

**COMPLEMENTARY AND ALTERNATIVE MEDICINES AND
TREATMENT ON VITILIGO**

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ABSTRACTS

Vitiligo, a common depigmenting skin disorder, has an estimated prevalence of 0.5–2% of the population worldwide. The disease is characterized by the selective loss of melanocytes which results in typical nonscaly, chalky-white macules. In recent years, considerable progress has been made in our understanding of the pathogenesis of vitiligo which is now clearly classified as an autoimmune disease. Vitiligo is often dismissed as a cosmetic problem, although its effects can be psychologically devastating, often with a considerable burden on daily life. In 2011, an international consensus classified segmental vitiligo separately from all other forms of vitiligo, and the term vitiligo was defined to designate all forms of nonsegmental vitiligo.

Vitiligo is a common, acquired disorder of skin pigmentation that can significantly impact quality of life. It often represents a therapeutic challenge, which has resulted in interest in alternative treatments.

INTRODUCTION

Vitiligo, a depigmenting skin disorder, is characterized by the selective loss of melanocytes, which in turn leads to pigment dilution in the affected areas of the skin. The characteristic lesion is a totally amelanotic, nonscaly chalky-white macule with distinct margins. Considerable recent progress has been made in our understanding of the pathogenesis of vitiligo, and it is now clearly classified as autoimmune disease, associated with genetic and environmental factors together with metabolic, oxidative stress and cell detachment abnormalities.

Vitiligo is the commonest acquired pigmentary disorder, affecting 0.1–2% of the population worldwide^[1,2], with no incidence difference between male and female. While it can affect people of all ages, vitiligo appears more frequently before 20 years of age. It is characterized by the progressive disappearance of skin melanocytes resulting in cosmetically white patches of skin depigmentation, occasionally associated with premature whitening, or graying of the hairs, eyelashes, eyebrows, beard, or mucous membranes, usually without clinical symptoms. However, vitiligo has devastating impacts on the quality of life in affected individuals. Patients with vitiligo present lowered self-esteem, which, in turn, affects social life, frequently culminating in the development of depression.^[3,4,5] Clinically, vitiligo is broadly categorized into segmental vitiligo and nonsegmental vitiligo.

We are in an era of modern medicine that is defined by rapid change. The pathogenesis of vitiligo is multifactorial, and includes three main factors: genetic, immunological, and environmental. Clinically, environmental factors are important in the development of vitiligo. Trauma, eczema, chemical agents, and fragility of keratinocytes play a role in development of vitiligo, so treatment decisions should be made taking these factors into account. Recently various treatment modalities have been introduced, and treatment options and outcomes have been improving. Excimer laser, phototherapy, epidermal grafts, and lifestyle modification have improved the results of treatment and quality of lives of patients with vitiligo. South Korea is a country (approximately 1/7th the size of Texas) with excellent modern medical facilities for the treatment of vitiligo. There are 130 practices where excimer lasers are commonly used and more than 70 practices can provide surgical management (epidermal grafts). Nevertheless, many patients seek alternative medical options, including oriental medicines and folk remedies for treatment of their vitiligo.^[6,7]

AIM: Complementary and alternative medicines and treatment on vitiligo.

OBJECTIVE

1. To improve efficacy and safety of patients.
2. To identify natural health products (NHP) such as vitamins, herbs and other supplement may have efficacy in treatment of vitiligo.
3. To provide an updated overview of most frequently used medicinal plants in treatment of vitiligo.
4. To study complementary and alternative medicine and evaluate their efficacy and safety to validate their reliability.

5. To study about camouflage as an effective method for vitiligo for improving quality of life.

TYPES OF VITILIGO^[8,9]

There are three major types of vitiligo are as follows:

- Segmental Vitiligo
- Non-Segmental Vitiligo
- Mixed Vitiligo

- **Segmental Vitiligo**

Segmental vitiligo starts as well as stays in one side of body. It is an autoimmune disease. It is clearer in early age groups, affecting about 30 percent of children diagnosed with vitiligo. It responds well to topical treatment.

- **Non-Segmental Vitiligo**

It is an autoimmune disease as well as often mirrors on both sides of the body. It is most common type of vitiligo observed in 90% cases. They often appear on skin that is commonly exposed to the sun, such as the face, neck, and hands.

- **Mixed Vitiligo**

Mixed Vitiligo intersection of both types in the rare cases where segmental becomes non-segmental.

SYMPTOMES AND CAUSES^[9,10]

The elementary symbol of vitiligo is loss of skin color. Discoloration first shows on sun-exposed areas like hands, lips, arms and face.

Vitiligo Signs Include

- Occasional loss of skin color.
- Premature whitening of the hair on your scalp, eyelashes, eyebrows or beard.
- Loss of color in the tissues that line the inside of your mouth and nose (mucous membranes).
- Change in color of the inner layer of the eyeball (retina).

CAUSES

Vitiligo occurs when the melanocytes die or stop functioning. Melanocytes are nothing but cells producing melanin. It is pigment that gives color to eye skin and hair. Vitiligo may cause due to.

- A disorder in which your immune system attacks and destroys the melanocytes in the skin.
- Family history (heredity).
- A trigger event, such as sunburn, stress or exposure to industrial chemicals.
- Stressful events
- A virus
- Vitiligo is not contagious. One person cannot fasten it from alternative.

THERAPEUTIC APPROACHES FOR VITILIGO PATIENTS^[11,12]

Vitiligo treatments aim to provide good cosmetic outcomes, extend remission periods, prevent recurrences, and ensure patient satisfaction. Based on the described scenario, current medical strategies basically aim to offer antioxidant supplementation, immune system modulation, and melanocyte precursor mobilization. Recently, due to the progressive loss of functional melanocytes associated with failure to spontaneously recover pigmentation, it has been proposed to treat vitiligo as a degenerative disease. Accordingly, along with pharmacological treatment, several cell-based and cell-free regenerative approaches have been proposed.

A) Medical Therapies

Commonly used re pigmentation therapies for vitiligo include topical immunosuppressor agents (corticosteroids, calcineurin inhibitors, calcipotriol) and UV light (whole-body irradiation or UV targeted to lesions). Corticosteroids repress the cellular immune response and melanocyte destruction while stimulating melanocyte regeneration and melanogenesis. Topical corticosteroids are the foremost treatment for localized vitiligo, while low-dose systemic corticosteroids are used for the stabilization of the rapidly progressive disease.^[13,14]

B) Introduction to Interventional Therapies

From a general point of view in humans, the term “regeneration” is used to describe the replacement of specialized tissue by proliferation and differentiation of undamaged cells. However, in the skin and mucosa, normal replacement of individual cells is a continuous process, even in absence of specific stimuli. In the case of vitiligo, lack of repigmentation

suggests that persistent stress-induced melanocyte damage may demand a permanent regenerative request leading to an abnormal turnover of melanocyte stem cells, resulting in the loss of regeneration ability. On the other hand, the lack of spontaneous skin color recovery may reflect the persistent loss of physiological skin homeostasis, suggesting that in white areas the entire microenvironment needs to be treated or reprogrammed to achieve normal pigmentation^[15] Repair is an adaptation to loss of tissue integrity and leads to production of scar tissue, sometimes without complete recovery of the normal structure and function.

C) Light Therapies

Phototherapy with narrow band ultraviolet B (UVB) has been shown to stop or slow the progression of active vitiligo. It might be more effective when used with corticosteroids or calcineurin inhibitors. You'll need therapy two to three times a week.

VITILIGO AND LIFESTYLE MODIFICATION^[16]

The location of vitiligo can give clues as to its triggers or causes. In stress-induced cases, skin lesions are frequently localized to the seborrheic area (Figure 1A). In traumatic types, the lesions are usually localized to sites of injury or pressure (Figure 1B). In dermatitis-associated types, depigmented lesions tend to occur in areas of a specific pre-existing dermatitis. Doctors can often assume predisposing and aggravating factors that can help identify vitiligo etiology, and thereby advise patients to alter modifiable living habits.



Figure 1 A Figure 1 B

PATHOGENESIS

Vitiligo is a multifactorial disorder characterized by the loss of functional melanocytes^[2, 17,18] Multiple mechanisms have been proposed for melanocyte destruction in vitiligo. These include genetic, autoimmune responses, oxidative stress, generation of inflammatory mediators and melanocyte detachment mechanisms. Several mechanisms might be involved in the

progressive loss of melanocytes, and they consist either of immune attack or cell degeneration and detachment. The “convergence theory” or “integrated theory” suggests that multiple mechanisms may work jointly in vitiligo to contribute to the destruction of melanocytes, ultimately leading to the same clinical result.^[1,19,17,20,21]

Genetics of Vitiligo^[22,34]

Strong evidence from multiple studies indicates the importance of genetic factors in the development of vitiligo, although it is clear that these influences are complex. Epidemiological studies have shown that vitiligo tends to aggregate in families however, the genetic risk is not absolute. Around 20% of vitiligo patients have at least 1 first-degree relative with vitiligo, and the relative risk of vitiligo for first-degree relatives is increased by 7- to 10-fold. Monozygotic twins have a 23% concordance rate, which highlights the importance of additional stochastic or environmental factors in the development of vitiligo. Large-scale genome-wide association studies performed in European-derived whites and in Chinese have revealed nearly 50 different genetic loci that confer a vitiligo risk. Several loci are components of the innate and adaptive immune system and are shared with other autoimmune disorders, such as thyroid disease, type 1 diabetes and rheumatoid arthritis. Tyrosinase, which is encoded by the TYR gene, is an enzyme that catalyzes the rate-limiting steps of melanin biosynthesis. Tyrosinase is a major autoantigen in generalized vitiligo. A genome-wide association study has discovered a susceptibility variant for NSV in TYR in European white people that is rarely seen in melanoma patients.

Oxidative Stress^[35,44]

Pathogenesis of vitiligo suggests that oxidative stress may be the initial event in the destruction of melanocytes. Indeed, melanocytes from patients with vitiligo were found to be more susceptible to oxidative stress than those from unaffected individuals and are more difficult to culture *ex vivo* than those from healthy controls. Reactive oxygen species (ROS) are released from melanocytes in response to stress. In turn, this causes widespread alteration of the antioxidant system: An imbalance of elevated oxidative stress markers (superoxide dismutase, malondialdehyde, ROS) and a significant depletion of antioxidative mechanisms (catalase, glutathione peroxidase, glutathione reductase, thioredoxin reductase and thioredoxin, superoxide dismutases, and the repair enzymes methionine sulfoxide reductases A and B) in the skin and in the blood. It has been suggested that this imbalance between pro-oxidants and antioxidant in vitiligo is responsible of the increased sensitivity of melanocytes to external pro-

oxidant stimuli and, over time, to induce a presenescent status. The generation and buildup of ROS can in turn cause DNA damage, protein oxidation and fragmentation, and lipid peroxidation, thus impairing their cellular function.

Innate Immunity^[45,48]

Innate immunity in vitiligo bridges the gap between oxidative stress and adaptive immunity in vitiligo. It is likely that the activation of innate immune cells occurs early in vitiligo, by sensing exogenously or endogenously induced stress signals released from melanocytes and possibly keratinocyte. Genomic expression analysis on the skin of patients with vitiligo has highlighted an abnormally heightened innate immunity in the local microenvironment of melanocytes in vitiligo skin, particularly natural killer cells. Indeed, natural killer cells have been found to infiltrate clinically normal skin of patients with vitiligo, suggesting that natural killer cells are early responders to melanocyte stress. Melanocytes seem to communicate stress to the innate immune system through the excretion of exosomes. Human melanocytes were found to secrete exosomes in response to chemically induced stress. These exosomes contain melanocyte-specific antigens, miRNAs, heat shock proteins and other proteins that act as damage-associated molecular patterns.

Adaptive Immunity^[48,49]

Both humoral and cell-mediated immune abnormalities are implicated in the pathogenesis of vitiligo. Antibodies to surface and cytoplasmic melanocyte antigens have been identified in the past in the sera of vitiligo patients. These antibodies can induce the destruction of melanocytes grown in culture by complement-mediated lysis and antibody-dependent cellular cytotoxicity.

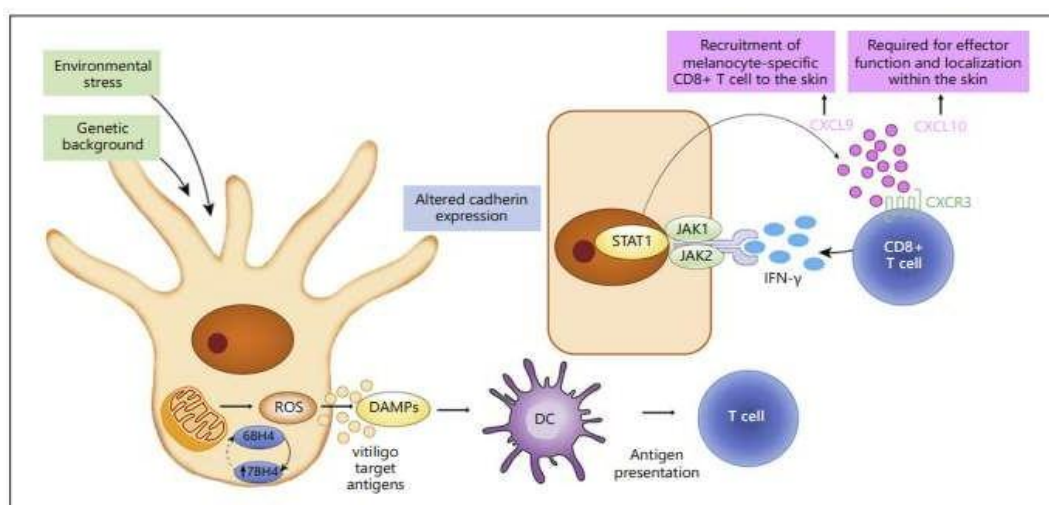


Figure 2: Mechanisms of Action.

CLASSIFICATION

In 2011, an international consensus classified SV separately from all other forms of vitiligo, and the term vitiligo was defined to designate all forms of NSV. “Mixed vitiligo” in which SV and NSV coexist in one patient, is classified as a subgroup of NSV (Table 1). Distinguishing SV from other types of vitiligo was one of the most important decisions of the consensus, primarily because of its prognostic implications.

Type Of Vitiligo	Subtype
NSV	Focal Mucosal Acrofacial Generalized Universal Rare variants of vitiligo (leukoderma punctata, hypochromic vitiligo, follicular vitiligo)
SV	Focal Unisegmental Bi -or multisegmental
Mixed (NSV +SV)	Concomitant occurrence of SV and NSV According to severity of SV
Unclassified	Focal at onset, multifocal asymmetrical nonsegmental, mucosal (one site),

1. Generalized vitiligo is characterized by bilateral, often symmetrical, depigmented macules or patches occurring in a random distribution over the entire body surface. It often affects areas that tend to experience pressure, friction and/or trauma. It may begin in childhood or early adulthood.



Fig. 3: Generalized Vitiligo.

2. Acrofacial vitiligo is characterized by depigmented macules limited to the distal extremities and/or the face. A distinctive feature is depigmentation of the distal fingers and facial orifices. It may later progress to include other body sites and be better

classified as generalized or universal. The lip-tip variety is a subcategory of the acrofacial type in which lesions are restricted to the cutaneous lips and distal tips of the digits.



Fig. 4: Acrofacial Vitiligo.

3. Mucosal vitiligo typically involves the oral and/or genital mucosae. It may occur in the context of generalized vitiligo or as an isolated condition. An isolated mucosal vitiligo which remains so after at least 2 years of follow-up is defined as unclassified.^[2]
4. Vitiligo universalis (Fig. 5) refers to complete or nearly complete depigmentation of the skin (80–90% of body surface). It is usually preceded by generalized vitiligo that gradually progresses to complete or near complete depigmentation of the skin and hair.



Fig. 5: Vitiligo Universalis.

5. Focal vitiligo refers to a small, isolated, depigmented lesion without an obvious distribution pattern and which has not evolved after a period of 1–2 years. It can evolve into SV or NSV.
6. Punctate vitiligo, refers to sharply demarcated depigmented punctiform 1- to 1.5-mm macules involving any area of the body^[50] If these lesions do not coexist with classical vitiligo macules, they should be referred to as “leukoderma punctata.
7. Hypochromic vitiligo or vitiligo minor is characterized by the presence of hypopigmented macules in a seborrheic distribution on the face and neck associated with hypopigmented macules of the trunk and scalp. It seems to be limited to individuals with dark skin types.



Fig. 6: Monosegmental vitiligo of the left abdomen.

8. Follicular vitiligo presents with leukotrichia in the absence of depigmentation of the surrounding epidermis.^[51] SV refers to depigmented macules distributed in a segmental pattern and is typically associated with leukotrichia and a rapid onset. The characteristic lesion is clinically similar to the macule seen in NSV: a totally amelanotic, nonscaly, chalky-white macule with distinct margins.

The head is involved in more than 50% of cases.^[42,53] The most commonly involved dermatome is that of the trigeminal nerve. The next common locations in decreasing order of frequency are the trunk (Fig. 6), the limbs, the extremities and the neck.^[52,55]



Fig. 7: Mono segmental vitiligo.

LIFE, EXERCISE, STRESS

Living Habits

Patients may need to change their living habits depending on their individual clinical presentation of vitiligo. For example, since severe stress can aggravate vitiligo lesions, positive thinking and reducing stress could help reduce them. Adequate rest and antioxidants are important for patients with vitiligo, particularly those with lesions in a seborrheic distribution. Patients ought to reduce smoking, a habit that siphons beneficial antioxidants from the body. It is necessary to reduce the risk of koebnerization in vitiligo through friction or trauma. For example, tight-fitting shoes or jeans, and elastic stockings should be avoided.

Identification of possible occupational trauma is important as well. Figures 2A & 2B suggest that occupational trauma such as burns or chemical irritation (*e.g.*, by discharge in an electric arc or argon welding) can exacerbate vitiligo. The patient in Figure 2C, working in a disposable mask, developed vitiligo in the perioral area where the mask was fitted. As expected, the skin lesions improved with switching to a cotton mask and excimer laser treatment for one month.

Exercise Repetitive movements in exercise can induce vitiligo due to trauma to or friction with certain body areas. If this is consistent with a patient's story of the appearance of certain vitiligo lesions, the patient should consider modifying or discontinuing the exercise. Common occurrences include lesions of the dorsal shin in soccer, inner thigh and groin for horseback riders, protuberant areas in contact with protective headgear, and pressure points on the hands and palms when gripping golf clubs.

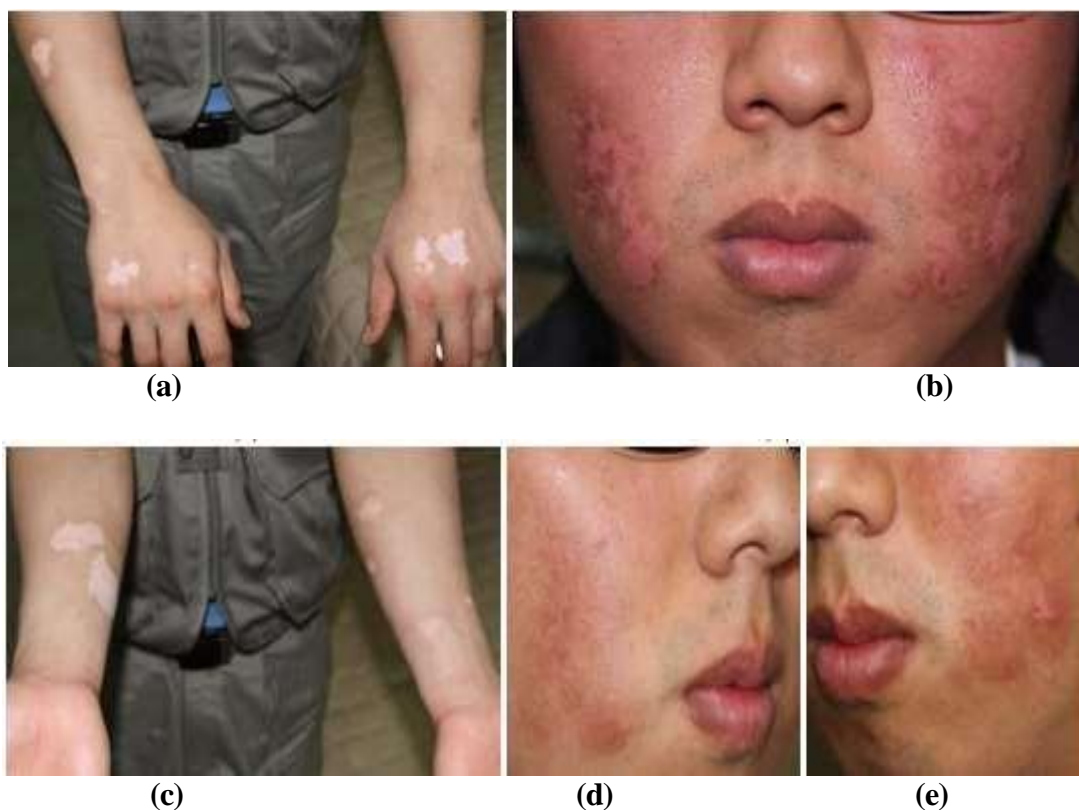


Fig. 8 (a) and (b): Occupational vitiligo induced by welding. (c) (e). Vitiligo on areas in contact with a disposable mask, before (c) and one month after treatment (d, e)

DIAGNOSIS^[56,60]

The diagnosis of vitiligo is generally straightforward, made clinically based upon the finding of acquired, amelanotic, nonscaly, chalky-white macules with distinct margins in a typical distribution: periorificial, lips and tips of distal extremities, penis, segmental and areas of friction. The diagnosis of vitiligo may be facilitated by the use of a Wood's lamp, a hand-held ultraviolet (UV) irradiation device that emits UVA. It helps identify focal melanocyte loss and detect areas of depigmentation that may not be visible to the naked eye, particularly in pale skin. Under the Wood's light, the vitiligo lesions emit a bright blue-white fluorescence and appear sharply demarcated.

Dermoscopy can be used to differentiate vitiligo from other depigmenting disorders. Vitiligo typically shows residual perifollicular pigmentation and telangiectasia, which are absent in other hypopigmentation disorders.

TREATMENT

Many treatments are accessible to benefit restore skin color or even out skin tone. Results vary and are unpredictable. Some treatments have serious side effects. Sometimes doctor may

recommend that, you first try improving the appearance of your skin by applying self-tanning products or makeup. Even if treatment is successful for a while, the results may not last or new patches may appear.

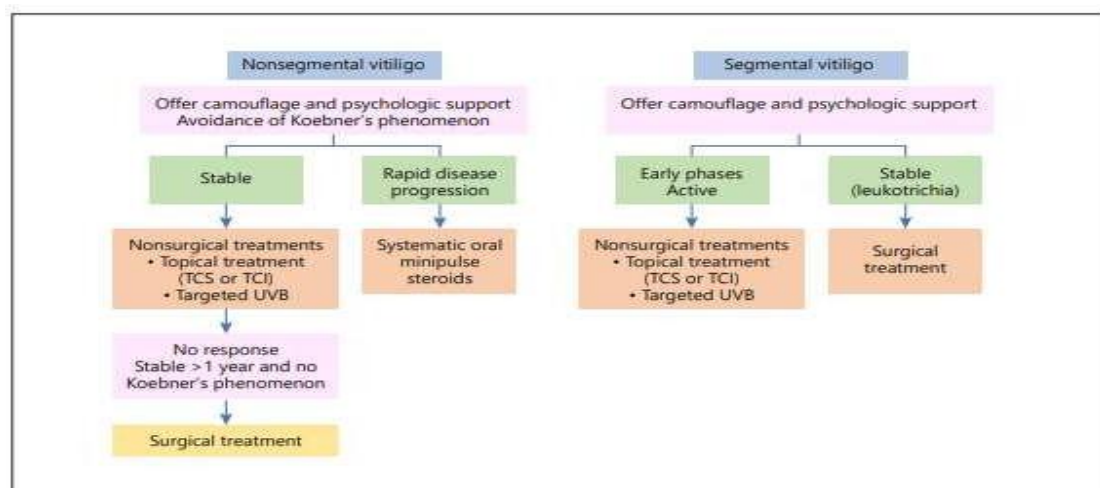
No drug can stop the process of vitiligo. However, some drugs used alone or with light therapy, can help restore some skin tone.

- ❖ Use of corticosteroid cream
- ❖ Depigmentation
- ❖ Skin grafting
- ❖ Blister grafting
- ❖ Tattooing (Micro pigmentation)
- ❖ Kapalbhati is helpful in the treatment of vitiligo.
- ❖ Photochemotherapy
- ❖ Piperine an alkaloid from black pepper show anti vitiligo activity.
- ❖ An arthritis drug - Tofacitinib citrate - has shown some promise. It inhibits Janus kinase, an enzyme that seems to be implicated in the etiology of vitiligo.

MANAGEMENT

The treatment of vitiligo is still one of the most difficult dermatological challenges. An important step in the management of vitiligo is to first acknowledge that it is not merely a cosmetic disease and that there are safe and effective treatments available.

These treatments include phototherapy, topical and systemic immunosuppressants, and surgical techniques, which together may help in halting the disease, stabilizing depigmented lesions and stimulating re pigmentation.



DIET

Diet is not considered very important in the treatment of vitiligo. However, a healthy, balanced diet with nutrients from a variety of sources can be helpful in vitiligo. According to complementary and alternative medicine (CAM) practitioners, there are foods that are considered either beneficial for or detrimental in vitiligo, but they differ in opinion about these foods and they often lack medical evidence to substantiate their claims. Often, recommendations are determined by a food's composition of antioxidants, vitamins, and microelements. On the other hand, the detrimental effects of foods or food additives are often based on the risk of allergic reactions and irritation, either of which could trigger or exacerbate vitiligo.

COMPLEMENTARY AND ALTERNATIVE MEDICINE FOR VITILIGO

A) Traditional Chinese medicine (TCM)

The history of TCM dates back thousands of years. The variety and usage of these medicines is almost identical throughout Korea, China, and Japan thanks to long-term cultural exchange among nations.^[61]

Among the decoctions of herbs which TCM primarily uses, the most effective medicines have been shown to be the xiaobailing decoction, Chang-ye powder, and three-yellow powder. These medicines include various medicinal plants such as *Xanthium strumarium*, *Sophora flavescens*, *Atractylodes japonica*, and *Arisaema amurense*. The TCM medicines.

Scientific Name	Common name Or Ayurvedic name	Proposed mechanism of action
<i>Angelica sinensis</i>	Dong Quai	Phototoxic
<i>Arisaema amurense</i>	Tian Nan Xing	Antioxidant
<i>Astragalus membranaceus</i>	Mangolian milkvetch	Immunity modulator
<i>Atractylodes japonica</i>	Japanese Atractylodes	Phototoxic
<i>Carthamus tinctorius</i>	Safflower	Antioxidant
<i>Cassia occidentalis</i>	kasaundi, stinking weed	Melanoblast differentiation and migration
<i>Cnidium officinale</i>	Chuanxiong rhizome	Phototoxic
<i>Codonopsis pilosula</i>	Tangshen	Strengthen Immunity
<i>Cuscuta chinensis/japonica</i>	Dobber seed	Antioxidant
<i>Eclipta prostrata</i>	Bhangrach	Antioxidant
<i>Gentiana scabra</i>		Anti-inflammatory
<i>Liquidambar formosana</i>	Sweetgum fruit	Promotes circulation,
<i>Lycium chinense</i>	Wolfberry fruit	Nutrient, Antioxidant
<i>Paeonia lactiflora</i>	White peony root	Anti-inflammatory
<i>Picrorhiza kurroa</i>	Red peony root	Anti-inflammatory
<i>Pleuropterus multiflorus</i>	Katuki, kutki	Anti-cancer
<i>Prunella vulgaris</i>	Prunella spike	Anti- inflammatory

Prunus persica	Peach kernel	Anti-inflammatory
Rehmania glutinosa	Chinese foxglove	Anti-inflammatory
Salvia miltiorrhiza	Red sage	Antioxidant, Anti-inflammatory, Promotes circulation
Sesamum indicum	Black sesame	Antioxidant
Spatholobus suberectus	Climbing stem of S.suberectus	Promotes circulation
Tribulus terrestris	Gokshura, sarrata	Phototoxic
Xanthium strumarium	Common cocklebur	Phototoxic

B) Traditional Indian medicines^[62,65]

Traditional Indian medicine has thousands of years of history. Its branches include Ayurveda, Yoga & Naturopathy, Unani, and Siddha medicine. Due to a long history of active trading between China and India through the Silk Road (via Central Asia, transHimalayan, or sea-route), there are similarities in the medicinal plants utilized and their indications. Cassia occidentalis, Eclipta prostrata, Curcuma longa, Picrorrhiza kurroa, Psoralea corylifolia, and Tribulus terrestris are commonly used in both Ayurvedic medicine and TCM.

However, there are fundamental differences between Ayurveda and TCM. Despite having common drugs, Ayurvedic medicine and TCM use them for different applications. Ayurvedic medicine primarily uses mineral-based and herbal drugs that act as photosensitizers and blood purifiers. Photosensitizing agents include Psoralea corylifolia, Semicarpus anacardium (marking nut), and Ficus hispida. They are administered locally as well as systematically in conjunction with sun exposure. Sun exposure is advised three hours after drug administration.

Among these, Aristolochia indica root contains aristolochic acid, so it can cause a renal failure or cancer. Both the hepatotoxicity of Psoralea corylifolia, and its phototoxicity are mentioned due to its possible applications in vitiligo. Ayurvedic medicine as well as TCM acknowledge the risks of the use of arsenic and mercury.

C) Homeopathic treatment

Homeopathy is a form of alternative medicine that originated in 18th century Germany. Many countries have adapted and transformed these practices in accordance to their cultures. India is particularly well known for its wide application of various homeopathic treatments that claim a high “cure” rates, but there is a lack of medical evidence substantiating this. Poisonous materials such as arsenic sulph falvus, arsenic album (arsenic trioxide), baryta muriaticum (barium chloride) and baryta carbonicum (barium Carbonate), are often employed by practitioners in highly diluted preparations. The collective weight of scientific evidence has found homeopathy to be no more effective than placebo.

D) Folk remedies in Korea^[65,67]

There are various Korean folk remedies for vitiligo. Apart from TCM, folk remedies include the root of *Rumex crispus* or leaves of the common fig tree (*Ficus carica*) which contain strong phototoxic agents (mainly furocoumarine). These phototoxic agents are less effective than modern medicine (i.e., psoralen) because these preparations are affected by many variables, such as active ingredient concentration, treatment frequency, and application or administration methods. Foreign body reactions using various irritants that add pigment to the skin (i.e., tattooing) are often harmful and have no benefits. Bee venom is regarded as ineffective and dangerous because it induces systemic inflammation. However, purified honey bee venom (apitoxin) may be effective in vitiligo.

E) Other Treatments

Serrano et al reported that repeated photodynamic therapy (PDT) with low concentrations of aminolevulinic acid (ALA, 1-2%) is helpful in the vitiligo. We have had similar experiences in patients with alopecia totalis. We treated patients with a very low concentration of ALA (0.5%), and asked them to wait 2 hours before exposing themselves to window glass-filtered sunlight for 30 minutes once every two weeks. If similar treatment is repeated in vitiligo, it may work. This may be due to the protoporphyrin IX produced by ALA that strongly absorbs UVA. Aghaei and Ardekani reported that diphenylcyclopropenone (DPCP) showed some efficacy in the treatment of vitiligo. DPCP is thought to act as a local irritant when applied topically.

However, based on our clinical experience, this agent seems to be quite dangerous and unreliable.^[68,69]

COMOUFLAFE OF VITILIGO

The majority of patients who suffer from vitiligo want to conceal their exposed vitiligo lesions because of psychosocial reasons. Patients conceal lesions on the face, head and neck, arms, legs, and hands with clothing or other methods. Concealment is a useful way to improve social functioning and patient quality of life. Camouflage can take the form of: micropigmentation which lasts for months to years (tattoos and semi- permanent tattoos/permanent makeup), dihydroxyacetone and selected fruit juices that last for several days, and dyes or makeup concealers which last for 1- 2 days.

Long-acting camouflage**Micropigmentation**

Micropigmentation is a method in which pigments are injected directly into dermis and last for months to years at a time. This can be in the form of tattooing or semi-permanent tattoos (permanent makeup) depending on the features of pigments utilized. Tattoos have been used widely throughout the world for thousands of years, as part of cultural and ethnic activities to recreational purposes.^[68]

Permanent makeup

uses digitalized tattoo machines and need re-touching when colors begin to fade after treatment (around one month). Permanent makeup has the advantage of lasting for a long time. Eyebrows or lips can be concealed naturally with permanent makeup. The common problem with micropigmentation is dissatisfaction with shape and tone. It is difficult for even the most experienced tattooists to make pigments with accurate tone, depths, and symmetry, particularly for the eyebrows and lips. Furthermore, adverse events are a possibility with these procedures, and include infection, allergic reactions, tattoo granulomas, keloid formation, and magnetic resonance imaging (MRI) complications. Magnetic responsive dyes in tattoo can cause cutaneous reactions when patients undergo MRI testing.^[69-71]

Intermediate-acting camouflage

Dihydroxyacetone (DHA) is an ingredient in self-tanning products. This dyeing method camouflages lesions of vitiligo temporarily because of browning by the Maillard reaction. DHA can mask lesions of vitiligo relatively well and lasts for 3-6 days. According to our experience, many patients combine DHA with conventional makeup. Korean patients with vitiligo effectively conceal lesions using DHA concentrations of 5-15%. Since DHA can make lesions slightly reddish brown, it is not well-suited for patients with yellow skin tones. DHA is not very effective in damaged or inflamed stratum corneum. It may also interfere with the effects of phototherapy by inhibiting ultraviolet rays. Patients need to practice application techniques for the most natural-appearing camouflage because final coloring appears several hours after application.^[72,73]

Short-acting camouflage

Dyes such as potassium permanganate, indigo carmine, and bismarck brown can be used to camouflage vitiligo. These dyes provide an immediate, natural, amber-like shade with single or repeated applications, and can be easily removed by washing. Special makeup products are

also helpful. Cosmetics are limited by their easy removability (can be washed away by sweat) and they can be messy (get on clothing), however tend to give vitiligo lesions the most natural skin color. Many patients prefer makeup, which can achieve cosmetically acceptable results in an investment of 20 minutes a day.^[74]



Fig. 9 (A) Concealer cosmetic set for vitiligo patients.

(B) Patient before and after makeup.

CONCLUSION

Vitiligo is a common pigmentary disorder with significant psychosocial effects. Autoimmunity and oxidative stress have been proposed as potential mechanisms of melanocyte damage, however, the exact cause leading to clinically depigmented patches remains to be elucidated. Patients and doctors can safely combine modern medicines with reliable CAM all while encouraging healthy lifestyles in order to prevent vitiligo exacerbation. CAM is less effective for vitiligo compared to modern medicine although it has shown some merit in making use of the phototoxic, anti-congestion, anti-oxidant, anti-stress, and immune modulation properties of specific herbs and herbal combinations. Various natural foods and products can be another option for the treatment of vitiligo.

Camouflage is an efficient method for vitiligo in terms of cost-benefit ratio and improving quality of life. Various CAM modalities including TCM, health foods, good living habits, and camouflage combined with Western medicine, in the form of oral or topical medications, phototherapy, or excimer laser, can help these patients live happier lives with decreased disease burden.

REFERENCES

1. Cardo M, Dell'Anna ML, Ezzedine K, Hamzavi I, Harris JE, Parsad D, et al. Vitiligo. *Nat Rev Dis Primers*, 2015 Jun; 1(1): 15011.
2. Ezzedine K, Lim HW, Suzuki T, Katayama I, Hamzavi I, Lan CC, et al.; Vitiligo Global Issue Consensus Conference Panelists. Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. *Pigment Cell Melanoma Res.*, 2012 May; 25(3): E1–13.
4. Ezzedine K, Grimes PE, Meurant JM, Seneschal J, Léauté-Labrèze C, Ballanger F, et al. Living with vitiligo: results from a national survey indicate differences between skin phototypes. *Br J Dermatol.*, 2015 Aug; 173(2): 607–9.
5. Howitz J, Brodthagen H, Schwartz M, Thomsen K. Prevalence of vitiligo. Epidemiological survey on the Isle of Bornholm, Denmark. *Arch Dermatol.*, 1977 Jan; 113(1): 47–52.
6. Boisseau-Garsaud AM, Garsaud P, CalèsQuist D, Hélénon R, Quénéhervé C, Claire RC. Epidemiology of vitiligo in the French West Indies (Isle of Martinique). *Int J Dermatol.*, 2000 Jan; 39(1): 18–20.
7. Alikhan, A.; Felsten, LM.; Daly, M. & Petronic-Rosic, V. Vitiligo: A comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. *J Am Acad Dermatol.*, September 2011; 65(3): 473-491.
8. Felsten, LM.; Alikhan, A. & Petronic-Rosic, V. (2011). Vitiligo: A comprehensive overview Part II: Treatment options and approach to treatment. *J Am Acad Dermatol.*, September 2011; 65(3): 493-514.
9. Lakhani, D.M. and Deshpande, A.S. "Various Treatments for Vitiligo: Problems Associated and Solutions", *Journal of Applied Pharmaceutical Science*, 2014; 4(11): 101-105.
10. Talia, K., "Vitiligo in children: a review of classification, hypotheses of pathogenesis and treatment", *World J Pediatric*, 2009; 4: 265-268.
11. Craiglow, B.G. and King, B.A. "Tofacitinib citrate for the treatment of vitiligo: a pathogenesis-directed therapy, *JAMA Dermatology*, 2015; 151(10): 1110-1112.
12. Bellei, B.; Pitisci, A.; Ottaviani, M.; Ludovici, M.; Cota, C.; Luzi, F.; Dell'Anna, M.L.; Picardo, M. Vitiligo: A possible model of degenerative diseases. *PLoS ONE*, 2013; 8: e59782. [CrossRef]
13. Bellei, B.; Migliano, E.; Tedesco, M.; Caputo, S.; Papaccio, F.; Lopez, G.; Picardo, M.

- Adipose tissue-derived extracellular fraction characterization: Biological and clinical considerations in regenerative medicine. *Stem. Cell Res. Ther.*, 2018; 9: 207. [CrossRef]
14. Daniel, B.S.; Wittal, R. Vitiligo treatment update. *Australas J. Dermatol.*, 2015; 56: 85–92.
 15. Luger, T.; Paul, C. Potential new indications of topical calcineurin inhibitors. *Dermatology*, 2007; 215(Suppl. 1): 45–54.
 16. Yannas, I.V. Similarities and differences between induced organ regeneration in adults and early foetal regeneration. *J. R. Soc. Interface*, 2005; 2: 403–417. [CrossRef] [PubMed]
 17. Taïeb, A. & Picardo, M. Clinical practice. Vitiligo. *N Engl J Med.*, January 2009; 362(2): 160–169.
 18. LePoole IC, Das PK, van den Wijngaard RM, Bos JD, Westerhof W. Review of the etiopathomechanism of vitiligo: a convergence theory. *Exp Dermatol.*, 1993 Aug; 2(4): 145–53.
 19. Rodrigues M, Ezzedine K, Hamzavi I, Pandya AG, Harris JE; Vitiligo Working Group. New discoveries in the pathogenesis and classification of vitiligo. *J Am Acad Dermatol.*, 2017 Jul; 77(1): 1–13.
 20. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet.*, 2015 Jul; 386(9988): 74–84.
 21. Andoval-Cruz M, García-Carrasco M, Sánchez-Porras R, Mendoza-Pinto C, Jiménez Hernández M, Munguía Realpozo P, et al. Immunopathogenesis of vitiligo. *Autoimmune Rev.*, 2011 Oct; 10(12): 762–5.
 22. Richmond JM, Frisoli ML, Harris JE. Innate immune mechanisms in vitiligo: danger from within. *Curr Opin Immunol.*, 2013 Dec; 25(6): 676–82.
 23. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. *Pigment Cell Res.*, 2003 Jun; 16(3): 208–14.
 24. Majumder PP, Nordlund JJ, Nath SK. Pattern of familial aggregation of vitiligo. *Arch Dermatol.*, 1993 Aug; 129(8): 994–8.
 25. SK, Majumder PP, Nordlund JJ. Genetic epidemiology of vitiligo: multilocus recessivity cross-validated. *Am J Hum Genet.*, 1994 Nov; 55(5): 981–90.
 26. Spritz RA, Andersen GH. Genetics of Vitiligo. *Dermatol Clin.*, 2017 Apr; 35(2): 245–55.
 27. Jin Y, Birlea SA, Fain PR, Ferrara TM, Ben S, Riccardi SL, et al. Genome-wide association analyses identify 13 new susceptibility loci for generalized vitiligo. *Nat*

- Genet., 2012 May; 44(6): 676–80.
28. Jin Y, Mailloux CM, Gowan K, Riccardi SL, LaBerge G, Bennett DC, et al. NALP1 in vitiligo-associated multiple autoimmune disease 25
 29. Spritz RA. The genetics of generalized vitiligo: autoimmune pathways and an inverse relationship with malignant melanoma. *Genome Med.*, 2010 Oct; 2(10): 78.
 30. Birlea SA, Jin Y, Bennett DC, Herbstman DM, Wallace MR, McCormack WT, et al. Comprehensive association analysis of candidate genes for generalized vitiligo supports XBP1, FOXP3, and TSLP. *J Invest Dermatol.*, 2011 Feb; 131(2): 371–81.
 31. Spritz RA. Six decades of vitiligo genetics: genome-wide studies provide insights into autoimmune pathogenesis. *J Invest Dermatol.*, 2012 Feb; 132(2): 268–73.
 32. Spritz RA, Hearing VJ Jr. Genetic disorders of pigmentation. *Adv Hum Genet.*, 1994; 22: 1–45.
 33. Aharav E, Merimski O, Shoenfeld Y, Zigelman R, Gilbrud B, Yechezkel G, et al. Tyrosinase as an autoantigen in patients with vitiligo. *Clin Exp Immunol*, 1996 Jul; 1.
 34. Rezaei N, Gavalas NG, Weetman AP, Kemp EH. Autoimmunity as an aetiological factor in vitiligo. *J Eur Acad Dermatol Venereol.*, 2007 Aug; 21(7): 865–76.
 35. Jin Y, Birlea SA, Fain PR, Gowan K, Riccardi SL, Holland PJ, et al. Variant of TYR and autoimmunity 3 loci in generalized vitiligo. *N Engl J Med.*, 2010 May; 362(18): 1686–97.
 36. Dell'Anna ML, Maresca V, Briganti S, Camera E, Falchi M, Picardo M. Mitochondrial impairment in peripheral blood mononuclear cells during the active phase of vitiligo. *J Invest Dermatol.*, 2001 Oct; 117(4): 908.
 37. Eeckhaert R, Dugardin J, Lambert J, Lapeere H, Verhaeghe E, Speckaert MM, et al. Critical appraisal of the oxidative stress pathway in vitiligo: a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol.*
 38. Uri N, Mojamdar M, Ramaiah A. In vitro growth characteristics of melanocytes obtained from adult normal and vitiligo subjects. *J Invest Dermatol.*, 1987.
 39. Dell'Anna ML, Picardo M. A review and a new hypothesis for non-immunological pathogenetic mechanisms in vitiligo. *Pigment Cell Res.*, 2006 Oct; 19(5): 406–11.
 40. V, Roccella M, Roccella F, Camera E, Del Porto G, Passi S, et al. Increased sensitivity to peroxidative agents as a possible pathogenic factor of melanocyte damage in vitiligo. *J Invest Dermatol.*, 1997 Sep; 109(3): 310–3.
 41. H, Pehlivan M, Alper S, Tomatir AG, Onay H, Yüksel SE, et al. Lack of association between catalase gene polymorphism (T/C exon 9) and susceptibility to vitiligo in a

- Turkish population. *Genet Mol Res.*, 2011 Oct; 10(4): 4126–32.
42. mbow K, Chen H, Park JS, Thomas PD. Increased sensitivity of melanocytes to oxidative stress and abnormal expression of tyrosinaserelated protein in vitiligo. *Br J Dermatol.*, 2001 Jan; 144(1): 55–65.
43. Dell'Anna ML, Ottaviani M, Albanesi V, Vidolin AP, Leone G, Ferraro C, et al. Membrane lipid alterations as a possible basis for melanocyte degeneration in vitiligo. *J Invest Dermatol.*, 2007 May; 127(5): 1226–33.
44. Bickers DR, Athar M. Oxidative stress in the pathogenesis of skin disease. *J Invest Dermatol.*, 2006 Dec; 126(12): 2565–75.
45. Challreuter KU, Bahadoran P, Picardo M, Slominski A, Ellassiuty YE, Kemp EH, et al. Vitiligo pathogenesis: autoimmune disease, genetic defect, excessive reactive oxygen species, calcium imbalance, or what else? *Exp Dermatol.*, 2008 Feb; 17(2): 139–60.
46. den Boorn JG, Picavet DI, van Swieten PF, van Veen HA, Konijnenberg D, van Veelen PA, et al. Skin-depigmenting agent monobenzene induces potent T-cell autoimmunity toward pigmented cells by tyrosinase haptenation and melanosome autophagy. *J Invest Dermatol.*, 2011 Jun; 131(6): 1240–51.
47. R, Broady R, Huang Y, Wang Y, Yu J, Gao M, et al. Transcriptome analysis reveals markers of aberrantly activated innate immunity in vitiligo lesional and non-lesional skin. *PLoS One.*, 2012; 7(12): e51040.
48. Naughton GK, Eisinger M, Bystryrn JC. Detection of antibodies to melanocytes in vitiligo by specific immunoprecipitation. *J Invest Dermatol.*, 1983 Dec; 81(6): 5.
49. K, Van Geel N, Naeyaert JM. Evidence for an autoimmune pathogenesis of vitiligo. *Pigment Cell Res.*, 2003 Apr; 16(2): 90–100.
50. Falabella R, Escobar CE, Carrascal E, Arroyave JA. Leukoderma punctata. *J Am Acad Dermatol.*, 1988 Mar; 18(3): 485–94.
51. Gan EY, Cario-André M, Pain C, Goussot JF, Taïeb A, Seneschal J, et al. Follicular vitiligo: A report of 8 cases. *J Am Acad Dermatol.*, 2016 Jun; 74(6): 1178.
52. Hann SK, Lee HJ. Segmental vitiligo: clinical findings in 208 patients. *J Am Acad Dermatol.*, 1996 Nov; 35(5 Pt 1): 671–4.
53. Arona MI, Arrunátegui A, Falabella R, Alzate A. An epidemiologic case-control study in a population with vitiligo. *J Am Acad Dermatol.*, 1995 Oct; 33(4): 621–5.
54. Hann SK, Park YK, Chun WH. Clinical features of vitiligo. *Clin Dermatol.*, 1997 Nov Dec; 15(6): 891–7.
55. Hann SK, Chang JH, Lee HS, Kim SM. The classification of segmental vitiligo on the

- face. *Yonsei Med J.*, 2000 Apr; 41(2): 209.
56. Mofty AM, el-Mofty M. Vitiligo. A symptom complex. *Int J*
57. Khan A, Felsten LM, Daly M, PetronicRosic V. Vitiligo: a comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. *J Am Acad Dermatol.*, 2011 Sep; 65(3): 473–91.
58. Zedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet.*, 2015 Jul; 386(9988): 74–84.
59. Zzedine K, Silverberg N. A Practical Approach to the Diagnosis and Treatment of Vitiligo in Children. *Pediatrics*, 2016 Jul; 138(1): 138.
60. äieb A, Picardo M; Vitiligo European Task Force Members. The definition and assessment of vitiligo: a consensus report of the Vitiligo European Task Force. *Pigment Cell Res.*, 2007 Feb; 20(1): 27–35.
61. Gawkrödger DJ, Ormerod AD, Shaw L, Mauri-Sole I, Whitton ME, Watts MJ, et al.; Therapy Guidelines and Audit Subcommittee, British Association of Dermatologists; Clinical Standards Department, Royal College of Physicians of London; Cochrane Skin Group; Vitiligo Society. Guideline for the diagnosis and management of vitiligo. *Br J Dermatol.*, 2008 Nov; 159(5): 1051–76.
62. Thatte SS, Khopkar US. The utility of dermoscopy in the diagnosis of evolving lesions of vitiligo. *Indian J Dermatol Venereol Leprol.*, 2014 Nov-Dec; 80(6): 505–8.
63. Bark, KM.; Heo, EP.; Han KD.; Kim, MB.; Lee, ST.; Gil, EM. & Kim, TH. Evaluation of the phototoxic potential of plants used in oriental medicine. *J Ethnopharmacol.*, January 2010; 127(1): 11-18.
64. Dharmananda, S. (August, 2011). *Ayurvedic Herbal Medicine and its Relation to Chinese Herbal Medicine*, 22/08/2011.
65. Sarveswari, KN. (2010). Cosmetic camouflage in vitiligo. *Indian J Dermatol.*, July 2010; 55(3): 211-214.
66. Arlt, VM.; Stiborova, M. & Schmeiser, HH. Aristolochic acid as a probable human cancer hazard in herbal remedies: a review. *Mutagenesis.*, July 2002; 14(4): 265-277.
67. Saper, RB.; Kales, SN.; Paquin, J.; Burns, MJ.; Eisenberg, DM.; Davis, RB. & Phillips, RS. Heavy metal content of ayurvedic herbal medicine products. *JAMA.*, December 2004; 292(23): 2868-2873.
68. Jeon, S.; Kim, NH.; Koo, BS.; Lee, HJ. & Lee, AY. Bee venom stimulates human melanocyte proliferation, melanogenesis, dendricity and migration. *Exp Mol Med.*,

October 2007; 39(5): 603-613.

69. Serrano, G.; Lorente, M.; Reyes, M.; Millan, F.; Lloret, A; Melendez, J.; Navarro, M. & Navarro, M. Photodynamic therapy with low-strength ALA, repeated applications and short contact periods (40-60 minutes) in acne, photoaging and vitiligo. *J Drugs Dermatol.*, June 2009; 8(6): 562-568.
70. Aghaei, S. & Ardekani, GS. Topical immunotherapy with diphenylcyclopropenone in vitiligo: a preliminary experience. *Indian J Dermatol Venereol Leprol.*, November 2008; 74(6): 628-631.
71. Tanioka, M.; Yamamoto, Y.; Kato, M. & Miyachi, Y. Camouflage for patients with vitiligo vulgaris improved their quality of life. *J Cosmet Dermatol.*, March 2010; 9(1): 72-75.
72. De Cuyper, C. Permanent makeup: indications and complications. *Clin Dermatol.*, January 2008; 26(1): 30-34.
73. Fusaro, RM. & Rice, EG. (2005). The maillard reaction for sunlight protection. *Ann N Y Acad Sci.*, June 2005; 1043: 174-183.
74. Sarveswari, KN. (2010). Cosmetic camouflage in vitiligo. *Indian J Dermatol.*, July 2010; 55(3): 211-214.