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ABSTRACT

Cosmetics are products used to enhance the appearance of one's and cosmeceuticals take the concept of cosmetics and elevate it to another level by using various compounds for that not only beautify the appearance but also takes care of the skin. With the desire of looking young for as long as possible cosmeceuticals are at the center of attention. Cosmeceuticals incorporate various substances like vitamins, minerals, peptides, growth factors and botanical extracts for the protection of the skin. Vitamins A, B, C, E and K all find their use in skin protection and healing. Vitamin A and beta-carotene finds its use in the anti-aging preparations as well as in the treatment of acne vulgaris. Vitamin B₃ (nicotinamide) is frequently used in cosmeceuticals. Vitamin C in its active form and other esters is a competent cosmeceuticals agent. Vitamin E is termed as the "protector" vitamin of its UV protective properties while Vitamin K also is an important because of its blood clotting factor. This review puts light on the role of these various compounds used in the formulation of cosmeceuticals backed by the relevant scientific data from various experiments and studies including both in-vitro as well as in-vivo studies performed over the years.

KEYWORDS: Cosmetics, Cosmeceuticals, Vitamin, Antioxidant, Anti-aging, Acne, Photo-aging.

Abbreviations used

UVA: - Ultraviolet A; UVB: - Ultraviolet B; ROS: -Reactive Oxygen Species; DNA: - Deoxyribonucleic Acid; RNA: - Ribonucleic Acid; AP: - Activator protein; MMP: - Matrix Metalloproteinase; NF: - Nuclear Factor; TGF-B: - Transforming Growth Factor-b.

1. INTRODUCTION

Cosmetics are readily available goods that are used to enhance the skin's look.^[1] Cosmetics are items designed to be rubbed, poured, sprinkled, sprayed, injected into, or otherwise applied to the human body for washing, beautifying, boosting attractiveness, or altering the look without affecting structure or function, according to the Food, Drug, and Cosmetic Act.^[2] More than 25 years ago, Albert Kligman of the University of Pennsylvania coined "cosmeceutical" to designate products the term containing active ingredients but not being either pharmaceuticals or cosmetics.^[3] Products with active substances that can change structure or function are to as cosmetics referred or pharmaceuticals, respectively.^[4,5] Cosmeceuticals may be chemically made or biologically derived. The ideal ingredients for cosmeceuticals should be those that can be digested by skin and are safe, effective, new, stable, economical to produce, and all of the above.^[6] People want to seem young for as long as possible, which is why there is an

increasing desire for products that lessen the cosmetic signs of ageing.^[7]

The medications included in cosmeceutical treatments still have a lot of hot-button issues, including their modes of action, ideal concentrations, physiologically active forms, formulation stability, penetration, and retention in the skin.^[8] These substances are represented by vitamins, peptides, growth factors, and botanical extracts and can be found in a variety of formats.^[7] Vitamins are necessary substances for a variety of bodily processes. While certain vitamins can be produced, others must be obtained from a balanced diet. The most crucial ones are folic acid, vitamins A, B, C, D, E, and K.

It is hypothesized that the molecular mechanisms of photo-aging, which also affect all other organs, are the same for chronologic skin ageing.^[9] Chronologic ageing is connected to two significant pathways. One is the gradual shortening of the telomere, which is followed by its disruption from low-grade oxidative damage. This is a result of aerobic cellular mitochondrial metabolism and also has an impact on other cellular components. Reactive oxygen species (ROS), often known as free radicals, are what start damage.^[10] Consequences include oxidation of membrane lipids, which affects transport and transmembrane signaling, damage to DNA leading

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to mutations, reduction in protein functions, and decline in protein functions over time.^[11] The daily and continuous application of sunscreen that blocks both UVB and UVA is the most crucial precaution to take in order to prevent photo damage.^[12] The potential impact of topically applied and systemically administered antioxidants that improve ROS neutralization is another strategy.^[11](**Fig.1**)

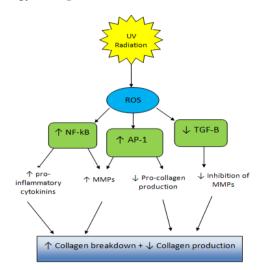


Fig 1. Effects of UV radiation on skin. Reactive Oxygen Species (ROS), which are driven on by UV, can damage DNA and have an impact on variety of transcription factors in the nucleus. Collagen production is adversely affected, and it is extensively destroyed. AP: - Activator protein; MMP: - Matrix Metalloproteinase; NF: - Nuclear Factor; TGF-B: -Transforming Growth Factor-b.

Some of these effects can be produced by growth hormones, hydroxy acids, and topical vitamins. When these items are utilized prior to and following the completion of procedures offered by cosmetic dermatology, the outcomes are better.^[13] Cosmeceutical products are expected to be as safe as cosmetics and not behave like drugs. They exhibit performance traits that point to possible pharmacological effect, although they are registered (as required) and offered for sale as cosmetics.^[14]

They frequently cost a lot of money, have little to no effect, and offer the myth of permanent beauty. On the other hand, there is a lot of evidence to support the use of topical vitamins, particularly vitamin A, in the treatment of acne vulgaris. Pharmaceuticals employ vitamin A more commonly than cosmeceuticals do. Acne is a multifactorial disease characterized by excessive sebum production by the sebaceous glands in response to an increase in androgen levels at the beginning of puberty, ductal hyper cornification of the follicles, and proliferation of Propionibacterium acnes and other bacteria that activate the toll like receptors, attracting lymphocytes, neutrophils, and macrophages.^[15,16,17]

Niacinamide, also known as vitamin B_3 , is an additional treatment for some types of acne and ageing skin. It is a component of cosmetic and cosmeceutical products. Because of its mild anti-inflammatory properties, potential role in the decrease of sebum production, and potential improvement of the skin barrier, nicotinamide is valuable as a supplemental medication.^[18,19,20]

2. Role of Different Vitamins

2.1. Vitamin A

Beta-carotene (pro vitamin A), vitamin A and its derivatives, and other ingredients have long been used as cosmetic additives. Beta-carotene can be found in foods like tomatoes, carrots, and other vellow vegetables. The main sources of vitamin A are animal products like liver and egg yolk. A powerful lipid-soluble antioxidant that serves as a precursor to vitamin A, beta-carotene can quench the highly reactive free radical singlet oxygen. Singlet oxygen has the ability to cause DNA damage and is mutagenic.^[21,22] It has been demonstrated that betacarotene has topical photo protective properties. It has been shown through research on the skin of mice and guinea pigs to offer UVA radiation protection.^[23, 24] Betacarotene and vitamin A were also discovered to be photo protective by reducing the amount of lipid peroxyl radicals in UV-exposed murine skin.^[25]

Since many years ago, retinyl palmitate, a vitamin A ester, has been included in cosmetics. It is stable in formulation and has a high molecular weight. However, it is regarded as the least potent topical retinoid.^[26] There is evidence that topical retinyl palmitate has some benefits for the skin. It has been reported to boost epidermal thickness in human skin.^[27] In a different study, hairless mice received topical retinyl palmitate for fourteen consecutive days, which raised the amount of protein, collagen, DNA, and thickneed the epidermis.⁽²⁸⁾

For almost 40 years, topical retinoids have been used to treat acne. A retinoid was originally a substance with properties that resembled those of retinol. Three generations of topical and systemic retinoids—the non-aromatics (retinol, tretinoin, and isotretinoin), the mono-aromatics (etretinate and acitretin), and the poly-aromatics (arotinoid, adapalene, and tazarotene)—have been produced as a result of variations in this molecule.^[29]

The preferred vitamin A component in cosmetics nowadays is retinol. It is a clinically effective addition to skin care products when stabilized in the mix by guarding it from disintegration from oxygen and light. According to one study, applying retinol to human skin in-vivo boosted epidermal thickness and the mRNA levels of the proteins that bind retinoic acid and retinol in cells.^[30]

All-trans-retinoic acid, often known as tretinoin, is unquestionably the gold standard for retinoid action on the skin. Tretinoin was first used to treat acne, and Kligman was the one to identify and document its advantages for photo damaged skin.^[31,32,33] When applied to photo damaged skin, tretinoin's clinical effects on wrinkles and roughness were improved, and lentigines and melasma were lightened.^[34,35,36] Reduced corneocyte adhesion and epidermal hyperplasia, increased Langerhan cells, and enhanced collagen, elastin, and angiogenesis are some of the objective histologic alterations brought on by tretinoin.^[37]

Two more topical retinoid agents, isotretinoin and tazarotene, have shown some advantages, although the degree of evidence is less strong.^[38] The optimal concentrations of tretinoin cream (0.025%, 0.05%, and 0.1%), as well as isotretinoin (0.1%), and tazarotene (0.1%), usually cause moderate to severe skin irritation. Additionally, because they are still considered prescription medications, there is rising interest in using other retinoids (retinol, retinaldehyde, retinyl propionate, and retinyl palmitate), which are approved as ingredients in cosmeceutical products, to achieve the same results.^[39,40] Another effective topical medication for the treatment of photoaged skin is retinaldehyde (0.05%). Though less effective than tretinoin, it causes irritation less frequently. Sadly, hardly many clinical trials have examined this intriguing drug.^[41,42]

2.2. Vitamin B

When applied topically, the vitamin B₃ form, niacinamide, also known as nicotinamide, has been proven to offer some fascinating advantages. Acne has been demonstrated to improve as a result of niacinamide's anti-inflammatory characteristics.^[43,44] Niacinamide's pyridine ring is thought to be the source of its anti-inflammatory properties.^[45] Additional research on the anti-inflammatory properties of niacinamide has revealed suppression of antigen-induced lymphocyte transformation and inhibition of inflammation caused by potassium iodide.^[46]

Additionally, topical niacinamide showed promise for the treatment of rosacea, pityriasis rubra pilaris, psoriasis, and isonizid-induced pellagra-like skin eruptions.^[47,48,49] Vitamin B₃ also protected immunosuppression and skin cancer in UV irradiated mice, like some other topically applied vitamins.^[50] Such a discovery points to some photo protection, possibly via antioxidant action. The ability of niacinamide to function as both a protease inhibitor and a stimulant of DNA repair may be one of its other anti-carcinogenic properties.^[51,52]

2.3. Vitamin C

L-ascorbic acid, also known as vitamin C, is the most prevalent antioxidant in human skin. The majority of creatures and plants are able to produce vitamin C. Humans are an exception to this rule because humans are no longer able to generate the enzyme required for its creation, L-gulonogamma-lactone-oxidase.^[53] The rise in skin vitamin C content, even with extensive oral supplementation, is modest.^[54]

The capacity of vitamin C to immediately squelch UVinduced free radicals and renew vitamin E, another effective antioxidant, is one reason for its interest as a cosmetic element.^[55,56] Due to its capacity to promote collagen formation, vitamin C is also regarded as a component of anti-aging products.^[57] In the aqueous compartment of the cell, water-soluble vitamin C works by giving electrons, dissipating free radicals, and shielding intracellular structures from oxidative stress.^[58]

Recent research has shown that vitamin C affects collagen production by increasing its transcription and stabilizing pro-collagen messenger ribonucleic acid, acting independently of hydroxylation.^[59] Inhibiting the biosynthesis of elastin is another way that ascorbate aids in the treatment of photo damaged skin.^[60]

In one research, topical ascorbyl palmitate was found to be thirty times more efficient than ascorbic acid at inhibiting some of the biochemical factors linked to the development of skin tumours in mice.^[61] After UV burning, application of ascorbyl palmitate reduced redness 50% faster than untreated areas on the same patient.^[62] Ascorbyl palmitate therapy has demonstrated clinical improvement in other dermatologic disorders such psoriasis and asteototic dermatitis, which involve inflammation as a part of the disease process.^[63]

Magnesium ascorbyl phosphate was discovered to shield hairless mice from UVB radiation-induced lipid peroxidation.^[64] Magnesium ascorbyl phosphate was shown to be equal to ascorbic acid in stimulating collagen synthesis and to be stable at a neutral pH in an in-vitro examination of monolayer human fibroblast cells.^[65] An additional in-vitro experiment using fibroblasts from human skin in culture showed improved collagen synthesis and cell proliferation.^[66] When using a 10% magnesium ascorbyl phosphate cream, melasma and senile freckles showed a clinical improvement in an in-vivo study conducted on human skin.^[67] Another ascorbate derivative that stimulated cultured human skin fibroblasts in-vitro and enhanced collagen synthesis was 2-alpha-D-glucopyranosyl-L-ascorbic acid, which is also stable in solution and throughout a wide pH range.^[68]

The most bioactive form of vitamin C, L-ascorbic acid, has been demonstrated to have several positive effects on the skin. Although this type of vitamin C is water soluble, it needs to be made at low pH in order to be stable. It enhances the mRNA for type I and type III pro-collagen in cultured human skin fibroblasts.^[69,70] Ascorbic acid levels were 20 times higher after 3 days of daily treatment of a 15% solution of L-ascorbic acid, and tissue levels of the vitamin were saturated.^[71] As a free radical scavenger, ascorbyl-6-palmitate is superior to L-ascorbic acid in various ways.^[72]

2.4. Vitamin E

Due to its capacity to lower lipid peroxidation, vitamin E is said to provide several systemic health advantages for the eyes and cardiovascular systems.^[73,74] Due to its

physical characteristics, vitamin E absorbs UV light in the part of the solar spectrum that causes the majority of the harmful physiological impacts of the sun.^[75]

The word "protector" has been used to describe the effects of vitamin E and its derivatives because of their capacity to squelch free radicals, particularly lipid peroxyl radicals. Numerous studies have demonstrated their capacity to lessen the erythema and edoema, sunburn cell development, and lipid peroxidation caused by UV radiation.^{([76,77,78,79,80,81]} Reduced skin wrinkling and skin tumour growth have been linked to clinical improvement in the obvious indications of skin ageing.^[82,83,84,85,86]

Although vitamin E's main active form is tocopherol, studies have demonstrated that when given topically, vitamin E esters can also permeate the epidermis.^[87]

2.5. Vitamin K

Phytonadione, a form of vitamin K_1 , is required for the liver to produce a variety of clotting factors. It was discovered that using topical vitamin K at a concentration of 1% twice daily was useful in both hastening the healing of existing bruises and preventing new ones.^[88]

For under-eye circles, a similar product containing retinol has been tested and is readily available.^[89] Topical vitamin K can be used to treat and prevent some of the vascular symptoms of ageing since parental vitamin K reduces extended bleeding time.

Table1. Summary	of functions of vitamins in	prevention of photo-aging.

Vitamins	Functions	
Vitamin A	• UV induced collagen breakdown may be prevented	
	Promotes the growth of fibroblast and collagen	
	Increases thickness of epidermal lining	
	Reduces level of MMP	
	• Reduces keratinocytes and melanocytes cell atypia preventing promotion of skin cancer	
Vitamin B	Reduces hyperpigmentation of skin	
	Increases production of collagen	
Vitamin C	May protect skin from damage caused by UV radiation	
	Promotes collagen production	
Vitamin E	• Shows good antioxidant properties protecting the skin from from UV induced photo-	
	damage	
Vitamin K	Reduces photo-aging's vascular symptoms	

3. CONCLUSION

The market of cosmetics and cosmeceuticals is growing at a much faster rate at this time due to the fact that people are becoming more and more conscious of their looks and their appearance. The fact that a lot of cosmeceuticals provide the much needed care required by the skin while enhancing the appearance of the skin backed by considerable scientific data makes them even more desirable.

The incorporation of vitamins in cosmeceuticals due to their various beneficial effects has been a popular subject of study for over half a century now. With the advancements in technology it is safe to say we will see much more of these products with improved skin care and anti-aging properties. Vitamins much as A and E work as excellent additives in the smoothening of the skin and also in the treatment of skin conditions such as acne, psoriasis, etc. Vitamin C has remarkable antioxidant properties and is regularly incorporated in the preparations. The topical application of all these vitamins incorporated into a suitable combination provides desirable effects on the skin and its benefit in the protection of skin and prevention of photo-aging. (**Table.1**) The exciting world of cosmeceuticals offers much more to us and further research and evaluation of different compounds will ultimately help in creating the perfect product to be used by us.

4. REFERENCES

- Mary P. Lupo, MD, Introduction, Antioxidants and Vitamins in Cosmetics, Clinics in Dermatology, 2001; 19: 467–473.
- 2. U.S. Food and Drug Administration Centre for Food Safety and Applied Nutrition. 2002. "CFSAN/Office of Cosmetics and Colors Fact Sheet: Is it a Cosmetic, a drug or both? (Or it is Soap?)" (*online*). Retrieved from http: //www.cfsan.fda.gov/dms/cos-218.html
- Kligman AM. Introduction. What is cosmeceuticals. In: Draelos ZD, editor. Cosmeceuticals. 1st ed. Philadelphia: Elsevier Saunders, 2005; 1-2.
- 4. Elsner, P. and H. I. Maibach. 2000. *Cosmeceuticals: Drugs vs Cosmetics*. New York: Marcel Dekker.
- Millikan, L. E. 2001. "Cosmetology, Cosmetics, Cosmeceuticals: Definitions and Regulations." *Clinics in Dermatology*, 19(4): 371-374.
- Dooley, T. P. 1997. "Is There Room for A Moderate Regulatory Oversight?" in. W. Hori (ed.). Drug Discovery Approaches for Developing

Cosmeceuticals: Advanced Skincare and Cosmetics Products. Southborough: IBC Library Series.

- Dahiaya A, Romano JF. Cosmeceuticals: a review of their use for aging and photoaged skin. Cosmet Dermatol, 2006; 19: 479-84.
- Abdulmajed K, Heard CM, McGuigan C, Pugh WJ. Topical delivery of retinyl ascorbate co-drug 2. Comparative skin tissue and keratin binding studies. Skin Pharmacol Physiol, 2004; 17: 274-82.
- 9. Fischer GJ, Kang S, Varani J, et al. Mechanisms of photoaging and chronogical skin aging. Arch Dermatol, 2002; 138: 1462-70.
- Kosmadaki MG, Gilchrest BA. The role of telomeres in skin aging/ photoaging. Micron, 2004; 35: 155-9.
- 11. Pinnell SR. Cutaneous photodamage, oxidative stress, and topical antioxidant protection. J Am Acad Dermatol, 2003; 48: 1-19.
- 12. Hawk JLM. Cutaneous photoprotection. Arch Dermatol, 2003; 139: 527-30.
- Rokhsar CK, Lee S, Fitzpatrick RE. Review of photorejuvenation: devices, cosmeceuticals or both? Dermatol Surg, 2005; 31: 1166-78.
- 14. Kligman AM. Cosmetics. A dermatologist looks to the future: promises and problems. Dermatol Clin, 2000; 4: 699-709.
- 15. Gollnick H, CunliffeW, Berson D, et al. Management of acne. A report from a global alliance to improve outcomes in acne. J Am Acad Dermatol, 2003; 46: S1-S38.
- 16. Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. J Am Acad Dermatol, 2003; 49: S200-10.
- 17. Berson DS, Chalker DK, Harper JC, et al. Current concepts in the treatment of acne: report from a clinical roundtable. Cutis, 2003; 72: 5-19.
- Griffiths CEM. Nicotinamide 4% gel for the treatment of inflammatory acne vulgaris. J Dermatol Treat, 1995; 6: S8-S10.
- 19. Bisset DL. Topical niacinamide and barrier enhancement. Cutis, 2002; 70S: 8-12.
- 20. Bisset DL, Oblong JE, Berge CA. Niacinamide: a B vitamin that improves aging facial skin appearance. Dermatol Surg 2005; 31: 860-6.
- DiMascio P, Wefers H, Do-The HP, et al. Singlet molecular oxygen causes loss of biological activity in plasmid and bacteriophage DNA and induces single-strand breaks. Biochem Biophys Acta, 1989; 1007: 151–7.
- 22. DiMascio P, Menck CFM, Nigro RG, et al. Singlet molecular oxygen induced mutagenicity in a mammalion SV40-based shuttle vector. Photochem Photobiol, 1990; 51: 17–20.
- Evelson P, Ordonez CP, Llesuy S, et al. Oxidation stress and in-vivo chemiluminescence in murine skin exposed to UVA radiation. Photochem Photobiol B: Biol, 1997; 38: 215–9.
- 24. Carraro C, Pathak MA. Studies on the nature of invitro and in-vivo photosensitization reactions by

psoralens and porhyrins. J Invest Dermatol, 1988; 90: 260–75.

- 25. Khettab B, Amory MC, Briand G, et al. Photoprotective effect of vitamin A and E on polyamine and oxygenated free radical metabolism in hairless mouse epidermis. Biochimie, 1988; 70: 1709–13.
- Boerman, MHEM, Napoli JL. Cellular retinolbinding protein-supported retinoid acid synthesis. J Biol Chem, 1996; 271: 5610–16.
- 27. Duell EA, Kang S, Voorhees JJ. Unoccluded retinol penetrates human skin in-vivo more effectively than unoccluded retinyl palmitate or retinoic acid. J Invest Dermatol, 1997; 109: 301–9.
- Counts DF, Skreko F, McBee J, et al. The effects of retinyl palmitate on skin composition and morphometry. J Soc Cosmet Chem, 1988; 39: 235– 40.
- 29. Rigopoulos D, Ioannides D, Kalogeromitros D, Katsambas AD. Comparisn of topical retinoids in the treatment of acne. Clin Dermatol, 2004; 22: 408-11.
- Kang S, Duell EA, Fisher GJ, et al. Application of retinol to human skin in-vivo induces epidermal hyperplasia and cellular retinoid-binding proteins characteristic of retinoic acid but without measurable retinoic acid levels or irritation. J Invest Dermatol, 1998; 105: 549–56.
- Kligman LH, Do CH, Kligman AM. Topical retinoic acid enhances the repair of ultraviolet damaged dermal connective tissue. Connect Tissue Res, 1984; 12: 139–50.
- Schwartz E, Cruickshank FA, Mezich JA, et al. Topical all-trans-retinoic acid stimulates collagen synthesis in-vivo. J Invest Dermatol, 1991; 96: 975– 8.
- Kligman AM, Grove GL, Hirose R, et al. Topical tretinoin for photoaged skin. J Am Acad Dermatol, 1986; 15: 838 – 59.
- Rafal ES, Griffiths CEM, Ditre CM, et al. Topical tretinoin (retinoic acid) treatment for liver spots associated with photodamage. N Engl J Med, 1992; 326: 368 –74.
- 35. Weiss JS, Ellis CN, Headington JT, et al. Topical tretinoin improves photoaged skin. JAMA, 1988; 259: 527–32.
- Griffiths CE, Finkel LJ, Ditre CM. Topical tretinoin (retinoic acid) improves melasma. A vehiclecontrolled clinical trial. Br J Dermatol, 1993; 129: 415–21.
- Pepine ML, Calderone DC, Fenske NA. The therapeutic role of topical tretinoin in photoaging. J Ger Dermatol, 1996; 4: 156–68.
- 38. Stratigos AJ, Katsambas AD. The role of topical retinoids in the treatment of photoaging. Drugs, 2005; 65: 1061-72.
- 39. Stratigos AJ, Katsambas AD. The role of topical retinoids in the treatment of photoaging. Drugs, 2005; 65: 1061-72.

L

- Oblong JE, Bisset DL. Retinoids. In: Draelos ZD, editor. Cosmeceuticals. 1st ed. Philadelphia: Elsevier Saunders, 2005; p. 35-45.
- Creidi P, Vienne MP, Ochonisky S, et al. Profilometric evaluation of photodamage after topical retinaldehyde and retinoic acid treatment.J Am Acad Dermatol, 1998; 39: 960-5.
- Didierjean L, Tran C, Sorg O, et al. Biological activities of retinaldehyde. Dermatology, 1999; 199(suppl 1): 19-24.
- Shalita AR, Smith JG, Parish LC, et al. Topical nicotinamide compared with clindamycin gel in the treatment of inflammatory acne vulgaris. Int J Dermatol, 1995; 34: 434 –7.
- 44. Griffiths CEM. Nicotinamide 4% gel for the treatment of inflammatory acne vulgaris. J Dermatol Treat, 1995; 6: S8-S10.
- 45. Bernstein JE, Lorincz AL. The effects of topical nicotinamide, tetracycline, and dapsone on potassium iodideinduced inflammation. J Invest Dermatol, 1980; 74: 257–8.
- 46. Burger DR, Vanderbark AA, Daves P. Nicotinamide: suppression of lymphocyte transformation with a component identified in human transfer factor. J Immunol, 1976; 117: 797– 801.
- Binnick SA. Pityriasis rubra pilaris responding to aminonicotinamide. Arch Dermatol, 1978; 114: 1348-9.
- Zackheim HS. Treatment of psoriasis with 6aminonicotinamide. Arch Dermatol, 1975; 111: 880 -2.
- 49. Comaish JS, Felix RH, McGrath H. Topically applied niacinamide in isoniazid-induced pellagra. Arch Dermatol, 1976; 112: 70 –2.
- 50. Gensler, HL. Prevention of photoimmunosuppression and photocarcinogenesis by topical nicotinamide. Nutr Cancer, 1997; 29: 157–62.
- 51. Troll W. Anticarcinogenic action of protease inhibitors. Adv Cancer Res, 1987; 49: 265–83.
- 52. Licastro F, Walford RL. Modulatory effect of nicotinamide on unscheduled DNA synthesis in lymphocytes from young and old mice. Mech Age Devel, 1986; 35: 123–31.
- 53. Nishikimi M, Fukuyama R, Minoshima S, Shimizu N, Yagi K. Cloning and chromosomal mapping of the human nonfunctional gene for L-gulono-gamma-lactone oxidase, the enzyme for L-ascorbic acid biosynthesis missing in man. J Biol Chem, 1994; 269: 13685-8.
- 54. Levine M, Wang YH, Padayatty SJ, Morrow J. A new recommended dietary allowance of vitamin C for healthy young women. Proc Natl Acad Sci U S A, 2001; 98: 9842-6.
- 55. Darr D, Combs S, Dunston S, et al. Topical vitamin C protects porcine skin from ultraviolet radiationinduced damage. Br J Dermatol, 1992; 127: 247–53.

- Chan AC. Partners in defense, vitamin E and vitamin C. Con J Physiol Pharmacol, 1993; 71: 725– 31.
- 57. Phillips CL, Combs SB, Pinnell SR. Effects of ascorbic acid on proliferation and collagen synthesis in relation to the donor age of human dermal fibroblasts. J Invest Dermatol, 1994; 130: 228 –32.
- Farris PK. Cosmeceuticals Vitamins: Vitamin C. In: Draelos ZD, editor. Cosmeceuticals. 1st ed. Philadelphia: Elsevier Saunders, 2005; p. 51-6.
- 59. Nusgens BV, Humbert P, Rougier A, et al. Topically applied vitamin C enhances the mRNA level of collagen I and III, their processing enzymes and tissue inhibitor of matrix metalloproteinase I in the human dermis. J Invest Dermatol, 2001; 116: 853-9.
- 60. Farris PK. Topical Vitamin C: a useful agent for treating photoaging and other dermatologic conditions. Dermatol Surg, 2005; 31: 814-8.
- 61. Smart RC, Crawford CL. Effect of ascorbic acid and its synthetic, lipophilic derivative ascorbyl palmitate on phorbol ester-induced skin-tumor promotion in mice. Am J Clin Nutr, 1991; 54: 1266S–73S.
- 62. Perricone NV. The photoprotective and antiinflammatory effects of topical ascorbyl palmitate. J Ger Dermato, 1993; 1: 5–10.
- 63. Perricone NV. Topical vitamin C ester (ascorbyl palmitate). J Ger Dermato,l 1997; 5: 162–70.
- 64. Kobayashi S, Takehana M, Itoh S, et al. Protective effect of magnesuim-L-ascorbyl-2-phosphate against skin damage induced by UVB irradiation. Photochem Photobiol, 1996; 64: 224–8.
- 65. Geesin JC, Gordon JS, Berg RA. Regulation of collagen synthesis in human dermal fibroblasts by the sodium and magnesium salts of ascorbyl-2phosphate. Skin Pharmacol, 1993; 6: 65–71.
- 66. Hata R, Senoo H. L-ascorbic acid 2-phosphate stimulates collagen accumulation, cell proliferation, and formation of a three-dimensional tissuelike substance by skin fibroblasts. J Cell Physiol, 1989; 138: 8–16.
- 67. Kameyama K, Sakai C, Kondoh S, et al. Inhibitory effect of magnesium-L-ascorbyl-2-phosphate (VC-PMG) on melanogenesis in-vitro and in-vivo. J Am Acad Dermatol, 1996; 34: 29–33.
- Yamamoto I, Muto N, Murakami K, et al. Collagen synthesis is human skin fibroblasts is stimulated by a stable form of ascorbate, 2-0-alpha-Dglucopyranosyl-L-ascorbic acid. J Nutr, 1992; 122: 871–7.
- 69. Geesin JC, Darr D, Kaufman R, et al. Ascorbic acid specifically increases type I and type III procollagen mRNA levels in human skin fibroblasts. J Invest Dermatol, 1988; 90: 420–4.
- Pinnell SR, Murad S, Darr D. Induction of collagen synthesis by ascorbic acid. Arch Dermatol, 1987; 123: 1684–6.
- 71. Pinnell SR, Yang HS, Omar M, et al. Topical Lascorbic acid: percutaneous absorption studies. Dermatol Surg, 2001; 27: 137-42.

L

- 72. Perricone NV. The photoprotective and antiinflammatory effects of topical ascorbyl palmitate. J Geriatr Dermatol, 1993; 1: 5-10.
- Vama SD, Beachy NA, Richards RD. Photoperoxidation of lens lipids: Prevention by vitamin E. Photochem Photobiol, 1982; 36: 623–6.
- 74. Meydani M. Vitamin E. Lancet, 1995; 345: 170-5.
- 75. Thiele JJ, Ekanayake-Mudiyanselage S, Hsieh SN. Cosmeceuticals vitamins: vitamin E. In: Draelos ZD, editor. Cosmeceuticals. 1st ed. Philadelphia (Pa): Elsevier Saunders, 2005; 47-54.
- 76. Trevithick JR, Xiong H, Lee S, et al. Topical tocopherol acetate reduces post-UVB sunburn-associated erythema, edema, and skin sensitivity in hairless mice. Arch Biochem Biophys, 1992; 296: 575–82.
- 77. Roshchupkin DI, Pistosov MY, Potapenko AY. Inhibition of ultraviolet light-induced erythema by antioxidants. Arch Dermatol Res, 1979; 266: 91–4.
- 78. Darr D, Dunston S, Faust H, et al. Effectiveness of antioxidants (vitamin C and E) with and without sunscreen astopical photoprotectants. Acta Dermatol Venereol, 1996; 76: 264–8.
- Ritter EF, Axelrod M, Mina KW, et al. Modulations of ultraviolet light-induced epidermal damage: Beneficial effects of tocopherol. Plant Reconstr Surg, 1997; 100: 973– 80.
- Lopez-Torres M, Thiele JJ, Shindo Y, et al. Topical application of alpha-tocopherol modulates the antioxidant network and diminishes ultravioletinduced oxidative damage in murine skin. Br J Dermatol, 1998; 138: 207–15.
- Yuen KS, Halliday GM. Alpha-tocopherol an inhibitor of epidermal lipid peroxidation, prevents ultraviolet radiation from suppressing the skin immune system. Photochem Photobiol, 1997; 65: 587–92.
- Jurkiewicz BA, Bissett DL, Buethner GR. Effect of topically applied tocopherol on ultraviolet radiationmediated free radical damage in skin. J Invest Dermatol, 1995; 104: 484–8.
- Bissett DL, Chatterjee R, Hannon DP. Protective effect of a topically applied antioxidant plus an antiinflammatory agent against ultraviolet radiationinduced chronic skin damage in the hairless mouse. J Soc Cosmet Chem, 1992; 43: 85–92.
- 84. Bissett DL, Chatterjee R, Hannon DP. Photoprotective of superoxide-scavenger antioxidants against ultraviolet radiation-induced chronic skin damage in the hairless mouse. Photodermatol Photoimmunol Photomed, 1990; 7: 56–62.
- 85. Bissett DL, Hillebrand GG, Harnon DP. The hairless mouse as a model of skin photoaging: Its use to evaluate photoprotective materials. Photodermatol, 1989; 6: 228 –33.
- Ginsler HL, Magdaleno M. Topical vitamin E inhibition of immunosuppression and tumorigenesis induced by ultraviolet radiation. Nutr Cancer, 1991; 15: 97–106.

- 87. Beijersbergen van Henegouwan GMJ, Junginger HE, de Vries H. Hydrolysis of RRR-alphatocopheryl acetate (vitamin E acetate) in the skin and its UV protecting activity (an in-vivo study with the rat). Photochem Photobiol B: Biol, 1995; 29: 45– 51.
- 88. Elson ML. Topical phytonadione (Vitamin K1) in the treatment of actinic and traumatic purpura. Cosmet Dermatol, 1995; 8: 25–7.
- 89. Elson ML, Nacht S. Treatment of periorbital hyperpigmentation with topical vitamin K/vitamin A. Cosmet Dermatol, 1999; 12: 32–4.

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