

SKIN DISORDERS IN HIGH ALTITUDE AREAS AND THEIR TREATMENTS: A REVIEW

¹Shalini Kumari, ²Meenakshi Bajpai

^{1,2}Institute of Pharmaceutical Research GLA University Mathura Uttar-Pradesh Pin code- 28140

ABSTRACT

Higher exposure to ultra violet light, less humidity and other factors such as extreme subzero temperature in winter is difficult to resist. When the body does not achieve enough oxygen that condition is refer to as high altitude illness. Due to the extreme height there are many modification in the environmental condition the very low oxygen as well as exposure to UV light more than 3 times over the plane, 14% to 20% low humidity and subzero temperature in winters makes the high altitude area difficult for residence. There are several skin diseases that occur frequently from neonates to elderly people and may cause harm. So, to avoid the risk of skin infection or skin disorder it is important to keep the body healthy as well as protected from harmful ultra violet radiations. Skin disorders can develop through winter weather prevailing in the high altitude areas such disorder are cold sores, chill blains, xerosis, rosacea, actinic keratosis etc. Certain wild plants or part of plant are used in the traditional system of medicine for the treatment of these skin disorder. The use of plant for the treatment is very older method and treatment through plants is cheaper and safer as compared to conventional system of medicine.

Keywords: High altitude areas, skin disorders, ultra violet radiation, medicinal plants

INTRODUCTION :

Around 140 million population from all over the world reside at high altitudes. In India, part of northwest Kashmir, northern part of Sikkim as well as Tenga valley of Arunachal Pradesh, as well as Ladakh region are regarded as the inhabiting area of high altitude areas. Higher exposure to ultra violet light, less humidity and other factors such as extreme subzero temperature in winter is difficult to resist. High altitude usually refers to 8000-12000 feet above sea level. Extremely higher altitude refers to 18000 feet above sea level. When the body does not achieve enough oxygen that condition is refer to as high altitude illness. When a person travels lower altitude to higher altitude the body adjust itself with respect to change in oxygen level.[1,2] Certain symptoms of higher altitude illness are Nausea, Dizziness, Fatigue, Increase heart rate etc. and which may also include several skin diseases which usually cause due to UV radiation from the sun or the extreme cold climate at high altitude. Due to the extreme height there are many modification in the environmental condition the very low oxygen as well as exposure to UV light more than 3 times over the plane, 14% to 20% low humidity and subzero temperature in winters makes the high altitude area difficult for residence. Prolong exposure to ultra violet radiation directly lead to chronic skin disorders. Certain factors at high altitude region lead to cause skin disorder are cold and heat climate condition, higher altitude and water [3, 4]

Environmental and physical factors such as low humidity, low atmospheric pressure, high wind velocity, serve cold and high intensity of solar radiation are responsible for physiological of body. Certain major problems linked with soldiers going on high altitude involves high altitude pulmonary edema, acute mountain sickness, high altitude cerebral edema, lack of appetite, lethargy, stomach upset, muscle and

bone degradation etc. due to which the person become depressed mentally as well as physically. General disease such as high altitude pulmonary edema, high altitude cerebral edema, thromboembolic condition occurs in high altitude. Xerosis, UV related skin infections, cold injuries, skin carcinoma etc. are also detected in high altitude areas [4, 5]

SKIN :

Skin is usually regarded as the largest organ of the body and covers the extremely surface of the body. On the basis of height and body mass, it weigh between 3.5 and 10kg and surface area of about 1.5 to 2sq meter. It serve a lot of different action. It could be termed as stable but flexible outer covering that act as a barrier. Skin safeguard from the body from harmful things from the atmosphere such as moisture, the sun rays, germs as well as toxic particles. Certain modification in the color of the skin and structure could be a symptoms of the medical condition. [6] **Skin** plays crucial role in the maintenance of temperature. It averts dehydration and protects from negative effects of too cold or heat .skin also grant the body to feel certain sensations. It is considers as the storeroom for the body. Deeper layer of skin store metabolic layer products, fats as well as water and produces hormones that play an important part in body functioning. Skin is usually composed of intricate network that serves as the barrier for the pathogens as well as ultra violet radiation. It also maintains the homeostasis of the body. The most important parameter are skin pH, epidermal hydration, Sebum excretion and transdermal water loss. Skin also constitute of 15-20 lyres of fully cornfield keratinocytes- comocytes. [6, 7]

Skin has a major role in immunological surveillance, control of insensible fluid loss and sensory perception At the time of injury, the supply of the blood to the site of the injured tissue increase so as impart various substances to wound to protect it from infections and can heal faster. Skin mainly composed of three main layers: Epidermis, dermis and sub cutis. Older people usually have thinner skin as compared to younger people and women have thinner than men. [8]

Outer layer :

Epidermis is the outer most layer of the skin which is composed of cell that produce **keratin**. The coenocytes are closely packed and seal the off from the atmosphere. The epidermal layer continually renews itself. The new cells are produce in the lower layer of the epidermis. Constant renewal of the epidermal layer replace the cells they are lost and fall as tiny flaks of the skin.

The thickness of the epidermis various according to the site. It is 0.3mm thick on elbows and beak of the knees, 4mm thick on other part of the body such as soles of your feet and palms of hands. [9, 10]

Epidermis also consists of other cells-

Melanocytes

Lymphocytes and Langerhans cell

Markel cells

Middle layer :

Dermis is present below the epidermis it is made up of dense network of elastic collagen fibers. Dermis is responsible for making the skin strong sturdy as well as stretchy. Dermis also consists of network of nerve fibers and very small blood vessels. Oxygen and nutrients are supplied through the capillaries. It also helps to cool the body

The deepest layer :

Subcutaneous layer and hypodermis is composed of fat and connective tissues. Tiny cavities are present between the folds of dermis which are filled with storage tissues. Fat present the cavity act as shock absorber and protect the joints and bones and it also provide insulation. Vitamin D is a hormone present in skin. [11, 12]

SKIN RELATED DISORDERS IN HIGH ALTITUDES :

Xerosis :

Xerosis is a condition which experienced by majority of people. Exogenous factors that usually contribute to xerosis include the living in colder climate specifically in the winter month. Extreme bathing could also dry skin. Certain skin cleanses contain surfactants that emulsifying the skin lipids .The concentration of water in the skin declines due to low relative humidity as well as temperature collaterally with high wind velocity, xerosis is skin disorders that start to cause pertussis and cracks in the skin as well as oozing and fissuring The utilizations of soap should be reduced especially over face, hands, groins and armpits. Utilization of emollients such as oils or lotion (coconut or olive oil) after bath may be effective. Scalp area could become dry application of steroids or antibiotics in harmful. Weekly use of soap or miler shampoo along with conditioner should be use. [14, 15, 16]

UV Related Skin Disorder :

Solar radiation leads to certain abnormal cutaneous reaction such as photomelanosis, acute and chronic sunburn, chronic actinic dermatitis, tanning, polymorphic light eruption, actinic cheilits etc. Maximum intensity of ultraviolet for radiation lies between 10a.m and 3p.m. both UV- A and UV- B are catastrophic for the skin but UV_B components is the reason for acute skin infection. [1, 17]

Acute Effects of Ultraviolet Radiation :

Erythema as well as enhanced melanogenesis is the major acute of uv rays. Various broad range of acute effects involves immunosuppressive, Vitamin D synthesis and DNA photo damage.Erythema or sunburn inflammation generally requires 12-24hrs to become peak and faded after 1-3days and it is then retrieved by pigmentation. Melanogenesis is usually common in mountaineers and it could be elevated by the so called "albedo effect". Generally a major part of the ultra violates rays i.e. 90% is reflected by the snow while 9-7% is reflected from the ground covered by grass. [1, 18]

Prolong Exposure of UV :

Leakage of the median and hyperpigmentation into the dermis and is taken up by meloanophores that lead to the dermal of and is taken exfoliation to HA. Long term exposure to the sun rays at higher altitude

could cause tanning over exposed areas of body usually on face, dorsum of hands as well as on 'V' area of neck. The commonest site of chronic dermatitis is dorsum of both hands and nape of the neck. Acute cheilitis refers to the erosion or over the lower lip. Certain use of sunscreen which constitute mixture of organic UVA and UVB filters are as well as inorganic filters are very efficacious. Gentle application of sunscreen over the face or hands should be done. And it should be reapplied after 3-4hrs. While dermatitis or chronic actinic generally needs to utilization of oral steroid or immunosuppressant. [1, 18]

Skin carcinoma :

Human being having light skin or eyes is more prone to skin cancer. A prolonged effect of uv radiation on white skin people is the skin cancer generally basal cell carcinomas and malignant melanoma. [19]

Cold related injury (chilblains, frost bite):

In wintertime, the temperature in the high altitude area declines down to -30°C while snow founded mountains it may dip down to -60°C. so people should to precariously move down to prevent themselves from chilblains or frost bite. It is usually an inflammatory skin disorder which characterized by pain and itching well as redness. It generally attacks the fingers, nose tip or ear pinna. People having low (BMI) or genetic predisposition are more to prone chilblains. Application of emollients, soaking the feet in lukewarm water and wearing nylon socks are some precautionary steps against chilblains. Unusual symptoms of chilblains are firmness, stinging numbness, and clumsiness, throbbing, furring or electric current-like sensation, coldness. [21, 22] When frost bite is more severe i.e. when it affected the deeper tissue it would be labeled as 2nd, 3rd and 4th degree. The fourth degree frost bite would be damage the muscles, tendons and bones that might result in the loss of certain tissue to cure it the patient require surgical medication such as amputation. [1, 23]

Cold sore :

Cold sore is affiliated with typical itching or tingling around the lips. The causative agent is a type of contagious herpes virus already present in their body but that do not cause cold sore most of the time. Herpes labialis could be related to the formation of painful blister specifically on one side of the lips but these blister are spreadable. Survey done in north Wales to regulate the frequency, duration, incidence and severity of cold sores revealed that out of 1855 adults 46% were the victim of cold sore at some time but 25% continued to have one or more a year. Cold sore from a painful vesicular eruption that lead to the formation of unsightly crusting that cause physiological discomfort and cosmetic disfigurements no cure is available for cold sore, and it reoccurs annually. [24]

Actinic keratosis :

It is usually regarded as a field disease that restricted to single clinically apparent lesion. These are linked to cutaneous lesion correlated with chronic exposure to ultraviolet radiation. Actinic keratosis is present as scaly, erythematous plaque. These are mostly found in fair-skinned people or the person whose immune system is suppressed. It could be stable or may get transformed to invasive SCC. The major mechanisms for the formation of actinic keratosis are inflammation, immunosuppressant, oxidative stress, mutagenesis, tissue remodeling and deregulations of cell growth and proliferation. Actinic keratosis could also occur as a result of adverse action of UV radiation on the keratin DNA that would

lead to certain change that decrease skin immunity. Due to prolonged sun exposure it could progress to non-melanoma skin cancer. [25, 26]

Rosacea :

It is chronic inflammatory skin disorder that usually affects the nose, cheeks forehead and chin in other words it is a chronic facial skin disease. It affects women more than men. The activation of immune system occurs through the multiple stimuli which also include the increase levels of cathelicidin and kallikerin5, toll-like receptor3, mast cell with in cells. It could be treated through gently skin cleansing, avoidance of excel bating factors and photo portion such as modification in ultraviolet light, alcohol and some foods , temperature and stress . Certain primary feature such as flushing, pustules, telangies classes, non-transient redness, popular would indicate rosacea. Symptoms and severity fluctuates between periods of exacerbation and remission. [27, 28, 29]

TREATMENT OF SKIN DISORDER THROUGH AYVURVEDA, ALLOPATHIC AND HOMEOPATHIC :

Ayurvedic treatment of skin related disorder :

The drugs which are obtained from the plant are attaining popularity due to certain advantages that may include their better therapeutic efficiency lesser side effects, better patient tolerance and they are comparatively cheaper than the synthetically obtained as well as easily acceptable by a wide range of people due to the long history of use, along with the such advantage herbal drugs also provide the rational means treatment of various disease that are incurable obstinate in other system medicine for such reasons wide varieties of plant and tree have been studied and researcher so as to obtain natural drug from than for the treatment of skin related disorders ranging from itching to skin cancer. [30] By far the investigation some plant have been reported which gives the evidence of their effectiveness in various skin diseases, some are mention below

Table no-1 List of medicinal plant with their formulation against skin disorders

S.no	Plant names	Family	Uses	Formulations	Ref.
1	Neem <i>Azadirachta indica</i>	Meliaceae	Anti-inflammatory Anti-septic also used in rosacea, eczema, psoriasis	Topical formulations and body wash	31,32,33

2	Turmeric <i>Curcuma longa</i>	Zinziberaceae	Anti-inflammatory agent. Antimicrobial Used in pains and bruises. In cosmetics	Gel, cream, ointments and oral formulations	34
3	Onion <i>Allium cepa</i>	Liliacea	Scar softness, redness, texture	Gels, creams	35,36
4	Garlic <i>Sativa</i>	Liliaceae	Cellular defense system	Gels	37
5	Neem <i>Azadirachta indica</i>	Meliaceae	Anti- acne	Moisturizer	32,33
6	Devil's horsewhip <i>Achyranthes aspera</i>	Amaranthaceae	carcinogenesis	Gel, extraction	38
7	Wallich spurge <i>Euphorbia walachii</i> , <i>Euphorbia hirta</i> ,	Euphorbiaceae	Skin infection Antimicrobial activity	Cream, ointment	39,40
8	Fig <i>Ficus carica</i> , <i>Ficus racemosa</i> , <i>Ficus bengalensis</i>	Moraceae	Pimples, itches, sabies	Topical formulations	41, 42

9	Henna <i>Lawsonia inermis</i>	Lythraceae	Impetigo, anti-pyretic anti-inflammatory, and analgesic	topical formulations	43,44
10	Purslane, Pigweed, Little Hogweed <i>Portulaca oleraceae</i> ;	Portulacaceae	treat burns, earache, insect stings, inflammations, skin sores, ulcers, pruritus (itching skin), eczema	Topical application of the aqueous extract	45,46,47
11	Rosemary <i>Rosmarinus officinalis</i>	Labiatae	preventing cutaneous photo damage induced by UV radiations	Topical application of leaves extraction	48,49,50
12	Ashoka <i>Sarco asoca</i>	Caesalpinaceae	freckles and external inflammations, ulcers and skin diseases	bbing the crushed flower on the skin	51
13	Thyme <i>Thyme vulgaris</i>	Lamiaceae	pain, tenderness, edema, fever, chills and reddening of the skin	Topical formulation	52,30
14	Bitter gourd <i>Momordica charantia</i>	Cucurbitaceae	Carcinogenic	Topical application of fruits extraction	53
15	Four o'clock flower, Marvel of Peru <i>Mirabilis jalapa</i>	Nctaginaceae	allergic skin disorders and asthma	Root extraction of topical formulation	54

Conventional treatment of skin related disorder :

Conventional or oral drug delivery system produces a specific drug concentration in systemic circulation.

Table no-2 List of conventional formulations of skin disorders [55]

S.No	Drug	Uses	Formulations	Side effects
1	Mupirocin and Clindamycin hydrochloride	Prevent infections	Oral formulations	burning, stinging, and irritation,
2	Drithocrema, micanol	Reduce inflammation and can help treat psoriasis	Gels	diarrhea, headache, irritability
3	Lamisil, lotrimin and nizoral	Antifungal	Cream, gels and lotions	nausea, vomiting, dizziness and fatigue
4	Benzoyl peroxide	Used to treat acne	Cream , gels	mild stinging or burning; itching or tingly feeling; skin dryness and peeling
5	Corticosteroids	eczema	Foams, lotions, ointments and creams	osteoporosis, hypertension , diabetes, weight gain
6	Retinoid	Acne	Gels or creams	dryness, tightness, peeling, and redness
7	Salicylic acid	Used in acne and warts.	Lotions, gels,	burning, dryness, or

Homeopathic treatment of skin related disorder :

Usually homeopaths divided into three parts:

1. Local
2. Mental

General :

In local indicates the particularly a skins problems this means shows the skin related disorders, Mental indicates the factories of the person like personally and physiological features and the generals indicates the physical appearance pf person. In skin problems Arsenicum album and Sulphur largely similar in condition of the skin manifestation which is produce strongly itchy rashes which is feel like burning after scratching. [56] Rashes are prone to react to arsenicum bear to be on small roundish patches and flaky, while the above mentioned which reacts to sulfur commonly happen huge, red sphere, yet these distinction generally, not satisfactory and its generally challenging to be assure that which medication is designating on the basis of locals alone. [57] Homeopathy isn't the sole quite homeopathy and unless one among the pictures and unless one among the pictures define the above actually appear to suit , probably best left to practitioner. The counting of so called small homeopathic medicines is vast and many times symptoms specific, generally referred as "kyenot". These comprise to petroleum (made from crude oil). Keynote of the medicine perceptible with devolution in winters. This found utilitarian in children who gets thick cracked skin at knuckles. Many patients helped by this medicine have told me that although they need been prescribed steroid creams, they find Vaseline even as effective and use it instead of steroids. [58] Vaseline is of course made from petroleum. Favorite medicine for gardeners dermatitis is Rhus venenata. Typically these are the knee gardeners who get really itchy, blistery rash, presumably from contact with a plant, although it is difficult to figure out which one , the keynote here is that the sole thing that relives the itching is bathing the hands in extremely warm water. [60]

CONCLUSION :

In India more than 80% of the population basically depends on traditional system of medicine such as Ayurveda, allopathic, or homeopathic. Herbal medications have greater impact to cure variable types of skin disorders. Traditional medications are relatively of low cost and are of great benefit as compared to conventional medicine system. Herbal medicines constitute major source of active ingredients and are relatively more safer and cost effective. It is generally used for the treatment of minor to major skin disorders i.e., from rashes to dreadful skin cancer. Major of the plant materials i.e., approximately 50% of plant species are used for the treatment of skin disease. Very severe diseases that could get cure through medication include xerosis, cold sores, actinic keratosis, rosacea etc.

ABBREVIATIONS :

HAA: high altitude areas, **UV:** ultra violet, **DNA:** deoxyribonucleic acid, **BMI:** body mass index, **SCC:** squamous cell carcinoma

ACKNOWLEDGMENT :

The author express cordial and humble thanks to supervisor Prof. Meenakshi Bajpai, Head of the department and Institute of Pharmaceutical Research (GLA University Mathura) Uttar-Pradesh Pin code-281406

REFERENCES

1. Singh, L.C.G., 2017. High altitude dermatology. Indian journal of dermatology, 62(1), p.59

2. Singh G, Chatterjee M, Grewal R, Verma R. Incidence and care of environmental dermatoses in the high-altitude region of Ladakh, India. *Indian J Dermatol.* 2013;58:107–12
3. Director General Armed Forces Medical Service. *Medical Memoranda in Problems of High Altitude.* Vol. 140. New Delhi: Director General Armed Forces Medical Service; 1997. pp. 31–2
4. Dr. Naveen Nandal, Dr. Aarushi Kataria, Dr. Meenakshi Dhingra. (2020). *Measuring Innovation: Challenges and Best Practices.* *International Journal of Advanced Science and Technology*, 29(5s), 1275 - 1285.
5. Nisha Nandal, Dr. Naveen Nandal, Dr Aarushi. (2020). *Women Social Entrepreneurs: A growing trend in Indian Economy.* *International Journal of Advanced Science and Technology*, 29(4s), 2246 - 2253.
6. West JB. The atmosphere. In: Hornbein TF, Schoene RB, editors. *High Altitude an Exploration of Human Adaptation.* Vol. 161. New York: Mercel Dekker Inc; 2001. pp. 25–41.
7. Basnyat B, Murdoch DR. High-altitude illness. *Lancet.* 2003;7(361):1967–74.
8. Pascoe, D.D., Mercer, J.B. and de Weerd, L., 2007. *Physiology of thermal signals.* In *Medical infrared imaging* (pp. 89-108). CRC Press.
9. Yousef, H., Alhajj, M. and Sharma, S., 2019. *Anatomy, skin (integument), ep*
10. Boer, M., Duchnik, E., Maleszka, R. and Marchlewicz, M., 2016. *Structural and biophysical characteristics of human skin in maintaining proper epidermal barrier function.* *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*, 33(1), p.1
11. Nishigori, C., Hattori, Y. and Toyokuni, S., 2004. *Role of reactive oxygen species in skin carcinogenesis.* *Antioxidants and Redox Signaling*, 6(3), pp.561-570.
12. Aumailley, M., & Krieg, T. (1996). *Laminins: A family of diverse multifunctional molecules of basement membranes.* *Journal of Investigative Dermatology*, 106(2), 209-214.
13. Boulant, J. A. (2000). *Role of the preoptic-anterior hypothalamus in thermoregulation and fever.* *Clinical Infectious Diseases*, 31(Suppl. 5), S157-S161.
14. Caputo, R., & Peluchetti, D. (1977). *The junctions of normal human epidermis: A freeze-fracture study.* *Journal of Ultrastructure Research*, 61(1), 44-61.
15. D'Orazio, J., Jarrett, S., Amaro-Ortiz, A. and Scott, T., 2013. *UV radiation and the skin.* *International journal of molecular sciences*, 14(6), pp.12222-12248.
16. Blank, I.H., 1952. *Factors which influence the water content of the stratum corneum.* *Journal of Investigative Dermatology*, 18(6), pp.433-440
17. Pons-Guiraud, A., 2007. *Dry skin in dermatology: a complex physiopathology.* *Journal of the European Academy of Dermatology and Venereology*, 21, pp.1-4.
18. Engelke M, Jensen JM, Ekanayake-Mudiyanselage S, Proksch E. *Effects of xerosis and ageing on epidermal proliferation and differentiation.* *Br J Dermatol.*
19. Hawk JL, Young AR, Ferguson J. *Cutaneous photobiology.* In: Burn T, Breathnach S, editors. *Rook's Textbook of Dermatology.* 7th ed. Vol. 2. Oxford: Blackwell Publishing; 2004. pp. 24.6–24.9.
20. Walker SL, Hawk JLM, Young AR. *Acute and chronic effects of ultraviolet radiation on the skin.* In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. *Fitzpatrick's dermatology in general medicine.* 6th ed. New York: McGraw-Hill Companies Inc; 2003. pp. 1275–82.

21. Matsumura Y, Ananthaswamy HN. Toxic effects of ultraviolet radiation on the skin. *Toxicol Appl Pharmacol.* 2004;195:298–308.
22. Ramirez, C.C., Federman, D.G. and Kirsner, R.S., 2005. Skin cancer as an occupational disease: the effect of ultraviolet and other forms of radiation. *International journal of dermatology*, 44(2), pp.95-100
23. Goette DK. Chilblains (perniosis) *J Am Acad Dermatol.* 1990;23(2 Pt 1):257–62.
24. DeGroot DW, Castellani JW, Williams JO, Amoroso PJ. Epidemiology of U.S. army cold weather injuries, 1980-1999. *Aviat Space Environ Med.* 2003;74:564–70.
25. DeGroot DW, Castellani JW, Williams JO, Amoroso PJ. Epidemiology of U.S. army cold weather injuries, 1980-1999. *Aviat Space Environ Med.* 2003;74:564–70
26. Singh GK, Datta A, Grewal RS, Suresh MS, Vaishampayan SS. Pattern of chilblains in a high altitude region of Ladakh, India. *Med J Armed Forces India.* 2015;71:265–9
27. Cappaert TA, Stone JA, Castellani JW, Krause BA, Smith D, Stephens BA. National Athletic Trainers' Association. National Athletic Trainers' Association position statement: Environmental cold injuries. *J Athl Train.* 2008;43:640–58.
28. Goldenberg, G. and Perl, M., 2014. Actinic keratosis: update on field therapy. *The Journal of clinical and aesthetic dermatology*, 7(10), p.28.
29. Nagpal BM, Sharma R. Cold injuries: The chill within. *Med J Armed Forces India.* 2004;60:165–71.
30. Rainer, B.M., Kang, S. and Chien, A.L., 2017. Rosacea: Epidemiology, pathogenesis, and treatment. *Dermato-endocrinology*, 9(1), p.e1361574
31. Rosen, T. and Stone, M.S., 1987. Acne rosacea in blacks. *Journal of the American Academy of Dermatology*, 17(1), pp.70-73.
32. Tabassum, N. and Hamdani, M., 2014. Plants used to treat skin diseases. *Pharmacognosy reviews*, 8(15), p.52.
33. Arora N, Bansal MP, Koul A. Azadirachta indica exerts chemopreventive action against murine skin cancer: Studies on histopathological, ultrastructural changes and modulation of NF-kappaB, AP-1, and STAT1. *Oncol Res.* 2011;19:179–91.
34. Arora N, Bansal MP, Koul A. Azadirachta indica acts as a pro-oxidant and modulates cell cycle associated proteins during DMBA/TPA induced skin carcinogenesis in mice. *Cell Biochem Funct.* 2013;31:385–94.
35. Rasheed A, Shama SN, Joy JM, Reddy BS, Roja C. Formulation and evaluation of herbal anti-acne moisturizer. *Pak J Pharm Sci.* 2012;25:867–70
36. Limtrakul P, Lipigorngoson S, Namwong O, Apisariyakul A, Dunn FW. Inhibitory effect of dietary curcumin on skin carcinogenesis in mice. *Cancer Lett.* 1997;116:197–203.
37. Draelos ZD. The ability of onion extract gel to improve the cosmetic appearance of postsurgical scars. *J Cosmet Dermatol.* 2008;7:101–4.
38. Shams-Ghahfarokhi M, Shokoohamiri MR, Amirrajab N, Moghadasi B, Ghajari A, Zeini F, et al. In vitro antifungal activities of Allium cepa, Allium sativum and ketoconazole against some pathogenic yeasts and dermatophytes. *Fitoterapia.* 2006;77:321–3.
39. Das I, Saha T. Effect of garlic on lipid peroxidation and antioxidation enzymes in DMBA-induced skin carcinoma. *Nutrition.* 2009;25:459–71

40. Chakraborty A, Brantner A, Mukainaka T, Nobukuni Y, Kuchide M, Konoshima T, et al. Cancer chemopreventive activity of *Achyranthes aspera* leaves on Epstein-Barr virus activation and two-stage mouse skin carcinogenesis. *Cancer Lett.* 2002;177:1–5
41. Tantray MA, Tariq KA, Mir MM, Bhat MA, Shawl AS. Ethnomedicinal survey of shopian, Kashmir (J and K), India. *Asian J Tradit Med.* 2009;4:1–6.
42. Chanda S, Baravalia Y. Screening of some plant extracts against some skin diseases caused by oxidative stress and microorganisms. *Afr J Biotechnol.* 2010;9:3210–7
43. Bohlooli S, Mohebipoor A, Mohammadi S, Kouhnavard M, Pashapoor S. Comparative study of fig tree efficacy in the treatment of common warts (*Verruca vulgaris*) vs. cryotherapy. *Int J Dermatol.* 2007;46:524–6
44. Joshi AR, Joshi K. Ethnomedicinal plants used against skin diseases in some villages of Kali Gandaki Bagmati and Tadi Likhu watersheds of Nepal. *Ethnobotanical Leaflet.* 2007;11:235–46
45. Kingston C, Jeeva S, Jeeva GM, Kiruba S, Mishra BP, Kannan D. Indigenous knowledge of using medicinal plants in treating skin diseases in Kanyakumri district, Southern India. *Indian J Tradit Knowl.* 2009;8:196–200.
46. Yucel I, Guzin G. Topical henna for capecitabine induced hand-foot syndrome. *Invest New Drugs.* 2008;26:189–92.
47. Leung AY. 2nd ed. Wiley-Interscience Publication: John Wiley; 1996. *Foster's Encyclopedia of Common Natural Ingredients used in Foods, Drugs and Cosmetics.*
48. Quisumbing E. Quezon City, Phillipines: Katha Publishing Company, JMC Press; 1978. *Medicinal Plants of the Phillipines.*
49. Lim YY, Kim HM, Park WS, Kim JH, Shin HJ, Kim MN, et al. Anti-inflammatory and anti-pruritic effects of *Portulaca oleracea* L. extract using in vitro and in vivo inflammation model: LPS-treated raw264.7 cells, keratinocytes, NC/Nga mice and hairless SKH-1 mice. *Korean J Asthma Allergy Clin Immunol.* 2011;31:199–206
50. Martin R, Pierrard C, Lejeune F, Hilaire P, Breton L, Bernerd F. Photoprotective effect of a water-soluble extract of *Rosmarinus officinalis* L. against UV-induced matrix metalloproteinase-1 in human dermal fibroblasts and reconstructed skin. *Eur J Dermatol.* 2008;18:128–35.
51. 56. Fu Y, Zu Y, Chen L, Efferth T, Liang H, Liu Z, et al. Investigation of antibacterial activity of rosemary essential oil against *Propionibacterium acnes* with atomic force microscopy. *Planta Med.* 2007;73:1275–80.
52. 57. Huang MT, Ho CT, Wang ZY, Ferraro T, Lou YR, Stauber K, et al. Inhibition of skin tumorigenesis by rosemary and its constituents carnosol and ursolic acid. *Cancer Res.* 1994;54:701–8.
53. Cibir TR, Devi DG, Abraham A. Chemoprevention of two-stage skin cancer in vivo by *Saraca asoca*. *Integr Cancer Ther.* 2012;11:279–86
54. Renu S. Treatment of skin diseases through medicinal plants in different regions of the world. *Int J Compr Pharm.* 2010;4:1–4
55. Singh A, Singh SP, Bamezai R. *Momordica charantia* (Bitter Gourd) peel, pulp, seed and whole fruit extract inhibits mouse skin papillomagenesis. *Toxicol Lett.* 1998;94:37–46
56. Maxia A, Sanna C, Salve B, Kasture A, Kasture S. Inhibition of histamine mediated responses by *Mirabilis jalapa*: Confirming traditional claims made about antiallergic and antiasthmatic activity. *Nat Prod Res.* 2010;24:1681–6

57. <http://www.webmd.com/skin-problems.treatments/./medications-skin-co>
58. Itamura, R., 2007. Effect of homeopathic treatment of 60 Japanese patients with chronic skin disease. *Complementary therapies in medicine*, 15(2), pp.115-120
59. Waisse S. Severe acute thromboinflammation: case report of individualized homeopathic treatment. *Homeopathy*. 2021 May;110(02):132-6.
60. Nwabudike LC. Homeopathic Treatment of Long-Standing Psoriasis--Two Case Reports and Discussion. *American Journal of Homeopathic Medicine*. 2020 Mar 1;113(1)
61. Frei H. Polarity Analysis in the Homeopathic Treatment of Skin Disease.
62. Ranade SR, Hulekar S. Common skin disease "corns" with effective homeopathic medicine Silicea.