

Safety and Efficacy of Herbal Extracts in the Treatment of Vitiligo

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Abstract: Vitiligo, a skin condition characterized by depigmented patches, has a long history dating back over 1500 years BC. Ancient civilizations, including those of pre-Hindu Vedic India and Egypt, documented its existence and attributed it to a lack of melanin. Traditional healers, such as Hakims and Vaidyas, employed various remedies to treat vitiligo. In Egypt, a mixture of tar, honey, and oil was commonly used, while in India, herbal formulations were administered to stimulate melanin production. The AYUSH system, encompassing Ayurveda, Siddha, and Unani, offers a comprehensive approach to vitiligo treatment. In Ayurveda, Bakuchi (*Psoraleacorylifolia*) seeds, both in powder and topical forms, are widely used. Siddha medicine categorizes vitiligo (*Venpadai*) into three types based on the imbalance of vital humors: *VathaVenpadai*, *PithaVenpadai*, and *KabaVenpadai*. Unani medicine, founded by Hakim IbnSina (*Avicenna*) in 980 CE, emphasizes the restoration of bodily balance to induce repigmentation. While modern medicine offers synthetic treatments to inhibit vitiligo and stimulate melanin production, these often come with adverse side effects. This review aims to explore the potential of herbal remedies, particularly those derived from the AYUSH system, as a safer and more effective alternative for vitiligo management..

Keywords: Vitiligo, a skin condition caused by a lack of melanin, has been treated with various therapies, including herbal remedies. To evaluate the efficacy of these herbal treatments, researchers often analyze their active ingredients using techniques like High-Performance Liquid Chromatography (HPLC) and UV spectroscopy. These methods help identify and quantify the specific compounds responsible for the therapeutic effects of herbal medicines.

I. INTRODUCTION

HISTORY

The earliest records of vitiligo date back over 3000 years. The Roman physician Celsus and ancient Egyptian medical texts, such as the Ebers Papyrus, described conditions that likely correspond to vitiligo. Indian Ayurvedic texts, including the Atharva Veda and the Ashtanga Hridaya, also discussed depigmentation disorders. In Japan, Shinto prayers from 1200 BC mentioned depigmentation.

It took nearly 4000 years for scientists to identify the underlying cause of vitiligo. In 1879, Moritz Kaposi's discovery of the DOPA reaction shed light on the role of melanocytes and the enzyme tyrosinase in melanin synthesis.

INTRODUCTION:

Vitiligo is a common autoimmune skin disorder that causes loss of skin color. While not life-threatening or contagious, it can significantly impact a person's quality of life. Affecting approximately 0.5 to 2% of the global population, vitiligo often appears in the mid-twenties. In India, the prevalence is particularly high, ranging from 0.46% to 8.8%.

Vitiligo can manifest in various patterns:

- * Vitiligo Vulgaris: The most common type, accounting for 64.9% of cases.
- * Focal Vitiligo: Affecting specific areas of the body, representing 18.6% of cases.
- * Acrofacial Vitiligo: Primarily affecting the hands, feet, and face, comprising 0.8% of cases.
- * Mucosal Vitiligo: Involving the mucous membranes, accounting for 14.8% of cases.
- * Segmental Vitiligo: Affecting one side of the body, representing 8.2% of cases.

Vitiligo :

Vitiligo is often linked to imbalances in the three doshas (Vata, Pitta, and Kapha) in Ayurvedic medicine. While modern medicine primarily attributes vitiligo to autoimmune disorders, both traditional and contemporary approaches aim to manage the condition and improve quality of life. Effective prevention and treatment strategies can vary from person to person, making personalized care essential.

Pathogenesis of Vitiligo :

Here is the paragraph translated to Spanish:

El vitiligo es un trastorno poligenético multifactorial con una patogénesis compleja. Está relacionado con factores tanto genéticos como no genéticos.

Aunque se han propuesto varias teorías sobre la patogénesis del vitiligo, la causa precisa sigue siendo desconocida.

Las teorías incluyen:

- * Teoría autoinmune y de citotoxicidad
- * Defecto intrínseco y melanocitos
- * Hipótesis neural
- * Mecanismo oxidante-antioxidante

El vitiligo es asintomático excepto en el vitiligo inflamatorio, que se asocia con prurito y se caracteriza por lesiones elevadas y margen eritematoso.

The FOXP3 gene located on the X chromosome was also the risk factor of the Vitiligo)[3]

Causes of Vitiligo:

Autoimmune disease: A problem with the body’s immune system

- * Family history: Having a relative with vitiligo
- * Environmental factors: Stress, severe sunburn, skin injury, or exposure to certain chemicals
- * Lack of pigment: Not producing enough melanin, the pigment that gives skin its color
- * Sun exposure: Damage to skin cells from the sun’s UV rays
- * Nutrient deficiencies: Low levels of iron or copper in the body
- * Chronic inflammation: Long-term inflammation in the body
- * Parasitic infections: Infestation with certain types of worms.

Symptoms:

Vitiligo is characterized by the following symptoms:

- * Depigmentation: Patches of skin that lose their color, often appearing on the hands, face, and areas around body openings.
- * Premature hair whitening: Loss of color in hair on the scalp, eyelashes, eyebrows, and beard.
- * Mucous membrane depigmentation: Loss of color in the tissues lining the inside of the mouth and nose.
- * Ocular involvement: Changes in the color of the retina.

Types of Vitiligo-

Types of Vitiligo

Segmental Vitiligo

- Less common
- More common in children
- occurs along a spinal nerve
- or
- on one side of he body

Non Segmental

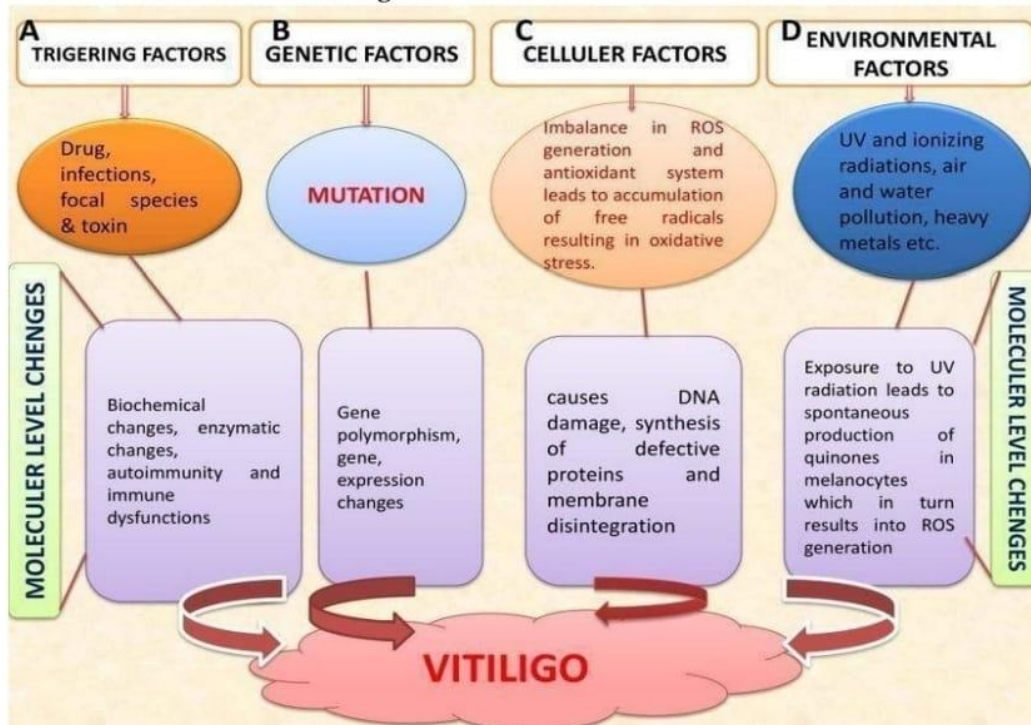
- More common
- Affects any age group
- can occur on any side - sometimes as mirror image
- c/a generalised vitiligo

A) Non-Segmental Vitiligo:

Vitiligo can also be classified as bilateral or generalized. This type is characterized by symmetrical depigmentation, meaning white patches appear on both sides of the body in a mirrored pattern. It is the most common form of vitiligo, affecting approximately 90% of individuals with the condition.

B) Segmental Vitiligo :

Another type of vitiligo is segmental vitiligo, also known as unilateral or localized vitiligo. In this form, white patches are confined to one specific area of the body, unlike the symmetrical pattern seen in bilateral vitiligo. While less common overall, segmental vitiligo is more prevalent in children compared to non-segmental vitiligo. It typically has an earlier onset and affects around 3% of individuals with the condition.



Therapies used In Vitiligo:

Light therapy :

The selection of a treatment plan for vitiligo is influenced by several factors, including:

- * Age: The patient’s age can impact treatment choices.
- * Extent of involvement: The amount of skin affected by depigmentation.
- * Location of lesions: The specific areas of the body involved.
- * Rate of progression: The speed at which the condition is advancing.

Optimal dosing frequency: Three times per week.

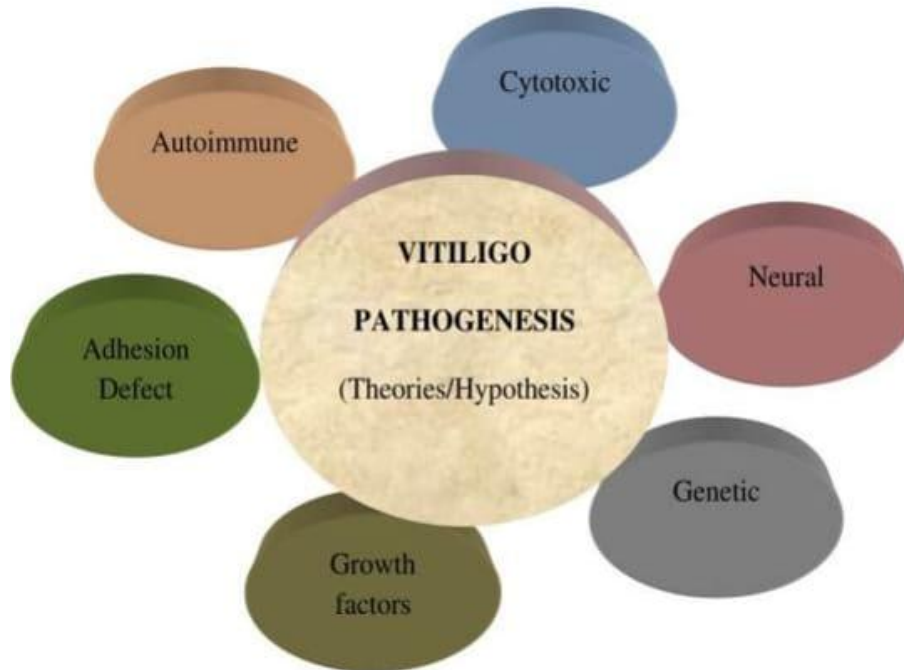
Acceptable dosing frequency: Two times per week.

Surgical Therapy :

A)Surgical Grafting: This procedure involves transplanting small pieces of healthy, pigmented skin to areas affected by depigmentation.

Blister Grafting: In this technique, blisters are created on healthy, pigmented skin, typically using suction. The tops of these blisters are then transplanted to the depigmented areas.

Cellular Suspension Transplant: This method involves taking pigmented skin, isolating the cells, and suspending them in a solution. The cell suspension is then transplanted onto the affected areas.



Animal Models of Vitiligo that develop spontaneously:

Some animals, like pigs, can get vitiligo. This happens because their bodies attack their own skin cells.

1) Swine:

These animals were specifically bred to have a high rate of melanoma. Approximately 54% are born with melanoma, and 85% develop it within their first year of life. However, in 90% of cases, these tumors spontaneously regress, accompanied by localized depigmentation of the skin and hair. Between the fourth and sixteenth weeks of life, depigmentation may spread from the original site, often affecting the skin, hair, and melanocytes in the iris of the eye.

2) Horses:

The mechanisms underlying vitiligo in horses with antibodies against melanocyte surface antigens remain poorly understood. These animals could serve as valuable models for studying antibody formation in vitiligo, especially considering the large volumes of serum available for antibody purification. Additionally, the gray allele in Lipizzaner horses provides a natural model for studying vitiligo.

Toxicology occur in Vitiligo:

Acute oral toxicity: Short-term poisoning from swallowing the substance.

* Short-term inhalation toxicity: Short-term poisoning from breathing in the substance.

* Short-term oral toxicity: Short-term poisoning from swallowing the substance.

* Chronic oral toxicity: Long-term poisoning from repeated swallowing of the substance.

* Skin irritation: Skin inflammation or damage caused by contact with the substance.

* Cytotoxicity: The ability of the substance to kill cells.

* Genotoxicity: The ability of the substance to damage genetic material (DNA).

* Antimutagenicity: The ability of the substance to prevent or reduce the occurrence of mutations.

Prevention of Vitiligo:

Sun Protection: Shield your skin from harmful UV rays.

* Tanning Avoidance: Refrain from using tanning beds or sun lamps.

* Skin Care: Minimize skin damage by avoiding cuts, scrapes, and burns.

* Informed Tattooing: Understand the potential risks associated with tattoos.

* Healthy Lifestyle: Boost your immune system through a balanced diet and regular exercise.

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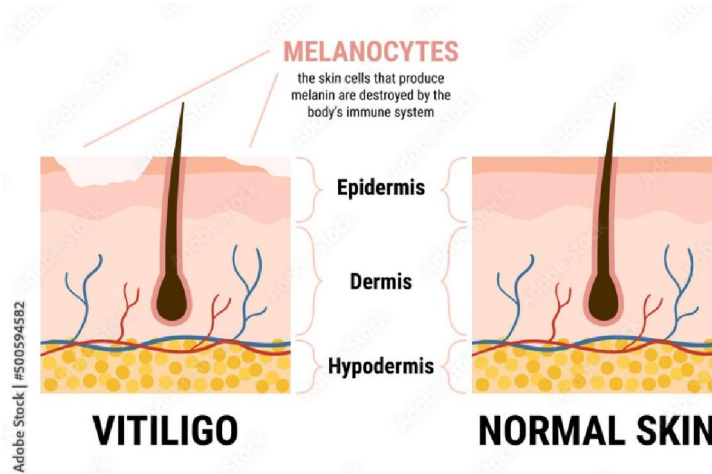
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- * Mental Well-being: Prioritize mental health by practicing stress management techniques.
- * Community Support: Connect with others who have vitiligo for emotional support and shared experiences.
- * Hydration and Nutrition: Stay hydrated and nourish your body with a diet rich in essential nutrients.

1) Immunotherapy :

Adaptive immunity in Vitiligo: Several studies suggest that CD8+ T cells, which target specific antigens, play a key role in destroying melanocytes in people with vitiligo. Early research showed that T cells infiltrate the skin affected by vitiligo. CD8+ T cells were found near dying melanocytes in the skin’s outermost layer. Additionally, the number of CD8+ T cells in the blood of vitiligo patients that recognize melanocyte antigens correlates with the severity of the disease. These cells can also kill melanocytes.



General Mechanism Of vitiligo:

Melanocytes are skin cells that produce melanin, a pigment that gives skin its color. When harmful bacteria or other foreign invaders enter the body, the immune system sometimes overreacts and produces antibodies to attack them. In some cases, the immune system mistakenly attacks melanocytes. This destruction of melanocytes leads to the formation of white, milky patches on the skin, a condition known as vitiligo.

Synthetic drugs that are used in treatment of Vitiligo:

Treatment	Drug	Indications	Side effect
1)Corticosteroid	Betamethasone dipropionate,clobetasol dipropionate,	Localized Vitiligo both on adults and children	Skin atrophy,Telangiectasias, acneic lesions,hypertrichosis
2)Immunomodulators	Tacrolimus , pimecrolimus	Adult patients as a substitution option of corticosteroid	Photosensitivity,Burning sensation erythema, flushing increased risk of cutaneous.
3)Orally Administered	Ruxolitinib(opzelura)	Medication approved by U.v, high risk myelofibrosis	Urinary tract infection Other bleeding Increased risk of infection Weight gain

Herbal drug used in the treatment of vitiligo:

Capsaicin
Walnut
Green tea
Basil Leaves
Giloy

1)Capsaicin	Curcumas' – melo(muskmelon, fixed 4 to16%)proteins,capsanthin, carotene	They are responsible for red pigment.
2)walnut	Gallic acid,ethyl gallate, pyrogallol,vanillic acid,protocatechuic acid	They contain copper which is needed to produce melanin pigment.
3)Green Tea	Caffeine,catechin,epigallocatechin, theanine,epicatechin,gallocatechin	Antioxidants Act as booster for
		pigmentation and melanin production.
4)Basil Leaves	Methyl cinnamate (70.1%) linalool(17.5%)B. elemene	Anti aging Stimulate production of melanin on the skin
5)Giloy	Giloy,tinospora acetate , Tinosporidine sinapic acid,octacosanol	A herb that helps treat and correct the abnormalities of one's immune system

Capsicum:

Capsicum peppers were first documented in the mid-1400s by a doctor who accompanied Columbus on his voyages to the West Indies.



Dose of capsicum:- Children-0.025%- 0.075%
Pregnancy- high level of dose avoided
Adults- apply 3 to 4 times a day
Dosage form and Strength[9]

Topical Cream- 0.025%-0.035%, 0.075% to 0.1%

Topical gel- 0.025%

Topical liquid- 0.025%

Solvent suitable for extraction:

Solvents:

- * Ethyl acetate
- * Dichloromethane
- * Acetone
- * Acetonitrile
- * Methanol
- * Acetic acid
- * Toluene

Surfactants:

Glycerol

Please note that while glycerol is often used in cosmetic and pharmaceutical formulations for its moisturizing properties, it's not typically considered a traditional surfactant like soaps or detergents.

Validation method in Vitiligo :

Developing a UV spectrophotometric method to measure the amount of capsaicin in ethanol solutions.

HPLC Analysis of Capsaicin:

Mobile Phase: A mixture of methanol and deionized water (66:34, v/v) was used for High-Performance Liquid Chromatography (HPLC) analysis of capsaicin.

UV Spectrophotometry:

- * Validation: A double-beam UV-visible spectrophotometer was used to validate a method for analyzing capsaicin in ethanol.
- * Maximum Absorption: Capsaicin exhibited peak absorbance at wavelengths of 227 nm and 280 nm.

Capsaicin:

- * Synonyms: Capsicum extract, chili, cayenne pepper
- * Family: Solanaceae
- * Source: Oleoresin extracted from dried, ripe fruits of *Capsicum annuum* var.
- * Chemical Composition:
 - * 0.5-0.9% capsaicin (colorless, crystalline, pungent compound, volatile above 65°C)
 - * 4-16% fixed oil
 - * Protein
 - * Pigment (responsible for red color)
 - * Thiamine
 - * Ascorbic acid
- * Geographical Source: East Africa, West Africa, India (Andhra Pradesh, Uttar Pradesh, Gujarat, Maharashtra, Assam, Tamil Nadu)

Uses of Capsaicin:

- * Anti-inflammatory and Antioxidant Properties: Capsaicin possesses potent anti-inflammatory and antioxidant effects.
- * Vitiligo Treatment: Capsaicin has been studied for its potential to halt cellular damage in vitiligo.
- * Melanocyte Protection: Cucumis melo (melon) may prevent melanocyte destruction caused by oxidative stress, a crucial step in vitiligo development.

Mechanism of Action:

- * Antioxidant and Anti-inflammatory Effects: Capsaicin, in combination with curcumin, chili pepper, capsanthin, and carotene, exhibits antioxidant and anti-inflammatory properties.
- * TRPV1 Receptor Inactivation: Capsaicin binds to the TRPV1 receptor, leading to its inactivation.
- * Cellular Damage Prevention: By inhibiting the TRPV1 receptor, capsaicin helps prevent cellular damage caused by reactive oxygen species (ROS), which play a significant role in oxidative stress.

Basil leaves:



Synonyms: Sweet basil, Basilic commune, Basilic Grand, Krishna Tulsi

- * Family: Lamiaceae
- * Chemical Constituents: Methyl cinnamate (70.1%), linalool (17.5%), elemene (2.6%), camphor (1.5%)
- * Geographical Sources: Tropical Asia, Africa, America, and India
- * Biological Source: Basil is derived from the leaves of *Ocimum basilicum* L. (Sweet basil).

Uses of Basil:

- * Melanin Production: Basil leaves stimulate the production of melanin, a pigment responsible for skin color.
- * Antimicrobial Properties: Basil exhibits antibacterial and antifungal properties.
- * Anti-inflammatory Effects: Basil has anti-inflammatory effects.

Mechanism of Action:

- * Anti-Aging Properties: Basil leaves possess anti-aging properties.
- * Melanin Stimulation: A paste made from basil leaves and lime juice, applied to the skin for 20 minutes, can help increase melanin production.

3) Walnut-



- Synonym Juglandaceae (Latin), English walnut, Black walnut

Family- Juglandaceae

Chemical Composition:

- * Ash: 3.4%
- * Lignin: 50.3%
- * Hemicelluloses: 22.4%
- * Cellulose: 23.9%

Geographical Origin: Ancient Persia, USA, China, Turkey

Extraction Method: Ultrasound

Uses of Walnut:

- * Vitis Treatment: Walnuts can help reduce the appearance of white patches associated with vitiligo.
- * Antioxidant Properties: Walnuts possess antioxidant properties.
- * Anti-inflammatory Effects: Walnuts may help reduce inflammation.

Mechanism of Action:

- * Daily Consumption: Consuming 5-7 walnuts daily can be beneficial.
- * Topical Application: A paste made from crushed walnuts and water can be applied to affected areas (white patches).
- * TRPV1 Receptor Activation: This application may help activate the TRPV1 receptor in the body.
- * Patch Reduction: Activation of the TRPV1 receptor can contribute to reducing the appearance of white patches.

Giloy



- Synonyms ;Gulvel ,Tinsopora, Giloy,Amrita

Family -Menispermaceae

Chemical Constituents: Tinosporine, tinosporic acid, tinospora L, giloin, berberine, syringin, tinosporidine, tinosporaside

* Biological Source: Dried leaves and stem pieces of the woody climber *Tinospora cordifolia* Miers

* Geographical Source: [Specify the geographical source, if known]

Uses of *Tinospora Cordifolia*:

- * Anti-inflammatory Properties: It possesses anti-inflammatory properties.
- * Antioxidant Effects: It exhibits antioxidant effects.
- * Melanin Stimulation: It can stimulate melanin synthesis.

Mechanism of Action:

* Consumption and Application: Giloy (giloin) can be consumed in powdered form, as a decoction (kadha), or applied topically as a paste.

* JAK Receptor Inhibition: Giloy binds to the JAK receptor, which is involved in signaling pathways that lead to melanocyte destruction.

* Reduced Melanocyte Destruction: By binding to the JAK receptor, giloy helps minimize the destruction of melanocytes.

Tea-



Synonym-Camellia thea

Family-Theacea

Chemical Composition:

- * Rich in caffeine (1-3%)
- * Contains theobromine and theophylline (minor quantities)
- * Gallotannic acid (15%)
- * Yellow volatile oil

Geographical Source:

India, Sri Lanka, China, Indonesia, and Japan

Biological Source:

Prepared leaves and leaf buds of *Thea sinensis* (L.) Kuntze

Uses of Green Tea:

- * Skin Improvement: Green tea can help improve skin texture.
- * Antioxidant Properties: It possesses antioxidant properties.
- * Anti-inflammatory Effects: It exhibits anti-inflammatory effects.

Mechanism of Action:

Vitiligo Treatment: Green tea is considered a potential home remedy for managing the discomfort associated with vitiligo.

II. CONCLUSION

This review will explore the use of herbal remedies for vitiligo. Vitiligo is a complex condition with multiple contributing factors. While human studies are essential, they often rely on observational data. Combining these observations with mechanistic studies in animal models can provide a more comprehensive understanding of vitiligo and lead to the development of new treatments.

Herbal medicines offer a potential alternative due to their diverse bioactive compounds and lower risk of side effects. However, more research is needed to establish their safety, efficacy, and optimal dosage for vitiligo treatment. The lack of standardized formulations and quality control in herbal medicine presents challenges for widespread adoption. Animal models offer a valuable platform to study vitiligo pathogenesis. This review will also delve into the analysis and extraction of herbal compounds using suitable spectroscopic methods.

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