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Full Length Research Paper

Ethanomedicinal trends in Indian tradition for treatment of vitiligo

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Vitiligo is an acquired disorder of pigmentation, caused by decreased production of melanin as a result of dysfunction of melanocytes. The present work is collection of information regarding plants having potential in treatment in vitiligo, used in the traditional Indian system of medicine. The plants used are enlisted by their botanical name, families, parts used, chemical components, recommended doses and adverse effects. In the traditional system 38 plants of 30 genera were found to have potential in the treatment of vitiligo. These are being used in the form of therapeutical and topical preparations.

Key words: Vitiligo, ethanomedicinal study, hypopigmentation.

INTRODUCTION

Vitiligo is an acquired disorder of pigmentation, characterized by depigmented macules, as a result of the disappearance of melanin from the epidermis. This is cosmetically disfiguring especially in dark-skinned individuals and makes the lesional skin more sensitive to sunburn. It affects 0.1 to 2% of the world's population, irrespective of gender and race (Moretti et al., 2006). The histologic picture shows loss of melanocytes and melanin in the affected skin and an inconstant lympho-mononuclear infiltrate in the advancing margins of the lesions (Ogg et al., 1998). Diagnostic criteria are mainly clinical, based on the findings of acquired, well-demarcated white areas of the skin, with no associated inflammation that tend to enlarge centrifugally. A recent classification subdivides vitiligo into two clinical types: segmental (type B) and nonsegmental (type A) (Koga and Tando, 1988). Type B is rarer and has a dermatomal distribution; after a rapid onset and evolution usually exhibits a stable course. Type A is more common, has a potential of life long evolution, frequently with autoimmune diseases such as sutton nevus, thyroid disorders, juvenile diabetes mellitus, pernicious anemia and Addison's disease. The pathogenic basis of the disease is disappearance of melanin from the achromic patches (Nordlund and Lerner, 1982; Castanet and Ortonne, 1997). Regarding this mechanism, three possible pathways could occur and are supported by experimental evidence: an apoptotic process (Van der Wijngaard et al., 2000), a necrotic event (associated with the inflammatory process), (Lee Pole et al., 2004) and a melanocythorragy or detachment, following trauma or friction, as a result of an impaired function of cell to cell or cell to matrix adhesion (Gauthier, 2003; Gauthier et al., 2003). A crucial point is whether in vitiligo depigmented skin melanocytes completely disappear. Specific stainings such as the Masson Fontana method for melanin or dihydroxyphenylalanine technique for tyrosinase generally show absence of melanocytes from vitiligo lesions (Birbeck et al., 1961). Accordingly, specific autoantibodies for melanocytic lineage give no evidence of melanocytes in completely vitiliginous skin (Lee Pole et al., 1993; Dippel et al., 1995). These histologic data are also supported by electron microscopy, which fail to identify melanocytic cells in vitiligo achromic patches (Morohashi et al., 1997). In addition, cultured melanocytes can be obtained from pigmented (nonlesional) skin of vitiligo patients (Medrano and Nordlund, 1990), and occasionally from depigmented (lesional) skin of vitiligo patients (Tobin, 2000).

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METHODOLOGY

In Indian system of medicine local remedies are used according to “ayurveda and unani” medical discipline for treatment of vitiligo. This study is an endeavourer to pile up all the traditional trends for the treatment of vitiligo including remedies used, type of formulation used by vaidhyas and tribal people, active components of the plants, their role in treatment of vitiligo and amount to be given as therapeutic against vitiligo. All the plants are collected and kept in herbarium for further studies. The plants are collected from the forests of Lalitpur district on Bundelkhand region and from the Gwalior Chambal region. The herbarium is authenticated from the botanist of Central Ayurvedic Research Institute Gwalior (M.P) 474001.

RESULTS

The result is concluded in the Table 1. In the present study we enlisted 38 plants of 30 genera having potential against vitiligo. The plants are listed by their botanical names, their families, recommended doses for vitiligo patients, harmful effects if over dose is provided and their chemical constituents. These plants are used in the form of therapeutics and topical, on the affected skin. The parts of the plant most used for medicinal purposes are leaves, root, stem, fruits, the complete aerial parts, the whole plant, barks (root and stem) and flowers (including the flowering heads) in decreasing order. Juice (almost mix with water and goat's or cow's milk) and paste are the main methods of preparation, either for oral or for external administration. For topical use, the most important methods used are direct application of the paste or ointment (with oil). These remedies are medicated by the ayurvedic clinicians because ayurveda is the ancient medicinal custom of India. Ayurveda is a good supplement of regional medicinal values. Tribes are using these remedies very frequently and 76% of patients are even concerning the allopathic clinicians.

DISCUSSION

These plants work against vitiligo because they have chemical constituents, which are basically alkaloids, flavonoids, terpenoids, vitamin E, vitamin C, selenium, amino acids and steroids. In vitiligo melanocytes are absent from the affected area. Antioxidants are compounds that protect cells against the damaging effects of reactive oxygen species, such as singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals and peroxynitrite. An imbalance between antioxidants and reactive oxygen species results in oxidative stress,leading to cellular damage. Oxidative stress has been linked to cancer, aging, atherosclerosis, ischemic injury, inflammation and neurodegenerative diseases (Parkinson's and Alzheimer's). Tyrosinase is a key enzyme required for melanin synthesis. Tyrosinase catalyzes thehydroxylation of tyrosine to dihydroxyphenyl alanine (DOPA), which is the rate limiting step of melanin synthesis (Hearing, 1999). DOPA undergoes oxidation of dopaquinone, which is immediately converted to DOPAchrome and then to 5, 6 di hydroxyl indole (DHI). TRP2 (tyrosine related protein 2) convert dopachrome to dihydroxyindole carboxylic acid (DHICA). DHI and DHICA further polymerize to form eumenalin (Figure 1).

Cystine/glutathione reacts with dopaquinone to produce cysteinyldopas that undergo further cyclization to benzothiazines and higher condensates give rise to confer photo protection to the skin from ionization radiations (Hearing, 1999). Keratinocytes are the cell where storage of melanin takes place. Human keratinocytes are the cells that make up majority of the epidermis, express only beta 2 adrenergic receptors. Normal epidermal keratinocytes can endogenously generate epinephrine, they may be provided local stimulation of this beta 2 AR mediated pathway for melanogenesis in the normal melanocytes. Synthesis of beta blocker can lead to exacerbation of vitiligo in some patients. Since beta 2 AR stimulation activates melanogenesis *in vitro*, blockage of beta 2 AR on melanocytes *in vivo* may contribute to the decrease in melanin synthesis seen in vitiliginous skin. Patients with Vitiligo exhibit increased plasma and urine concentrations of norepinephrine and its degradation products (Cucchi et al., 2003). Intracellular calcium levels are increased in keratinocytes in vitiliginous epidermis. In vitiliginous skin, free radicals inhibit tyrosinase. These herbal antioxidants scavange the free radical generated due to stress, sun exposure and autoinnunity (Figure 2).

Role of flavonoids

Flavonoids are polyphenolic compounds that are ubiquitous in nature and are categorized according to chemical structure, into flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins and chalcones. Over 4,000 flavonoids have been identified, many of which occur in fruits, vegetables and beverages (tea, coffee, beer, wine and fruit drinks). The flavonoids have aroused considerable interest recently because of their potential beneficial effects on human health-they have been reported to have antiviral, anti-allergic, antiplatelet, anti-inflammatory, antitumor and antioxidant active-ties. Flavonoids may help provide protection against these diseases by contributing, along with antioxidant vitamins and enzymes, to the total antioxidant defense system of the human body.

Epidemiological studies have shown that flavonoid intake is inversely related to mortality from coronary heart disease and to the incidence of heart attacks. The recognized dietary antioxidants are vitamin C, vitamin E, selenium, and carotenoids. However, recent studies have demonstrated that flavonoids found in fruits and vegetables may also act as antioxidants. Like alpha-tocopherol (vitamin E), flavonoids contain chemical structural elements that may be responsible for their

Table 1. List of botanical names of plants, their family, amount used by the vaidhyas for treatment of vitiligo, side effects if overdosed, part used and their chemical composition.

Botanical name/ authentication number	Family	Amount (gm)	Adverse effect	Part of plant	Chemical constituents
Cuccuta chinensis CRI/1	Cuscutaceae	7 to 14	Lungs and hot temperature persons.	Stem	Phenolics, steroids and tanins
Caccia fistula CRI/2	Caesalpiniaceae	20 to 40	Gripping and diarrohea.	Fruit pulp	Sugar ~50 %, anthraquinone derevatives& combined sannidin.
Emblica officinales CRI/3	Euphrobiaceae	3 to 5	Colic and constipation.	Fruits	Gallic acid, ellagic acid, glucose.
Ficus carica CRI/4	Moraceae	32 gm dry, 40 fresh n ripe.	Teeth, liver, week stomach, itching.	Fruit	Glycosides, phenolics 4.5%, terpenes, resins.
Asarum europeanum CRI/5	Aristolochiaceae	2 to 5	Lungs	Rhizomes	α-agrofuran, α-asaroon, diaasaron, trans& cis isoasaron.
Berbaris aristata CRI/6	Berbiaceae	2 to 4	Post digestive effect	Bark	Berbarin, isobebarin, barbinoids.
Prunus dulcis CRI/7	Poaceae	7 to 11 seeds	Nil	Kernels	Pentosane, hemicelluloses, oxalic acid, riboflavin, nicotinic acid, folic acid iron.
Foeniculum vulgare CRI/8	Apiaceae	5 to 7	Nil	Fruits and roots.	Fruits contain: anethol, iodine, thiamine, riboflavin, niacin, ascorbic acid.
Senecarpus anacardium CRI/9	Anacardiaceae	4 to 6	Corrosive	Seed oil	Flavonoids, resins & glycosides.
Cyclonia oblonga CRI/1	Rosaceae	3 to 9 g seed powder, 30-40 g soaked seeds.	Nil	Seed mucilage	Steroids, glycosides, tannin and volatile oils.
Eclipta alba CRI/11	Asteraceae	5 to 7	Nil	Whole plant	Alkaloid, ecliptine and nicotine.
Swetaria chirayita CRI/12	Ceentianaceae	5 to 7	Nil	Whole plant	Chiratin and ophelic acid.
Cinnamomum zeylanicum/CRI 13	Lauraceae	1 to 2	Urinary bladder.	Bark	Eugenol
Menthe piperata CRI/1	Laminaceae	3 to 5	Nil	Whole plant	Menthol, esters.
Punica granatum CRI/15	Punicaceae	3 to 5	Headache	Flower	Alchohal soluble matter, acid soluble ashes.
Terminalia chebula Gaertu. CRI/16	Combretaceae	5 to 7	Nil	Fruit	Tannins.

Table 1. Contd.

Terminalia chebula Rest.CRI/17	Combretaceae	9 to 12	Nil	Fruit	Tannic, tannic acid, gallic acid.
Citrus colocynthis CRI/18	Cucurbitaceae	1 to 2	Gripping pain	Fruit	. Colocynthin, colocynthttin.
Psoralea corylifolia CRI/ 19	Rutaceace	1 to 3	Increase bile	Seeds	. Psoralen, bakuchiole, isobavachin, bavachinin
Cymbopogon jawarancus CRI/20	Poaceae	5 to 7	Nil	Roots	Citral, citronella glycosides, phenolics and tannins
Nigella sativum CRI/ 21	Ranunculaceae	3 to 7	Renal and urinary system, lung, increase headache	Seeds	Alkaloids, glycosides & terpeniods.
Apium graveolens CRI/22	Apiaceae	5 to 7	. Harmful for high temperature people.	Roots	. Apiin, glycosides, traces of copper and arsenic.
Aethae officinalis CRI/ 23	Malvaceae	5 to 10	Stomach	Seeds	Saponins, resins and volatile oils
Vitus venifera CRI/ 24	Vitaceae	9 to 11	Kidney	Fruits	Tartaric acid, tannin, calcium, iron, potassium, ashes.
Glycyrrhiza glabra CRI/ 25	Fabaceae	3 to 7	Kidney and spleen	Roots	Glycyrrhizin, glycyrrhizic acid, glycyrrhetic acid, liquiritin, isoliquiritin.
Adiantum capillus CRI/ 26	Polypodiaceae	5 to 7	Spleen	Leaves and branches.	Glycosides, tannin, resins.
Cassia angustifolia CRI/ 27	Caesalpinaceae	3 to 5	Nil	Leaves and pods.	, Glycosides, kaempheral, anthraquinone, chrysophanic acid, isoahamneten, flavones, resin, emodin.
Pterocarpus santalinus CRI/ 28	Caesalpinaceae	5 to 10	Diminish sexual appetite.	Stems.	Santalin, pterostillbene, pterocarpin and homopterocarpin.
Tephrosia purpurea CRI/ 29	Fabaceae	7	Nil	Whole plant	Tephrosin, deguelin, isotophrosin rotenone. Leaves glycoside, osyritun.
Plumbago zeylanica CRI/ 30	Plumbaginaceaea	4 to 5 g	Alimentary canal	Bark	Alkaloid plumbaginaceae.
Nardastachys jatamansi CRI/ 31	Valerianceae	3.5 to 4.5 g	Kidney	Bark	Jatamansic acid

Table 1. Contd.

Aloe barbadensis CRI/ 32	Liliaceae	5 to 10 g	Nil	Leaves	Aloin, isobarbaloin, emodin, gum, resin.
Raphanus sativus CRI/ 33	Brassicaceae	1 to 3 g	Kidney and liver	Roots	Essential oils.
Merremia turpethum CRI/ 34	Convolvulaceae	3 to 5 g	Produce unconsciousnes	Stem	Glycosidic resin
Crocus sativurs CRI/35	Iridaceae	1 to 2 g	Loss of appetite, headache and weakness of kidney and lungs.	Flower, style and stigma.	Colchicines.
Cassia tora CRI/36	Caesalpiniceae	1 to 3 g	Intestine	Seeds	Oleic acid, linoleic acid, palmitic acid and lignoceric acid.
Zingiber officinale CRI/ 38	Zingiberaceae	1 to 2 g	Throat disorder	Rhizome	Glutaminine, aspartic acid, spartic acid, serine, gylcine, threonine, alanine, glutamic acid, minobutyric acid, valine, phenylalanine, histidine, leucine, camphene, pheliandrene, cine oil, zingeberene, zingeberol and shogoal, borneol, citral.

antioxidant activities. Dr Buhler and Miranda reported that flavonoids may be potentially useful in the prevention of human disease attributed to free radical damage. The observation that prenyl groups are important in conferring antioxidant activity to certain flavonoids, may lead to the discovery or synthesis of novel prenylated flavonoids as preventive or therapeutic agents against human diseases associated with free radicals.

Role of terpenoids

Fruit and vegetables contain an abundance of phenolic substances, terpenoids and other natural antioxidants that have been associated with protection from and treatment of chronic diseases such as heart disease or cancer. Terpenoids are a group of substances, which occur in nearly every natural food. Their main subclasses discussed as beneficial to maintain and improve health are monoterpenes (like limonene, carvone or carveol), diterpenes (including the retinoids) and tetraterpenes (which include all different carotenoids like α- and β-carotene, lutein, lycopene, zeaxanthine and cryptoxanthine). To be discussed as health promoting or biofunctional, the significant impact of a substance either on human metabolism or on well-defined and appropriate biomarkers must be shown (Wagner and Elmadfa, 2003). Terpenoids are preventive therapeutic agents against human diseases associated with free radicals.

Role of alkaloids

Among all elements found in the plants, alkaloids are the most powerful as well as very effective. The strength or effectiveness of the alkaloids commonly includes everything or all substances that are poisonous in the plants. Therefore, it would be right to state that the exploits of any kind of alkaloids on the human body is naturally traumatic and painful.

Alkaloids are the natural compounds found in all vegetables that include nitrogen and are considered to be disintegration of substances that comprises proteins. They are exuded in particular cells or tubes and can be of great use in safeguard against normal enemies as they have a bitter flavor. Generally, alkaloids are amalgams that do not have any scent and boast of a distinctive outcome on the animals' body mechanism or function. Alkaloids are preventive or therapeutic agents against human free radical associated diseases.

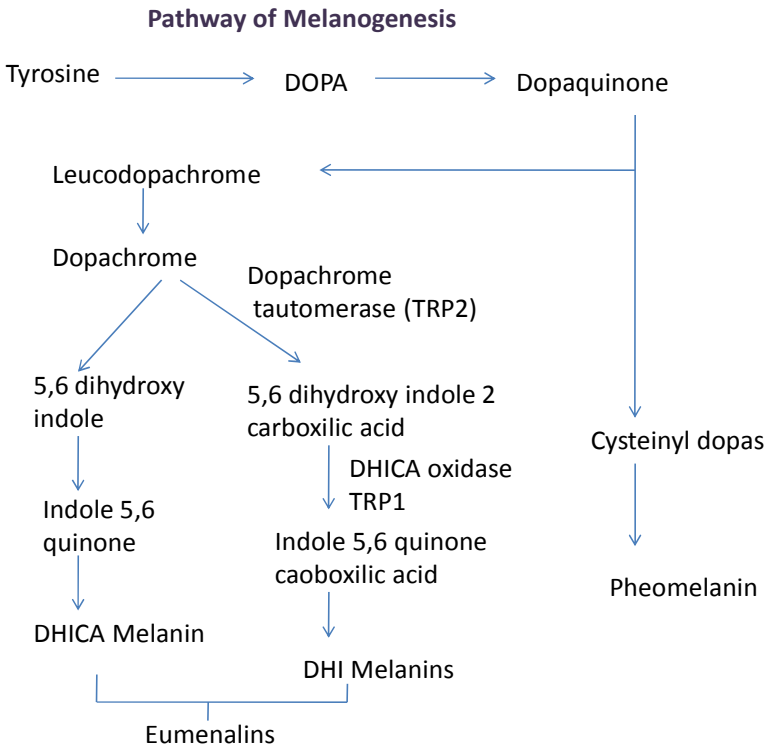

Figure 1. Pathway of melanogenesis, tyrosinase as key enzyme for melanin formation.

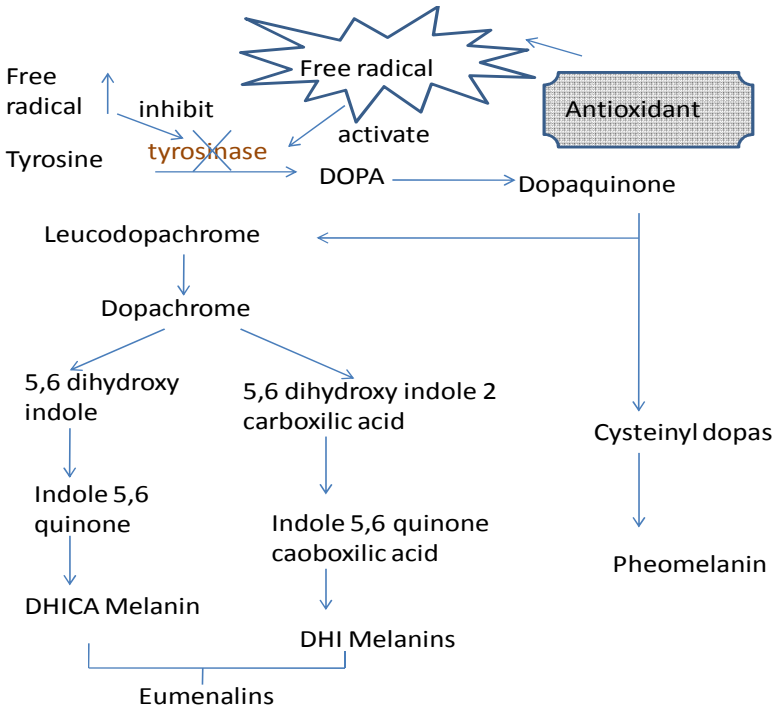

Figure 2. Role of antioxidants in regulating tyrosinase inhibition in vitiliginous skin.

Role of steroids

Reversible hypopigmentation of normal skin is a well known side effect of prolonged potent steroid application. The skin lightening effect of topical corticosteroid is ill-understood. Melanocytes respond to a wide variety of chemical mediators. The inhibitory effects of corticosteroids on the synthesis of mediators like prostaglandin and leukotriene may partly explain their effects on melanogenesis (Gupta et al., 2006). Potent or super potent steroids, when used alone, have been associated with good therapeutic responses (Kanwar and Dhar, 1994; Neering, 1975), but monotherapy is not recommended due to their frequent side effect.

Topical steroids are used in combination with other drugs for their synergistic effect and for the reduction of irritation from other products like retinoid. Various combinations with hydroquinone and retinoic acid have given good cosmetic results in clinical trials (Rendom et al., 2006). Adverse effects of topical steroids include irritation, rosacea-like dermatosis, atrophy, telangiectasia and hypertrichosis.

Conclusion

The present work is collection of information regarding plants having potential in treatment in vitiligo, used in the traditional Indian system of medicine. The plants used are enlisted by their botanical names and families, parts used, their active chemical components, recommended doses and adverse effects. In the traditional system 38 plants of 30 genera were found to have potential in the treatment of vitiligo. These are being used in the form of therapeutical and topical preparations.

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