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A Narrative Review On Skin Biology In Ayurveda

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Abstract
Exploration of the skin-related descriptions by Ayurveda scholars reveals that the physiology and anatomy of the skin, as well as its clinical and pathological features, have all been thoroughly investigated, nevertheless, the descriptions are dispersed throughout the Samhita under various parts. This article aims to compile all pertinent matters related to the development and physiological aspects of the skin along with pathological aspects in one frame and provide a probable scientific basis for it.
Based on Ayurvedic descriptions, the skin (Twacha), is the outermost layer that protects against the invasion of foreign substances, developed as cream formed over the heated milk. It is Updhatu of Mamsa Dhatu and Moola of Mamsavaha Shrotas, meaning that it gives the tissues below stability and nutrition. Skin is the primary site of Vata dosha, making it a sensory organ (Sparshanendriya Adhisthana) i.e., the seat of general sensations that processes all types of tactile senses including touch, pain, and pressure. The skin plays a significant part in the protection of the body, preserving metabolism and homeostasis, determining Prakriti (psychosomatic constitution) and Dhatu Sara (level of nourishment of bodily tissues) identifying illnesses, and deciding how best to administer medications through the skin for various conditions.
Ayurveda has considered skin as a vital route for delivering medication and treating ailments by utilising topically applied ointments, gels, or other methods like external oleation (vahya snehan), massage (abhyanga), and fomentation (swedan). It explores the connections of skin with nervous, immune, cutaneous, and endocrine functions and various biological mechanisms and the rationale behind administering drugs through the skin. This review will facilitate researchers and scholars of Ayurveda in better understanding of the biology of the skin, its involvement in different pathophysiological conditions, clinical examination, and the management of disorders in light of various recent biological mechanisms.
Keywords: *Skin, Bhrajak Pitta, Swedan, Abanga, Sparshindriya, Prakriti, Sara, Twacha.*

INTRODUCTION

The skin is the largest organ; it serves as a physical barrier, sensory and metabolic organ, a communication link with the internal organ systems and a window for displaying changes in the function of the interior organs. Intracutaneous interaction makes the skin vital to the immune, neurological, and endocrine systems. In addition to preserving fluid, electrolyte, and temperature homeostasis, it shields the body from hazardous environmental effects (physical, chemical, and microbial). Recent research has shown that the skin produces and breaks down signalling molecules, lipids, and structural proteins. These novel cutaneous roles are significant for clinical dermatology, dermatopathology, and dermato-pharmacology. [1]
Exploration of the skin-related topics described by Ayurveda scholars reveals that the physiology and anatomy of the skin, as well as its clinical and pathological features, have all been thoroughly investigated by ancient Ayurvedic experts; nevertheless, the descriptions are dispersed throughout the Samhita under various parts. Dosha (humour) and Dhatu's (tissues) roles concerning skin physiology are less clearly explained. Instead, the diverse pathogenic states are largely highlighted in developmental and the context of current scientific explorations.
According to Ayurveda, the skin (Twacha), the outermost layer that protects against the invasion of foreign substances, developed as cream formed over the heated milk. [2] It is Updhatu of Mamsa Dhatu[3] and Moola of Mamsavaha Shrotas [4], meaning that it gives the tissues below stability and nutrition. Skin is the primary site of Vata dosha, making it a sensory organ (Sparshanendriya Adhisthana) i.e., the seat of general sensations that processes all types of tactile senses including touch, pain, and pressure. [5] The variations in complexion, lustre and skin metabolism are imparted by the Bhrajaka pitta that resides in the skin[6] and also depends on the Mahabhuta permutation, the functional state of seven tissues (Sapta dhatu). However, Kapha imparts moisture, unctuousness and inherent immunity to the skin. [7] In addition, to protection, skin supports sweating, metabolism of medicaments, excretion,

and other processes. However, the science has now well established that skin complexion and lustre depend on nutritional status, haemoglobin content, melanin pigments and skin metabolism. The characteristics of the skin and its appendages have been regarded as significant traits in identifying a person's body type i.e. Prakriti (psychosomatic constitution). Yoga Ratnakar believes that the skin is an important component to examine [8] since it can reveal Dhatu's nutritional status and will aid in the assessment of Dhatu Sarata [9]. The skin-related specificities revealed by the imbalanced condition of Dhatu and Dhatu Mala can be used to diagnose a range of illnesses. Ayurveda has considered skin as a vital route for delivering medication and treating ailments by utilising topically applied ointments, gels, or other methods like external oleation (vahya snehan), massage (abhyanga), and fomentation (swedan) [10]
These descriptions of Ayurveda imply that the skin has an important role as a trait in determining Prakriti and Dhatu Sara, in maintaining homeostasis and metabolism, diagnosing disorders, and route of drug administration in the management of several disorders. Thus, by examining various biological mechanisms and the rationale behind administering drugs through the skin, this review will facilitate researchers and students of Ayurveda in better understanding of the biology of the skin, its involvement in different pathophysiological aspects, clinical examination, and the management of disorders in light of various recent biological mechanisms.

MATERIAL AND METHOD

In Ayurvedic texts such as Charak Samhita, Sushrut Samhita, Asthtang Hridya, etc., the description of the formation and development of skin, the physio-pathological aspects of Twacha in various contexts such as Dosha, Dhatu, Mala, Srotas, Prakriti, Sara, etc. have all been thoroughly examined. To comprehend skin physiology, published research data on the skin were comprehensively screened using appropriate keywords like skin development, origin, functions, keratinocytes, skin pigments, skin enzymes, thermoregulation etc. in standard e-databases such as PubMed, Science Direct, Web of Science, and Medline Plus. All of these reviewed contents related to Twacha have been comprehensively analysed in light of current science under two major categories: structural description, which focuses on the layers of the skin and their development, and physiological and therapeutic aspects, which considers relationships with Dosha, Dhatu, Updhatu, Srotas, Prakriti, etc.

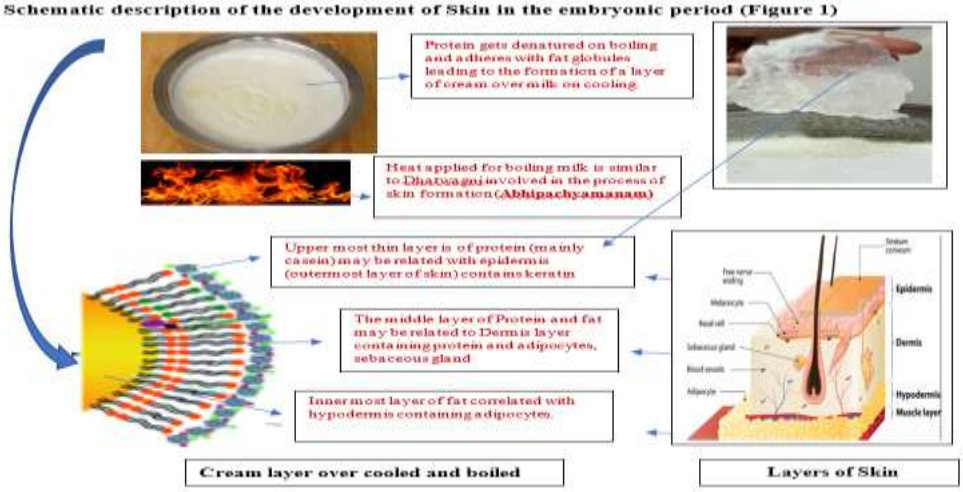
REVIEW AND DISCUSSION

Development and Functional Anatomy of Skin: The description regarding the development of Twacha is found in Garbhvyakran Sharir of Sushruta Samhita [11](and Angavibhaga Sharir of Ashtanga Hridayam [12].

Development of skin:

According to scholars of Ayurveda, the seven layers of Twacha (skin), i.e. Avabhasini, Lohita, Shweta, Tamra, Vedini, Rohini, and Mamsadhara develop in the embryo [13] (Su. Sa.4/4) during the metabolism of Rakta Dhatu by the action of Raktadhatvagni, [12] in a similar manner as the solid creamy layer is formed over the top layer of boiled milk [11]. The possible scientific interpretation of this parallel is shown in the schematic description that follows: A scientific interpretation of this analogy can be seen in the schematic explanation that follows:

Schematic description of the development of Skin in the embryonic period (Figure 1)



A close inspection of the layers of cream on boiling milk shows that the inner layer is soft, thick, and contains fat globules while the outermost thin layer is fibrous and translucent and is formed primarily of protein. It makes a layer

of defence that resembles skin as a physical barrier, blocking the admission of extraneous materials into milk and safeguarding internal structures; any discontinuity in the skin or cream allows the entry of foreign materials. The cream adheres tightly to the vessel and doesn't let things pass through, just like a semipermeable membrane/skin doesn't let in undesirable things. Ayurveda states about the formation of skin that the Rakta dhatvagni acts on Rakta Dhatu resulting in the development of the skin. Current scientific research on embryogenesis supports the validity of this description. Primitive erythroblasts, or blood cells, are the earliest cells produced in the yolk sac of the developing embryo during embryogenesis. Further, as various organs are formed, other specialised cells also develop. The skin's epidermis, which is its topmost layer, is derived from the ectoderm whereas the dermis, which is its deeper layer, is derived from mesenchyme. It implies that the development of skin layers and their sequential arrangement takes place at the same time as blood cell division. [14]

Position of the skin

The skin, which is the body's outermost layer, serves as the body's first line of defence and protects the other tissues and organs that are beneath. Ayurveda scholars have explained the position of the skin by analogy, as the cream forms an outermost covering over the surface of the boiled milk. Similarly, Twacha (skin) is also formed, covering and protecting the rest of the organ, and tissues beneath.

Time duration of development of skin:

According to Charak, the development of the skin and all other body parts begin in the 3rd month [15], however, the skin appendages nails, hair, and hair follicle development occurs in the 6th month of gestation [16]. At the end of the fourth week of life, the surface ectoderm begins to form the epidermis; however, for the first few weeks, the epidermis consists only of a basal layer of cuboidal cells. Between 12 and 14 weeks of proliferation result in the formation of epidermal ridges that protrude as troughs into the developing dermis beneath. By the 20th week, the epidermis starts to proliferate and differentiate to form four additional superficial strata: the spinosum, granulosum, lucidum, and corneum. Thus, the epidermis develops over four months [14]. Likewise, the Nails start to form after 10 weeks, while hair follicles appear between 9 to 12 weeks. Thus, the period needed for skin development is roughly equivalent to that outlined in Ayurveda.

Layers of epidermis:

Epidermal development in mammals is a multi-step process consisting of epidermal specification, commitment, stratification, terminal differentiation, and growth of epidermal appendages.[17] Stem cells in the basal layer continuously provide cells into the suprabasal layers, which include the spinous, granular, and cornified layers from below. The entire transformation from stratum basale to stratum corneum shows a variety of changes that took place, including a change in cell type, from cuboidal and nucleated cells to polyhedral prickle cells to anucleated squamous cells. These changes depict the transformation process, i.e. *Abhipachyamanam,* that Ayurvedic scholars have speculated for the formation of the skin.

Table 1: Skin Layers Described in Ayurveda: Potential Modern Correlations

Layers of Skin		**Measurement (in Vrihi)**	**Disease**	**Probable correlation with location**
As per Charak [18]	**As per Susruta [19]**			
Udakadhara	Avabhasini	1/18	Sidhma, Padmakantaka	Pityriasis versicolor (Stratum corneum) Papillomas(epithelial surface)
Asrigdhara	Lohita	1/16	Tilkalak, Nyaccha, Vyanga	Moles (epidermis) Melesma(epidermis/ dermis both)
3rd layer seat of Sidhma and Kilasa.	Sweta	1/12	Charmadala, Ajagallika, Mashaka	Dermatitis (Stratum corneum lipid layer)

4th layer seat of Dadru and Kustha	Tamra	1/8	Kilasa, Kushtha	Leprosy (all layers of epidermis)
5th layer seat of Alaji and Vidraddhi	Vedini	1/5	Kushtha, Visarpa	Leprosy Erysipelas(dermis)
6th layer deep-rooted ulcers	Rohini	1	Granthi,Apachi, Arbuda, Slipad, Galaganda	Lump, Tumour, Filariasis(hypodermis), Goitre
-	Mamsadhara	2	Bhagandara, Vidradhi, Arsha	Fitula-in-ano, Abscess (subcutaneous layer), Piles

Panchbhautika Composition of Skin and its Relation with Srotas:

Panchabhautika Composition of skin:

The human body and its organ are Panchabhautika [20], similarly the different biophysical characteristics in Twacha are imparted by Panchamahabhauta like Softness (Mriduta) and Unctuousness (Snigdhata) of Twacha are imparted by Jala Mahabhuta, Lusture (Abha) and Complexion (Varna) by Teja Mahabhuta, all kind of sensations by Vayu Mahabhuta, Skin pores and channel carrying sweat (Swedavahi Srotas), intracellular and extracellular space by Akasha Mahabhuta. Twacha is the site for general sensations (Sparshanendriya Adhisthana) which also is the main site of Vata dosha. [21].

Skin complexion: As per Ayurveda the normal complexion is determined by Doshaja Prakriti type, which remains the whole life [22]

Although the complexion depends on various factors namely:

i) The functional state of Dosha, Dhatu and Mala.

ii) Genetic constituent relating to individual Prakriti and constitution of Mahabhuat at the time of embryogenesis.

iii) Quality of Shukra(semen), Matruja Ahara Vihara (maternal dietary pattern and lifestyle).

iv) Desha (place) and Kala (season)[23]; external factors like exposure to sunlight, pollution etc.

v) Nutritional status or Dhatu Sara, and amount of Haemoglobin circulating in the body. Any alteration or abnormality in the functional state of these factors is reflected by the changes in the skin including complexion.

It has been suggested that human skin colour can be traced back to a genetic variation. There are four regions in the genome where variations can be predicted to change skin colour. One of the most prominent associated genetic regions is at the SLC 24A5 gene. Some of the other genes of interest are: - MFSD12 - OCA2 - HERC2 - Light skin pigmentation as observed in the population of African San shared by Europeans [24]. Prakriti (psychosomatic constitution) [25] remains the same throughout life and has specific traits like, Vata Prakriti person shows less lustrous skin with a darker complexion. Pitta Prakriti person has fair body colour and reddish black spots on their body. They have moles, wrinkles & and hairs that turn grey early. Pitta Prakriti person's body & his nails, eyes, lips, palms & and soles are copper coloured. The complexion of Kapha Prakriti person resembles the colour of a blue lotus (Nymphaea caerulea) they are beautiful, tender & and of fair colour.

Table: showing the composition of Mahabhut resulting in different complexion of skin at the time of embryogenesis. (Table 2)

Complexion	**Charak [26]**	**Sushrut [27]**
Gaura(fair)	Teja, Jala, Akash	Teja, Jala
Krishna (black)	Teja, Vayu, Prithvi	Teja, Prithvi
Shyama	All Mahabhut	-
Gaura Shyama	-	Teja, Jala, Akash
Krishna Shyama	-	Teja, Prithvi, Akash

Vagbhtta quoted that the colour of Shukra determines the complexion, if Shukra (semen) is of Shukla (white) colour like Ghritamanda (supernatant fluid of ghee), the colour of the offspring will be Gaura Varna (fair complexion) etc. [28] This may be the nutrients present in the semen like fructose, citric acid etc. which leads to differences in nutrient quality. Maternal lifestyle also affects skin complexion like if the mother indulges in Madhura (sweet foods) such as Kshira (milk) etc., and in water sports, the complexion of the child will be Gaura (whitish-yellow).

If we see the concept of Panchmahabhut regarding complexion, Sushrut has also mentioned that Teja Mahabhuta is responsible for the manifestation of all types of Varnas(complexion) of the skin [27] these Mahabhuta forms the external factors like ultraviolet radiations, exposure to sunlight etc, areas receiving higher UVR, have darker-skinned populations as the number of active (melanin-producing) melanocytes can be increased by UVR exposure, while areas having low-intensity UVR, is reflected by lighter-skinned inhabitants [29]. Exposure of human skin to UVR results in a profound alteration of the metabolism, structure, and function of epidermal cells. These activities include increased activation of melanocytes, augmentation of melanosome production, and an increase in the size of melanosome complexes incorporated within keratinocytes. [30]

Another factor responsible for normal complexion is Bhrajaka Pitta present in the skin, it may be related to the activity of melanin pigment secreted by melanocytes, which is the main determinant of the skin colour of darker-skinned humans. The determinant of people with light coloured skin is mainly the bluish-white connective tissue beneath the dermis and by the circulating haemoglobin in the veins of the dermis [31]. Charak has also quoted that Rakta(blood) causes differences in the complexion of the body [32]. Another important factor that determines the complexion is the nutritional status of the skin or the tissues which may be related to Sara in Ayurveda. Sara reflects the nutritional status of the body; good skin shows good nutritional status of the body. A person taking appropriate amounts of food and vegetables in the diet leads to positive associations with skin colour.

Skin as Updhatu:

According to Charak the skin and adipose tissues (Meda) are Updhatu of Mamsadhatu [3]; however, the skin's role is to shield the muscle from foreign substances rather than to nourish it. In addition to serving as a thermal insulator, shock absorber, body shape, and energy storage zone, the hypodermis of the skin, which is made up of fat cells (Meda), serves to secure the skin to the underlying muscle [14]. The Meda connects and supports the skin and the muscle, and it is composed of a network of fat cells (up to half of the body's fat) organised in lobules. Several recent investigations have shown that adipocytes and myocytes have mutually dependent metabolisms, with adiponectin and adipokines secreted by adipocytes and myokines secreted by muscle tissue respectively influencing the metabolic rates [33]. This suggests that the skin and fat are the Updhatu of the Mamsa Dhatu.

Relation with Srotas: Skin is described as one of the roots (Mulasthana) of Mamsavaha Srotas and Upadhtu of Masadhatu that is closely related to Swedavaha Srotas[4] Chakrapani has described Srotomoola as the organ or the structure of origin of pathogenesis or through which the characteristics of Srotodushti get manifested or can be examined [34]. Thus, the diseases of Manshavaha Srotas like Charmakeela(˜warts), and Granthi(nodule) are examined in the skin.

Swedavaha Srotas carrying the sweat have their root in the adipose tissue and hair follicles. The symptoms of their vitiation are less perspiration, burning sensation and dryness, excessive perspiration, and unctuousness manifested through the skin [4]

Physiological aspect:

Skin as a protective organ: Skin continuously challenges the external environment and serves as a primary defence system. Its protective functions include UV protection and antimicrobial functions. Stratum corneum, the outermost layer comprising of lipid matrix forms the first barrier for the skin, it prevents compounds from the external environment from permeating into the viable epidermal and dermal layer thus instigating an immune response.[35]. As per Ayurveda scholars, the Mriduta (softness) and Snigdhata (unctuousness) of skin are imparted by Kapha Dosha. This property of Kapha along with the properties of Meda dhatu forms an oily layer in the outermost layer of skin, thereby providing protection thus safeguarding tissues and, in this way, helping in imparting innate immunity. The immune system within the skin is in both major structural compartments: the epidermis and dermis and consists of several important types of immunocompetent cells. Main skin-resident immune cells, Langerhans cells (LCs) together with melanocytes that produce melanin, occupy the epidermis, whereas the other types of immune specialized cells such as various dendritic cell (DCs) subpopulations, macrophages, and several T cell types reside in a deeper layer—dermis. [36]

The innate immune system comprises all inborn defence mechanisms, thus protecting by inducing instant responses against potentially harmful microorganisms such as bacteria, fungi, and viruses. Innate immunity includes resident cells such as keratinocytes as well as dendritic cell (DC) and lymphocyte subsets. These cells serve as critical first responders in host defence. This includes epithelial cells, DCs, macrophages, mast cells, and innate lymphoid cells (ILCs)

Skin immune adaptive response is induced by dendritic cells present in the epidermis; they are responsible for the capture, processing, and presentation of antigens to T lymphocytes in local lymphoid organs.

The Langerhans cells are responsible for suitable adaptive response by blocking the miroenvironmental framework in which these cells bump into antigens.[37]

Immunoglobulins, also known as antibodies, are glycoprotein molecules produced by plasma cells (white blood cells). Epidermal cell derived IgG and IgA were found mainly in prickle cells and basal cells respectively. [38]. They act as a critical part of the immune response by specifically recognizing and binding to a particular antigen, such as bacteria or viruses, and aiding in their destruction.

Hydration of skin

Good skin hydration is essential to maintain a healthy and youthful complexion. The most important factor that regulates the hydration in stratum corneum are lipids, sebum, natural moisture factor and aquaporin in skin. Water content of stratum corneum depends on four key processes – water binding capacity and barrier properties of stratum corneum, water gradient across the stratum corneum, and its transporter function.[39] The study of skin hydration according to different Deha Prakriti lifestyle.

Vata Dosha has Vayu (air) and Akasha Mahabhuta (space elements) predominance which increases dryness of skin causing evaporation, thereby water cannot be retained for longer time, leading to dryness. Similarly, Pitta Dosha has Teja Mahabhuta (fire elements) predominance. Teja and Jala Mahabhuta in combination imparts little unctuousness to skin. In Kapha Prakriti, Kapha Dosha has predominance of Jala (water element) and Prithvi Mahabhuta(earth element). Since, Jala Mahabhuta (water element) has Drava (liquid), Stimit (wet or moist), Shita (cold) and Snigdha(unctous) property, it is responsible to maintain moisture in body, performs Snehana Karma (maintain oiliness). According to Hemadri, Sneha property causes Kledana (water-lodging retention of moisture) that moisturizes the skin.

Skin as sensory organ: The skin is the largest sensory organ in our body, and it further contributes to homeostasis by sensing various changes occurring at the border of the two environments, including thermal disturbances, and triggers defence responses [40]. Among five sense organs (Gyanendriya), Sparshanendriya (organ of general sensation) is a major sensory organ situated in skin [5], Vata Dosha is situated in Sparshanendriya, all the general and special sensations of the body are carried out through the Vata Dosha. Pitta dosha is involved in regulation of visual senses[41]. Along with Vata dosha, Rakta is also responsible for proper perception of sensations [42], absence of blood supply leads to decreased sensory activity.

These sensations may be altered in different clinical conditions like in case of Vata Kshaya(hypofunctional state) there is less responsiveness towards any stimulus, reflexes or sensations also gets diminished, leading to delayed walk and talk and inactiveness in any of the work [43], features like unwanted movements of the body, tremors, loss of consciousness, decreased strength and capacity of sensory organs are manifested in cases of hyperactivity of Vata Dosha. [44]

Hyperactivity of Pitta leads to weakness of the sense organs and hypoactivity leads to stiffness of the body and tremors.[45]

Table 3: Skin being seat of one of the sense organs has following five components (Indriyapanchapanchak

Indriya	Sparshana indriya (organ of general sensation)
Dravya	Vayu Mahabhuta (generation of receptor potential, action potential and transmission to the brain)
Adhishthana	Twak (skin)

Artha	Sparsha (sensations like touch, temperature, pain, pressure etc)
Buddhi	Sparsha Buddhi (respective cerebral cortical areas of brain of different kind of sensation)

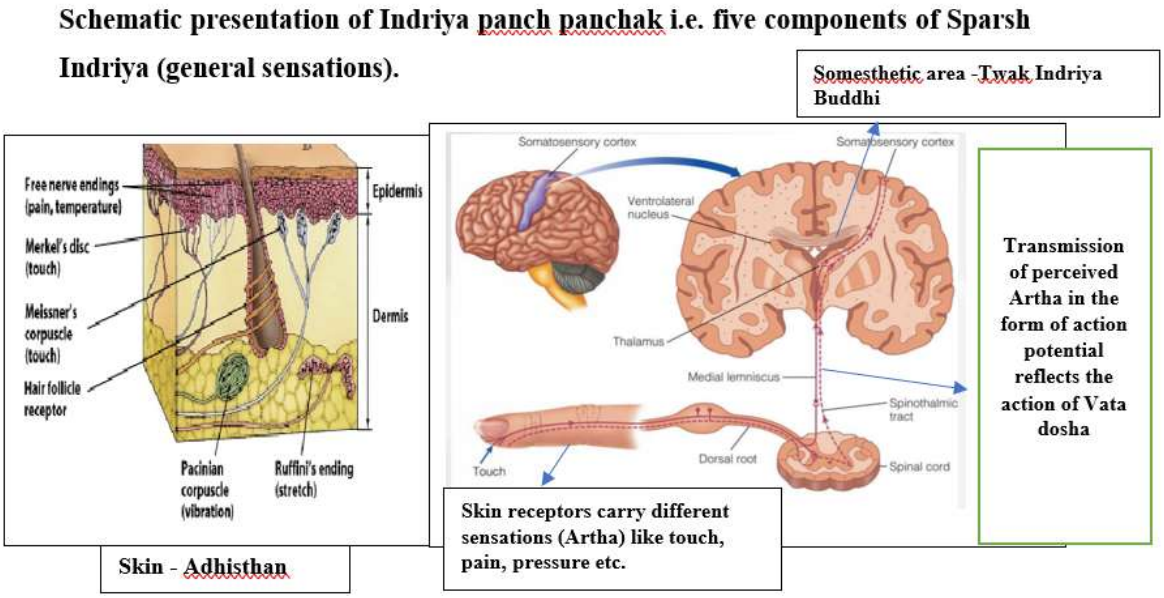


Figure. 2 Skin and psychosomatic relation:

Both the skin and nervous system are derived from ectoderm in the fetus, develop adjacent to each other and remain interconnected throughout life. Skin and brain continually interact through psycho-neuro-immunoendocrine mechanisms, thus any kind of mental stress can strongly affect the initiation or flaring of skin disorders. It is important to consider these mind-body interactions when planning treatments for specific skin disorders in individual patients.

Charak has described the skin (twacha) as 'chetah samvaayi' i.e., the skin has an eternal relationship with Manas (psyche/mind)[46]. Therefore, any mental stress due to any cause has a direct impact on the skin. Skin and mind grossly differ with each other but share some similar characteristics. Vata being the controller and stimulator of mind has an inseparable relation with the skin, which is responsible for tactile sensation. Among the five varieties of Vata, Prana Vata is situated in the brain and regulates activities of Buddhi (higher intellectual functions of brain), Chitta (mind), Hridya (brain & heart) and Indriya (senses)[47]. The function of skin depends on the functional state of Vata, Pitta and Kapha dosha. The tactile sensations are perceived through an association of skin and mind leading to different kind of emotions either pleasurable or painful. Skin is closely connected with the nervous system and is very sensitive to emotions. It turns pale and clammy during fear, it blushes when embarrassed and glows due to happiness. Anger, depression, etc cause different hormonal changes in the skin. In case of Kustha roga, aetiology involves indulging in different sinful acts (Papa-Karma) like disrespecting elders, abusing teachers etc causes fear, rage, sinking feeling etc, factors like chinta(stress), shoka(depression), bhaya(fear) and other forms of anti-social or anti ritual activities leads to stress which directly or indirectly plays major role in manifestation of skin diseases (Kustha Roga) [48] and no effective treatment for Kushtha is available till now. As per modern literature, now a days skin diseases run a chronic course and dermatologists ultimately end up in making use of corticosteroids to get symptomatic relief.

It is well acknowledged that psychological stress plays an important role in the pathophysiology of numerous skin disorders. However, the strength of association between stress response and the onset, recurrence or exacerbation of various skin diseases varies. The skin disease best known as the stress associated and by far the most intensively studied for this association is psoriasis, with 40-60% of cases triggered by stress. Stress activates various neural pathways. The main stress response systems are the sympathetic-adrenal medullary system and the hypothalamic-pituitary-adrenal (HPA) axis. Corticotropin hormone (CRH) is a central component of the HPA axis and regulates the expression of pro-opiomelanocortin (POMC) and POMC-derived peptides [adrenocorticotropin (ACTH), melanocyte-stimulating hormone (MSH) and endorphin] from the anterior pituitary gland. CRH has a pleotropic effect in the skin depending

on the cell type and experimental growth conditions. CRH-R1 activation, which modulates proliferation, differentiation, apoptosis and pro-or anti-inflammatory activities of skin cells.[49]

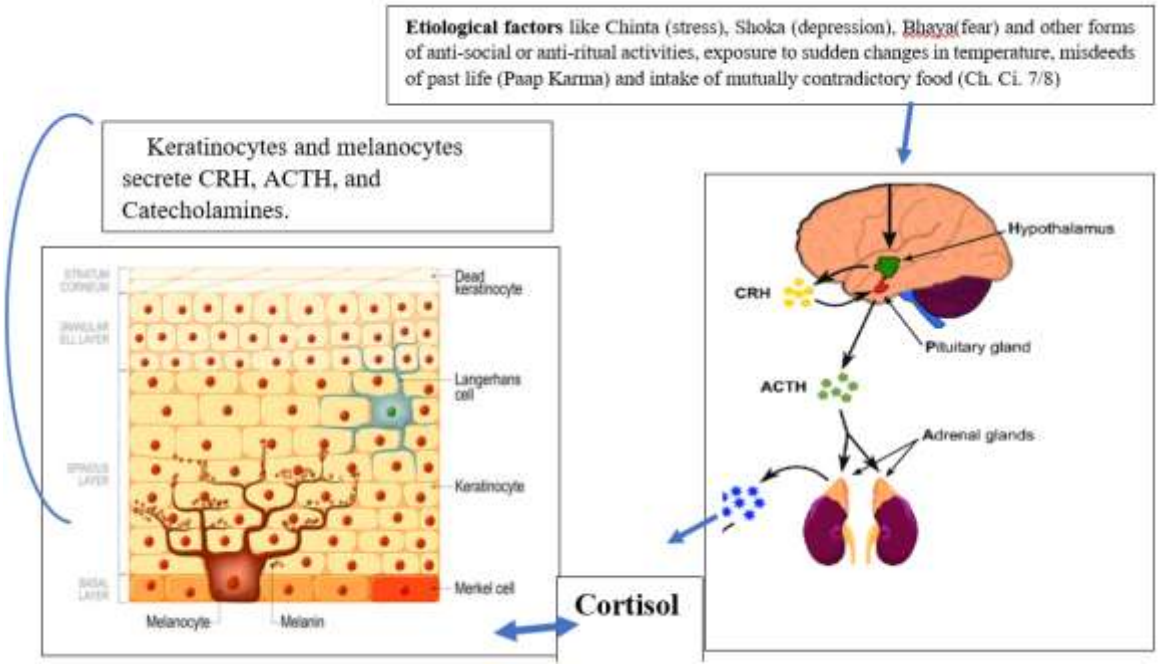


Figure 3. Skin and Psychosomatic interactions.

Role of skin in temperature regulation and Sweating mechanism

The body temperature is regulated by the functional state of Pitta Dosha [50]. Charak has described the mechanism of temperature regulation while describing the sweat formation. On exposure to the heat fraction of body water(udaka) which comes out from the roots or body pores of skin is Sweat.[51] . During the process of sweating there is loss of body heat along with sweat because of Aashraya Aashrayi relationship with Pitta Dosha[52]. Bhrajak Pitta residing in the skin also plays role in maintaining the shell temperature of the body. As we know epidermis is devoid of blood supply and the capillary network are present within dermis, there is presence of arteriovenous anastomoses at all levels in the skin which allow a direct shunting of up to 60% of the skin blood flow between the arteries and veins, from here nutrition or exchange of substances takes place, these vessels play important role in skin's functions of heat regulation [53]. Ayurveda has also recognised role of cutaneous blood flow and has described the role of vessels responsible for sweating in the form of network of triyaka Dhamni (diagonally placed vessels) supplying the skin. These vessels are basically 4 types but get divided into multiple times and form network just like that of the capillaries present beneath skin. These capillaries are related with hair follicles for the formation of sweat and for nutrition of the body[54].

Temperature regulation on exposure to cold and heat: when body gets exposed to heat, in adaptive response there is sweating to lower down the body temperature. Pitta Dosha is responsible for all kind of transformations i.e. digestion and metabolism resulting in heat production. Therefore, Sweat is helpful in maintenance of body temperature along with Pitta. On exposure to cold leads to sympathetic stimulation causing increased metabolism, heat production and vasoconstriction in skin vascular bed that prevents the heat loss. As per Ayurveda exposure of cold leads to hyperactivity of Vata dosha which causes the closure of body pores (Romakoopavrodha) thus prevents the external heat loss and the heat gets internalized.

Regulation of Sweating: Amount of sweating depends on the cutaneous circulation, on exposure to heat cutaneous circulation increases as an adaptive response to enhance sweating. Samana vata regulates Swedavaha srotas [55] and therefore formation of sweat. Vyan vata is responsible for secretion or oozing of sweat and for changes in circulation of blood beneath the skin. [56]. Therefore, this mechanism may be related with autonomic nervous regulation involved in thermoregulation.

There is an individual variation in the amount of sweating which has been described and the characteristics of Prakriti also, the rate of sweating also depends on quantity of Meda i.e. subcutaneous fat and adipose tissue in the body.

Charak has described that obese persons perspire more[57] and sweat is considered as mala(waste) of Meda Dhatu [58].

Skin as metabolic organ: the skin is a metabolically active tissue that contains enzymes able to metabolize endogenous chemicals such as carbohydrates, lipids, proteins, and steroid hormones as well as exogenous chemicals like topically applied drugs. Ayurveda states that it is the Bhrajak pitta in the skin, which is responsible for various chemical changes in the skin, it plays role in absorption and biotransformation of a drug. Sushrut has described this function of Bhrajak pitta as "Kriyadravyanampakta" for depicting its role in the metabolism of any medicaments applied topically in form of Abhyang (oil massage), spray (Paisheka), Tub bath (Awagaghan), etc.[59].

Skin a vital route for drug administration and site for management of diseases:

Skin is one of the routes for drug administration, through which different topically applied substances like ointments, dermal patches, spray etc. are absorbed and bio transformed. In Ayurveda various measures involving skin have been suggested for disease management, including therapies like external oleation (snehan) and sudation (swedan), which are a prerequisite in Panchkarma therapy, it balances Vata and Kapha dosha in the body, improves circulation, dislodge toxins and expel them through the pores of the skin along with sweat etc. [60] Ayurveda mentions the benefits of everyday Abhyanga practice for healthy and bright skin [61] Skin can be used as a site to treat various blood related disorders and other diseases by Raktamokshan (blood-letting therapy), lepa administration (topical cream, gel etc), Avagahan (tub fomentation). It is also used as a site for Agnikarma (therapeutic heat burn) to treat disorders like osteoarthritis, moles, warts etc.

All the enzymes present within the skin could be related with the functions of Bhrajak Pitta, most of them are found in keratinocytes and roots of hair follicles. The dermis also shows enzymatic activity, but it is much weaker than that of the epidermis. Some enzymes found in skin are: Cytochrome P450, Flavin-dependent monooxygenase, Cyclooxygenases, Alcohol dehydrogenase, Aldehyde dehydrogenase, NAD(P)H: quinone reductase, Carboxylesterase, Glutathione S-transferase, N-Acetyltransferase**. [62]**

Enzymes	Location	Function
Cytochrome P450	epidermis sebaceous glands	endogenous and exogenous substrate metabolism in the skin.
Flavin dependent monooxygenase (FMO)	epidermal keratinocytes	It mediate bioactivation of sulfamethoxazole and dapsone in human epidermal keratinocytes this signifies its role in drug metabolism.
Cyclooxygenases (COX)	COX-1 is present throughout the epidermis whereas COX-2 localizes mainly in supra basal keratinocytes	that COX-2 and COX-2-derived prostaglandins play a key role in keratinocyte differentiation
(ADH) Alcohol dehydrogenase (ALDH)Aldehyde dehydrogenase	epidermis, sebaceous glands, and hair follicles	important for the toxication and detoxication of some compounds which cause allergic contact dermatitis, such as trans-cinnamaldehyde and trans-cinnamic alcohol.
NAD(P)H quinone reductase	keratinocytes	its main role is to protect skin from the toxicity of quinones
Carboxylesterase	keratinocytes	Carboxylesterases 1 and 2 (CES1 and CES2) are involved in the metabolism of xenobiotics. For example, CES1 activates prodrugs of angiotensin-converting enzyme inhibitors and CES2 activates the anticancer prodrug CPT-11.
Glutathione S-transferase (GST)	foreskin	important contributor to the direct detoxification in the human skin of aromatic amines.

N. Acetyltransferase (NAT)	epidermal keratinocytes	an important contributor to the direct detoxification in the human skin of aromatic amines

It is also used as a site for Agnikarma (therapeutic heat burn) to treat disorders like osteoarthritis, moles, warts etc. Therefore, through Panckarma pre-procedure, Raktamokshan, Agni karma, Abhyanga, Avagaha, Alepa etc various diseases could be treated.

Factors Influencing the Enzymatic Activity of the Skin:

Anatomical Site and Gender: some enzymes are only found in specific regions of the body. The most prominent example is hydrocortisone 5α-reductase; activities of this enzyme were only found in the foreskin and scrotal skin.

Environmental factors [63] influencing enzyme activity are UV radiation and exposure to air pollutants like polycyclic hydrocarbons, generates reactive oxygen (ROS) species that leads to increased MMP activity in the skin and decreased Hyaluronic acid synthetase activity leads to extra cellular matrix damage and denaturation. ROS also causes DNA damage and mutation, promotes transcription of melanin genes thereby causing abnormal skin pigmentation.

Skin ageing:

Ageing is caused by a combination of internal factors (such as hormone levels, genotypes, endocrine metabolism, etc.), and external factors (such as ultraviolet radiation, nutritional levels, chemical pollution, etc.), it can be divided into chronological aging and photo-aging (or internal aging and external aging). Charak has talked about Kalaja(timely) death and Akalaja(untimely) death of an individual [64].As per Vagbhatt, dominance is seen in circadian rhythms ie in morning there is dominance of Kapha Dosha, in afternoon Pitta Dosha and in night Vata Dosha [65] In case of Kalaja death, person ages in chronological manner different changes occurs as per age like Pitta and Kapha Dosha decreases in old age leading to decreased nourishment to the cells and tissues of the body. However, dryness, wrinkling etc. shows increased activity of Vata Dosha in old age.

In case of Akalaja death various factors like faulty diet and unhealthy lifestyle, exposure to sunlight etc. lead to premature ageing causing vitiation of Bhrajaka Agni leading to its malfunctioning and therefore causing early ageing. Following changes takes place in the skin with ageing:

- The most consistent structural change in aged skin is that the dermo-epidermal junction gets flattened by more than a third, it happens due to the loss of dermal papillae as well as a significant reduction between layers [66] which in turn causes less resistance to shearing forces and an increased vulnerability to insult, suggesting reduction in the functional state of the kapha dosha [67] and increased activity of Vata dosha.
- As the epidermis shrinks and turnover slows, keratinocytes, as the skin gets older, shrink in size, becoming smaller and fatter while corneocytes grow larger due to reduced epidermal turnover, this may be due to hypofunctional state of Kapha dosha and decreased activity of Bhrajaka pitta leading to decreased turnover rate.
- Due to reduction in the activity of Bhrajak pitta uneven pigmentation and enzymatic activity is altered as one ages, tissue also functions at a slower rate and there is reduction in sebum production upto 60% indicating decreased activity of kapha dosha and Meda Kshaya.
- Global lipid content of the aged skin is reduced as much as 65%. Changes in the amino acid composition in aged skin may reduce the amount of cutaneous natural moisturizing factor, thereby decreasing its capacity for water binding [68] may be understood in way of Dhatu Kshya in old age.
- Dermis thickness decreases with age, thinning is accompanied by a decrease in both vascularity and cellularity. There is also a decrease in the number of mast cells and fibroblasts. The amount of glycosaminoglycans in the dermis declines with age, as does the amount of hyaluronic acid produced by fibroblasts and the amount of interfibrillar ground substance this may be understood as reduced Dhatwagni and Dhatu kshya.

Skin a site of clinical examination

Ashtavidha pariksha **(eight-fold of examinations)** mentioned by Yogaratnakara includes 8 specific sites of clinical examinations including skin, which are helpful in diagnosing different disorders. Charak while describing Pratyksh praman (knowledge by direct perception) has mentioned Sparsh pariksha (tactile perception) [69], different touch perception could be sensed by this examination, like in case of functional state of Vata Dosha there is roughness and dryness in skin and cold perception while in its altered form excessive dryness, roughness, hyperpigmentation and hypothermia is seen, likewise in case of normal Pitta Dosha, , skin is moist in consistency and the skin temperature is imparted, when this gets altered hot flushes, rashes, burning sensation, small eruptions, elevated mole etc. is observed.

While assessing The skin moisture, unctuousness, coldness, thick in consistency is imparted by Kapha Dosha, while in its abnormal condition excessive oily skin with flabbiness etc. is found. In pathological conditions altered tactile perception is observed, like in Kustha roga there is excessive unctuousness or roughness, profuse sweating or absence of sweating, burning sensation, numbness etc is seen [70], in Prameha(Diabetes mellitus) numbness and burning sensations in various parts of body, fever etc. are seen [71]. In Rajyakshama(Tuberculosis), raised temperature is present, burning sensation over hands, fever[72]. Skin tests can help to diagnose allergies, infections, other problems, detects sensitivity reaction. The most common skin tests include Patch test, Prick tests, Intradermal tests, Skin biopsies. In case of abnormal functional state of Dosha Dhatu mala may be observed and may be helpful in detection of their functional state.

Table 5: Skin characteristics as per prakriti reflects the genetic variation skin[73]

Prakriti	**Vatala**	**Pittala**	**Sleshmala**
Features	Roughness in skin, Intolerance to cold, often getting afflicted with cold, shivering and stiffness, abundance of tendons and veins, Roughness of hair of the head, face and other parts of the body, nails, teeth, face, hands and feet.	Intolerance to hot things, having hot face, tender and clear body of port-wine mark, freckles, black moles, excessive hunger and thirst, quick advent of wrinkles, greying of hairs and baldness, presence of some soft and brown hair on the face, head and other parts of the body. voiding of sweat in large quantity leading to putrid smell of axilla, mouth, head and body in excess	Smoothness of organs. Pleasing appearance, tenderness, clarity of complexion, appearance, and voice.

Table 6: Features of different Dhatu Sara reflected in skin [74]

Sara	**Twak**	**Rakta**	**Mamsa**	**Meda**	**Majja**	**Shukra**
Features in skin	Unctuous, smooth, soft, clear, lustrous	Face, palm sole, forehead genitals are unctuous and red	Body without depression, the bony joints are concealed	Complexion, voice, skin hairs, hairs unctuous	Unctuous complexion and sweet voice	Unctuous complexion and brilliant voice

Different characteristics related to functional state of Dhatu and Mala may be also observed in the skin which help in assessment of diseases.

Table 7: Sapta Dhatu karma(functions) and characteristics of Vriddhi (hyper-functional state), Kshya (hypo-functional state) of Dhatu reflected in skin.[75], [76],[77].

Dhatu	**Karma (Normal functions)**	**Kshaya (Hypo-functional state)**	**Vriddhi (Hyper-functional state)**
Rasa	Tarpayati(satiate), Vardhayati(increases) Dharyati (sustains)	Dryness, tremors, painfulsensation, pulsations.	Hypo pigmentation, cold and calmy touch, Angmarda (body ache), heaviness.

Rakta	Enhances complexion, perception to touch,	Dry, crack and lustreless skin	Redness in skin and eyes, prone to skin diseases
Mamsa	Lepan(smearing)	Dryness and pain all over the body,	Heaviness
Meda	Unctuousness in whole body. Provides support to body.	Dryness, emaciation, Crepitations in joints	Excessive unctuousness, weakness
Asthi	Deha dharan(maintains body posture and support body tissue)	Dry, crack skin, joints Pain, bony pain	Increased number of teeth.
Majja	Snehan (Unctousness), Asthi pooran (filling)	joints Pain, bony pain, Altered sensations	Heaviness all over body and eyes, deep rooted ulcer formation
Sukra	Harsha(happiness), priti(affection), deha bala(body strength)	Weakness, anaemic, body ache	-

Table 8: Dhatu pradoshja vicar (tissue related disorder) manifested over skin [78]:

Dhatu	**Disorders**
Rasa	Pandu (anemia), Akala vali,Akala palit(wrinkling of skin and greying of hair)
Rakta	Kustha(skin related disorders), Visarpa(erysiplas), Pidika(furuncles), Nilika(blue mole), Tilkalaka(black mole), Vyanga(blemishes), Gulma(lump), Akala palita (greying of hair),Kamla(jaundice), Piplika (portwine mark), Dradru (ring worm infection), Charmdala (dermatitis), Shwitra(vitiligo), Kotha (urticaria), Pama (scabies).
Mamsa	Adhimansa(granuloma), Arbuda(myoma), Upjihva, Galshundika, Alaji(boils)
Meda	Atisthaulya(obese), Atisweda(excessive sweating)
Asthi	Kesha loma,Nakha, shramshru dosha (abnormality of body hair, beard, nail), Vivarna(discoloration),.
Majja	Parva shola (joint pain), deep rooted abscess in joints.

Table 9: Manifestation of abnormal functional state of Dhatu mala in skin [79]:

Dhatu	Mala
Rasa	Lasika(lymph) it oozes out from injury site of the skin as an exudate[80]. The lymphatic system is an important component of the skin in regulating its interstitial pressure, mobilization of defense mechanisms, and in waste removal.[35]
Rakta	Ranjak pitta by Sharangdhar could be correlated with bilirubin metabolism and in case of hyperbilirubinemia yellowish color imparts over certain parts of the skin, nail beds and conjunctiva
Mamsa	kha mala secretions in outer openings of the body) probable correlation is excretions in ear, eye, nose, oral cavity, genitals this secretion protects their respective orifices. Eg. Ear wax protect the skin of the ear canal against bacteria, fungi, water.
Asthi	Kesha(hair) and loma (body hair).
Majja	Oily secretions from the skin (sebaceous secretions) and eye.
Meda	Sewda (sweat) (secretions in outer openings of the body) it is the dwelling site of the Pitta and has protecting function for skin and helps in thermoregulation
Shukra	Yuvanpidika (Acne) gets manifested over skin especially at puberty and Androgen hormone is responsible for its occurrence. Pitta prakriti are more prone to it.

CONCLUSION

Recently important biological roleplays of skin have been discovered and established in Immunologic, Endocrine, Metabolic, Psycho-social, Neuro-psycho-immunologic process apart from previous protective and thermoregulatory role. The descriptions of Ayurveda also imply that the skin has an important role in protection of the body, in maintaining homeostasis and metabolism. The characteristics of skin and its appendages has important role as a trait in determining Prakriti and Dhatu Sara, diagnosing disorders. Ayurveda has considered skin as an important route of drug administration in the management of several disorders.

This review may assist researchers gain a fundamental understanding of skin biology concerning Prakriti, Sara, Dosha, Dahtu, and other topics. It addresses the interactions of skin with neurological, immunological, cutaneous, and endocrine systems. It provides a wider understanding of Ayurveda's concepts of Psychodermatology, Neurodermatology, age-related changes, defensive functions, and enzymatic activity in the skin.

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