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Review

Human skin, aging and antioxidants

Barkat Ali Khan[1]*, Naveed Akhtar[1], Akhtar Rasul[1], Haroon Khan[2], Ghulam Murtaza[3], Atif Ali[1], Kamran Ahmad Khan[4], Shahiq-uz-Zaman[1], Adnan Jameel[1], Khalid Waseem[1] and Tariq Mahmood[1]

[1]Department of Pharmacy, Faculty of Pharmacy and Alternative Medicine, The Islamia University of Bahawalpur, Pakistan.
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gomal University Dera Ismail Khan, Pakistan.
[3]Department of Pharmaceutical Sciences, COMSATS Institute of Information Technology, Abbottabad, Pakistan.
[4]Department of Pharmaceutics, Faculty of Pharmacy, Gomal University Dera Ismail Khan, Pakistan.

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All health care professionals should have basic information about the structure and function of human skin inorder to be able to determine any type of change in normal skin, diagnose present skin problems and prescribe possible treatment for risk factors. Skin is also called the cutaneous membrane or the integumentry system as it has several accessory organs. In adults the skin has a surface area ranging from 1.2 to 2.2 m² and weighs about 5 kg. The skin is about 7% of the total body weight with a thickness of 0.02″ to 0.16″ range in the average adult. This review of literature covers all the aspects of human skin. Moreover, mechanisms of skin aging are discussed as well as the role of various natural and synthetic antioxidants in protecting skin are covered in this review with sagacity of understanding.

Key words: Skin, antioxidants, aging, vitamins.

INTRODUCTION

It is very important for all health care professionals to have basic information about the structure and function of human skin inorder to be able to determine any type of change in normal skin, diagnose present skin problems and prescribe possible treatment for risk factors (Bianchi and Cameron, 2008). Skin is also called the cutaneous membrane or the integumentry system as it has several accessory organs (Sylvia, 2005). In adults the skin has a surface area ranging from 1.2 to 2.2 m² and weighs about 5 kg. The skin is about 7% of the total body weight with a thickness of 0.02″ to 0.16″ range in the average adult (Elain, 2005). Skin has two types, hair-bearing skin that covers much of the body and hairless skin as that of palms of hands and soles of feet (John, 1995).

*Corresponding author. E-mail: barki.gold@gmail.com. Tel: 009263339732578.

SKIN FUNCTIONAL LAYERS

Mainly the skin is composed of two layers, the epidermis and dermis with a variable third layer, the subcutis or hypodermis (Alan and James, 2005).

Epidermis

Epidermis is the outer, protective and thinner layer of the skin. It is in contact with the outer environment. Sweet glands, hair follicles and other epidermal appendages are laying downgrowth of epidermis. Structurally, the surface of the epidermis is composed of protein plates known as Keratin which forms stratum corneum the superfacial tough and water repellent layer (Alan and James, 2005). The epidermis is translucent allowing the light to pass through it. It does not contain any blood vessel getting its nutrients and oxygen from the deep layers of the skin

Table 1. Nomenclature of the epidermal layers.

S/N	English nomenclature	Latin equivalent
1	Basal layer	Startum basal or stratum germinativum
2	Prickle cell layer	Stratum spinosum
3	Granular layer	Stratum granulosum
4	Keratin layer	Stratum corneum

(John, 2000). Traditionally epidermis is considered as stratified squamous epithelium but in fact only the outer three epidermal layers have a squamous configuration while the rest have cuboidal or polyhedral appearance (Alan and James, 2005).

Nomenclature of the epidermal layers

The English nomenclature for the epidermal layers and their Latin equivalent is composed of four layers from bottom to top as shown in Table 1.

In addition to these four layers a fifth layer, the stratum lucidum is also present in the thick skin of sole and palm. This layer has no structural or functional importance and may be an artifact or staining (Alan and James, 2005). Basal layer is also known as the dividing layer of epidermis, attached to a non-cellular basement membrane which separates the epidermis from the dermis. Basal layer have keratinocytes, markel cells and melanocytes. Markel cells have apparent sensory functions and melanocytes produce an important pigment called melanin that protects the human skin against the damaging effect of ultraviolet radiation (UVR) (Desmond, 2005). The cells of the basal layer have no blood vessels so they are not supplied with nutrients and oxygen. Thus, they eventually die and slough off (Sylvia, 2005). Keratinocytes of the basal layers move upwards, lose their nucleus and produce skin protein Keratins and lipids (John, 2000).

Unlike the basal layer, the prickle cell layer is thick of several cells. The cells of stratum spinosum are polyhedral joined by spine-like projections that is why they are referred to as prickle cells (David, 2001). The prickles are joined by Desmosomes to the neighbor's cells. Prickle cells produce a protein, the cytokeratin which aggregates to form intracellular fibrils called Tonofibrils (Barbara and John, 2005).

Granular layer is the most superfacial layer of the non-keratinized part of the epidermis having lost thier nuclei and are distinguished by the presence of dark clups of cytoplasmic materials. It is 1 to 3 cells thick. The cells of stratum granulosum contain a lot of keratohyalin granules hence this layer is called granular layer (Micheal et al., 2003).

Keratin layer is a thick zone of 20 to 30 cells making up to the three-quarters of the epidermal thickness. Keratin inthis layer protects the skin against abrasion. The glycolipid of this layer makes it water-proof. Stratum lucidum layer is a translucent band just above the stratum granulosum. It is composed of few rows of clear dead keratinocytes. It is mostly present in the exposed and abraded areas of the skin such as finger tips, soles and palms. It may be absent in other areas of the skin (Elain, 2005).

Cell types of the epidermis

Cells in the epidermis include keratinocytes, melanocytes, Merkel cells and langerhans cells (Keratinocytes are tightly bound to each other by Desmosomes. They arise from the deepest part of epidermis, the stratum basale by the process of mitosis, they produce the fibrous protein, keartin gives the epidermis the protective property. Body parts subjected to all-time friction have an accelerated production of both keratinocytes and keratin (Elain, 2005). Melanocytes in the stratum basale of the epidermis are scattered in the form of dendritic cells. They are present with the keratinocytes in a ratio of 1:4 to 1:10 in various parts of the body. Melanocytes have the capacity to replicate throughout whole life that is why melanin unit of the skin is maintained forever (Micheal et al., 2003).

Merkel cells are scattered very sparsely in the basal layer of epidermis (Barbara and John, 2005). They are mostly present in association with sensory nerves. Combination of sensory nerves and Merkel cells is known as Merkel disc or Merkel's corpuscle functioning as sensory receptor for touch (Elain, 2005). Although Langerhans cells are present in all layers of epidermis but enormous in Prickle cell layer (Stratum spinosum). They have the function of recognizing antigen thus working as a component of immune system. Normally they are present in small number but in case of inflammation/chronic atopic dermatitis Langerhans cells are increased in number (Alan and James, 2005).

Dermis

Dermis is much thicker than the epidermis which may be as thick as 3000 µm. It is largely composed of a protein called Collagen which accounts for 75% of the total

weight of dermis. Collagen of the dermis is responsible for the elasticity of human skin. Collagen molecules are bound together by elastic fibers made of a protein called Elastin. Dermis also contains glycoprotein responsible for holding a large amount of water. Hyaloronic acid is also present in the dermis which has the ability to attract and hold water (John, 2000). The dermis may be divided into two types, the papillary layer that is very close to the epidermis and the deep reticular layer. The papillary layer has a thin collagen of just 10 mm where as the reticular has collagen of 50 mm. Fibers of smooth muscle are present in the deeper part of the dermis of the penis, scrotum of tetes and nipple of breast. Hair follicles, sweet glands and sebaceous glands are present in the dermis (Bradbury, 1975).

Hypodermis/subcutis

It is also known as the subcutaneous fat layer that is connected to the dermis of muscles and bones. It acts as an insulator to store body heat. The subcutaneous fat is arranged into fat lobules keep separated by collagen fibers. When these lobules are extended in length they attain a specific shape called cellulite (John, 2000). The hypodermis may act as food store and shock absorber (Alan and James, 2005).

SPECIAL SKIN STRUCTURES

The human skin has some very important appendages with specialised functions. Sebaceous glands are sac like glands present all over human skin except the hairless skin, palms and soles. Mostly they are associated with hair but in case of lips they occur independently. They are alveolar in shape (Bradbury, 1975). Sebaceous glands secrets an oily substance called Sebum. Sebum has the function to soften and lubricate the hair and skin thus preventing the hair and skin from becoming brittle. The sebum also prevents water loss when the external humidity is low. Androgen stimulates sebum secretion. The sebaceous glands are inactive during childhood and become activated on puberty (Elain, 2005). The sebum is acidic in nature with a pH 4.2 to 5.6 that is why it is some time known as acid-mantle (John, 2000).

Sweet glands are divided into two types on the basis of their structure and mechanism of secretion. These two types include: Eccrine or merocrine sweet glands and apocrine sweet glands (Micheal et al., 2003).

Eccrine sweet glands are coiled tubular secreting a watery secretion onto the skin surface. The process by which water (sweat) is secreted is known as Merocrine secretion. The coiled shape of the sweet glands is very important for thermoregulation. Eccrine sweet glands are supplied with cholinergic neurons. Body heat and fear stimulate sweating (Barbara and John, 2005). Apocrine glands are limited to some part of body like nipple, axila aerola, anus skin and external genitelia. Apocrine glands have large lumen with coiled tubular shape but may be branched some time (Micheal et al., 2003).

Hair follicles have both epidermal and dermal components. Epidermis provides the root sheaths while the dermis provides connective tissues sheath (Bradbury, 1975). The hair follicles open on to the epidermal surface of the skin. They have tubular epithelial structures. Hair follicles have a specialized expanded area at their lower end called hair papilla. Papilae are enervated with mylinated and non-mylinated neurons as well as blood vessels. Internally root sheath of hair follicles are composed of three layers: A single cell layer called Henle's layer, a thicker layer with esinophilic granules, the overlapping keratin plates called Cuticles (Alan and James, 2005).

Functions of skin and allied organs

The skin and its allied organs have to perform a variety of functions which may affect body metabolic system. Being the outer most system, the skin is susceptible to mechanical abrasion, bacteria, temperature as well as various chemicals (Elain, 2005). The skin has four major functions (Barbara and John, 2005).

Protection from the environment/ biological barrier

Skin is the most apparent organ of human body. It is the frontier between the interior and exterior of human body. It protects the body from the pessimistic sway of external environment. The most protective function of the skin is to protect the body from the lethal effects of solar rays. The electromagnetic solar irradiations may be divided into ultra violet (UV) irradiation; visible and infra-red irradiations. Irradiations are further divided into UVB (290 to 320 nm λ), UVA (230 to 400 nm λ) and UVC (100 to 290 nm λ). UVB causes sunburn which results in painful engorgement and erythema of the skin. UVB irradiations are the main cause of skin cancergenesis. UVA irradiations lead to photo (extrinsic) aging (Skin care forum, 2009).

Protection in the form of a barrier

Skin works as a chemical, physical and biological barrier. As a chemical barrier melanin, acid mantle, low pH, the natural antibiotic human defensin and cathelicidin contribute. As a physical barrier keratinized cells mainly contribute. Glycolipid of the epidermis prevents in and out of water and hydrophilic substances (Elain, 2005).

Sensation

Human skin is richly supplied with exteroceptors including

Miessner's corpuscles and Merkel discs. These receptors allow us to feel and create awareness about the touching of our clothes with our skin as well as other irritating chemicals (Elain, 2005).

Thermoregulation

During high temperature and exercise our skin cools our body as well as maintains temperature homeostasis because water present in the sweat evaporates (Robert, 2004). In case when the body is too cold it is insulated by the presence of deep adipose tissues preventing heat loss from the body (Barbara and John, 2005).

Synthesis of vitamin D/ metabolic function

Vitamin D in the human skin is synthesized in two stages starting with the production of previtamin D after irradiation of 7-dehydrocholesterol by ultraviolet B (UVB) irradiations with wavelength 280 to 315 nm. UVB irradiations struck to the skin cells which isomerise 7-dehydrocholesterol (7DHC) to previtamin D3. Following this initial isomerisation, the previtamin D3 undergoes a heat isomerisation in the skin to Vitamin D3. This process takes several hours (Ann and Ola, 2006).

SKIN AND AGING

Like other organs of the human body skin also experiences aging, however as skin is in direct contact with the external environment so aging is a result of environmental damage. The main environmental cause of skin aging is UV irradiations (Fisher et al., 2002).

Extrinsic aging /photo aging

Extrinsic aging or photo aging occurs because of external environment particularly solar irradiations. Photo aging has a particular affect on the dermis which results in the changes in the chemical structures of skin proteins, collagen and elastin. Photo aging causes the epidermis to become thick because the quantity of collagen and elastin increases with disorganized structures (John, 2000). Photo aging depends upon the degree and time of sun exposure. People who live outdoor or live in sunny area are more prone to photo aging (Fisher et al., 2002).

Intrinsic aging/chronological aging

Skin aging which occurs with the passage of time and which is natural and unavoidable is known as intrinsic or chronological aging. In case of intrinsic aging the skin becomes thinner losing much of its elasticity. In chronological aging epidermis and dermis comes close to each other, dermis becomes wither and the quantity of dermal blood vessels falls down (John, 2000). Chronological aging depends upon the passage of time (Fisher et al., 2002).

Wrinkle

Wrinkles are thin furrows in the epidermal layer of the human skin. There are two types of wrinkles: Permanent wrinkles and non-permanent wrinkles. Permanent wrinkles occur at the sun exposed area of the body like face, neck and forehead where as the non-permanent wrinkles occur at the sun protected area of the body like abdomen and back (John, 2000). Comparatively, there is little information regarding the biological features of sun-induced wrinkling, even though it is accepted that this may be due to loss of extracellular matrix, the collagen and fibrin (Rebecca et al., 2001).

Wrinkles versus age and food intake

Wrinkles have a positive relation with the age. It has been suggested that taking vegetables, olive oil, fish and legumes, may cause less skin damage. Taking dairy food, butter, margarine and sugar products, may cause more skin damage. The only fatty acid, which has protective effect on the skin wrinkling, is monosaturated fatty acid. More ever retinol, Vitamin C, calcium, phosphorus, magnesium, iron and zinc also have protective effect on skin wrinkling (Martalena et al., 2001).

Reactive oxygen species (ROS) /oxidizable substrate

This term is used preferably for oxygen radicals (both free and non-free radicals) or oxidants, which cause oxidation. Examples include superoxide ($*O_2^-$), hydroxyl peroxide (*OH) and HOCl (free radicals) while hydrogen peroxide (H_2O_2) and singlet oxygen (O_2) are non-free radical (Barry, 1995). Radiations like UV light, drugs like bleomycin and toxic chemicals like paraquat are the sources of ROS (Minireview, 1997).

Antioxidants

This term is used for a substance, which delays or prevents oxidation of oxidizable substrate provided that it should be present at low concentration in comparison to oxidizable substrate. Examples include Vitamin E, Vitamin C, supeoxide dismutase, glutathione, β carotenes and polyamines. When reactive oxygen species (ROS) are produced in the body various types of antioxidants

Table 2. Human skin and vitamins.

Name of vitamins	Role in skin
Retinoid (Vitamin A)	Decrease sebum production in acne, put on a normal footing the production, of keratinocytes, used in the treatment of photodamage and cellulite.
Calciferol (Vitamin D)	Downregulate the cutaneous immune system, epithelial propagation and encourage differentiation.
Ascorbic acid (Vitamin C)	Regulates collagen sysnthesis, acts as antioxidant and synthesizes lipids of stratum corneum barrier.
Tocopherol (Vitamin E)	Acts as membrane antioxidant, grants photo protection synergistically with Vitamin C.
Coenzyme Q	Acts as regenerator of Vitamin E, provides photo protection.

come to play their role depending on the type of ROS produced and target of damage for example, when ROS NO_2 or O_3 are produced in the plasma then the antioxidant uric acid plays its role rather any other antioxidant (Barry, 1995).

Mechanism of damage by ROS

ROS have the potential to react with nucleic acids, carbohydrates and proteins but the more susceptible molecules are polyunsaturated fats, which instigate lipid peroxidation. ROS alter the structures and functions of proteins. They can also modify the individual nucleotide bases; break the single-strand and cross-linkage of nucleic acid (Minireview, 1997).

Human skin and carotenoids

Beta carotenes are commonly referred to as “sun protectants” that is, his ability in preventing UV radiations damage of human skin (Hans and Ute, 2001). UV light renders the human skin to photo oxidative damage because of the formation of ROS such as singlet oxygen, peroxyl and superoxide radicals. ROS have a damage effect on the DNA, proteins and lipids and is known to be a cause of erythema, skin aging and cancer. Beta carotenes, other carotenoids and tocopherols are effective ROS scavengers. Among all the naturally occurring ROS scavengers carotenoids are most efficient (Wilhelm, 2000).

Human skin and flavonoids

Flavonoids are polyphenolic compounds which universally occur in the fruits and vegetables of plant kingdom. Because of their wide pharmacological actions, flavonoids are very important plant constituents. The pharmacological activity of the flavonoids is attributed to their inhibitory action on certain enzymes and strong antioxidant activity.

It is generally accepted that flavonoids have excellent free radical scavenging activity. Flavonoids interfere with both the propagation reactions and formation of free radicals (Saskia et al., 1996). It has been established by a number of studies that flavonoids especially quercetin is a potent tyrosinase inhibitor thus decreases sun induced melanin (Robert et al., 2004). Flavonoids have also anti-inflammatory activity and in recent times their topical application got interest. Flavonoids from hamamelis prevent human UV radiations induced erythema (Francesco et al., 1996).

Human skin and vitamins

Table 2 shows the role of various vitamins in the skin described by Stanley and Claude (2001).

Topical vitamin C as antioxidant in skin aging

Chemically, Vitamin C is an alpha ketolactone shown in Figure 1. It is monovalent hydroxyl anion at physiologic pH. It is the main water soluble non enzymatic antioxidant interacting with a variety of free radicals thus providing a front line defense against free radicals. Dermatologically Vitamin C can be used in wound healing, cutaneous aging and prevention of skin cancer. In the past Vitamin C has been marketed in cosmetic industry for the treatment of hyperpigmentation. Vitamin C has the advantage of stimulating dermal fibroblasts for the synthesis of collagen thus preventing photoaging (Roy and Sheldon, 1996).

CONCLUSIONS

Understanding of human skin, skin aging and anti-oxidants lead to a basic knowledge of preventing various

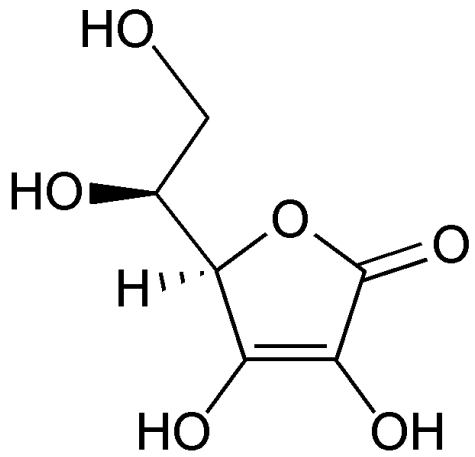

Figure 1. Chemical structure of Vitamin C.

skin disorders. Sustained disclosure to UV irradiations may contribute to photoaging. From this review we concluded that it refreshes the importance of anti-oxidants in skin aging and presents new information such as human skin and vitamins especially topical Vitamin C as antioxidant in skin aging. Moreover, mechanisms of skin aging are discussed as well as role of various natural and synthetic antioxidants in protecting skin are covered with sagacity of understanding.

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