the scalp, face, and chest [64]. Squalene and triglycerides were lower in SD individuals, whereas cholesterol and free fatty acids were significantly higher [38, 44]. The increased amounts of cholesterol and free fatty acids might be the consequence of *Malassezia*'s lipase breaking down triglycerides; these metabolites encourage *Malassezia* development and draw inflammatory infiltrators into the epidermis.

Permeability of the epidermal barrier

As a barrier against water loss and the entrance of germs and hazardous substances from the environment, the stratum corneum (SC), the anucleated outer layers of the epidermis, serves as an example [65]. Constructed by specific intercellular cell adhesion structures known as corneodesmosomes, the SC is made up of many layers of terminally developed keratinocytes, or "corneocytes," enclosed in lipid lamellae. Epidermal permeability barrier (EPB) function might be affected by any changes in the number of corneodesmosomes, thickness of the SC, size or shape of corneocytes, or content of lamellar lipids. Electron microscopy, which contained intercellular *Malassezia* yeasts, has shown structural anomalies in the barrier in dandruff scalp.

Etiology

The genesis of seborrheic dermatitis (D/SD) and dandruff is reliant upon three factors: individual predisposition, microbial metabolism

(particularly, *Malassezia* yeasts), and sebum. The significance of *Malassezia* in particular may be better understood because to developments in microbiological and analytical methods. Due to their adaptability and lipid need, *malassezia* can only thrive in a specific niche on skin that produces a lot of sebum. The goal of our lab's work and that of our partners has been to thoroughly analyze gene expression and biochemistry in order to comprehend these changes. We have demonstrated the presence of *Malassezia globosa* and *M. restricta* on dandruff-affected scalps, the induction of dandruff-like elimination by oleic acid alone, the likelihood that *M. globosa* is the most likely initiating organism due to its high lipase activity, and the proliferation of *M. globosa* lipase on human scalps. Considering into account how significant *M.*

We have sequenced the genomes of *M. globosa* and *M. restricta* in Dandruff/SD (and the general significance of commensal fungus). The results of genomic research point to major skin environment modifications, some of which provide crucial hints about the involvement of *Malassezia* in human illness. This research has the potential to identify novel D/SD therapies that modify the expression or function of *Malassezia* genes.

Types of Dandruff:-

1. Dry Skin- related dandruff: This is the most common type of dandruff which usually occur during the winter months from cold, dry weather, and is linked with using hot water shampoo the hair (which dried out the scalp)

2.Oil-related dandruff:-This occurs from a buildup of sebum (oil) on the scalp. the oil can

clump the dead skin cells on the scalp together with oil, forming itchy flakes.

3.Yeast-related dandruff:- This is caused by *Malassezia* yeast, which is a type of fungus that lives on excess oil. It produces a byproduct that cause the skin cells to clump together, which is the cause of the white flakes seen in dandruff.

4.Seborrheic dermatitis:-Trusted source occur more often in people with oily skin dandruff in addition to flakes,this common scalp condition can caused scaly patches and itching .one of the most effective ways to treat dandruff caused by seborrheic dermatitis is with a shampoo that contains zinc pyrithione.

5.Eczeme:- it also known as atopic dermatitis, eczema is characterized by patches of flaky, itchy skin, and sometimes a red rash.when it appears on human scalp,this inflammatory condition can cause flakes that are usually larger than dry skin dandruff flakes .so many times may noticed red, irritation on the scalp.

6.Psoriasis:- Psoriasis is a skin condition that often affects the knees, elbows, trunk, and scalp. Psoriasis is a widespread, incurable, chronic illness that lasts a long time. It may hurt, disrupt sleep, and make it difficult to focus. The illness usually flares up for a few weeks or months, then goes into remission for a time. For those who have a hereditary propensity to psoriasis, common triggers include infections, burns, or wounds, as well as ascertain drugs.Thought to be it is an autoimmune condition in which skin cell grow too quickly, causing thick, scaly patches to form on the skin scalp psoriasis my appear as fine,powdery flakes.



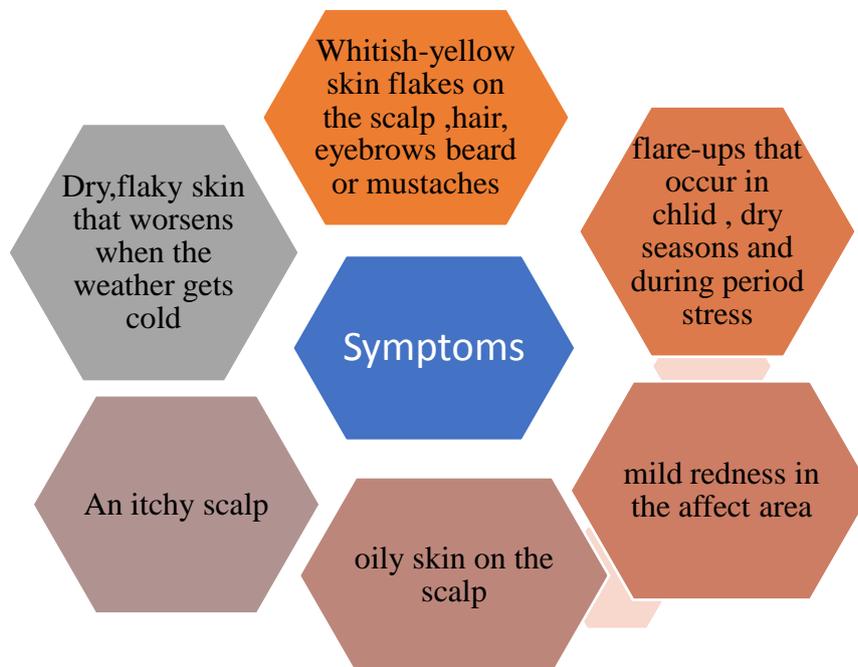
Fig. 2: dandruff on scalp



Fig 3: seborrheic dermatitis

Symptoms of Dandruff-

Where is the first sign that a person has dandruff is the aspect of white flakes of dead skin on the hair or shoulders, as well as an itchy scalp. The Other symptoms of dandruff can vary, depending on the type of dandruff.



Treatment

Over-the-counter (OTC) shampoos that contain the following types of ingredients may help reduce or prevent flaking:

- **Pyrithione zinc.** Helps destroy bacteria and fungus on the scalp. Shampoos with this ingredient, also known as zinc pyrithione, are appropriate for most hair types.
- **Coal tar.** Slows the process of skin cell death on the scalp. These shampoos may cause some discoloration to light-colored hair.
- **Salicylic acid.** Treats excessive oil on the scalp. Many shampoos with this ingredient can be used every day, while others are recommended for use 2 to 3 times a week.
- **Selenium sulfide.** Fights fungus on the scalp. This ingredient can cause some hair discoloration if you don't thoroughly rinse your hair after washing.
- **Ketoconazole.** Another inflammatory skin disease that causes skin flaking, skin plaques, and redness is psoriasis, which is commonly treated with ketoconazole. Many times, a yeast-like fungus causes these skin plaques. Psoriasis flare-ups may require the prescription drug ketoconazole. and the verity of shampoos is available OTC and in prescription strength.
- **Zinc pyrithione:** Zinc pyrithione (or pyrithione zinc) is collaborating complex of zinc. It is capable to restrict the division of fungal cell known as fungistatic and retard the partitioning of bacterial cells wall known as bacterioststic moreover its used in the treatment of SD and Dandruff, flaky scalp, itchy skin.

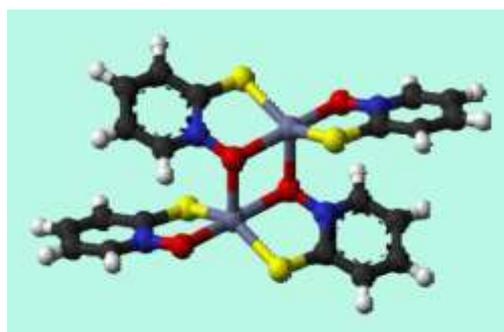
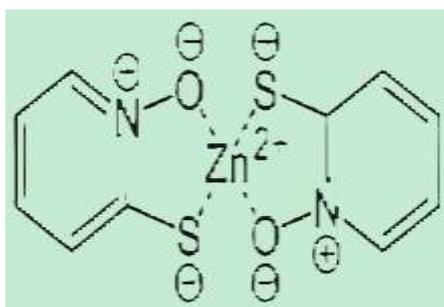


Fig. 4 Mol. structure of zinc pyrithione Fig. 5 3D structure of zinc pyrithione

IUPAC name: bis(2-pyridylthio)zinc 1,1'-dioxide
 Other names: ZnPT, Pyrithione Zinc, Zinc OMADINE, ZnPT
 Chemical formula: $C_{10}H_8N_2O_2S_2Zn$
 Molar mass: 317.70 g/mol
 Appearance: colourless solid
 Melting point: 238°C-240 °C (464 °F; 513 K)
 (decomposition)[1]

Boiling point: decomposes

Solubility in water: 8 ppm (pH 7)

The rigid crystal lattice structure exists in the solid-state where two bridging oxygens form a pseudo-dimer between two ZnPT molecules. The rigid crystal lattice structure exists in the solid-state where two bridging oxygens form a pseudo-dimer between two ZnPT molecules.

Mechanism of zinc pyrithione

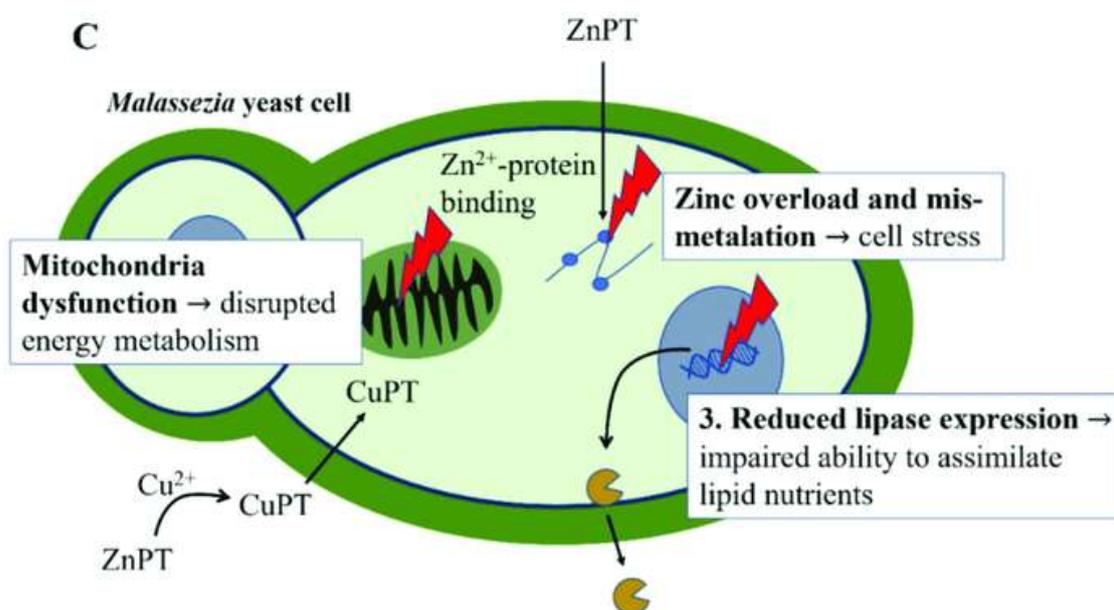


Fig 6: The three key actions of ZnPT on Malassezia yeast, resulting in zinc-induced cellular stress, disrupted energy metabolism and impaired ability to assimilate lipid nutrients for growth.

The mechanism of action of ZPT has been characterized using different model of fungal organism rather than Malassezia ermolayevae suggested that ZPT leads to membrane depolarization either directly or indirectly, thereby, inhibiting proton pump-mediated membrane transport. They suggested that this inhibition might be caused solely by pyrithione, because zinc salt is believed to dissociate after ZPT is transported into the cytosol, and that pyrithione alone acted in this manner. However, membrane depolarization occurs at a significantly higher concentration of pyrithione, which is beyond the inhibitory concentration for the fungi therefore, it is difficult to assert that the mechanism of action of ZPT on fungi involves membrane depolarization.

Firstly, as Pyrithione it is also known as zinc ionophore, Zinc Pyrithione causes elevated intracellular zinc levels in yeast cells to the extent

that it results in incorrect metallation and cellular stress.

This excess intracellular copper can inactivate aconitase, which is an enzyme involved in fungal energy production within the mitochondria. In study it also demonstrated that zinc pyrithione inhibits the membrane transport of nutrients needed for yeast growth by inducing membrane depolarization.

USES-

Zinc pyrithione (ZPT) is an active material that has been used for over 50 years to effectively treat dandruff and seborrheic dermatitis.

It also has antibacterial properties and is effective against many pathogens from the Streptococcus and Staphylococcus genera.

It can be used in wide categories. they are followings:-

- Medicine
- Paint
- House hold Sponges
- Clothing

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