Summer Training at
Mankind Pharma Ltd.,
Delhi

Dermat- Insight of Therapies and Medico Marketing of Emollients, Keratolytics and Demyelinising Agents

By
Aditya Delu

Under the guidance of
Dr. Sandeep Narula

MBA Pharmaceutical Management
2015-2017

The IIHMR University, Jaipur
2016

INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

CERTIFICATE

This is to certify that Aditya Delu has undergone Summer Training in Mankind Pharmaceutical, Delhi from 1st April to 31st May 2016.

The candidate himself completed the project assigned to his during summer training. His approach to the project was sincere and proactive. This summer training is partial fulfillment of the course requirement recommended for the award of MBA in Pharmaceutical Management.

I wish his success in all her future endeavors.

Dr. Sandeep Narula
(Associate Professor)
IIHMR Jaipur

Col. (Dr) Ashok Kaushik
Dean (Academic and Student Affair)
IIHMR Jaipur

Mankind

Serving Life

31.05.16

To Whomsoever It May Concern

This is to certify that **Mr. Aditya Delu,** student of **MBA Pharmaceutical Management** from **IIHMR University** has successfully completed his training with **Mankind Pharma Ltd.** in **Product Management Team** from **01.04.2016 to 31.05.2016.**

Mr. Aditya was found to be hardworking, sincere & honest during his training period.

We wish him all the best for future endeavors.

For Mankind Pharma Ltd.

Authorized Signatory

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ACKNOWLEDGEMENT

I would like to express my special thanks ***to Mr. R. C. Juneja (Chairman) & Mr. Rajeev Juneja (CEO) of*** **Mankind Group*, New Delhi*** *for providing me an opportunity to join his prestigious Company.*

I would like to express my deep sense of gratitude to ***Dr. Sanjay Koul, and Satender Singh*** *for giving me valuable suggestions and encouragements and providing a cooperative environment for work.*

I am equally grateful to ***Dr. Sandeep Narula, Associate Professor, Indian Institute of Health Management and Research, Jaipur*** *for his guidance and encouragement for my summer training.*

I am also grateful to ***Dr. Ashok Kaushik, Dean, Indian Institute of Health Management and Research, Jaipur*** *for his encouragement.*

I feel very proud to say that due to the keen knowledge of ***Mr. Sunil Thakur*** *about IMS software make very easy for me to complete this project.*

*I would like to express my sincere gratitude to my parents**.** There are not enough words to express my feelings towards them.*

I also wish to acknowledge all of my friends and well wishers for their love, support and encouragement.

ADITYA DELU

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Introduction

Mankind Pharma, one of the top 5 leading pharmaceutical companies in India, started its journey in 1995. The company name 'Mankind' was inspired from the belief that health is the most precious gift to mankind and this ethos is enshrined in Mankind's aim of working together to preserve this most precious gift.

Today, it have 11,000 employees and are heading towards a turnover of **INR 50000 million**. It's vast network includes 50 C&F agents and 7500+ stockists. Mankind provide a wide range of products – Antibiotic, Antifungal, NSAIDs, Gastrointestinal, Anthelmintic, Cardiovascular, Dermal, Erectile Dysfunction, and several other categories – across the nation.

It take great pride in the success of its products ranging from Pharma, OTC and FMCG brands like Manforce Condoms, Manforce Tablets, Manforce Staylong Gel, Unwanted 72, PregaNews, Adiction, Gas-O-Fast, Kaloree 1, and our latest launch, Heal-O-Kind.

Today, Mankind operates in 11 overseas destinations across Asia, Africa, South-East Asia and Gulf countries. Targeting the competitive markets of Commonwealth Independent States, the company will soon begin operations in regions like Uzbekistan and Tajikistan.

Motto of 'Serving Life' encompasses 3 major pillars:

Affordability : The very foundation of the company was laid on the belief that affordable medicine is the right of every citizen. Mankind is committed to making medicines accessible to the people.

Reach : Since more than 50% of the total population of India resides in villages, their medical needs often go unattended. Along with metros and Class-I towns, Mankind has concentrated in Class II to VI towns and rural areas to ensure that affordable medicine reaches to every part of India.

Quality : Mankind's unending commitment to quality has made it the most reliable pharmaceutical company. Delivering quality medicines at affordable prices makes healthcare accessible to the people.

Acquire and merger-

- In 2007, Mankind acquired Magnet Labs Pvt Ltd, establishing a marketing presence in the antipsychotic segment.
- Later in January 2010, the company acquired the former brand of UCB Belgium, Longifene.

Awards & Recognition

Mankind has been awarded for its work done in the pharmaceutical industry. Some of its major achievements are as follows:

- Awarded for 'Achieving Business Excellence' by Citi Commercial Bank in 2012.

- Acknowledgement of participation and support of Mankind in the 49th Annual National Conference of IAP by the Organisation Committee of Pedicon, 2012.
- Honoured for the spirit of entrepreneurship with 'Udyami Samman' by Axis Group and Zee News (UP) in 2011.
- Awarded 'India Business Icon (Pharma) Award' by Network 18 for the year 2011.
- Awarded 'Entrepreneur Of The Year' by Ernst and Young in 2011.
- Won the 'Amity HR Excellence Award for Team Effort' at the Global HR Summit in 2009.
- Certified by Hindalco (Aditya Birla Group) as Most Potential & 'A' Grade Vendor of 2008 in Supply Chain Management.
- Won 'Emerging Company of 'The Year at Pharma Excellence Award in 2007'.
- Awarded 'Indian Express Pulse Award' for overall performance in 2005.

Skin –

The human skin is the outer covering of the body. In humans, it is the largest organ of the integumentary system. The skin has multiple layers of ectodermal tissue and guards the underlying muscles, bones, ligaments and internal organs. Human skin is similar to that of most other mammals. Though nearly all human skin is covered with hair follicles, it can appear hairless.

There are two general types of skin,

- Hairy
- Glabrous skin.

Skin is composed of three primary layers:

- The epidermis,
- The dermis and
- The hypodermis

Epidermis –

The epidermis is composed of the outermost layers of cells in the skin. It forms the waterproof, protective wrap over the body's surface which also serves as a barrier to infection and is made up of stratified squamous epithelium with an underlying basal lamina. The epidermis contains no blood vessels, and cells in the deepest layers are nourished almost exclusively by diffused oxygen from the surrounding air. The main type of cells which make up the epidermis are Merkel cells, keratinocytes, with melanocytes and Langerhans cells. The outermost layer of the epidermis consists of 25 to 30 layers of dead cells.

Epidermis is divided into the following 5 sublayers or strata:

- Stratum corneum
- Stratum lucidum
- Stratum granulosum
- Stratum spinosum
- Stratum germinativum /stratum basale

Dermis –

The dermis is a layer of skin between the epidermis and subcutaneous tissues, that consists of connective tissue and cushions the body from stress and strain. The dermis is tightly connected to the epidermis through a basement membrane. Structural components of the dermis are collagen, elastic fibers, and extrafibrillar matrix. It also contains mechanoreceptors that provide the sense of touch and thermoreceptors that provide the sense of heat. In addition, hair follicles, sweat glands, sebaceous glands, apocrine glands, lymphatic vessels and blood vessels are present in the dermis. Those blood vessels provide nourishment and waste removal for both dermal and epidermal cells.

Dermis is divided into the following 2 sublayers

- Papillary dermis
- Reticular dermis

Hypodermis –

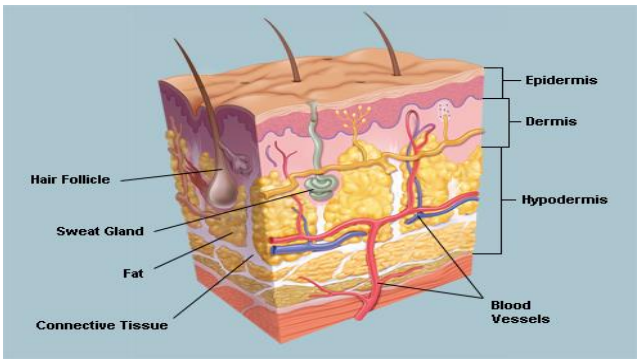
The hypodermis is not part of the skin, and lies below the dermis. Its purpose is to attach the skin to underlying bone and muscle as well as supplying it with blood vessels and nerves. It consists of loose connective tissue, adipose tissue and elastin. The hypodermis contains 50% of body fat

The main cell types which make hypodermis are –

- Fibroblasts,
- Macrophages and
- Adipocytes

Function of skin –

- Protection of the human body
- Temperature regulation
- Enables movement and growth without injury
- Excretion from the body of certain types of waste materials
- Endocrine function e.g. re. Vitamin D
- Sensation i.e. transmitting to the brain information about surroundings.
- As a reservoir for food and water
- As a major role player in regulating blood pressure and the flow of the blood
- As a producer of keratin.



Disease related to skin -

- Eczema: Skin inflammation (dermatitis) causing an itchy rash. Most often, it's due to an overactive immune system.
- Psoriasis: An autoimmune condition that can cause a variety of skin rashes. Silver, scaly plaques on the skin are the most common form.
- Acne: The most common skin condition, acne affects over 85% of people at some time in life.
- Rosacea: A chronic skin condition causing a red rash on the face. Rosacea may look like acne, and is poorly understood.
- Warts: A virus infects the skin and causes the skin to grow excessively, creating a wart. Warts may be treated at home with chemicals, duct tape, or freezing, or removed by a physician.
- Seborrheic keratosis: A benign, often itchy growth that appears like a "stuck-on" wart. Seborrheic keratoses may be removed by a physician, if bothersome.
- Herpes: The herpes viruses HSV-1 and HSV-2 can cause periodic blisters or skin irritation around the lips or the genitals.
- Viral exantham: Many viral infections can cause a red rash affecting large areas of the skin. This is especially common in children.
- Shingles (herpes zoster): Caused by the chickenpox virus, shingles is a painful rash on one side of the body. A new adult vaccine can prevent shingles in most people.
- Ringworm: A fungal skin infection (also called tinea). The characteristic rings it creates are not due to worms.

RESEARCH METHODOLOGY

Type of study - Descriptive Study

Sampling - Judgmental Non Probability

Secondary Data - IMS

EMOLLIENTS

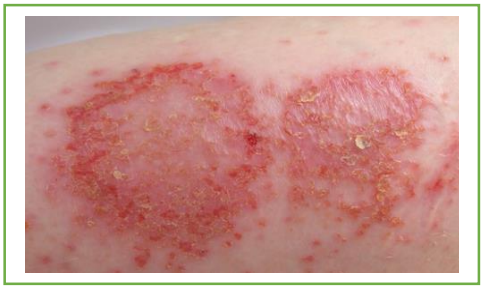
Emollients are bland oily substances which sooth and soften skin. They form an occlusive film over the skin preventing evaporation thus restoring elasticity of cracked and dry skin.

Eczema

Eczema is an itchy, red rash. It can appear all over the body. Many people have it on their elbows or behind their knees. Babies often have eczema on the face, especially the cheeks and chin. They can also have it on the scalp, trunk and outer arms and legs.

Types of Eczema-

1. Atopic dermatitis
2. Irritant contact dermatitis
3. Allergic contact dermatitis
4. Nummular dermatitis
5. Stasis dermatitis
6. Seborrhoeic dermatitis
7. Asteatotic eczema



Atopic Dermatitis

Atopy meaning “out of place” or strange, to signify the hereditary tendency to develop allergies to food and inhalants substances. Tendency to develop atopic dermatitis is inheritance pattern do not follow strict mendelein patterns and the overall prevalence of atopic disease is increasing. A child is at increased risk of developing atopy if either parents are affected.

Atopic Dermatitis can be divided into three stages

1. Infantile atopic dermatitis - occurring from 2 month to 2 years of age
2. Childhood atopic dermatitis – from 2 to 10 years
3. Adult atopic dermatitis

- Infantile Atopic Dermatitis

60% of cases of atopic dermatitis present in the first year of life. Eczema in infancy usually begins as erythema and scaling of cheeks. Worsening of atopic dermatitis is often observed after immunizations and viral infections. Partial remission may occur during summer with relapse in winter. This may relate to the therapeutic effects of UV and humidity in many atopic patients, and the aggravation by wool and dry air in winter.

- Childhood Atopic Dermatitis

During childhood lesions are apt to be less exudative. The classic location are the antecubital and popliteal fossae, flexor wrist, eyelids, and around the neck. Several atopic dermatitis involving more than 50% of the body surface area is associated with growth retardation.

- Atopic Dermatitis in adolescents

Atopic dermatitis may occur as localized erythematous, scaly, exudative or lichenified plaques. In adolescent the eruption often involves the classic antecubital and popliteal fossae front and slide of the neck, forehead, and area round the eye. In older adults the distribution is generally less characteristic, and chronic hand eczema may predominate.

Irritant Contact Dermatitis

It is provoked by contact with water, detergents and other subsequently occurs most commonly on hands.

- **Allergic contact dermatitis**

  It occurs when there is sensitization to usually tolerated environmental contact such as nickel, perfume, hair dye or preservative.

- **Nummular dermatitis**

It is particularly chronic eczema characterized clinically by papules which coalesce into coin shaped patches. Histological changes vary with chronicity. Early lesions show moderate spongiosis with mild acanthosis and exocytosis of inflammatory cells.

- **Statis dermatitis**

It is common condition affecting the legs secondary to impaired venous circulation. Spongiosis is usually mild with foci of parakeratosis and scale crust. Dermal changes are prominent with neovascularization, haemosiderin, deposition and varying degree of fibrosis.

- **Seborrheic dermatitis**

  It is most commonly occur at scalp and face secondary to toxic substances produced by yeasts. Histologically there is spongiosis which may be acute, subacute or chronic depending upon the lesion biopsied. More chronic lesion show progressive psoriasiform hyperplasia of the epidermis with less spongiosis.

- **Asteatotic eczema**

It is developed as a result of very dry skin. It is most common in the elderly and on the lower limbs. Histologically the most common finding is a mild subacute spongiotic dermatitis. The stratum corneum is compact and slightly irregular.

PATHOPHYSIOLOGY OF ECZEMA

The exact cause of eczema is unknown. But it is thought to involve dry sensitive skin alteration of the immune system, genetic factor

Eczematous conditions primarily affect the outermost layer of epidermis.

Skin damage due to sun burn, use of harsh soaps, certain cosmetics or environmental factors can reduce the content of ceramides.

This results in increasing water loss causing dry irritated and itchy skin.

Immunologic dysfunctions have been noted in patients with eczema. Increased IgE production and increased cytokine levels have been detected.

Although some patient don't have elevated IgE levels, approx. 80% with various types of atopic disease will show increased levels.

EPIDERMOLOGY OF ECZEMA

Prevalence of eczema has increased three-fold since 1960s

1. 10-20% of children in industrialized country eg. USA, Europe, New-Zealand
2. 1-3% of adult
3. 16% and 17% in Japan and Nigeria respectively
4. 1.1% in Iraq
5. Lower prevalence in agricultural economic country eg. India, China

Prevalence is higher in Australia, North Europe while lower in Asia and Central Eastern Europe

Prevalence in India

Rare data is available which is based on hospital studies

Northern region 0.42%

Eastern region 0.55%

Kerla 2.4-6%

Bihar 0.38%

THERAPY AREA

1. Mild soap and moisturizer.
   Use mild soap or soap substitute that don't dry skin. Generally soap known as syndets are available. Soap containing bleach is helpful in eczema. Bleach help to kill the bacteria of eczema
2. Medication therapy
   A. Hydrocortisone – OTC hydrocortisone cream or ointment is used in eczema
   B. Antihistamine – oral antihistamine such as Benadryl OTC is used
   C. Ultra violet therapy – in case very severe eczema
   D. Corticosteroid
   E. Immunosupressent
   F. Vitamin A & D, Zinc Oxide Petroalatum lanolin
   G. Dimethicone Tropical Emollient
   H. Betamethasone valerate

CURRENT/ FUTURE THERAPIES

- Barrier-Restoring Therapies
  Emollients, both creams and ointments, improve the barrier function of stratum corneum by providing it with water and lipids. Studies on atopic dermatitis and barrier repair treatment show that adequate lipid replacement therapy reduces the inflammation and restores epidermal function.
- Development of the IL-12/23 antagonist ustekinumab in psoriasis

  Ustekinumab is a human monoclonal antibody (mAb). It is manufactured in the Netherlands. It is directed against interleukin 12 and interleukin 23, naturally occurring proteins that regulate the immune system and immune-mediated inflammatory disorders. Since 2009, Ustekinumab is approved in Canada, Europe and the U.S.

  Ustekinumab binds the p40 subunit common to IL-12 and IL-23, key cytokines in psoriasis pathogenesis. The therapeutic mAb was developed using human gamma-1 immunoglobulin (IgG)-expressing transgenic mice, which created a molecule with endogenous IgG_1 biologic properties and low immunogenicity.
- Cannabinoid system as a possible target for future therapy in skin disease.
  Cannabinoids seem to have immunosuppressive properties and could be considered as potential anti-inflammatory drugs. Recently, Karsak et al. reported that the endocannabinoid system could be involved in attenuation of allergic response to contact allergens. In their experiments, double knockout mouse, without expression of CB_1R and CB_2R ($CB_1R^{-/-}/CB_2R^{-/-}$), stimulated by 2,4-dinitrofluorobenzen, an obligate contact allergen, developed significantly more severe ear dermatitis compared with wild-type mouse. Increased level of granulocytes and higher activity of myeloperoxidase, an indicative of enhanced neutrophil recruitment, were observed in knockout group compared with wild-type one. Moreover, knockout mouse demonstrated elevated

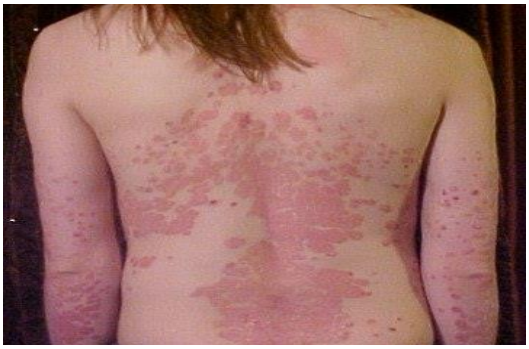
number of MHC II antigen-positive cells in the inflamed area. Remarkably, 2,4-dinitrofluorobenzen treatment resulted in significant elevation of 2-AG and AEA levels in the skin. Interestingly, experiments with single deletion of either CB_1R or CB_2R revealed that both receptors are involved in the attenuation of contact allergic reaction. These results were confirmed by the use of CB_1R and CB_2R antagonists that induced increase in ear swelling in treated mouse compared with controls. Furthermore, a significantly decreased allergic response was observed in FAAH knockout mouse with retarded degradation of AEA. Interestingly, it was also observed that substance P induced bronchoconstriction and airway oedema could be alleviated by CB_2R activation. In addition, activation of peripheral CB_2R decreased the spinal cord inflammation in animal model of multiple sclerosis. These observations carried out in different organs indirectly may support the idea that cannabinoids could also be important in the reduction of cutaneous inflammation.

PSORIASIS

Psoriasis is a common, chronic, and recurrent inflammatory disease of skin characterized by circumscribed, erythematous, dry scaling plaques of various sizes. The lesions are usually covered by silvery white lamellar scales. The lesions have a predilection for the scalp, nails, extensor surface of the limbs, umbilical region, and sacrum.

The early lesions are small erythematous macules, which from the beginning are covered with dry, silvery scales. The lesions are increased in size by peripheral extension and coalescence. The scales are micaceous, meaning that they peel in layers.

Types of Psoriasis



1. Seborrheic-like Psoriasis
2. Inverse Psoriasis
3. Napkin Psoriasis
4. Guttate Psoriasis
5. Pustular Psoriasis
6. Erythrodermic Psoriasis

SEBORRHEIC LIKE PSORIASIS

Some cases of psoriasis overlap with seborrheic dermatitis. Seborrheic lesion may predominate on the face, under the breast, and the scalp, flexures, and axillae. Lesion in this area are moist and erythematous, with yellow, greasy, soft scales, rather than dry and micaceous scale.

INVERSE PSORIASIS

This form selectively and often exclusively involves folds, recesses, and flexor surfaces such as the ears, axillae, groins, inframammary folds, navel, intergluteal creases, penis, lips and webspaces. Other area such as the scalp and nail may be involved

NAPKIN PSORIASIS

Napkin psoriasis in the diaper area is characterized seen in infant between 2 and 8 months of age. Lesions appear as brightly erythematous, sharply, demarcated patches of skin involving much of the diaper area. The lesion typically clear with topical therapy, but psoriasis may reappear in adulthood.

GUTTATE PSORIASIS

In this distinctive form of psoriasis typically lesions are the size of water drops, 2-5 mm in diameter. Lesions are typically occur as an abrupt eruption following some acute infection, such as streptococcal pharyngitis. It occur mostly in patient under 30 age.

- **PUSTULAR PSORIASIS**

Typical patients have had plaque psoriasis and often psoriatic arthritis. The onset is sudden with formation of lakes of pus periungually on the palms, and at the edge of psoriatic plaques. Pruritus and intense burning are often present. Mucus membrane lesions are common.

- **ERYTHRODERMIC PSORIASIS**

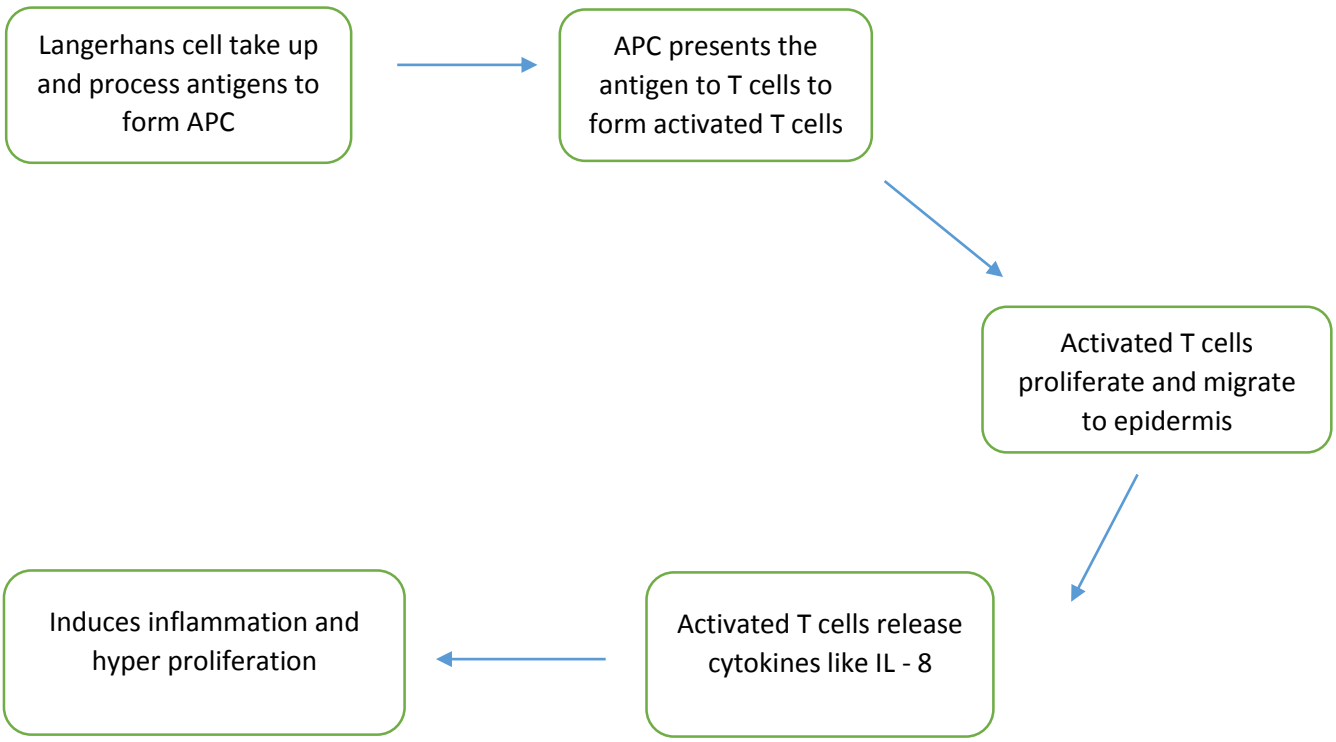
Patient with psoriasis may develop a generalized erythroderma. Erythodermic psoriasis is covered in great detail under exfoliative dermatitis.

EPIDERMIOLOGY OF PSORIASIS

1. Peak incidence – 22.5 years of age
2. Incidence 60 per 1,00,000 person a year
3. Accounts to 2,60,000 new cases yearly
4. Psoriasis may affect about 2.3 million people world wide
5. 2% population is affected by psoriasis in US
6. Less frequently in tropical regions
7. Less common in North Americans and West African people

Lymphoma may occur with an increased incidence in these patients.

PATHOPHYSIOLOGY OF PSORIASIS



THERAPY USED

1. **Tropical Treatment**
   - Corticosteroids
     Tropical application of corticosteroid in creams, ointment, lotions, and sprays is most frequently prescribed therapies for psoriasis. Class I steroids are suitable foe 2 week courses of therapy on most body area. On the scalp corticosteroid in propylene glycol, gel, foam, and spray bases are preferred by most white patients.
   - Tars
     Crude coal tar and tar extracts such as liquor carbonis detergens can be compounded into agents for tropical use. Tar bath oils and shampoos are readily available.
   - Anthralin
     Anthralin is effective but is irritating and stains skins, clothing, and bedding. To avoid these drawbacks short contact anthralin treatment can be helpful, with anthralin washed off after 15-30 min. Anthralin exerts a direct effect on keratinocytes and leukocytes by suppressing neutrophil and inhibit monocyte derivative IL-6, IL8, and TNF- alpha
   - Tazarotent
     It is nonisomerizable retinoic acid receptor specific retinoid. It appear to treat psoriasis by modulating keratinocyte differentiation and hyperproliferation, as well as by suppressing inflammation.
   - Calcipotriene
     Vitamin D3 affects keratinocyte differentiation partly through its regulation of epidermal responsiveness to calcium. Treatment with the Vit.D3 analog calcipotriene (Dovonex) in ointment, cream, and solution form has been show to be very effective in the treatment of scalp psoriasis.
   - Macrolactams (calcineurin inhibitors)
     Tropical macrolactums such as tacrolimus and pimecrolimus are specially helpful for this lesions in area prone to atrophy or steroid acne. The burning commonly associated with these agents can be problematic but may be avoided by prior treatment with a corticosteroid, and by application to dry skin, rather than after bathing.
   - Salicylic acid
     It is used as a kretatolytic agent in shampoos, creams and gels. It can promote the absorption of other topical agents.
2. **Ultraviolet Light**
   In most cases sunlight improves psoriasis. However, burning of skin may cause Koebner's phenomenon and an exacerbation. Artificial UVB light is produced by fluorescents bulbs in broad spectrum. Maximum effect is achieved at (MED) minimal erythemogenic doses.
3. **Goeckerman Technique**
   It remain as effective and cost effective method of treatment. In its modern form, 2% to 5% tar preparation is applied to the skin, and a tar bath is taken at least once a day. The excess tar is removed with mineral, vegetable oil and UV light is given.
4. **Ingram Technique**
   It consist of daily coal tar bath in a solution such as 120 ml liquor carbonis detergens to 80L of arm water. This is followed by daily exposer to UV light for increasing periods.
5. **PUVA Therapy**
   High intensity longwave UV radiation given 2 hr. after ingestion of 8-methoxypsoralen, twice a week is highly effective even in severe psoriasis. Although PUVA therapy is highly effective in patients with less than 50% of skin surface is affected.
6. **Surgical Treatment**

In patient with pharyngeal colonization by streptococci, an excellent response has been reported after tonsillectomy. More effective antibiotic regimens such as 10 day course of dicloxacillin combined with rifampin have largely replaced tonsillectomy.

7. **Systemic Treatment**
   - Methotrexate
     The folic acid agonist remain the standard against which other systemic treatment are measured. Methotrexate has a great affinity for Dihydrofolic acid reductase than has folic acid. The synthesis of DNA is blocked when dihydrofolic acid reductase is bound and thereby cell division is reduced.
   - Cyclosporine
     The therapeutic benefit of cephalosporin in psoriatic disease may be related to downmodulation of proinflammatory epidermal cytokines. The microemulsion formulation Neoral has greater bioavailability and is now standard.
   - Corticosteroid (Discussed in tropical treatment)
   - Dapsone - Dapsone use is limited to palmoplantar pustulosis or other variants of pustular psoriasis.
   - Retinoids

   Oral treatment with the aromatic retinoid ethylester, etretinate is effective in many patients with psoriasis, especially in pustular disease. Because of its long halg life drug is replaced by acitretin.

8. **Biological agent**
   A no. of biological agents are available that can produce dramatic response in some patients with psoriasis, all are expensive. Three agents block TNF-alpha infliximab is a chimeric monoclonal antibody to TNF alpha and requires intravenous infusion, etanercept is a fusion protein of human TNF type II receptor and the Fc region of IgG1 monoclonal antibody to TNF-alpha.
9. **Combination Therapy**
   In more severe forms of psoriasis a combination of treatment modalities may be employed. Combinational therapy has the potential to reduce overall toxicity if the toxicities of each agent are different.

GUIDELINES FOR EMOLLIENTS

1. Very greasy ointments

A. White soft paraffin in liquid paraffin (50:50)
For very dry skin or acute flares. Low risk of sensitivity.

2. Greasy ointments

A. Emulsifying ointments
White soft paraffin(50%)+Emulsifying wax(30%)+Liquid Paraffin(20%)
Good for night time, very dark skin or scaly patches requiring softening.

B. Zeroderm ointment
White soft paraffin(30%)+Emulsifying wax+Liquid Paraffin(40%)
Good for night time, very dark skin or scaly patches requiring softening.

C. Hydromol ointment
Yellow soft paraffin(30%)+Emulsifying wax(30%)+Liquid Paraffin(40%)
Good for night time, very dark skin or scaly patches requiring softening.

3. Creams/Gels

A. ZeroAQS
Liquid paraffin(6%)+white soft paraffin(15%)+macrogol cetostearyl ether 1.8%

B. Aquamax
White soft paraffin(20%)+ Liquid Paraffin(8%)

C. Zerocream

White soft paraffin(14.5%)+ Liquid Paraffin(12.6%)+anhydrous lanolin 1%

D. Double base gel
   Isopropyl myristate 15%+liquid paraffin15%
E. Cetraben cream
   White soft paraffin(13.2%)+Light liquid paraffin(10.5%)+Emulsifying wax

4. Lotion

A. E45 Lotion
   White soft paraffin(10%)+Light liquid paraffin(4%)+hypoallergenic anhydrous lanolin 1%
   Lighter formulation suitable for application to hairy areas, skin folds, face or scalp
B. QV Skin Lotion
   White soft paraffin(5%)+ Liquid Paraffin
   Lighter formulation suitable for application to hairy areas, skin folds, face or scalp

5. Preparations containing anti-microbials

A. Dermol 500 lotion
   Liquid paraffin 2.5% + benzalkonium chloride 0.1%+chlorhexidine dihydrochloride 0.1%+isopropyl myristate2.5%
   Short term use to wash or as a leave on emollient during skin infection only
B. Dermol cream
   Liquid paraffin(10%)+ benzalkonium chloride 0.1%+chlorhexidine dihydrochloride 0.1%+isopropyl myristate10%
   Short term use to wash or as a leave on emollient during skin infection only
C. Eczmol cream
   Chlorhexidine gluconate solution 1% + liquid paraffin and white soft paraffin

6. Preperation containing urea

A. Balneum cream
   Urea 5% + Ceramides 0.1%
   Useful where a keratolytic is required e.g. hyperkeratosis, ichthyosis, extremely dry or fissured skin on hands and feet
B. Aquadrate cream
   Urea 10% + white soft paraffin

7. Spray emollient

A. Emollin
   White soft paraffin and liquid paraffin (50:50)
   For very painful and fragile skin where there is difficulty with hands on application of cream or ointment only

- Used in the specified or exceptional situation only

8. Bath emollients or wash products

A. Hydromol bath and shower emollients
   Light liquid paraffin 37.8% + isopropyl myristate 13%
   To wash dry scalp or as substitutes where other emollients are unsuitable or not tolerated
B. QV Bath oil
   Light liquid paraffin 85.09%
C. Dermol 600 bath emollients with antimicrobial
   Liquid paraffin 25% + benzalkonium chloride 0.5% + isopropyl myristate 25%
   Short term use during skin infection only tissue variability – leg ulcer wash only

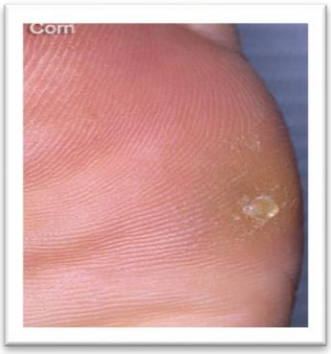
KERATOLYTICS

Keratolytics dissolve the intercellular substance in the horny layer of skin. The epidermal cells swell, soften, and then desquamate. These drugs are used on hyperkeratotic lesions like corns, warts, psoriasis, chronic dermatitis, ringworm, athletes foot, etc.

CORNS

Corns are hard, thickened areas of skin that form as a consequence of rubbing, friction or pressure on the skin. Corns form on the feet and can make walking painful.

Corns generally occur on the tops and sides of the toes. A hard corn is a small patch of thickened, dead skin with a small plug of skin in the center. A soft corn has a much thinner surface, appears whitish and rubbery, and usually occurs between the toes. Seed corns are clusters of tiny corns that can be very tender if they are on a weight-bearing part of the foot. Seed corns tend to occur on the bottom of the feet, and some doctors believe this condition is caused by blocked sweat ducts.



TYPES OF CORNS

- **Hard Corns**

  Hard corns (heloma durums) are the most common type. They are caused primarily by ill-fitting shoes and toe deformities. They usually develop on the tops and tips of the toes and on the sides of the feet

- **Soft Corns**

  Soft corns (heloma molles) typically develop between the fourth and fifth toes when one of the toe bones (phalanges) is slightly too wide. Normally, phalanges are hourglass-shaped and the ends are wider than the middle. Soft corns result when the ends of the toe bones are too wide, causing friction in between the toes. This problem is aggravated by tight-fitting shoes.

THERAPY USED

A. Tropical Treatment

- Salicylic acid-

  10-20% solution in alcohol or propylene glycol is used to treat Corns. More effective when applied under occlusive dressing.

- Liquid corn remover

  This medication is used on the skin to treat common skin. Salicylic acid helps cause the wart to gradually peel off. This medication is also used to help remove corns.

- Surgery

  In rare instances, it may be recommend surgery to correct the alignment of a bone causing friction.

- Antibiotic ointment

  In some cases applying an antibiotic ointment to reduce the risk of infection. It is also used to treat drain the pus and remove the affected skin.

B. Intravenous Treatment

Filler injections:

A retrospective evaluation of the use of fluid silicone in treating loss of plantar fat reveals a unique treatment option for corns.

PATHOPHYSIOLOGY OF CORN

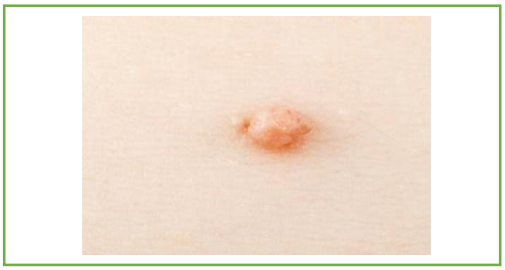
Corns are the result of mechanical trauma to the skin culminating in hyperplasia of the epidermis. Most commonly, friction and pressure between the bones of the foot and ill-fitting footwear cause a normal physiological response—proliferation of the stratum corneum. One of the primary roles of the stratum corneum is to provide a barrier to mechanical injury. Any insult compromising this barrier causes homeostatic changes and the release of cytokines into the epidermis, stimulating an increase in synthesis of the stratum corneum. When the insult is chronic and the mechanical defect is not repaired, hyperplasia and inflammation are common. With corns, external mechanical forces are focused on a localized area of the skin, ultimately leading to impaction of the stratum corneum and the formation of a hard keratin plug that presses painfully into the papillary dermis, which is known as a radix or nucleus.

EPIDERMOLOGY

1. Corns are one of the most common foot conditions in the United States, particularly amongst older patients.
2. Hyperkeratotic lesions of the foot (including corns and calluses) have been reported to affect 20-65% of people aged 65 or older
3. African Americans had a significantly higher rate of corns and calluses compared with non-Hispanic white and Puerto Rican participants (70% vs 58% vs 34.1%)
4. The prevalence of foot conditions amongst a diverse sample of adults from the northeastern United States revealed a significant difference in rates of corns amongst ethnic groups

WARTS

A wart is a small, rough growth resembling a cauliflower or a solid blister. It typically occurs on humans' hands or feet but often in other locations. Warts are caused by a viral infection, specifically by one of the many types of human papillomavirus (HPV). There are as many as 10 varieties of warts, the most common considered to be mostly harmless.



Types of warts

1. Common wart (*Verruca vulgaris*)
2. Flat wart (*Verruca plana*)
3. Filiform or digitate wart,

4. Genital wart
5. Mosaic wart
6. Periungual wart
7. Plantar wart

- **Common wart** –

Common warts are a significant cause of concern and frustration on the part of the patient. Social activities can be affected, lesions can be uncomfortable or bleed, and treatment is often painful and frustratingly ineffective. HPV-1, -2,-4,-27,-57 and -63 causes common warts. Common warts occur largely between the ages of 5 and 20 and only 15% occur after the age of 35.

- **Filiform wart**

It is most commonly occur on the face, especially near the eyelids and lips.

- **Flat wart**

HPV-3, -10, -28, and -41 most often causes flat warts. Children and young adults are primarily affected. Flat warts present most typically as 2 to 4 mm flat topped papules that are slightly erythematous or brown on pale skin and hyperpigmented on darker skin. They are generally multiple and grouped on the face, neck, dorsa of the hands, wrists, elbows, or knees.

- **Mosaic wart**

It is a group of tightly clustered plantar-type warts, commonly on the hands or soles of the feet.

- **Genital warts**

Genital warts are symptoms of a highly contagious sexually transmitted disease caused by some types of human papillomavirus (HPV). It is spread through direct skin-to-skin contact, usually during oral, genital, or anal sex with an infected partner. Warts are the most easily recognized symptom of genital HPV infection. Despite the fact that some types of HPV cause cervical cancer and anal cancers, these are not the same types of HPV that cause genital warts. About 90% of those who contract HPV will not develop genital warts, but the remaining 10% who are infected can still transmit the virus

- **Periungual warts**

Periungual warts are warts that cluster around the fingernail or toenail. They appear as thickened, fissured cauliflower-like skin around the nail plate. Periungual warts often cause loss of the cuticle and paronychia. Nail biting increases susceptibility to these warts. Warts of this kind often cause damage to the nail either by lifting the nail from the skin or causing the nail to partially detach. If they extend under the nail, then the patient may suffer pain as a result. Sometimes periungual wart infections resemble the changes that are found in onychomycosis. In worst cases, if the infection causes injury or damage to the nail matrix, deformity in the nail may become permanent.

- **Plantar wart**

A plantar wart also known as veruca, myrmecia and *veruca plantaris* is a wart caused by the human papillomavirus (HPV) occurring on the sole (Latin *planta*) or toes of the foot. HPV infections in other locations are not plantar. Plantar warts are usually self-limiting, but treatment is generally recommended to lessen symptoms (which may include pain), decrease duration, and reduce transmission.

PATHOPHYSIOLOGY

HPV enters into cells of the basal layer of the epidermis, penetrating skin and mucosal microabrasions in the genital area.

A latency period of 3 weeks to 9 months may ensue. Viral DNA, capsids, and particles are produced warts

Host cells become infected and develop the morphologic atypical koilocytosis of genital

Most frequently affected are the penis, vulva, vagina, cervix, perineum, and perianal area.

EPIDERMIOLOGY

1. Warts are estimated to affect approximately 7-12% of the population.
2. Annual incidence is 1%, in USA and genital warts are considered the most common sexually transmitted disease.
3. A 4-fold or more increase in prevalence has been reported in the last 2 decades; prevalence reportedly exceeds 50%
4. In school-aged children, the prevalence is 10-20%.
5. Prevalence is greatest in persons aged 17-33 years, with a peak incidence in persons aged 20-24 years.
6. Prevelence is least in developing and under developing countries than USA

THERAPY USED

- **Electrodesiccation**

  Cryosurgery, which involves freezing the wart (generally with liquid nitrogen), creating a blister between the wart and epidermal layer after which the wart and the surrounding dead skin supposedly fall off by themselves, although this was tested by the NHS to be ineffective. An average of 3 to 4 treatments are required for warts on thin skin. Warts on calloused skin like plantar warts might take dozens or more treatments
- **Surgical Method**

- ✓ Laser treatment – often with a pulse dye laser or carbon dioxide (CO_2) laser. Pulse dye lasers (wavelength 582 nm) work by selective absorption by blood cells (specifically haemoglobin). CO_2 lasers work by selective absorption by water molecules. Pulse dye lasers are less destructive and more likely to heal without scarring. CO_2 laser works by vaporizing and destroying tissue and skin. Laser treatments can be painful, expensive (though covered by many insurances), and not extensively scarring when used appropriately. CO_2 lasers will require local anaesthetic. Pulse dye laser treatment does not need conscious sedation or local anesthetic. It takes 2 to 4 treatments but can be many more for extreme cases. Typically, 10–14 days are required between treatments. Preventative measures are important.
- ✓ Infrared coagulator – an intense source of infrared light in a small beam like a laser. This works essentially on the same principle as laser treatment. It is less expensive. Like the laser, it can cause blistering pain and scarring

- **Duct tape occlusion therapy** involves placing a piece of duct tape over the wart. The mechanism of action of this technique still remains unknown, and despite several clinical trials the evidence for the efficacy of duct tape therapy is inconclusive.Despite the mixed evidence for efficacy, the simplicity of the method and its limited side-effects leads some researchers to be reluctant to dismiss it.
- **Garlic extract therapy**- fat soluble garlic extracts have been shown to clear greater than 90% of cases. The extract is applied twice daily and covered with a bandaid. Improvements show within 2–4 weeks and total clearing in an average of 6–9 weeks.

- **Medication**

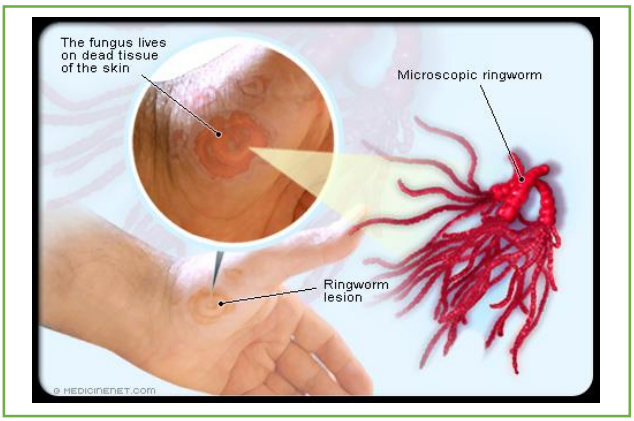
- ✓ Salicylic acid can be prescribed by a dermatologist in a higher concentration than that found in over-the-counter products. Severalover-the-counter products are readily available at pharmacies and supermarkets of roughly two types: adhesive pads treated with salicylic acid, and bottled concentrated salicylic acid solution.
- ✓ Imiquimod is a topical cream that helps the body's immune system fight the wart virus by encouraging interferon production. It has been approved by the U.S. Food and Drug Administration (FDA) for genital warts.
- ✓ Cantharidin, found naturally in the bodies of many members of the beetle family Meloidae, causes dermal blistering. It is used either by itself or compounded with podophyllin. Not FDA approved, but available through Canada or select US compounding pharmacies.
- ✓ Bleomycin is not US FDA approved and can cause necrosis of digits and Raynaud syndrome. The usual treatment is one or two injections.
- ✓ Dinitrochlorobenzene (DNCB), like salicylic acid, is applied directly to the wart. Studies show this method is effective with a cure rate of 80%. But DNCB must be used much more cautiously than salicylic acid; the chemical is known to cause genetic mutations, so it must be administered by a physician. This drug induces an allergic immune response resulting in inflammation that wards off the wart-causing virus.
- ✓ Cidofovir is an antiviral drug which is injected into HPV lesions within the larynx (laryngeal papillomatosis) as an experimental treatment.

RINGWORM

Tinea, often called ringworm, is any of a variety of skin mycoses. Tinea is a very common fungal infection of the skin. Tinea is often called "ringworm" because the rash is circular, with a ring-like appearance.

TYPES OF TYPES

1. Tinea pedis
2. Tinea unguium
3. Tinea manuum
4. Tinea cruris
5. Tinea corporis
6. Tinea capitis
7. Tinea faciei
8. Tinea barbay
9. Tinea imbricate
10. Tinea nigra
11. Tinea versicolor
12. Tinea incognito



- **Tinea pedis** Athlete's foot is a common and contagious skin disease that causes itching, scaling, flaking, and sometimes blistering of the affected areas. Its medical name is *tinea pedis*, a member of the group of diseases or conditions known as tinea, most of which are dermatophytoses, which in turn are mycoses. Tinea pedis is caused by fungi such as *Epidermophyton floccosum* or fungi of the *Trichophyton* genus including *T. rubrum* and *T. mentagrophytes*. These fungi are typically transmitted in moist communal areas where people go barefoot, such as around swimming pools or in showers, and require a warm moist environment like the inside of a shoe to incubate. Fungal infection of the foot may be acquired in many ways, such as by walking in an infected locker room, by using an infested bathtub, by sharing a towel used by someone with the disease, by touching the feet with infected fingers (such as after scratching another infected area of the body), or by wearing fungi-contaminated socks or shoes.
- **Tinea unguium**

  Onychomycosis (*tinea unguium*) is a fungal infection of the nail. It is the most common disease of the nails and constitutes about half of all nail abnormalities. This condition may affect toenails or fingernails, but toenail infections are particularly common. It occurs in about 10 percent of the adult population.

  There are four classic types of onychomycosis - Distal subungual onychomycosis , White superficial onychomycosis, Proximal subungual onychomycosis, Candidal onychomycosis
- **Tinea manuum**

  Tinea manuum is a fungal infection of the hand. It is typically more aggressive than tinea pedis but similar in look. Itching, burning, cracking, and scaling are observable and may be transmitted sexually or otherwise, whether or not symptoms are present.
- **Tinea cruris**

Tinea cruris is adermatophyte fungal infection of the groin region in any sex, though more often seen in males. In the German sprachraum this condition is called *tinea inguinalis* whereas *tinea cruris* is used for a dermatophytosis of the lower leg. Tinea cruris is similar to, but different from Candidal intertrigo, which is an infection of the skin by *Candida albicans*. It is more specifically located between intertriginous folds of adjacent skin, which can be present in the groin or scrotum, and be indistinguishable from fungal infections caused by *tinia*. However, candidal infections tend to both appear and disappear with treatment more quickly. It may also affect the scrotum.

- **Tinea corporis**

Tinea corporis is a superficial fungal infection (dermatophytosis) of the arms and legs, especially onglabrous skin; however, it may occur on any part of the body, it present as annular, marginated plaque with thin scale and clear center.

- **Tinea capitis**

Tinea capitis is a superficial fungal infection of the scalp. The disease is primarily caused by dermatophytes in the *Trichophyton* and *Microsporum* genera that invade the hair shaft. The clinical presentation is typically single or multiple patches of hair loss, sometimes with a 'black dot' pattern, that may be accompanied by inflammation, scaling, pustules, and itching. Uncommon in adults, tinea capitis is predominantly seen in pre-pubertal children, more often boys than girls.

- **Tinea faciei**

Tinea faciei is a fungal infection of the face. It generally appears as a red rash on the face, followed by patches of small, raised bumps. The skin may peel while it is being treated.

Tinea faciei is contagious just by touch and can spread easily to all regions of skin.

- **Tinea barbae**

Tinea barbae is a fungal infection of the hair. Tinea barbae is due to a dermatophytic infection around the bearded area of men. Generally, the infection occurs as a follicular inflammation, or as a cutaneous granulomatous lesion, i.e. a chronic inflammatory reaction. It is one of the causes of folliculitis. It is most common among agricultural workers, as the transmission is more common from animal-to-human than human-to-human. The most common causes are Trichophyton mentagrophytes and T. verrucosum.

- **Tinea imbricate**

Tinea imbricata is a superficial fungal infection of the skin limited to southwest Polynesia, Melanesia, Southeast Asia, India, and Central America. It is associated with Trichophyton concentricum.

- **Tinea nigra**

Tinea nigra is a superficial fungal infection that causes dark brown to black painless patches on the palms of the hands and the soles of the feet.This infection is caused by the fungus formerly classified as Exophiala werneckii, but more recently classified as Hortaea werneckii. The causative organism has also been described as Phaeoannellomyces werneckii.

- **Tinea versicolor**

Tinea versicolor is a condition characterized by a skin eruption on the trunk and proximal extremities, hypopigmintation macule in area of sun induced pigmentation. During the winter the pigment become reddish-brown. Recent research has shown that the majority of tinea versicolor is caused by the Malassezia globosa fungus, although Malassezia furfur is responsible for a small number of cases. These yeasts are normally found on the human skin and only become troublesome under certain circumstances, such as a warm and humid environment, although the exact conditions that cause initiation of the disease process are poorly understood.

- **Tinea incognito**

Tinea incognito is a fungal infection of the skin caused by the presence of a topical immunosuppressive agent. The usual agent is a topical corticosteroid. As the skin fungal infection has lost some of the characteristic features due to suppression of inflammation, it may have a poorly defined border, skin atrophy, telangiectasia, and florid growth. Occasionally, secondary infection with bacteria occurs with concurrent pustules and impetigo.

EPIDERMIOLOGY

1. It is a common infection more often seen in typically hot, humid climates.
2. Microsporum canis is the third most common causative organism and associated with 14% of tinea corporis infections
3. Kuwait that included 2730 patients reported that fungal skin infections remain prevalent in that country.
4. They included Trichophyton mentagrophytes (39%), M canis (16%), T rubrum (10%), Epidermophyton floccosum (6.2%), Trichophyton violaceum (2.4%), and Trichophyton verrucosum(0.4%).
5. Prevalence is highest in preadolescents.

PATHOPHYSIOLOGY

Fungi preferentially inhabit the nonliving, cornified layers of the skin, hair, and nail, which is attractive for its warm, moist environment conducive to fungal proliferation.

↓

Fungi may release keratinases and other enzymes to invade deeper into the stratum corneum

↓

Nonspecific host defense mechanisms that can include the activation of serum inhibitory factor, complement, and polymorphonuclear leukocytes.

↓

The active border has an increased epidermal cell proliferation with resultant scaling. Creates a partial defense by way of shedding the infected skin and leaving new, healthy skin central to the advancing lesion

THERAPY USED

- **ANTIFUNGAL AGENTS**

The antifungal agents can be grouped by structure and mechanism of action. The two principal pharmacologic groups are the azoles and the allylamines.

❖ Tolnaftate

This narrow-spectrum antifungal has no antibacterial or anticandidal activity. It is effective in most dermatophytoses and for treatment of tinea versicolor. It is available as an over-the-counter medication and requires twice-daily application.

❖ Haloprogin

Introduced after tolnaftate, haloprogin combines equivalent efficacy with a broadened fungal spectrum (including yeasts). It is associated with higher rates of irritant dermatitis. It is applied twice daily.

❖ Ciclopirox

This broad-spectrum agent is effective against dermatophytes, yeasts, and some bacteria. It has in vitro antibacterial activity against gram-negative and gram-positive bacteria. It has been shown to be more effective than the nonprescription agent clotrimazole (Lotrimin) in the treatment of tinea pedis. It requires twice-daily application.

❖ Butenafine

This agent is similar in structure to that of the allylamines. Butenafine is fungicidal for dermatophytes in vitro. It is applied once daily and, after four weeks of use, is associated with high cure rates and a long disease-free interval.

❖ Azoles

This class includes many over-the-counter and prescription preparations. Members of this class include clotrimazole, econazole (Spectazole), ketoconazole (Nizoral), miconazole (Micatin), oxiconazole (Oxistat), and sulconazole (Exelderm). These agents have broad-spectrum activity, including activity against some gram-positive bacteria. Ketoconazole, sulconazole and oxiconazole require only once-daily application because of their long durability in the superficial layers of the skin. Clotrimazole, miconazole, and econazole require twice-daily application.

❖ Allylamines

Naftifine (Naftin) and terbinafine (Lamisil) are applied once-daily and remain active in the skin for up to one week after application. Both agents have fungicidal activity in vitro, but the clinical significance of this point is uncertain. Terbinafine has been compared with ketoconazole and miconazole. Terbinafine was more efficacious after one week than ketoconazole was after two weeks.

- **COMBINED STEROID/ANTIFUNGAL AGENTS**

In the United States, the only combination steroid/antifungal agent indicated for the treatment of dermatophytosis is clotrimazole-betamethasone (Lotrisone). This formulation combines an effective antifungal agent with a potent steroid.

Patients who have symptomatic inflammatory dermatophytosis with erythema, pruritus, and burning are optimally treated twice daily with this combination. The steroid component provides rapid symptomatic relief while the slower-acting antifungal agent eradicates the causative organism. Inflammation typically occurs in tineas caused by zoophilic dermatophytes.
A steroid/antifungal preparation should be used only when a diagnosis of fungal infection has been confirmed, not when it is in question. An analysis of the use of this product found that non dermatologists are more likely to use combination therapy. In the absence of fungi or inflammation, the added expense of this preparation is not justified.

CURRENT/ FUTURE THERAPIES

- Luliconazole
  Luliconazole is a novel, broad-spectrum, imidazole antifungal under development in the USA as a treatment for dermatophytic skin and nail infections. *In vitro*, luliconazole is one of the most potent antifungal agents against filamentous fungi including dermatophytes. Luliconazole has been formulated in a 10% solution with unique molecular properties, which allow it to penetrate the nail plate and rapidly achieve fungicidal levels in the nail unit.
- Echinocandin
  Echinocandins are antifungal drugs that inhibit the synthesis of glucan in the cell wall, via noncompetitive inhibition of the enzyme 1,3-β glucan synthase. Caspofungin, micafungin, and anidulafungin are semisynthetic echinocandin derivatives with clinical use due to their solubility, antifungal spectrum, and pharmacokinetic properties.
  Due to the large molecular weight of echinocandins, they have poor oral bioavailability and are administered by intravenous infusion. In addition, their large structures limit penetration into cerebrospinal fluid, urine, and eyes. In plasma, echinocandins have a high affinity to serum proteins. Echinocandins do not have primary interactions with CYP450 or P-glycoprotein pumps.

GUIDELINES FOR KERATOLYTICS

1. Salicylic acid
   Tropical preparations of 15-26% of SA, applied daily after removing thick keratin layer, with occlusive if possible. Continue for 3-4 months.
2. Cryotherapy
   Keep wart frozen for 15-30 sec. repeating every 2-4 week for at least 3 months for treatment.
3. Bleomycin
   A 0.1-1 mg/ml solution injected or pricked into affected area after local anesthesia – one to three treatment.
4. 5- Fluorouracil
   5% cream was applied daily + occlusive for 4-12 weeks.
5. Cantharidin
   0.7% solution applied every 3 week upto 4 times.
6. Glutaraldehyde
   A 10% solution applied daily after paring or rubbing down for 3 months
7. Cidofovir
   1% cream daily for 5 days each week under occlusion for 8 week.
8. Pyruvic acid
   A 70% solution was applied daily for upto 2 months.
9. Trichloroacetic acid
   Trichloroacetic acid 50-80% solution applied weekly for upto 8 weeks.

DEMELENIZING AGENTS

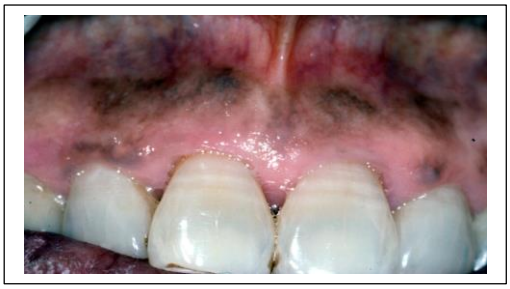
Melanin pigment is produced in melanocytes in the basal layer of the epidermis. The degree of rational pigmentation does not depend on the number of melanocytes present, but on their metabolic activity and the size and shape of their melanin producing organelles- the melanosome. Melanin synthesis is controlled by melanocyte stimulating hormone and is influenced by oestrogen and androgens. Melanocytes are also stimulated by UV-Radiation.
Excessive pigmentation in body is called hyperpigmentation and to treat this hyperpigmentation demelanizing agent are used.

SMOKER'S MELANOSIS

Smoker's melanosis

Smoker's melanosis is seen with the naked eye as a brown to black pigmentation of the oral tissue i.e. the gums, cheeks or palate as well as in larynx. It is most often seen in the lower labial gingiva of tobacco users. Most easily it is found in Caucasians, due to their lack of a genetically caused melanin pigmentation.
In the oral mucosa, where the ageing epithelial cells move faster to the surface compared to skin, a similar defence-mechanism seems to be present, but here acting to clean the mucosa from different toxic chemicals entering the mouth. Besides chemicals in tobacco also antimalaria-drugs cause an oral pigmentation. Smoker's melanosis is like the genetic melanin pigmentations a defence-system in action.

Causes



Smoking or the use of nicotine-containing drugs is the cause to Smoker's melanosis,. Also tar-components are known to stimulate melanocytes to melanin production, and other unknown toxic agents in tobacco may also be the cause. These chemical agents have a polycyclic, chain-like structure. Environmental tobacco smoke from parents is causing smoker's melanosis in their children. Swedish snuff causes a small elevation of oral melanin pigmented individuals from 3.0% to 4.7%. Nicotine tablets have shown to stimulate to melanin pigmentation of the oral mucosa.

PATHOPHYSIOLOGY

Nicotine appears to stimulate melanocytes.

→ Production of melanosomes takes place

↓ Increased deposition of melanin pigment along the basal cells of the lining epithelium of the oral mucosa.

EPIDERMIOLOGY

- In Sweden study of 31,000 whites, 21.5% of tobacco smokers exhibited smoker's melanosis.
- Whereas only 3% of nonsmokers had the lesion in Sweden.
- All had physiologic pigmentation, but tobacco users had significantly more oral surfaces displaying pigmentation.
- A Nigerian study reported a prevalence of 0.52% of pigmented sites in nonsmokers and 6% among smokers.
- A study of Turkish Army recruits revealed gingival pigmentation in 27.5% of smokers and 8.6% of those who never smoked.
- Females are affected by smoker's melanosis more than males.

THERAPY USED

- Quit Smoking
- Laser gum depigmentation

It is a procedure used in cosmetic dentistry to remove black spots or patches on the gums caused by excessive melanin. Melanocytes are cells which reside in the basal layer of the gingival epithelium. These cells produce melanin, which are pigments that cause discoloration or dark spots in gums. A dental laser can target and ablate the melanocytes, thus reducing the production of melanin in the gingival tissue.

- Gingival grafting
- Gum grafting, also known as a gingival graft or periodontal plastic surgery, is a surgical procedure to reverse gum recession. Gum recession exposes the roots of teeth, which can lead to sensitivity and put teeth at a higher risk of damage or disease due to the loosening of their attachment within the gums and bones of the jaw.
- Hydroquinone

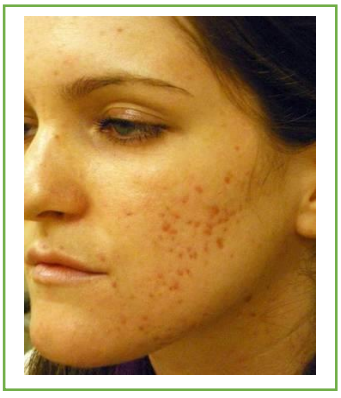
It is week hypopigmenting agent. It inhibits tyrosinase and other melanin forming enzymes, decreases formation of and increases degradation of melanosome. Regular application (2-6% lotion) for months is required melisma and melanosis.

ACNE SCARS

Acne scars are the result of inflammation within the dermal layer of skin, brought on by acne. The scar is created by an abnormal form of healing following this dermal inflammation. Scarring is most likely to occur with severe nodular acne, but may occur with any form of acne vulgaris. Acne scars are classified based on whether the abnormal healing response following dermal inflammation leads to excess collagen deposition or collagen loss at the site of the acne lesion.

TYPES OF ACNE SCARS

- Depressed acne scars
  - Rolling scars
  - Boxcar scars
  - Ice pick scars
- Raised acne scares
  - Keloid scars
  - Hypertrophic scars



Depressed acne scars –

Depressed or pitted acne scars are the most common. They are the result of inflammatory acne, or papulopustular acne. Papulopustular acne are lesions that consist of red blemishes, pimples, papules and pustules and larger swollen lesions.

Depressed scars as a result of inflammatory acne generally sit on collagen rich scar tissue, which prevents the skin from repairing the indentation.

- Rolling scars –

Rolling scars can be broad depressions in the skin, or shallow indentions in the skin. Rolling scars have rounded, sloping edges, hence the name 'rolling scars'. They often have a rough texture and a wavy or rippling appearance and they are the result of damage under the skin.

- Boxcar scars –

Boxcar scars can appear similar to rolling scars however these scars have steep, defined edges and resemble chicken pox scars. They are quite deep and in many ways, they can resemble the print left on the skin from pushing a finger nail into it.

- Ice pick scars –

  Ice pick scars are deep and narrow (usually less than 2mm across). They often resemble a large, empty pore on the skin and it is these scars that catch the light the most, so they are the most obvious and unfortunately as a result the most difficult to cover up.

Raised acne scars

Raised ace scars are less common than depressed acne scars, but they too are the result of inflammatory acne, as described above. In most cases, raised acne scars are more obvious than depressed acne scars. They present a tougher challenge in terms of treatment, because instead of healthy skin living on the surface, there is excess scar tissue on the surface. This manifests itself as a bumpy, uneven surface that catches the light.

- Keloid scars

Keloid scars are common in people with dark skin. Keloid scars are formed when scar tissue forms on the skin in excess, as a result of excess collagen production. This process begins when acne fails to run through a healing cycle and the skin is broken. Collagen gathers around the damage and builds it up, to help the wound seal over. Unfortunately, the body doesn't always do a good job in terms of smoothing or levelling, and collagen production spreads outside the wound, creating sometimes very large scars that are uneven.

- Hypertrophic scars –

Hypertrophic scars are what keloid scars would have been, had the body switched off its collagen production when the acne wound were filled. These are more common than keloid scars and initially they may be dark or red in appearance. Over time, usually within 2 years, these scars flatten out and become paler. However, although hypertrophic scars can be short-term scars, they often leave evidence of the original wound and when hypertrophic scars build up in one area, the result is a bumpy uneven surface

PATHOPHYSIOLOGY –

Cytokines produced by $CD4^+$ T cells and macrophages activate local endothelial cells to up-regulate inflammatory mediators

Follicular hyperkeratinization involves increased keratinocyte proliferation and decreased desquamation, leading to sebum- and keratin-filled micro comedones.

P acnes stimulates inflammation by producing pro inflammatory mediators that diffuse through the follicle wall.

EPIDERMIOLOGY –

- Black individuals are more prone to post inflammatory hyperpigmentation.
- Acne persists into the 20s and 30s in around 64% and 43% of individuals, respectively.
- The heritability of acne is almost 80% in first-degree relatives.
- Moderate-to-severe acne affects around 20% of young people and severity correlates with pubertal maturity.
- Acne is common in North American whites.
- During adolescence, acne is more common in males than in females. In adulthood, acne is more common in women than in men.

THERAPY USED –

- **Tropical treatment**

❖ Retinoids

Topical retinoids are comedolytic and anti-inflammatory. They normalize follicular hyperproliferation and hyperkeratinization. Topical retinoids reduce the numbers of microcomedones, comedones, and inflammatory lesions. Topical retinoids should be initiated as first-line therapy for both comedonal and inflammatory acne lesions and continued as maintenance therapy to inhibit further microcomedone formation.

The most commonly prescribed topical retinoids for acne include adapalene, tazarotene, and tretinoin. These retinoids should be applied once daily to clean, dry skin, but they may need to be applied less frequently if irritation occurs.

❖ Antibiotics

Topical antibiotics are mainly used for their role against *P acnes.* They may also have anti-inflammatory properties. Topical antibiotics are not comedolytic, and bacterial resistance may develop to any of these agents. Commonly prescribed topical antibiotics for acne vulgaris include clindamycin. Benzoyl peroxide products are also effective against *P acnes,* and bacterial resistance to benzoyl peroxide has not been reported. Benzoyl peroxide products are available over the counter and by prescription in a variety of topical forms, including soaps, washes, lotions, creams, and gels.

- **Systemic Treatment**

❖ Hormonal therapies

Some hormonal therapies may be effective in the treatment of acne. Estrogen can be used to decrease sebum production. Additionally, it reduces ovarian production of androgens by suppressing gonadotrophin release. Spironolactone may also be used in the treatment of acne. Spironolactone binds the androgen receptor and reduces androgen production. Adverse effects include dizziness, breast tenderness, and dysmenorrhea.

❖ Antibiotics

Discuss in tropical treatment

❖ Isotretinoin

Co-administration with steroids at the onset of therapy may be useful in severe cases to prevent initial worsening.

MELASMA

Melasma is a common skin problem. It causes brown to gray-brown patches on the face. Most people get it on their cheeks, bridge of their nose, forehead, chin, and above their upper lip. It also can appear on other parts of the body that get lots of sun, such as the forearms and neck.

It is not an infection therefore it is not contagious and it is not due to an allergy. It is not cancerous and will not develop into skin cancer.

There are various cause of hyperpigmentation, including over production of melanin, or pigment overexposure to the skin, hormonal changes to the body.

✓ Distribution Pattern

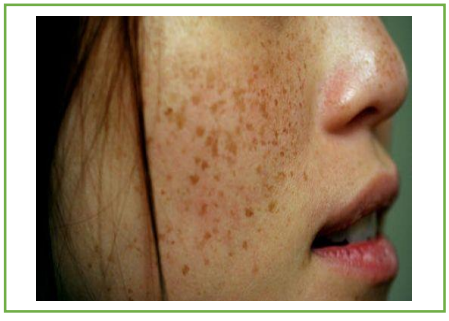
Melasma is typically distributed in any one of these patterns:

- 63% occurrence is around the nose and chin area.
- 21% over the cheeks and nose areas of the face.
- 16% known to occur around the lower jaw.
- Occurs very commonly in people who have darker skin or light brown skin where intense solar ultraviolet radiation exists. Thus people from East and south East Asian and Hispanic regions are prone to develop Melasma. It is more common in women than in men (9:1) and is rare before puberty, occurring most commonly in women of reproductive age.
- It is also known to affect 80% of pregnant women, and hence often referred to as the "Mask of Pregnancy".

TYPES OF MELASMA –

➢ **Epidermal**

The spots are usually light brown with well-defined margins. With this examination, hyperpigmentation is then, clearly visible.



Clinical features –

✓ Well defined border

✓ Dark brown colour

✓ Responds well to treatment

➢ **Dermal**

The colour of the spots ranges from grey-brown to light blue. They are less evident than in the previous case and with ill-defined margins.

Clinical features –

✓ Ill-defined borders

✓ Light brown or bluish in colour

- ✓ Responds poorly to treatment

- ➢ **Mixed**

  The spots are dark brown and less uniform, with more or less pigmented areas. The type of melisma has hyperpigmentation located in both layers mentioned above.

  Clinical features

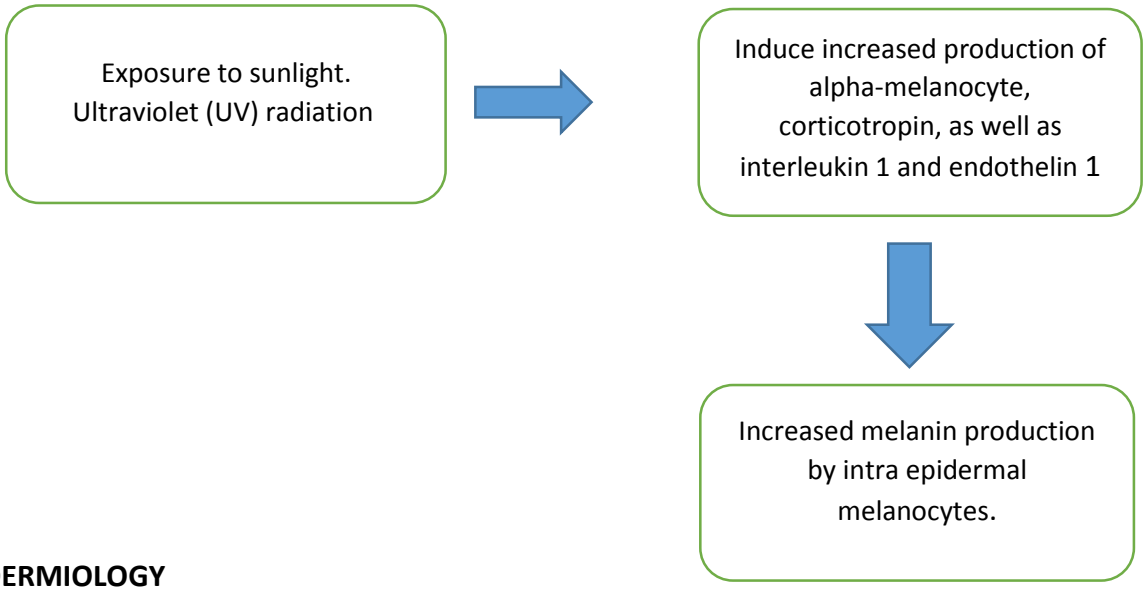
- ✓ The most common type
- ✓ Combination of bluish, light and dark brown patches
- ✓ Partial improvement with treatment

- ➢ **Intermediate**

  The type of melisma can't be classified with wood's light, as in the case of dark complexations.

PATHOPHYSIOLOGY

The pathophysiology of melasma is uncertain.



EPIDERMIOLOGY

- ➢ Melasma occurs more frequently in females than in males. (4:1)
- ➢ Women are affected in 90% of cases.
- ➢ Commonly develops or worsens during pregnancy and with the use of oral contraceptive pills.
- ➢ Melasma is present in 15-50% of pregnant patients.
- ➢ Melasma is much more common in constitutionally darker skin types than in lighter skin types.
- ➢ More common in light brown skin types, especially Latinos and Asians, from areas of the world with intense sun exposure.
- ➢ Malesma due to family history in india (31%)

- 38.5% in North Region (Highest)
- 18.2% in Eastern Region (Lowest)

- Predominant in southern region than northern region.

THERAPY USED –

- **Tropical Treatment**

There is no universally effective specific therapy for the disease—existing agents have varying degrees of effectiveness, and the condition, more often than not, relapses. Most cases are treated with topical agents, used alone, or in combinations. Topical agents are much more effective in the epidermal type of melasma.

- Hydroquinone

Hydroquinone also known as dihydroxybenzene, is a hydroxyphenolic compound that is structurally similar to precursors of melanin. It inhibits the conversion of DOPA to melanin by inhibition of the enzyme, tyrosinase. Hydroquinone affects not only the formation, melanization, and degradation of melanosomes, but it also affects the membranous structures of melanocytes and eventually causes necrosis of whole melanocytes. It is the most frequently prescribed depigmenting agent worldwide and it has remained the gold standard for the treatment of melasma, particularly of the epidermal type.

Adverse reactions of Hydroquinoline are related to its dose and the duration of treatment. Irritation is the most common complication; other adverse effects include erythema, stinging, colloid milium, irritant and allergic contact dermatitis, nail discoloration, transient hypochromia, and paradoxical postinflammatory hypermelanosis.

- Azelaic acid

Azelaic acid is a naturally occurring, nonphenolic, saturated, nine-carbon dicarboxylic acid that competitively inhibits tyrosinase. Azelaic acid was initially developed as a topical anti-acne agent but because of its effect on tyrosinase, it has also been used to treat hyperpigmentary disorders like melasma. Its mechanisms of action include the inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects toward the melanocyte. Topical azelaic acid has no depigmentation effect on normally pigmented skin; this specificity may be attributed to its selective effects on abnormal melanocytes.

A double-blind randomized study has shown that a 20% concentration of azelaic acid was equivalent to 4% hydroquinone in the treatment of melasma, but without its side effects. Adverse effects of azelaic acid include pruritus, mild erythema, and burning

- Kojic acid

Kojic acid is a naturally occurring, hydrophilic fungal product derived from certain species of Acetobacter*,* Aspergillus*, and* Penicillium It acts by inhibiting the production of free tyrosinase; it is also a potent antioxidant. It is generally univalent to other therapies but may be more irritating.

- Retinoids

Retinoids, such as tretinoin, were first used in combination with hydroquinone as penetration enhancers, but were later recognized to have their own effect on melanogenesis. Retinoids affect multiple steps in the melanization pathway. Tretinoin promotes the rapid loss of pigment through epidermopoiesis and increased epidermal turnover decreases the contact time between keratinocytes and melanocytes. Retinoic acid suppresses UVB-induced pigmentation by reducing tyrosinase activity.

The most common side effects include erythema, burning, stinging, dryness, and scaling. The inflammation may cause hyperpigmentation, particularly in people with dark skin. Patients must be advised to use sunscreens during treatment with retinoic acid.

- Tropical steroids

The mechanism of the skin-lightening effect of topical corticosteroids is ill-understood. Melanocytes respond to a wide variety of chemical mediators. The inhibitory effects of corticosteroids on the synthesis of mediators like prostaglandin and leukotriene may partly explain their effects on melanogenesis. Potent or superpotent steroids, when used alone, have been associated with good therapeutic responses, but monotherapy is not recommended due to their frequent untoward effects.

Adverse effects of topical steroids include irritation, rosacea-like dermatosis, atrophy, telangiectasia, and hypertrichosis.

- Glycolic acid

Glycolic acid is an alpha-hydroxy acid that is usually combined with other agents at a concentration of 5-10% for its skin-lightening property. The mechanism of its effect might be due to epidermal remodeling and accelerated desquamation, which would result in quick pigment dispersion on pigmentary lesions. It also directly reduces melanin formation in melanocytes by tyrosinase inhibition.

- Mequinol

Mequinol is a derivative of hydroquinone. Its mechanism of action is unclear however, being a substrate of tyrosinase, it may act as a competitive inhibitor of the formation of melanin precursor. It is currently marketed in the USA at a concentration of 2% in combination with 0.01% tretinoin as a penetration enhancer.

The untoward effects of this topical combination were in the form of erythema, burning/stinging/tingling, desquamation, pruritus, skin irritation, halo-hypopigmentation, and hypopigmentation.

- Arbutin

Arbutin, the *beta*-D-glucopyranoside derivative of hydroquinone, is a naturally occurring plant product which has been used successfully in the treatment of hyperpigmentary disorders. The glycosidic bond is hydrolyzed *in vivo* leading to the controlled release of hydroquinone. Arbutin acts by the inhibition of tyrosinase, thereby decreasing melanin formation. The normal skin microflora may also hydrolyze arbutin; the hydrolyzed hydroquinone shows more potent free-radical scavenging activity and tyrosinase inhibition than arbutin.

The action of arbutin is dose-dependent and less toxic than hydroquinone. This produces reversible skin-lightening by direct inhibition of tyrosinase.

- **Combination treatment**

Melanogenesis is a complex, multi-stage process in which precursor molecules are acted upon by the enzyme tyrosinase to produce the complex biopolymer named melanin in specific organelles called melanosomes. Melanized melanosomes are then transferred from melanocytes to the keratinocytes, eventually producing the visually apparent skin color. Various topical agents act on different stages of this process, thus providing a rationale for combinations of agents for better therapeutic effect.

In addition to having a synergistic effect, a particular drug may abrogate untoward effects of another drug formulated in the same vehicle. Various combinations of different topical agents have been studied and many are marketed by pharmaceutical companies. Hydroquinone is generally the main component of formulations. It is combined with drugs like glycolic acid, azelaic acid, kojic acid, retinoic acid, or corticosteroids. It was found to be effective in the treatment of melasma, ephelides, and post inflammatory hyperpigmentation.

FUTURE THERAPY-

- N-acetyl-4-S-cysteaminylphenol

  NCAP is a phenolic agent which acts as an alternative substrate for tyrosinase, thus inhibiting the enzyme's activity. It has been reported to be more stable and causes less irritation than hydroquinone.

- Non-Ablative laser
  Laser ablation is the process of removing material from a solid surface by irradiating it with a laser beam. At low laser flux, the material is heated by the absorbed laser energy and evaporates or sublimates. At high laser flux, the material is typically converted to a plasma. Usually, laser ablation refers to removing material with a pulsed laser, but it is possible to ablate material with acontinuous wave laser beam if the laser intensity is high enough.

GUIDELINES FOR DEMELENIZING AGENTS

- Topical preparation

1. Benzoyl peroxide
   - Benzoyl peroxide gel 5% - Good for patients with greasy skin, once daily application.
   - Benzoyl peroxide cream 10% - Good for patient with dry skin.
2. Erythromycin/ Zinc acetate lotion
   Reconstituted with ethanol based solvent, good for patient with greasy skin.
3. Clindamycin phosphate topical solution 1 %
   Used for greasy skin
4. Clindamycin phosphate lotion 1%
   Used for dry skin
5. Adapalene 0.1% cream
   Contraindicated in pregnancy. Good for patient with dry skin.
6. Adapalene 0.1% gel
   Contraindicated in pregnancy. Good for patient with greasy skin.
7. Isotretinoin 0.05% gel
   Contraindicated in pregnancy. Good for patient with greasy skin.
8. Adapalene 0.1% + benzoyl peroxide 2.5% gel
   Contraindicated in pregnancy. May need to apply a non-comedogenic moisturizer.

- Systemic preparation

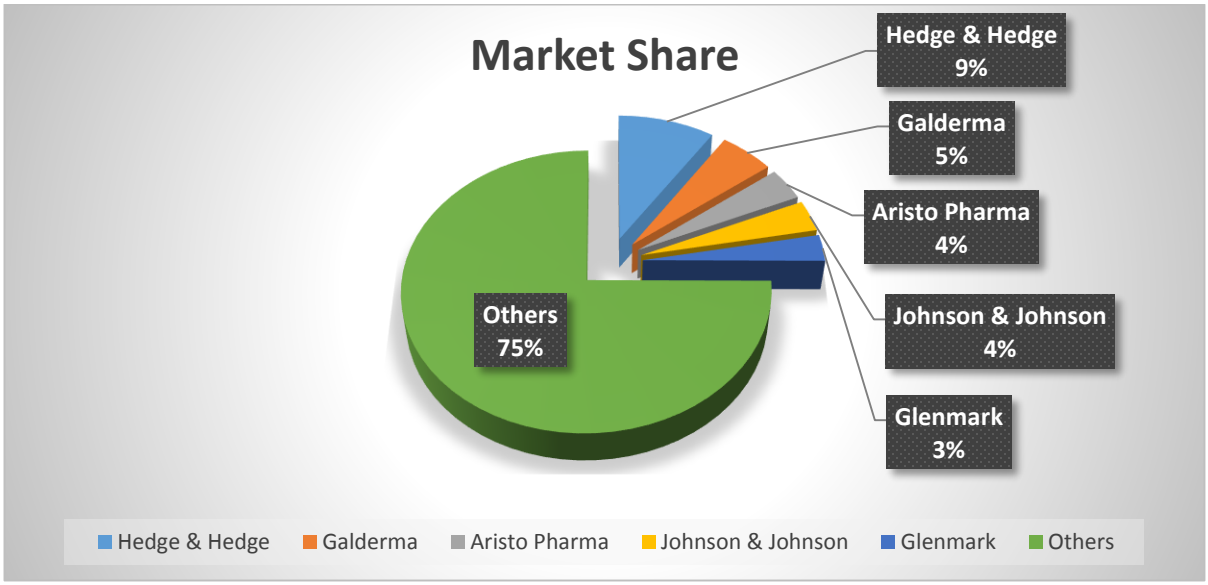
1. Doxycycline 100mg capsule
   1st line choice, take with food and plenty of water to reduce nausea, use sunscreen with sunshine exposure to minimize photosensitivity.
2. Trimethoprim 100, 200 mg tab
   For moderate severe resistant acne where topical treatment & systemic antibiotic therapy are ineffective or inappropriate.
3. Erythromycin 250mg gastro resistant tablet
   For use in pregnancy or contraindication/ intolerance to tetracycline.

MARKET SEGMENT ANALYSIS

Segment	MAT 03/2016 Rs. Crore	Growth	Total Unit
Dermatology	6,891	17.99%	1,358,346,351
Emollients	718	17.12%	81,240,749
Kreateolytics	1075	39.60%	255,542,193
Demelenizing agents	447	5.81%	39,523,858

EMOLLIENTS

Pharma Company	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Hedge & Hedge	67	16.62	6,523,177
Galderma	38	1.98	2,372,885
Aristo Pharma	27	31.45	3,551,970
Johnson & Johnson	26	15.85	6,598,784
Glenmark Pharma	22	4.21	1,599,265

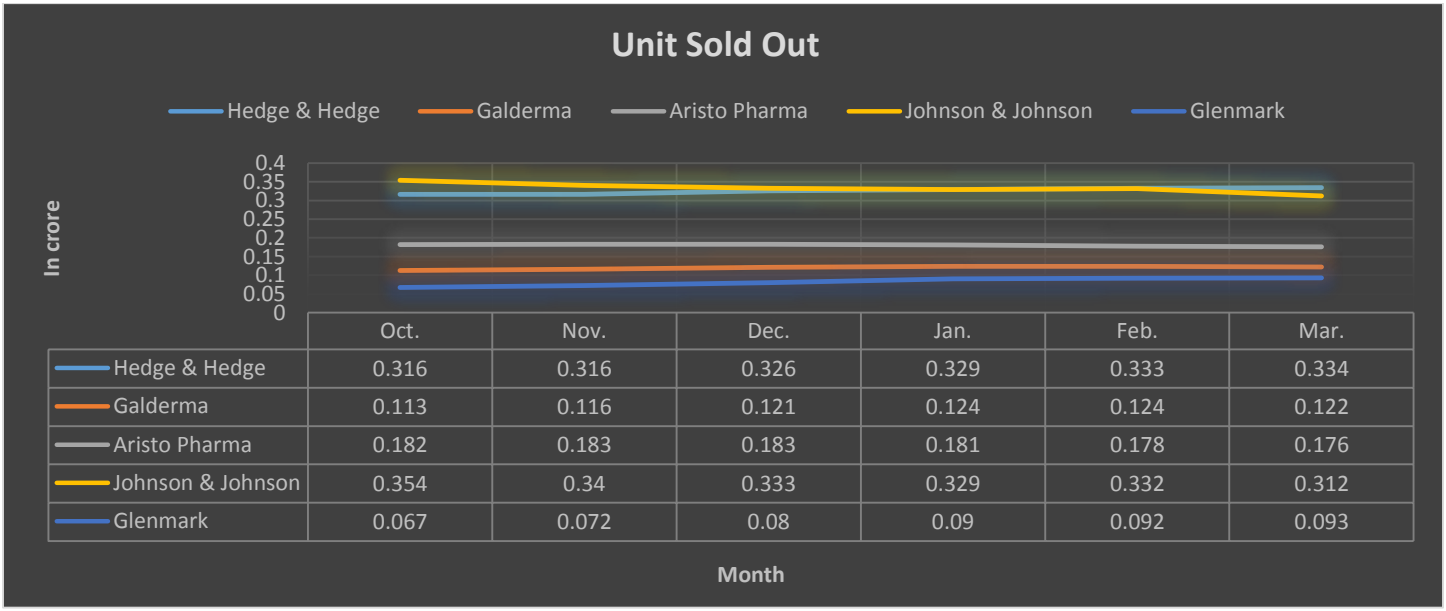


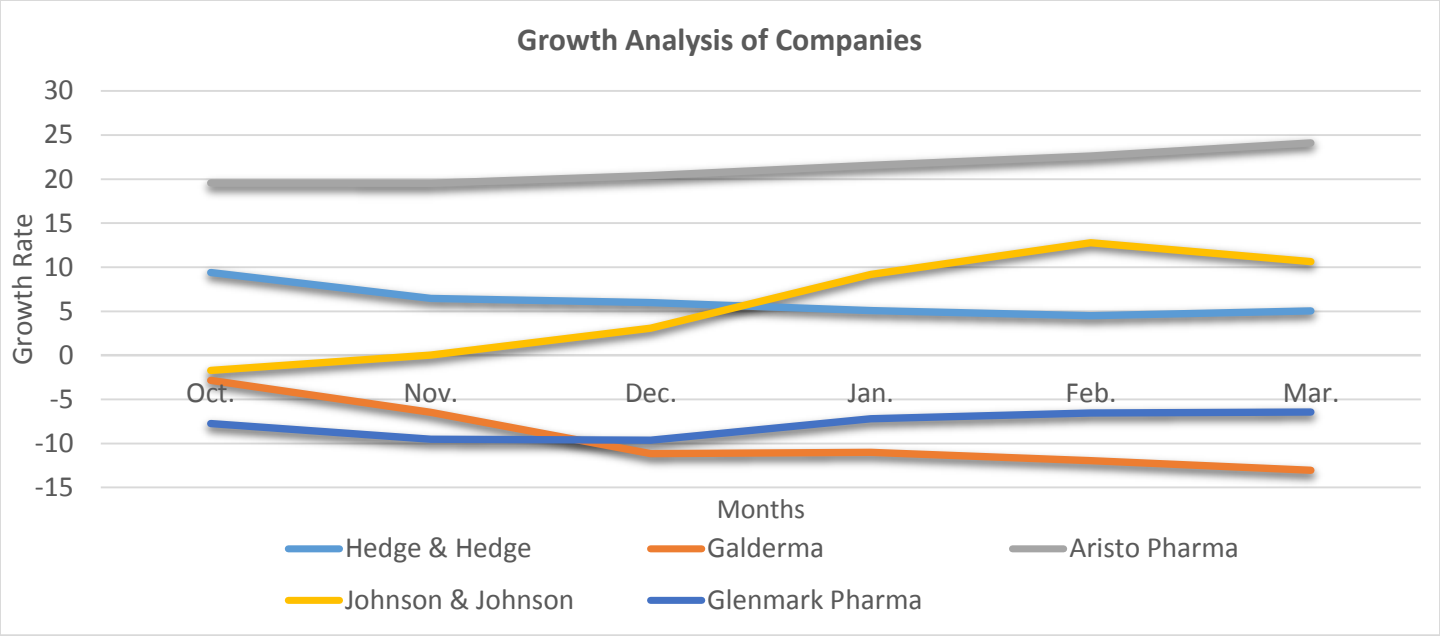
Analysis

1. Hedge & Hedge is the market leader in this segment by the second highest sales and the rate of unit is (0.97 unit/100 Rs.) comparatively low than the Galderma and Glenmark.
2. Gladerma with the very minute growth rate 1.98% acquire second position with the 5% of total market of Emollients and it consist highest rate (0.624 unit/100 Rs.) than all the companies.
3. Aristo Pharma with the highest growth rate and consist 4% of total market. Its rate of unit is low (1.31 unit /100 Rs.) in this top 5 companies.
4. Johnson & Johnson have acquire 0-5 year's age group. Its cost for unit is the lowest (2.53 unit/100 Rs.) among all. The sales of total unit is also the highest
5. Glenmark having least second growth rate with consist only 3% market. Its rate of unit is comparatively low than Gladerma but high than others. (0.72 unit/100 Rs.)

Sales analysis of 6 months

	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Company	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Hedge & Hedge	0.316	9.4	0.316	6.47	0.326	5.97	0.329	5.08	0.333	4.5	0.334	5.03
Galderma	0.113	-2.83	0.116	-6.49	0.121	-11.15	0.124	-11.00	0.124	-11.96	0.122	-13.06
Aristo Pharma	0.182	19.57	0.183	19.53	0.183	20.42	0.181	21.56	0.178	22.64	0.176	24.13
Johnson & Johnson	0.354	-1.72	0.340	0.02	0.333	3.07	0.329	9.18	0.332	12.78	0.312	10.62
Glenmark Pharma	0.067	-7.76	0.072	-9.51	0.08	-9.65	0.09	-7.20	0.092	-6.54	0.093	-6.43





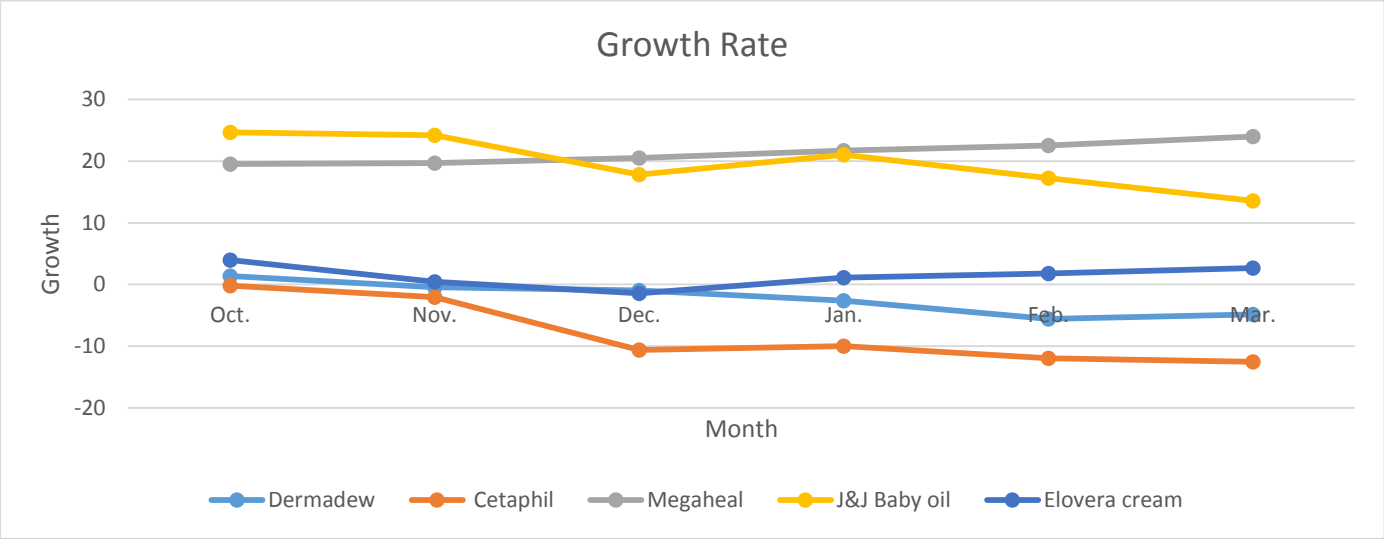
TOP PRODUCTS

Pharma Company Product	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Dermadew	23	3.76	2,545,221
Cetaphil	11	-1.61	581,758
Megaheal	18	30.23	3,028,060
J&J Baby oil	5	16.12	1,428,485
Elovera cream	13	18.61	971,150

Sales analysis of top 5products in last 6 months

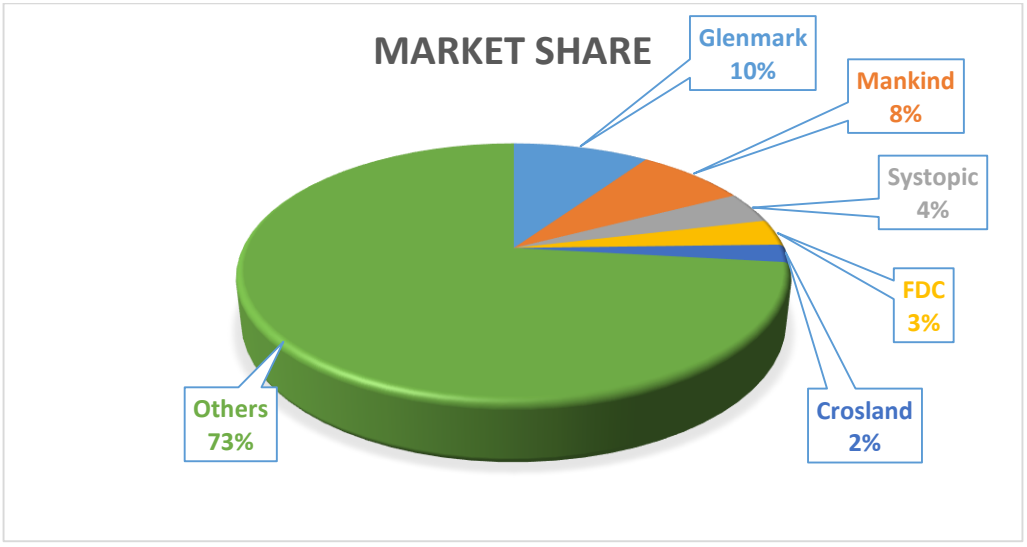
	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Product	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Dermadew	0.133	1.37	1.30	-0.47	0.129	-0.95	0.126	-2.64	0.122	-5.61	0.120	-4.88
Cetaphil	0.025	-0.17	0.027	-2.07	0.029	-10.65	0.032	-9.99	0.33	-11.98	0.33	-12.57
Megaheal	0.155	19.51	0.157	19.71	0.156	20.52	0.155	21.70	0.152	22.52	0.150	23.98

J&J Baby oil	0.081	24.65	0.076	24.20	0.072	17.8	0.068	21.03	0.064	17.24	0.061	13.57
Elovera cream	0.039	3.94	0.042	-0.44	0.048	-1.46	0.055	1.12	0.057	1.76	0.058	2.67



KREATEOLYTICS

Pharma Company	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Glanmark	103	36.805%	13,487,345
Mankind	84	49.76%	34,402,560
Systopic	42	313.255%	23,544,141
FDC	35	28.17%	19,683,159
Croslands	24	12.08%	3,293,407

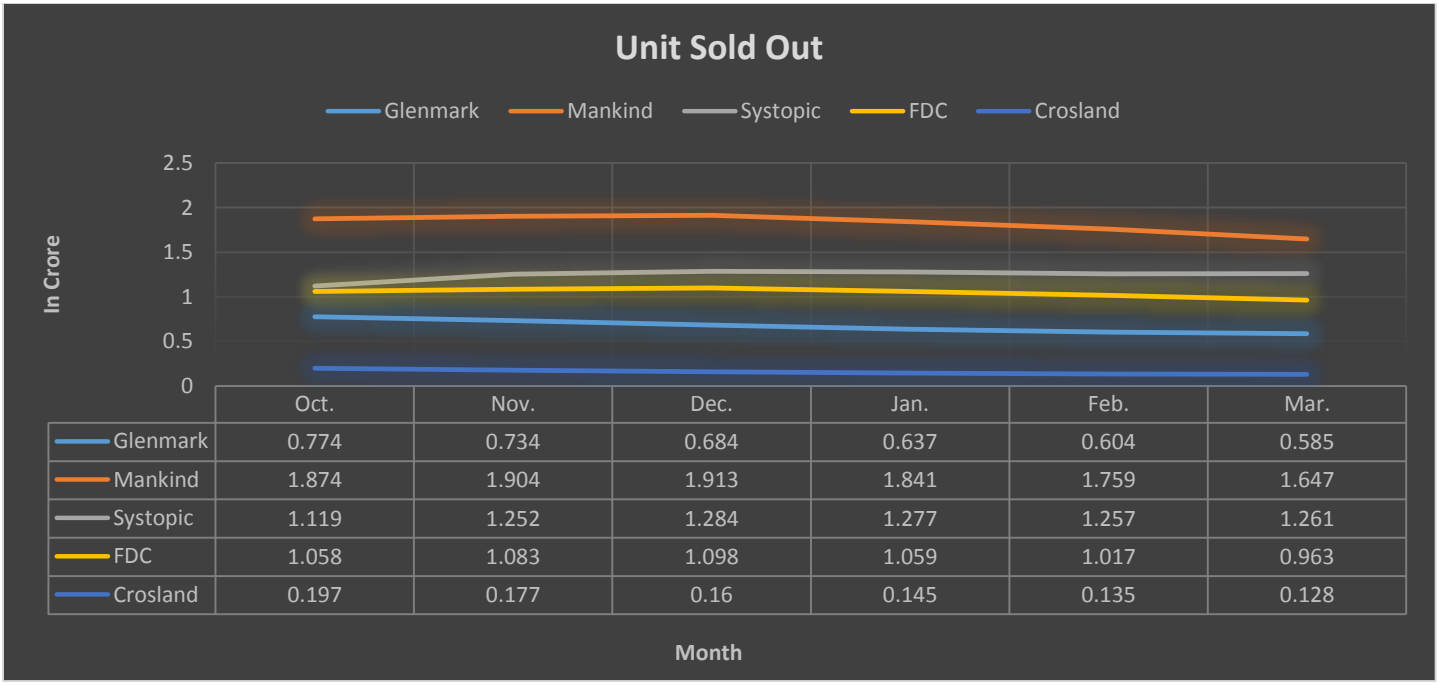


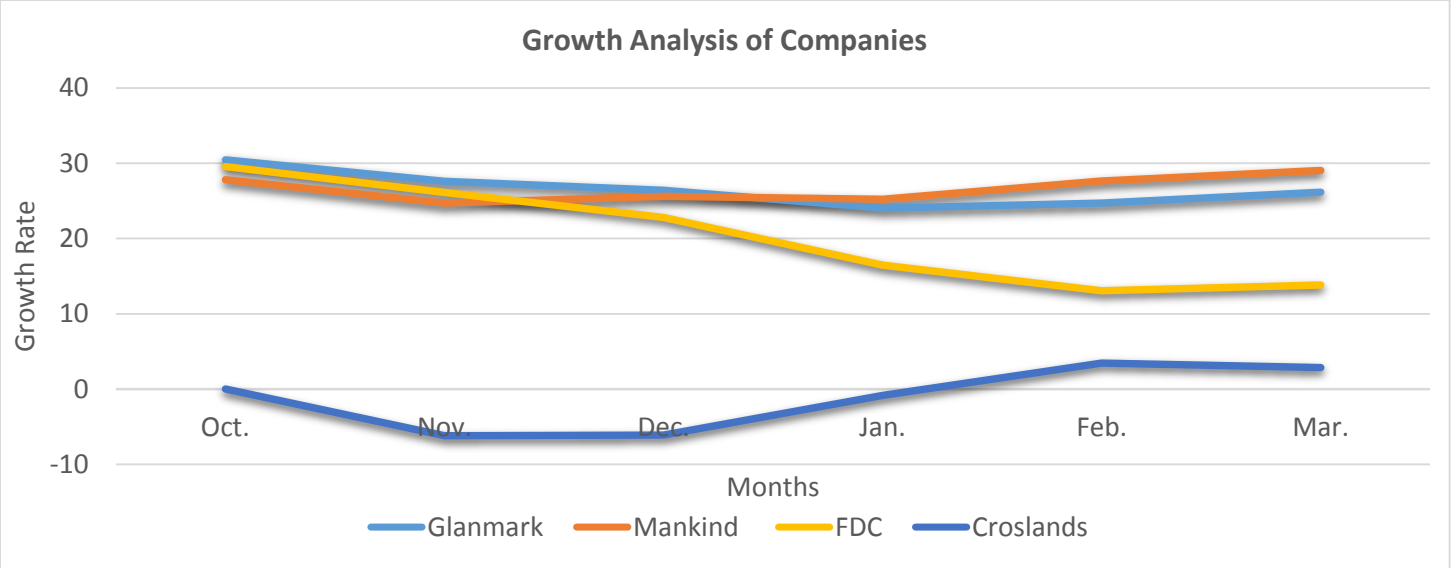
Analysis

1. Glenmark is the market leader in this segment and the rate of unit is (1.31 unit/100 Rs.) comparatively high among all.
2. Mankind with the second highest growth rate 49.76% acquire second position with the 8% of total market of Kreateolytics and it consist low rate (4.1 unit/100 Rs.) than Glenmark and Crosland. The sales of total unit is highest among all.
3. Systopic with the highest growth rate and consist 4% of total market. Its rate of unit is low (5.60 unit /100 Rs.) in this top 5 companies.
4. FDC with market contribution 3% in this category. Its rate for unit is the lowest (5.62 unit/100 Rs.) among all.
5. Crosland with the least growth rate. Its cost for unit is lower than Glenmark but higher than others. (1.37 unit/100 Rs.)

Sales analysis of 6 months

	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Company	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Glenmark Pharma	0.774	30.46	0.734	27.59	0.684	26.4	0.637	24.035	0.604	24.725	0.585	26.15
Mankind	1.874	27.84	1.904	24.71	1.913	25.59	1.841	25.21	1.759	27.67	1.647	29.06
Systopic	1.199	505.825	1.252	505.315	1.284	505.12	1.277	415.975	1.257	297.795	1.261	233.57
FDC	1.058	29.56	1.083	26.12	1.098	22.79	1.059	16.48	1.017	13.06	0.963	13.85
Crosland	0.197	0.03	0.177	-6.17	0.160	-6.08	0.145	-0.84	0.135	3.46	0.128	2.86





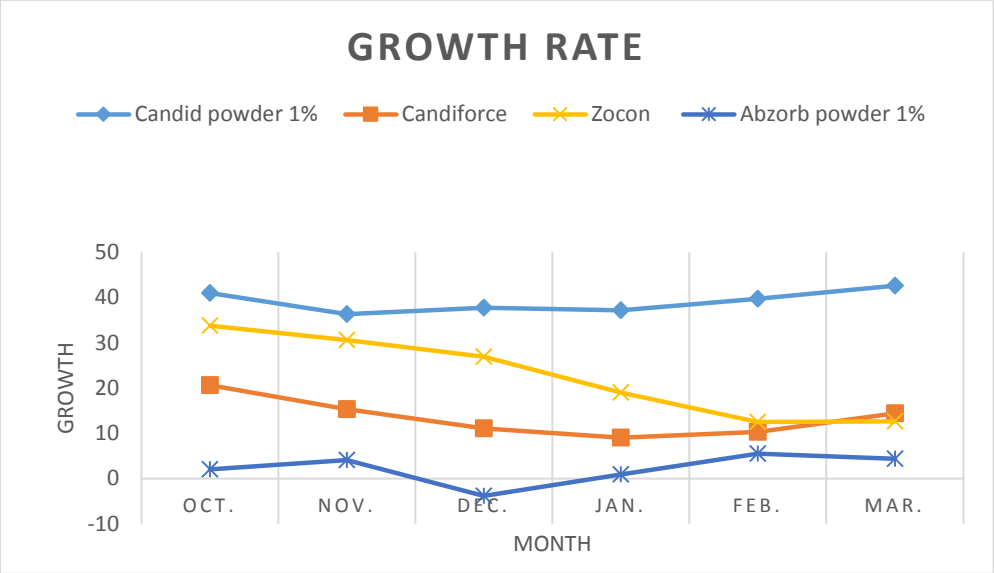
TOP PRODUCTS

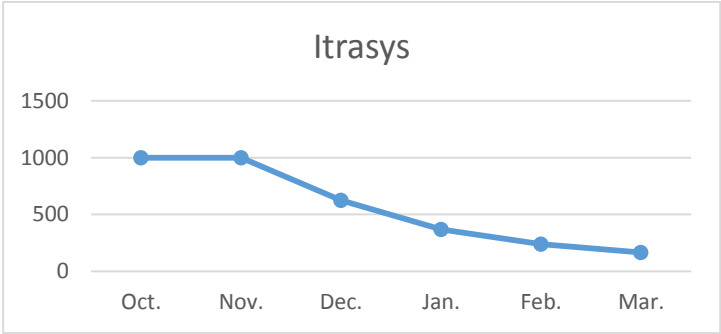
Pharma Company Product	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Candid powder 1%	25	43.54	3,221,761
Candiforce	36	34.51	6,964,529
Trasys	12	289.15	3,299,955
Zocon	21	28.75	15,698,755
Abzorb powder 1%	23	11.73	3,121,828

Sales analysis of top 5products in last 6 months

	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Product	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Candid powder 1%	0.198	41.00	0.171	36.35	0.148	37.72	0.134	37.22	0.125	39.72	0.124	42.61
Candiforce	0.357	20.66	0.362	15.35	0.362	11.11	0.359	9.01	0.354	10.30	0.349	14.41
Itrasys	0.162	999.00	0.170	999.00	0.178	625.31	0.179	368.32	0.180	237.41	0.180	164.94
Zocon	0.840	33.76	0.863	30.63	0.875	26.91	0.845	19.02	0.815	12.50	0.770	12.64

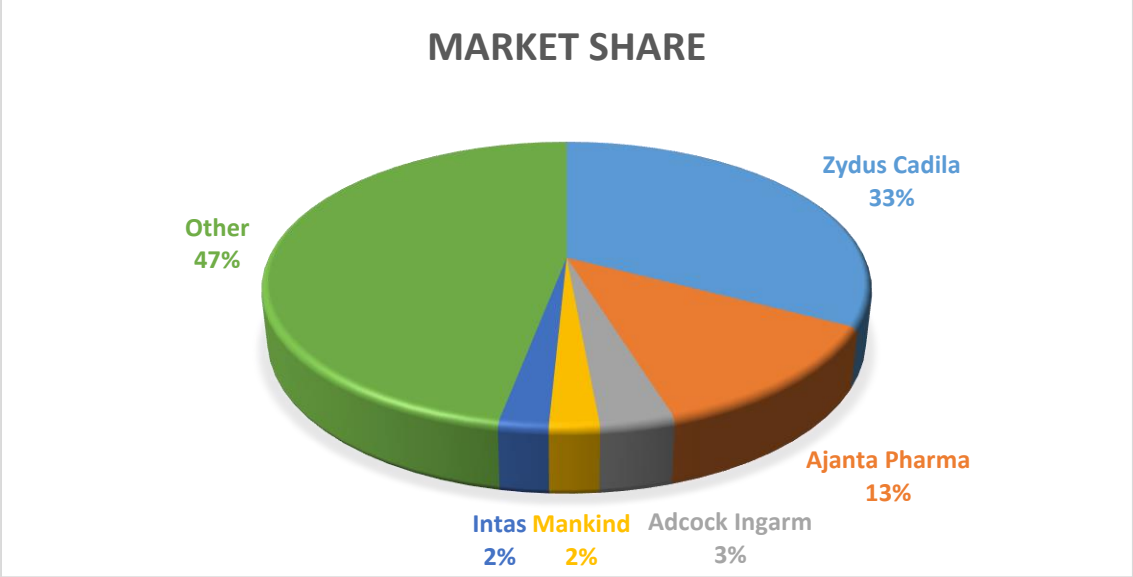
Abzorb powder 1%	0.186	2.05	0.167	-4.09	0.152	-3.81	0.138	0.92	0.128	5.51	0.122	4.39





DEMELANIZING AGENTS

Pharma Company	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Zydus Cadila	146	-8.89	12,043,484
Ajanta Pharma	56	-3.52	4,586,016
Adcock Ingarm	15	2.37	1,347,208
Mankind	10	35.69	1,342,504
Intas	10	-0.58	1,093,272

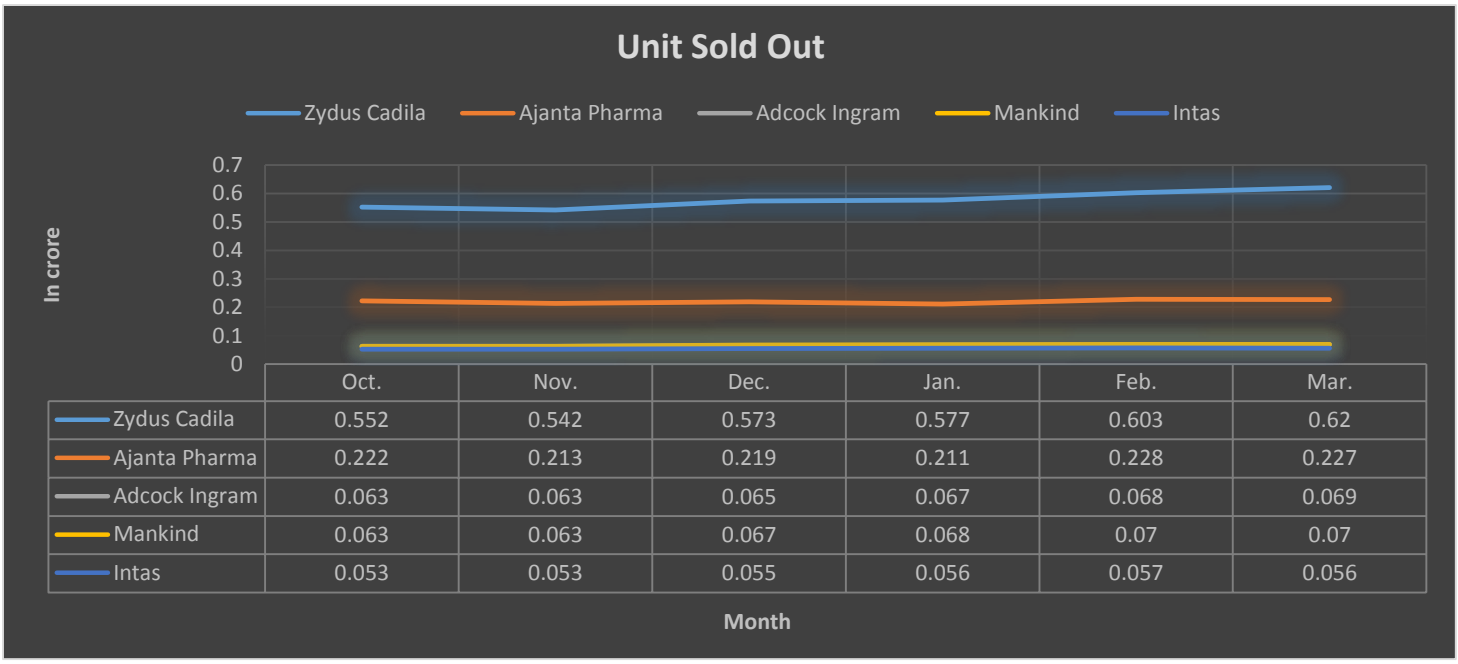


Analysis

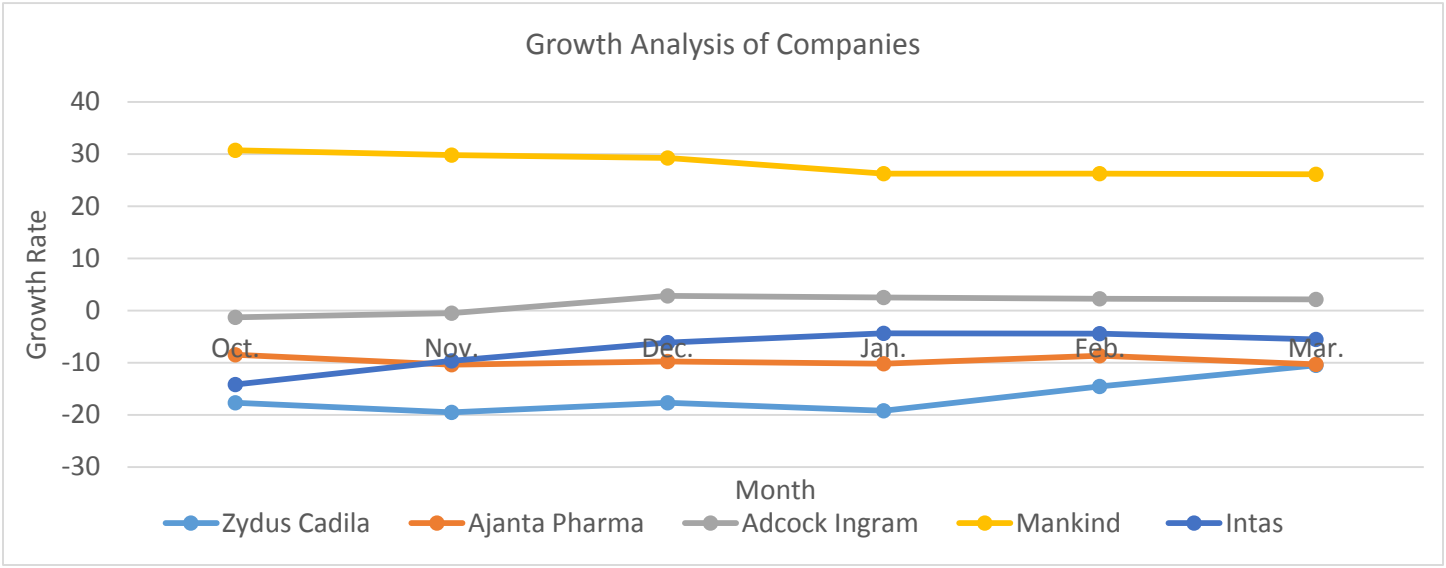
1. Zydus Cadila is the market leader with 33% of total market in Demelanizing agent. The rate of unit is (0.824unit/ 100 Rs.) is high then others but lower than Ajanta Pharma. The sales of total unit is highest among all.
2. Ajanta Pharma with 13% of total market is second leader. The rate of unit is (0.81unit/100 Rs.) highest then the remaining one. Ajanta Pharma is having declined growth rate.
3. Adcock Ingram with second highest growth rate 2.37% and its rate of unit is average (0.89 unit /100 Rs.)
4. Mankind with the highest growth rate acquire forth position with the 2% of total market of Demelanizing agents and it consist lowest rate (1.34 unit/100 Rs.) than others.
5. Intas pharma is very close but the growth rate is very far than the mankind. Its rate of unit is low (1.09 unit /100 Rs.) in this top 5 companies.

Sales analysis of 6 months

	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Company	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Zydus Cadila	0.552	-17.67	0.542	-19.5	0.573	-17.71	0.577	-19.20	0.603	-14.58	0.62	-10.54
Ajanta Pharma	0.222	-8.48	0.213	-10.39	0.219	-9.78	0.221	-10.21	0.228	-8.64	0.227	-10.34
Adcock Ingram	0.063	-1.33	0.063	-0.49	0.065	2.78	0.067	2.52	0.068	2.24	0.069	2.13
Mankind	0.063	30.71	0.063	29.81	0.067	29.26	0.068	26.23	0.070	26.21	0.070	26.10
Intas	0.053	-14.17	0.053	-9.65	0.055	-6.16	0.056	-4.40	0.057	-4.44	0.056	-5.54



	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.
Zydus Cadila	0.552	0.542	0.573	0.577	0.603	0.62
Ajanta Pharma	0.222	0.213	0.219	0.211	0.228	0.227
Adcock Ingram	0.063	0.063	0.065	0.067	0.068	0.069
Mankind	0.063	0.063	0.067	0.068	0.07	0.07
Intas	0.053	0.053	0.055	0.056	0.057	0.056



TOP PRODUCTS

Pharma Company Product	MAT 03/2016 Rs. Crore	Growth	Total Unit Sold Out
Skinlite cream	146	-8.49	12,043,484
Melacare	49	-2.96	4,091,242
Cosmelite cream	9	16.31	840,244

Melabest cream	10	35.69	1,342,504
Lomela cream	10	6.73	1,069,420

Sales analysis of top 5products in last 6 months Demelanizing agent

	Oct. 2015		Nov. 2015		Dec. 2015		Jan. 2016		Feb. 2016		Mar. 2016	
Product	Unit Sold Out	Growth	Unit Sold Out	Growth	Unit Sold	Growth	Unit Sold	Growth	Unit sold	Growth	Unit Sold	Growth
Skinlite cream	0.552	-17.67	0.542	-19.55	0.573	-17.71	0.577	-19.2	0.603	-14.58	0.620	-10.54
Melacare	0.198	-8.51	0.188	-10.70	0.195	-10.03	0.197	-10.48	0.204	-8.67	0.203	-10.66
Cosmelite cream	0.038	13.24	0.039	12.61	0.041	16.64	0.042	14.79	0.043	15.68	0.045	16.74
Melabest cream	0.063	30.71	0.063	29.81	0.067	29.26	0.068	26.33	0.070	26.21	0.070	26.10
Lomela cream	0.051	-1.99	0.053	4.83	0.055	7.06	0.056	8.52	0.057	10.34	0.056	8.97