

Topical Relief from Tropical Prickly Heat

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The Indian spring is a season of flowers and fruits, of sweet music of birds, of green nature, a season of new life and hope. Unfortunately spring just lasts for only a couple of months in India. It is followed by the long Indian summer and to me the worst season of the year. India has enough of heat throughout the year and summer only aggravates — adding fuel to fire. The burning heat of the blazing sun is oppressive enough for our comfort, and becomes all the more unbearable, when summer is accompanied by various ailments like sunstroke, measles and miliria. Although the brown skin of Indians gives reasonable protection from the summer heat and light, it has limitations to adapt itself to the harsh environment.

The structure of the human skin

The skin is no simple structure in the human body. This 1.7 m², protective cloak or barrier separates the vulnerable interior of the human body from potentially harmful and damaging stimuli in the environment. It controls loss of water from the body tissues and regulates body temperature. Various sensory nerve endings present on our skin help protect the human body. Skin prevents penetration of radiation and resists action against mechanical shock caused due to external agencies and protects the body from damage. Skin is composed of two main layers, the 'Epidermis', and the 'Dermis'.

The Epidermis

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.' It is very similar to the 'Stratum Corneum' 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' are 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.'
- * At the junction of the epidermis and dermis are present 'melanocytes' or 'melanin' containing branched cells. 'Malpighain cells' and the 'melanin' present in the deeper cells of the 'Stratum Germinativum' is produced by these melanocytes. Cytochrome secretion converts the fully formed 'melanin' granules from melanocytes to the malpighain cells. Melanin is a yellow to black pigment found in the Stratum Germinativum. It is formed on a specific cell particle, the melanosome within the melanocytes. Melanin contributes colour to the skin; moreover it protects one from the ultra-violet rays of solar radiation.

The Dermis

'Dermis' or the 'true skin' consisting of connective tissue, lies below the epidermal layer which it supports and binds to the underlying tissues. Chiefly made up of collagen and elastic fibre, it provides tensile strength. Structurally the superficial part of the dermis is compact and forms the papillary layer resembling innumerable finger-like projections into the prickle cell layer of the epidermis. The inner part of the dermis is made up of loose connective tissue containing fat. This layer constitutes the reticular layer of the dermis merging into the subcutaneous layer of fat. Fibroblasts cells from which the fibrous tissue of the dermis develops melanophores containing melanin pigments and cell belonging to the reticulo-endothelial system protecting the body from invading bacteria is also present in the dermis. Unlike the epidermis, the dermis has a well-organised lymphatic system and a luxuriant capillary blood vessel network supplying blood to the tip of the dermal papillae that play an important role in regulating temperature. Besides bundles of involuntary muscles and vasomotor nerves, the dermis has sensory nerve endings of different types that keep an individual informed about the surroundings.

Pear shaped sebaceous glands located in the dermis open

into the root of the hair follicles and secretes an oily material called as sebum. In places that are devoid of hair (sebaceous glands are not present at the palms and soles), the duct of the sebaceous glands opens directly to the surface of the skin. The sebaceous glands are very active during adolescence and when the secretion is improper, lodges in the ducts as whitehead, the outer portion of which may get oxidise to blacken and form a blackhead. The sebum is rich in fatty acids, cholesterol, cholesterol esters, triglycerides, wax esters, and other aliphatic components. The cholesterol present in sebum can absorb about 100% water and keep the surface of the skin moist. Irradiation of sebum creates vitamin D. Sebum behaves as a lubricant to prevent damage to the epidermis during summer and conserves heat during winter.

Sweat glands

Sweat glands are distributed throughout most of the skin. There are about 3 million active sweat glands in the body. The lower ends of the sweat glands reach the deep part of the dermis and act as islands for regrowth of epidermis in cases of injury and burns. Modified smooth muscle cells, known as the myoepithelial cells present at the base of the sweat glands surround their ducts in a manner that their contraction help in elimination of sweat. Sweat glands are of two types, Eccrine, and Apocrine.

Eccrine glands

Eccrine glands are distributed throughout the surface of the body. They are present in larger numbers on the palms and soles than on the head or the trunk. In humans, they may be present peaking at levels of 200 to 400 per square centimetres of skin surface. Their discharges are altered primarily due to changes in deep body temperature. Glands present at the palms and soles respond and secrete at times of emotional stress. Eccrine sweat composition depends on the blood constituents and contains sodium chloride, urea, lactates, creatinine, uric acid, ammonia, amino acids, glucose, water soluble vitamins B and C.

Apocrine glands

Apocrine glands are larger sweat glands and derived from the hair follicles. The distribution of these glands in humans varies from individual to individual and race to race. Apocrine sweat glands become active after puberty. Apocrine sweat has indoxyl, volatile fatty acids, hydroxy acids, ammonia, and other metabolic excretory products. Fresh perspiration is odourless. The bacterial activity in presence of these secretions contributes to the intensity and quality of odour.

Sweating in humans is of different types:

- * Insensible perspiration occurs even in cold climates, and amounts to about 600 to 800 ml per day
- * Psychic sweating, occurring chiefly in the palms, soles, axilla, head and neck in extreme emotional conditions.

Muscular exercises, eating spicy foods, sympathetic activity, nausea and vomiting, fainting, hypoglycaemia and asphyxia can induce sweating. Sweating is reduced by cold due to reduced cutaneous circulation. It is also reduced by dehydration, either by reduced fluid intake or by excess sweating. Drinking a glass of cold water dilutes the blood and this can induce sweating profusely.

- * Thermal sweating occurs in hot environmental temperature. As the environmental temperature increases, sweating rises and can under extreme conditions amount to 11 litres per day. Males start sweating excessively at temperatures above 28°C and females above 31°C.

Sweating is very important physiologically as active secretion plays a vital role in keeping the body cool and regulating body temperature. When the ambient temperature is higher than body temperature, sweating is the only means of keeping the body temperature normal. However excess sweating that takes place during summer, when the weather is hot and humid can cause prickly heat or Miliaria, an acute inflammation of sweat glands, characterised by the formation of patches of small red papules and vesicles, with intense itching and burning of skin.

Sweat rash

Sweat rash can also be caused by the blockage of the sweat gland opening (sweat pores) or the upper part of the ducts near the skin surface. The most frequently observed form known as 'miliaria crystallina', appears as a numerous delicate vesicle due to blockage of the pore right at the surface. If the pores are extensively, blocked, inflammation is produced with the eruption of red papules. Although there is no deep inflammation within the skin or considerable systemic disturbance, it causes unbearable prickling sensation or itching. This is more so in areas that come across clothing. Infants being more susceptible, suffer from lesions on the face as well, unlike elders who suffer on the trunk, neck, groins, axillae and elsewhere. It is postulated that the condition is aggravated with the increase in the density of aerobic bacteria, notably cocci. The secretion of toxins by these bacteria injures the luminal cells, blocking the sweat gland openings. The condition also called m. Rubra, lichen tropicus, strophulus, heat rash, sudamina and prickly heat. M alba, m crystallina, miliria, in which the contents of the vesicles are opaque and white, is called Sudamina crystallina or m rubra.

Chemicals used in treatment of prickly heat

An effective treatment for prickly heat is to cool the individual and prevent further sweating, using air conditioning, fans, cold water bandaging, etc. Topical application of anti-microbial and anti-inflammatory agents can bring relief from intense itching and burning of skin. Dusting powder containing actives on the affected area can provide relief from prickly heat.

Chlorphenesin

Chlorphenesin, is an antifungal agent used for topical applications. Chemically it is {3-(4-Chlorophenoxy)-1-2-propanediol, p-chlorophenyl a-glyceryl ether}, (C₉H₁₁ClO₃), with a molecular weight 202.64. The crystals of chlorphenesin has a melting point of 77-79°C. Solubility in water is less than 1%, but can be increased by the addition of solubilisers such as ethylene or propylene glycol. Chlorphenesin carbamate, malonate (C₁₀H₁₂ClNO₄), is some times also used.

Triclosan

Irgasan® DP 300, (Triclosan) or 2,4,4' trichloro-2 hydroxy diphenyl ether, an odourless or very faintly aromatic, off-white powder, with a molecular weight of 57± 1°C, effective against both gram positive and gram negative organisms, has been used extensively as a synthetic antibacterial agent, for more than three decades. Nowadays almost all major personal hygiene product manufacturers, use triclosan, at 0.2% to 0.3% (w/w) of the formulation to effectively reduce body odour, and fight harmful bacterial micro-organisms, in personal care products like skincreams, soaps, deodorants or talcum powder. Triclosan is stable in normal storage conditions, easy to incorporate in a talcum powder formulation. Thermal stability studies have proved that triclosan is relatively stable up to 150°C and upto 200°C, if not heated continuously for more than 2 hours. Triclosan is practically insoluble in water, moderately soluble in alkaline solutions, and readily soluble in most non-polar organic solvents (See Table).

Triclosan is lipid- soluble, antiseptic, incorporated at a level of 0.2% to 0.3% (w/w) of the formulation, dissolved in suitable solvents and added to personal care leave-on and rinse-off products like skin creams, soaps, deodorants, talcum powder, etc., to inhibit halitosis and fight against harmful germs. Triclosan usage will help in not only improving, but also maintaining, the high standard of personal hygiene necessary for complete body care. One of the most important features of triclosan is its anti-inflammatory activity. Triclosan is a potent inhibitor of cyclo-oxygenases and lipoxygenases, the main enzymes of the arachidonic acid metabolism. The inhibition of these enzymes results in reduced formation of the pro-inflammatory metabolites, prostaglandin E2 and leukotriene B4. Presence of triclosan at the site of affected skin has a soothing effect, and helps support healing of damaged skin.

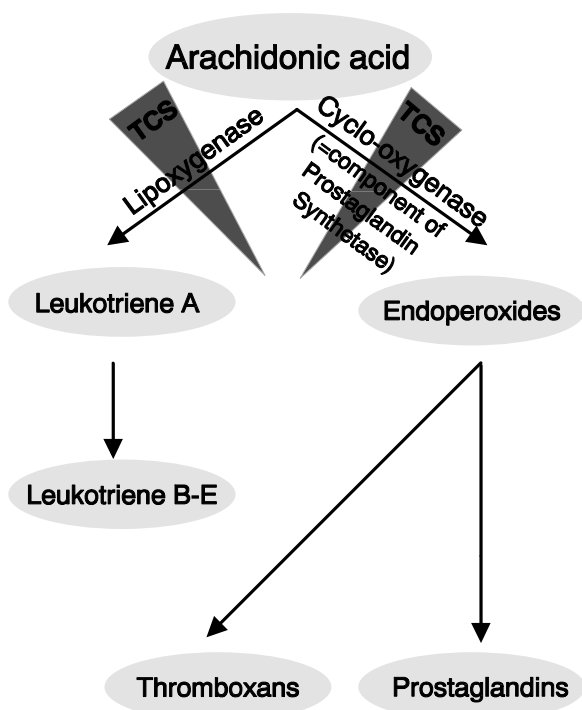
The intense itching and burning of skin that accompanies the acute inflammation of sweat glands, in miliaria can be reduced with the use of triclosan containing anti bacterial prickly heat powder. Triclosan is a broad-spectrum antimicrobial agent whose activity is dependent on the concentration and formulation of the product. Different experiments and extensive studies carried out to find the mode of action of triclosan concluded that the primary action of

SOLUBILITY OF TRICLOSAN IN SOME COMMON SOLVENTS

[Gms of triclosan per 100 g solvent at 25°C]

Solvent	Solubility
Distilled water 20°C	0.001
Distilled water 50°C	0.004
Distilled water / ethanol ratio	
* 75/25	0.06
* 70/30	0.17
* 65/35	0.42
* 60/40	1.0
* 30/70	> 100
* 5/95	> 100
1N Sodium hydroxide	31.7
0.1N Sodium hydroxide	2.35
1N Sodium carbonate	0.40
0.1N Sodium carbonate	0.32
Triethanolamine	> 100
Isopropanol	> 100
Benzyl alcohol	About 60
Propylene glycol	> 100
Dipropylene glycol	About 40
Polyethylene glycol 400	> 100
Ethyl cellosolve	> 100
Methyl cellosolve	> 100
Glycerine	0.15
Petroleum jelly white	About 0.5
Tween 20	> 100
Tween 80	> 100
Oleic acid	About 40
Olive oil	About 60
Castor oil	About 60
Amyl acetate	> 100
Ethyl acetate	> 100
Glycerin triacetate	> 100
Benzyl benzoate	> 100
Dimethyl phthalate	> 100
Diethyl phthalate	> 100
Dibutyl phthalate	> 100
Diocetyl phthalate	> 100
Isopropyl myristate	> 100

triclosan is directed against RNA and protein synthesis in bacteria, and not against DNA synthesis. It is considered that the uptake of nutrient molecules by the bacterial cell wall, as well as whole bacterial cells by diffusion, might be inhibited by triclosan, with the cytoplasmic membrane being the target. When exposed to low concentrations of triclosan, the bacterial cells do not die, but their growth and multiplication are inhibited. The degree may, however, not be the same for all nutrient molecules. Experimental findings support the hypothesis that bactericidal concentrations of triclosan



induce a release of cytoplasmic material from the bacterial cells, inducing a decrease in the optical density of the suspension and eventual death. Thus there is a difference between the bacteriostatic effect of triclosan that results due to the prevention of the uptake of nutrients by the cell membrane and the bactericidal effect that is caused due to the irreversible disruption and rupture of the cell membrane.

Acute toxicity studies reveal that triclosan is not a toxicant. The sub-acute and sub-chronic toxicity profile of triclosan has also been well documented. Studies conducted by the pathology-working group showed no evidence of carcinogenic potential at any level. Studies conducted to judge the mutagenicity of triclosan showed negative results. In a two-generation reproduction study, there were no adverse effects on the reproduction performance at any dose tested. In studies conducted to assess the development toxicity, triclosan was found to have no potential for tetratologic effect.

Triclosan is not skin sensitising and does not have photosensitising effect. Human safety studies conducted to determine the safety of triclosan showed no adverse effects. Blood chemistry and haematological measurements conducted during these studies showed no difference between control subjects and ones using triclosan. Triclosan containing talcum powders show an antibacterial effect against pathogenic gram-positive and gram-negative strains that are involved in numerous infections and disease. Gram positive cocci bacteria namely *Staphylococcus aureus*, are involved in the genesis of prickly heat and *Escherichia coli* as a

representative germ for gram-negative bacteria is involved in infectious diseases and unwanted on skin. Substantivity of an antimicrobial agent is a prerequisite for a long lasting effectiveness. Prickly heat powder containing triclosan shows excellent bacteriostatic effects against both test bacteria *staphylococcus aureus* and *Escherichia coli* under *in vitro* growth inhibition test conditions.

Triclosan for use in personal hygiene products should not only be analysed for its quantitative purity, but also for the presence of impurities, at trace levels of less than 1ng/Kg or 1 part per trillion. This is especially important for polychlorinated dioxins and furans such as the 2,3,7,8 isomers commonly known as Seveso-dioxins that are unwanted by-products during triclosan manufacture. Dioxins are highly toxic, persistent substances, with a wide range of adverse effects. Dioxins can produce a plethora of responses in animals and presumably in humans, which can lead to chloracne, carcinogenicity, reproductive and developmental effects, immunotoxicity, effects on circulating reproductive hormones, increased risk of diabetes, endometriosis and enzyme inductions. It is very important that only superior and approved quality triclosan is used in personal hygiene products. Irgacide® LP 10, a liquid formulation of triclosan upto 5% levels of which can also be used as an active with superior activity in place of triclosan. As it is a liquid it is easy to incorporate in cold manufacturing processes requiring, no pre-dissolving, no heating, and no time consuming mixing. It has low viscosity (which makes it pumpable) and so suitable for automatic dosage-systems.

Requirements of a prickly heat powder

A prickly heat powder containing triclosan is not very much different from a deodorant body powder. This naturally infers that the prickly heat body powder should also possess all the necessary attributes required for a deodorant body powder. We know that the function of a body powder is to mask minor imperfections, make skin look smooth to touch and hide unwanted shine caused mainly due to perspiration and other oily secretions or those caused due to the use of cosmetic formulations. Body powder or talcum powder should also act as a carrier for perfumes, producing a cooling sensation by its dissemination over a large surface area. Talcum powder acceptable for use confirms to the basic requirement of adhering to the skin and is resistant to the mixed body secretions.

A good covering power that is a prerequisite for any talcum powder formulation will also apply to a prickly heat powder. Titanium dioxide, zinc oxide, magnesium oxide, kaolin is used to enhance the covering power of talcum powder. Zinc oxide, when used, also imparts soothing properties, being a mild astringent unlike titanium dioxide. Zinc oxide also has

a slightly better sun screen property and helps in reducing minor skin irritations. The particle size of titanium dioxide and zinc oxide also plays a major role in the talcum powder formulation. The smaller the particles size, the better the spread on the skin, and thinner the spread, the greater its physical cover. However, if the particle size is smaller than the wavelength of light, i.e., below 0.25 μm there is a decrease in the opacity and subsequent decrease in covering power. Under similar conditions, the covering power of different pigments proportionally increases with their refractive index. Thus, it can be predicted that materials with higher refractive index have a better covering power. Magnesium oxide and superior grades of kaolin having a good covering power can also be used in combination with titanium dioxide and zinc oxide.

The next important requirement of a prickly heat body powder is its ability to absorb perspiration and the greasy sebaceous secretions to eliminate the unwanted oily shine on the skin to prevent aggravation of irritation and burn. The absorbing capacity of a talcum powder is increased by use of colloidal kaolin, precipitated chalk, magnesium carbonate, etc. Colloidal kaolin has very good water absorbing capacity and it's good covering power and adhesion to skin an added advantage. The relatively higher density of kaolin when compared to other components in a talcum powder helps in controlling the bulk density.

Special grades of starch are sometimes used as a base for talcum powder to increase absorptive properties and covering power imparting smoothness to the skin. However in a prickly heat formulation starch that has a tendency to swell and form cakes in presence of excessive perspiration and form a sticky paste can clog the opening of the hair follicles present on the surface of the skin and aggravate the problem. Starches being ideal nutrients may sometimes favour bacterial growth. Starch are best avoided in a prickly heat formulation.

Superior grades of precipitated calcium carbonate, pharmaceutical quality magnesium carbonate at 5% level can be used in prickly heat powder to effectively increase the absorbency and fluffiness of body talc. Adhesiveness or the ability of talcum powder to cling on to the body / skin for a sufficiently long time is imparted by the incorporation of stearic acid metallic soaps of zinc and magnesium. Present at 3 to 10% level, stearic acid soaps makes the talcum powder soft and fluffy increasing adhesion and water repelling properties. Addition of finely powdered pure silica in a talcum powder formulation increases the fluffiness of the product and behaves as an anti-caking agent.

Slip or the smoothness feeling caused by uniform and even spreading in a talcum powder is imparted by use of magnesium stearate, zinc stearate and talc. Chemically talc or

talcum is a naturally occurring mineral, hydrated magnesium silicate, $[\text{Mg}_6\text{Si}_8\text{O}_{20}(\text{OH})_4]$ is also the major component in prickly heat powder.

Prickly heat powders, as in case of body powder, contains over 75% of talc. 'Cosmetic grade talc' of very high quality and purity, white in colour with a slippery feel and good powers of oil absorption, inert to most chemical, having a hardness of 1 on the Moh's hardness scale and refractive index between 1.54 to 1.60, and density of 2.75 to 2.80. is preferred. It is to be ensured that talc used in prickly heat talcum powder should have a smooth feel with the particles passing through standard 200-mesh sieve. However it should be emphasised that only non-toxic materials giving no indications of adverse effects like irritation, skin sensitisation or subacute toxicity, allergy, carcinogenic, mutagenic or tetragenetic effects and that are environmentally acceptable be used. All ingredients used should comply with the relevant specifications laid down and permitted for use by The Drugs and Cosmetics Rules, framed by the regulatory authorities. Toxic metal impurities of arsenic, heavy metals, cobalt, chromium, nickel that may be present in inferior quality ingredients in substantial proportion could cause responses in humans in form of Allergic Contact Dermatitis. This condition of Allergic Dermatitis is chronic in nature and its symptoms remain even after the obvious source of contamination is removed. Good manufacturing practice is to be followed with utmost importance during manufacture to limit these impurities within acceptable limits, as it is suspected that even low level of these toxic impurities is sufficient to maintain Allergic Dermatitis.

Manufacturing body powder involves mixing of various ingredients in a horizontal mixer with a screw agitator. Micropulverisers, disintegrators, hammer mills, etc., and machines that mix and sieve automatically can be used. Talc, an airborne particulate, if uncontrolled in the manufacturing site can be a health hazard to workers. The exposure levels at the workplace must be monitored and adhered to the limits laid down by regulatory authorities. Reassessment and regular monitoring exercise are to be carried out to detect any changes in concentration levels in the atmosphere, resulting from wear and tear of the machinery, plant defects and changes in operator working habits. Packaging of powder is best carried out by use of vacuum filling devices to reduce dusting and extraneous contamination in container's compatible with the different ingredients. After a soothing spring, summer brings in with its hot blazing sun associated diseases and discomfort.

Talcum powder containing an effective antimicrobial like triclosan when topically applied, not only curbs unpleasant body odour to make one smell excitingly fresh, and keep skin healthy, but also provides, welcome relief, from prickly heat, making summer more comfortable.