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Niacinamide Potential: Boon in Management of Hyperpigmentation and Acne

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ABSTRACT :

Niacinamide is a hydro soluble form of vitamin- B3 that contributes to essential metabolic functions and its deficiency can cause pellagra which leads to dermatitis, diarrhea, and dementia. It is responsible for the synthesis of NAD+, contributing to redox reactions and cellular energy metabolism in cutaneous cells. From a cosmetic standpoint, niacinamide has become a key functional ingredient in diverse skincare products. Hyperpigmentation is a condition in which skin becomes darker due to various factors like excess melanin production, skin injuries such as cuts or burn and excessive sun exposure. Similarly, acne occurs when hair follicles become clogged with oil and dead skin cells, leading to the formation of pimples, whiteheads and blackheads. Niacinamide can reduce melanin production, also helps to regulate the production of sebum and by strengthening the skin's barrier, it helps to prevent infection.

This review unlocks the potential of niacinamide across diverse skin types and in management of hyperpigmentation and acne.

Keywords: Niacinamide,vitamin- B3,Skin problems,Hyperpigmentation,Acne,*Melanosome*,whiteheads,blackhead

1. Introduction :

The facial skin is a unique and significant part of the human body, involved in both protective and aesthetic functions. Facial skin is exposed to the external environment almost all the time, so it has a higher risk of being damaged than other areas. Moreover, facial skin is the most important part of the body for people's appearance and overall well-being and plays a vital role in interactions and self-esteem. So people are more concerned about their facial skin health.Anatomy and Composition of facial Skin. It has two main layers. The uppermost one is the epidermis. It is a stratified squamous keratinised epithelium. The second is the dermis, subjacent fibrous-collagenous-elastic tissue that hosts vessels, nerves, and sensory receptors. It supports the epidermis. The subcutaneous tissue hypodermis is the deepest layer, which in most instances consist largely of pads of adipose tissue.

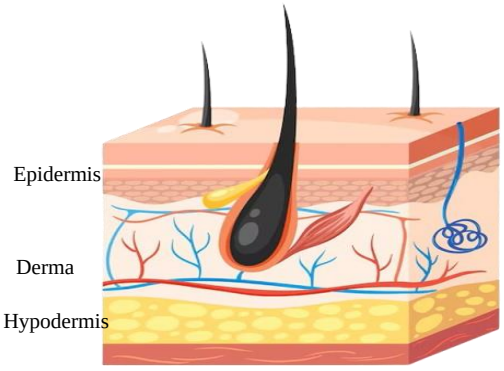


Fig1: Layer of skin

1.1. Layer of Facial Skin

- Epidermisy it is a stratified squamous epithelium which is continuously undergoing restoration. It is an outermost layer predominantly made up of keratinocytes, which constitute about 95% of the cells in the epidermis. This layer is thinner on the face compared to other parts of the body, allowing for greater flexibility and sensitivity.Has the keratinocyte progressively moves from its attachment to the basement membrane to the skin surface, it forms several morphologically distinct epidermal layers: stratum basale or stratum germinativum, stratum spinosum, stratum granulosum, and stratum corneum.Melanocytes can be seen between the basal cells of the epidermis; they are derived

from neural crest cells and migrate into the epidermis, where they produce melanin by enzymatic activity of tyrosine kinase and are stored in melanosomes. They form an umbrella-like cap over the nucleus, protecting it from the injurious effects of UV light.

- Dermis: The dermis is a connective tissue layer present between the epidermis and subcutaneous tissue. The dermis is a fibrous structure composed of collagen, elastic tissue, and other extracellular components that include vasculature, nerve endings, hair follicles and sebaceous glands, which produce sebum to keep the skin moisturized. It support and protect the skin and deeper layers, assist in thermoregulation[.It consists of 2 connective tissue layers, papillary and reticular, which merge without clear demarcation. The papillary layer is the upper dermal layer, which is thinner and composed of loose connective tissue which are rich supply of blood vessels that provide nutrients to the epidermis.The reticular layer is the deeper layer, which is thicker and less cellular.

- 3)Hypodermis: It also known as the subcutaneous fascia located beneath the dermis.Generally, it transforms into subcutaneous adipose tissue which contributes to thermal insulation and storage of energy, and it acts as a shock absorber.It has an important role in adipose homoeostasis and is particularly rich in G protein-coupled receptors, which regulate lipolysis, adiponectin and leptin secretion.

Common facial Skin problems

Facial skin condition is perceived as a vital indicator of the person's apparent age, perceived beauty, and degree of health.In an study to provide clinically relevant data regarding both dermatologic disease and skin care needs in the elderly, 68 noninstitutionalized volunteers, aged 50 to 91 years (average age, 74 years), were enrolled in a study consisting of a 33-item questionnaire and a total cutaneous examination. Two thirds of the entire group and 83% of the 23 octogenarians reported medical concerns regarding their skin[11].Thus a person can undergo different type of facial skin related problems throughout the Life which can affect confidence and attitude, there are several reasons which are responsible like hygiene, dieat,fungal,genetic or any disease

Classification of common Dermatoses condition

Category	***Conditions***
1. Infestations and Infections	*A) Parasitic Infestations*: Pediculosis capitis, Scabies
	B) Bacterial Infections: Pyodermas
	C) Viral Infections: Molluscum contagiosum, Warts, Herpes simplex, Chicken pox, Herpes zoster
	d) Fungal Infections: Tinea capitis, Tinea corporis, Pityriasis versicolor, Candidiasis
2. Dermatitis and Eczema	Infantile seborrheic dermatitis, Diaper or napkin dermatitis, Atopic dermatitis, Infective dermatitis
3. Urticaria	Urticaria
4. Exanthems	*Viral Exanthems*: Measles, Rubella, Roseola infantum, Erythema infectiosum
5. Drug Eruptions	Drug eruptions
6. Pigmentary Disorders	*A)Postinflammatory Pigmentation*
	B)Hypopigmentary
	C)Disorders: Pityriasis alba, Vitiligo, Leprosy, Nevus achromicus, Ash leaf macule, Albinism
7. Diseases of Hair and Nails	Tinea capitis, Alopecia areata, Diffuse alopecia, Twenty nail dystrophy

Three skin conditionsacne, dry skin, and hyperpigmentationhave been extensivelyinvestigated.Additionally, eotiologies of skin conditions are investigated and evaluated using relevant quality control tools has been done

1.2. Hyperpigmentation.

Hyperpigmentation is a common type of skin condition characterized by an overall darkening of the skin. This alteration in skin pigmentation can arise from a range of internal and external influences, such as hormonal fluctuations, inflammation, injuries, acne, eczema, specific medications, and exposure to UV rays. which is due to excess melanin production by melanocytes, the pigment-producing cells located in the epidermis.

Some frequently seen disorders linked to hyperpigmentation are melasma, post-inflammatory hyperpigmentation, freckles (ephelides), lentigines, among others.Melasma is a skin condition characterized by an acquired hypermelanosis, where uneven patches of light to dark brown or gray-brown lesions develop on areas of the skin that are exposed to the sun[16].Post-inflammatory hyperpigmentation occurs after various forms of skin inflammation or trauma, which can include exposure to chemicals, burns, wounds, psoriasis, atopic dermatitis, and acne. After the lesion has healed, the skin appears more pigmented and darker.

The skin epidermis is made up of two primary cell types: melanocytes, which are found at the basal layer of the epidermis and produce the protective pigment melanin, and keratinocytes, which are the most prevalent cells and found in all layers of the epidermis. Keratinocytes produce keratin to shield

epithelial cells from mechanical and non-mechanical stress.Melanin synthesis and transit within melanocytes, melanin transfer from melanocytes to keratinocytes, and melanin internalisation and processing by keratinocytes are the three processes that contribute to skin pigmentation.
Melanin synthesis and melanosome transport within melanocytes are well characterized.Melanosomes must be moved from the perinuclear area to the melanocyte dendrites in order to be transmitted to keratinocytes.Four theories have been put out thus far to describe this process: (a) keratinocytes cytophagocytose the tips of melanocyte dendrites; (b) melanocytes and keratinocytes fuse their membranes directly, creating filopodia that allow melanosomes to be transferred; (c) melanocytes transfer shed melanosome-loaded vesicles, which keratinocytes then internalise; and (d) melanocytes exocytose the melanin core and then internalise it.

1.3. Management of hyperpigmentation.

Although drugs for skin pigmentation have been acknowledged for quite some time, they have only recently gained broader accessibility. The main treatments for skin pigmentation are topical creams and oral medications are mostly used

- **Oral Medications:**

Tranexamic acid, one of several coagulation modifiers (Traxamac® 250 mg). it is use in treating eczema, melasm. Tranexamic acid assist tyrosinase in untangling tangles. This could prevent and stop hyperpigmentation by reducing melanin production.Mexameter® was used to assess the suggested lesional melanin index (MI) ranks and erythema index (EI) scores in 25 patients who received 1500 mg twice daily for two months. Each of these scores dropped dramatically.

- **Topical Agents:**

Topical agents are most commonly utilized to treat or manage localized skin hyperpigmentation and are developed into topical formulations like creams and gels. Hydroquinone, recognized as the gold standard for treating hyperpigmentation, has been applied topically since the 1960s, work by inhibiting tyrosinase to disrupt the synthesis of melanin.
Glycolic acid is a white crystalline alpha hydroxy acid extracted from sugarcane (Van Scott et al., 1996). The effect of glycolic acid is concentration dependent,It functions by inducing epidermolysis at greater concentrations and keratinocyte shedding at lower amounts.
Kojic acid is an organic compound generated by aerobic fermentationof foods material like soy sauce and rice wine by several fung, it effective cause reduction hyperpigmentation.
Laser Therapy: Different forms of laser treatments target pigmentation. These are usually considered when topical agents do not yield satisfactory results(Q switched ND:YAG 1064-nm laser therapy)**.**

1.4. How Niacinamide can use in treatment of hyperpigmenation

- **Inhibition of Melanosome Transfer:**

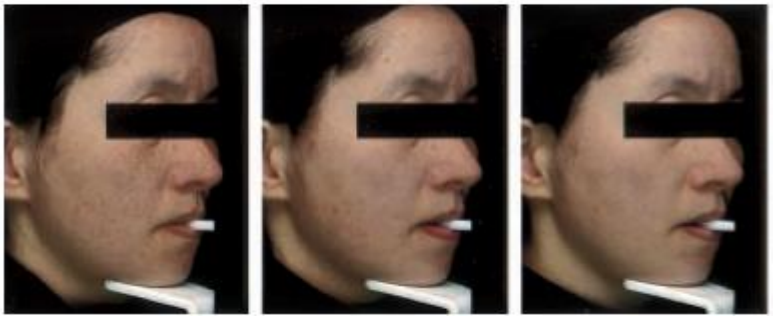
The primary mechanism by which niacinamide reduces hyperpigmentation is its ability to inhibit the transfer of melanosomes (which carry melanin, the pigment responsible for skin color) from melanocytes (the cells that produce melanin) to keratinocytes (the predominant cell type in the outer layer of the skin). Research has shown that niacinamide can inhibit this transfer by 35-68% in co-culture systems of melanocytes and keratinocytesand has been demonstrated to significantly reduce hyperpigmentation after four weeks of use.

- **Antioxidant and Anti-Inflammatory Effects of Niacinamid .**

Mechanistically, the skin's first reaction to environmental stresses is the production of reactive oxygen species (ROS) and free radicals, which change protein structure and enzyme function, damage DNA, and generate lipid peroxides. Under the influence of the Nrf2-antioxidant response element signalling pathway, this cellular damage can be reversed by endogenous antioxidant enzymes and small molecules, followed by increased production of antioxidant enzymes. Concurrently, inflammatory factors are synthesised and released to indicate the recruitment of an innate immune infiltrate.
As an antioxidant, niacinamide helps protect skin cells from oxidative stress caused by environmental factors such as UV radiation and pollution, which are known triggers for hyperpigmentation.According to Kamat et al., nicotinamide prevented lipid peroxidation of rat liver microsomes caused by the photosensitised reaction of methylene blue exposed to visible light in the presence of oxygen and scavenged singlet oxygen at a rate constant of $1.8 \times 108\ M^{-1}\ s^{-1}$. When exposed to UV light, nicotinamide reduced the production of inflammatory mediators such prostaglandin (PG) E2, IL-6, and IL-8 in human epidermal keratinocytes and full-thickness three-dimensional skin organotypic models.

1.5. Human Clinical Study: Reduction of hyperpigmentation by niacinamide.

Analysis of images. For the 5% niacinamide and vehicle control treatments, Figure shows the image analysis findings for the percentage change from baseline in the overall area of hyperpigmentation. Following four weeks of therapy, the overall hyperpigmented area on the niacinamide-treated side of the face decreased significantly ($P < 0Æ05$) in comparison to the vehicle-treated side.
After four weeks of therapy, the magnitude of the difference between niacinamide and vehicle treatments did not rise further, but it remained statistically different throughout the duration of the trial.
visual evaluation. The visual grading of the degree of hyperpigmentation for 5% niacinamide vs. the vehicle control shows the mean difference from baseline in Figure. Following 8 weeks of therapy, there was a significant decrease in hyperpigmentation on the niacinamide-treated side of the face compared to the vehicle-treated side. Figure illustrates that following treatment with both niacinamide and the vehicle, there were less regions of hyperpigmentation and that their colour lightened. Niacinamide and vehicle differences were significant for colour but not for the quantity of hyperpigmented regions**.**



Baseline **4 weeks** **8 weeks**

Fig2:Niacinamide-treated side couse reduction in hyperpigmentation

1.6. Dosage from of Niacinamide available in Market:

- PromaCare NCM(USP34)
- PromaCare NCM(Ultralow Nicotinic Acid)
- AaKo Vit NIA
- Niacinamide USP PC
- Niacinamid PC
- EcoCare VB3
- EcoGard PO
- EcoStat HP
- Tacodine (Niacinamide 99%)
- Nicotinamide
- Vitamin B3
- Macamin NC
- RonaCare Nicotinamide
- .Niacinamide, Nicotinamide

1.7. Acne:

Adolescence is a prevalent period for acne, an inflammatory condition of the pilosebaceous units(The pilosebaceous unit consists of the hair shaft, the hair follicle). characterized by clogged pores,open (black) and closed (white),pimples that give the skin a rough texture are the characteristic lesions.Almost all teenagers have acne, and half of those still continue to experience symptoms as adults.Acne's psychological effects have been extensively studied. A person's social life may be negatively impacted due to the acne, leading to low self-esteem, social isolation, anxiety, and despair.The mechanism of acne involves a number of factors, starting with seborrhoea, followed by sebum retention, and ending with inflammation. Originally, acne was thought to be associated to either the extent of bacterial presence in the skin's pores or the oil or sebum production in the skin.For the bacteria Corynebacterium acnes to colonise the pore, there must be a particular amount of oil production. These bacteria use the glycerol from the triglyceride as a carbon source and produce free fatty acids as a consequence of their life on the triglyceride in oil.The pore lining gets damaged by the free fatty acids, and in people who are genetically susceptible, the pore lining cells start to sludge up, adhere, and form microimpactions. At last, these show up as open and closed comedones. Inflamed papules or pustules form from these lesions if the follicle is attacked by an inflammation. When several papules sprout simultaneously or become inflamed, they manifest as cystic acne or nodules.

1.8. Type of Acne:

- ***Acne Vulgaris***

The most prevalent type of acne typically affects individuals between puberty and early adulthood. A common skin disorder called acne vulgaris is typified by the emergence of cysts, papules, pustules, comedones, nodules, and seborrhoea. It appears on parts of the skin such the face, legs, back, and upper chest where there is a lot of hair development. Sebecaous glands get clogged and diseased.
development of several eruptions, both big and minor.
A.Non-inflammatory lesions: These include *open comedones* (blackheads) and *closed comedones* (whiteheads).
B.Inflammatory lesions: These include *papules*, *pustules*, *nodules*, and *cysts.*

- ***Cystic Acne***

A severe kind of inflammatory acne, cystic acne develops beneath the skin as a result of clogged pores brought on by the buildup of bacteria, dry skin cells, and oil.The most affected are people of all ages who have greasy skin.Both inflammatory and non-inflammatory acne symptoms are common in most cystic acne sufferers.

- *Papulopustular Acne*: This type contains inflammatory lesions that present as papules and pustules. It can be further classified by severity into mild, moderate, and severe forms,Severe nodulocystic acne and scarring acne are assigned to the highest level of severity.
- *Acne Conglobata*: A rare and severe form of acne that consists of interconnected nodules and is often disfiguring. It tends to occur more commonly in males and can cause significant scarring.

1.9. Treatment of Acne:

- **Topical Retinoids**

Retinoids, first shown in the 1970s to be of value for treating acne, are derivatives of vitamin A that prevent comedone formation by normalizing desquamation of follicular epithelium. Tretinoin, adapalene, and tazarotene are the three primary topical retinoids. For a long time, tretinoin has been the gold standard by which new products are evaluated. According to a meta-analysis of five multicenter randomised investigator-blinded studies with 900 patients, tretinoin 0.05% gel and adapalene 0.1% gel decreased overall lesion counts by 53% and 57%, respectively.

- **Topical Antimicrobials**

Topical antimicrobials that are now on the market include benzoyl peroxide, tetracycline, erythromycin, and clindamycin. Due to its proven antibacterial effect against intrafollicular P acnes, azelaic acid may potentially be included in this category. Topical retinoids work well in combination with topical antibiotics. 249 participants with mild to moderate acne participated in a 12-week randomised controlled trial (RCT) that examined adapalene gel 0.1% + clindamycin 1%. A much higher overall decrease (P<.001).

- **Oral Antibiotics**

Antimicrobial and anti-inflammatory qualities are shared by systemic antibiotics used to treat acne vulgaris. By lowering P acnes inside follicles, they prevent the synthesis of inflammatory cytokines brought on by bacteria.while minocycline and doxycycline block matrix metalloproteinases and cytokines that are known to be involved in tissue deterioration and inflammation.

- **Hormonal Therapy**

Hormonal therapies for acne are tolerated in women only. Because androgens are necessary for the pathophysiologic development of acne, these therapies, which reduce androgen expression, are based on this fact.
Oral contraceptives (OCs) and androgen-receptor blockers like cyproterone acetate, flutamide, and spironolactone are examples of antiandrogenic substances. Nowadays, a number of OCs are authorised to treat acne. Each one has less than 35 µg of oestrogen. The US Food and Drug Administration has not authorised the use of any androgen-receptor blockers to treat acne.

1.10. How Niacinamide can use Treatment of Acne:

Nicotinamide seems to have several possible uses in the management of acne vulgaris. According to Draelos et al., topical nicotineamide at 2% significantly decreased the rate of sebum excretion.Furthermore, topical nicotinamide may have a bacteriostatic impact on P. acnes and aid in defending the skin's natural barrier against infection.At last, nicotinamide inhibits leukocyte chemotaxis to have an anti-inflammatory action by reducing the in vitro release of interleukin-8, a cytokine released by keratinocytes in response to infections (including P. acnes).

Oral nicotinamide
Two investigations on the treatment of acne vulgaris with oral nicotinamide.When compared to acne before therapy, Niren and Torok's combination product, which contained nicotinamide, zinc, copper, and folic acid, showed a notable improvement in acne vulgaris (Niren & Torok, 2006).
Combining the nicotinamide combination product with an oral antibiotic (name not specified in the primary publication) did not alter the acne lesions. Shalita et al. demonstrated a notable improvement in acne vulgaris as compared to acne before treatment using a combination product that contained nicotinamide, azelaic acid, zinc, pyridoxine, copper, and folic acid (Shalita et al., 2012).
It is unclear whether the treatment was the cause of the improvement in acne vulgaris because trial participants were allowed to follow their usual acne regimens. In both investigations, the person

1.11. Dosage from of Niacinamide available in Market:

- THE ORDINARY Niacinamide 10% + Zinc 1%
- Minimalist 10% Niacinamide Face Serum
- Cosrx The Niacinamide 15 Serum
- Paula’s Choice 10% Niacinamide Booster
- Dot & Key 10% Niacinamide Serum
- Kiehl’s Clearly Corrective Dark Spot Solution
- Derma Co 10% Niacinamide Face Serum
- Plum 10% Niacinamide Face Serum for Clear & Bright Skin
- OLAY AHA Face Serum with Niacinamide for Acne Spot Reduction

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