RESEARCH PAPER

"Role of Psoralea corylifolia *(Bakuchi)* in Melanogenesis and Repigmentation in Vitiligo: A Molecular Review"

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ABSTRACT
In Ayurveda, *Shwitra* is described in the chapter on *Kushtha Rogas* where pathogenesis is attributed mainly to the involvement of *Tridosha* especially *Bhrajaka Pitta*, *Kapha* and *Rakta Dushti*. It is correlated with Vitiligo in modern medicine. It is a chronic acquired depigmentary disorder characterised by loss of skin pigmentation due to destruction or dysfunction of melanocytes. Autoimmune mechanisms, oxidative stress, inflammatory mediators and genetic factors have been implicated in the disease development by current evidence. *Bakuchi* is a well-known *Shwitraghna* and *Varnya* drug in Ayurveda. It has attracted the attention of scientists as active constituents like psoralen, isopsoralen and bakuchiol have shown promise in stimulating melanocyte activity and melanogenesis.
Objective: - To study the molecular mechanism of *Bakuchi* in Vitiligo mainly in respect of melanocyte stimulation, melanogenesis, immunomodulation and repigmentation pathways.
Methods: - Literary review of Ayurvedic classical texts like Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Bhavaprakasha was done in this study. Research papers published in PubMed, Google Scholar, Scopus and various dermatology journals were also studied.
The study revealed that *bakuchi* contains psoralen, a potent photosensitising agent, which gets activated after exposure to UVA and increases the proliferation of melanocytes
Conclusion: -*Bakuchi* is a traditional Ayurvedic medicine and a scientifically proven melanocyte regenerative and melanogenic therapeutic agent at molecular level. It has an important role in the treatment of Vitiligo (*Shwitra*) through melanocyte stimulation, antioxidant activity and immune regulation.
Keywords: - *Shwitra*, Vitiligo, *Bakuchi*, psoralen, melanocyte, Melanogenesis**,**

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INTRODUCTION

The largest organ in our body is skin and it protects our body from the external environment. The colour of our skin is due to melanin, which is produced by cells called melanocytes. Whenever the melanocytes are destroyed or their ability to function is reduced for any reason, white patches appear on the human skin, which is called vitiligo in modern science.[1,2]
Prevalence Vitiligo affects about 0.5 to 2 percent of the world's population. This disease causes deep psychological disruptions, lowers self-confidence and has a substantial impact on the social life of an individual, so its increasing frequency in children is becoming a matter of special worry. The patient has problems in social interaction and is generally regarded with scorn by people. If it is about small children going to school then there can be problems like sharing tiffin with other children, sitting together, playing and doing normal social activities. Modern research shows it is a kind of autoimmune illness where the patient's immune system attacks its own melanocyte cells.[2] [3] Besides this, as per

oxidative stress theory, increase in Reactive Oxygen Species (ROS) is the reason of destruction of melanocytes.[4] Genetic predisposition is also an important factor in this disease where genes such as TYR, MITF, MC1R, TRP-1 and TRP-2 are involved.[5]

Acharya Charaka and Acharya Sushruta has discussed *Shwitra* under the heading of *Kushtha* in Ayurveda. Among the three *Doshas, Pitta, Kapha* and *Rakta Dushti* are considered predominant. Vitiation of *Bhrajaka Pitta* leads to loss of natural colour of the skin.[6,7] Different acharyas have described the *twacha* as having many layers. Acharya Charaka has classified *twacha* into six strata whereas Acharya Sushruta has identified seven layers of *twacha*. Acharya Charaka says that *Kilasa (Shwitra)* is produced in the third layer of *twacha*. On other side Acharya Sushruta has mentioned that *Kilasa* develops in fourth layer of skin called *Tamra* which is having thickness of 1/8th of *Brihi* (rice grain). Thus, from the Ayurvedic point of view, the beginning of *Shwitra* or *Kilasa* is in the superficial layers of the skin.

In Ayurveda *Bakuchi* is mentioned as *Shwitrahaghna*. It contains *Kushthaghna*, *Twachya* and *Varna*-promoting properties.various chemical constituents such as psoralen, isopsoralen, and bakuchiol [8,9] have been reported to be beneficial in promoting melanogenesis.[10,11]

Thus, the molecular review on the effect of *Bakuchi* on genes and melanocyte stimulation is very relevant. In modern science we find that vitiligo is an acquired depigmentary disorder in which the number of melanocyte cells that are present in the basal layer of the epidermis of the skin declines, or they are entirely eliminated.

MATERIALS AND METHODS

A comprehensive literature search was performed on the role of Psoralea corylifolia in melanogenesis and repigmentation in vitiligo, using the databases PubMed, Scopus, Web of Science, ScienceDirect and Google Scholar up to March 2026. The search terms included: “Psoralea corylifolia”, “Bakuchi”, “psoralen”, “isopsoralen”, “bakuchiol”, “bavachin”, “vitiligo”, “melanogenesis”, “repigmentation”, “melanocyte”, “tyrosinase”, “MITF”, “oxidative stress” and “immunomodulation”.

Original research articles, experimental studies, clinical trials and review articles described the phytochemistry, molecular mechanisms, melanogenic signalling pathways, antioxidant activity, immunomodulatory effects, and therapeutic potential of P. corylifolia in vitiligo. Exclusion criteria included articles not related to melanocyte biology and vitiligo, conference abstracts, duplicate research and non-English publications.

Data relevant to the study were collected and comprehensively reviewed to summarise the molecular pathways associated with P. corylifolia and its major bioactive components for melanocyte stimulation, melanin formation, immune modulation, and repigmentation.

1.AYURVEDA VIEW ON *SHWITRA*

1.1 *Shwitra Nidana: -*

- ***.Aharaja*: -**, *Drava, Snigdha*, and *Guru ahara*, *Navanna*, *Dadhi*, *Masha*, *Pishatanna*, *Viruddhahara* Excessive *amla* and *lavana rasa* Consuption, Excessive consumption of *Madya*, *kshar*, *Ajeernashana*, *asatmyabhojan*, *Garavisha* ,*Garbhajnidana*, Excessive *Kaphakaraahara* consumption by Garbhinistree causing *Shwitra* in baby.

- ***Viharaj*: -** *Chhardinigraha, Divaswapna, Ratrijagarana*

-Use cold water immediately after exposure to the blazing sun, effort or a stressful circumstance.

There are *agantuja* variables like *Vrana*, including *agnidagdhavrana*, and damage like cuts, scrapes, burns that can destroy pigment cells and lead to Vitiligo.

- ***Chikitsha sambandhi*: -** wrong use of *panchakarma* treatments

- ***Anya Nidana*: -** *Papkarma*, Gohatya, , Sadhu ninda or vadha or apamana Vipra guru Gharshana

1.2 *Samprapti Ghatak*: -

a) *Doshas: - Vata*-especially *Udana Vayu.*
b) *Dushya: - Rasa, Rakta, Mansa, Meda.*
c) Srotas: - *Rasavaha, Raktavaha, Mansavaha, Medovaha.*
d) *Sroto Dushti Lakshan: - Sanga, Vimargagaman.*
e) Marga: - Bahya Rogmarga.
f) Gati-: Tiryaka.
g) Adhishshthana: - Twacha

1.3 Bakuchi[14]: - Latin name: - Psoralea Corylifolia,

Family: - Fabaceae

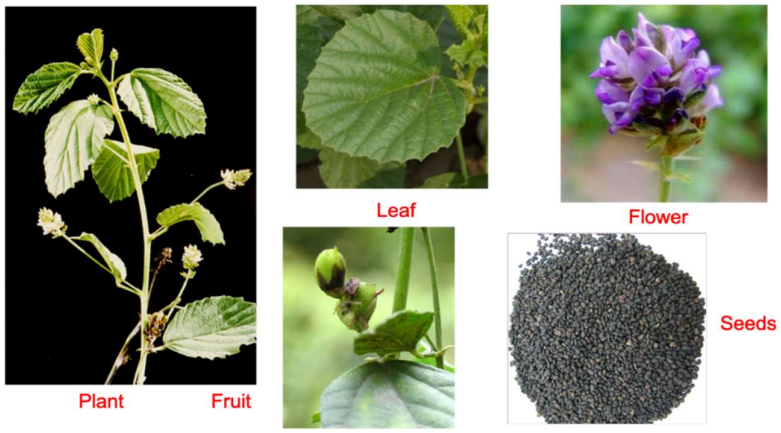


Fig.1 Morphological characteristics of *Bakuchi* (P*soralea corlifolia L*) : plant, leaves, flowers,Fruits and seeds.

Synonyms: -
Avalguj, Krishnaphala,Shashilekha Putiphali, Kushthagni, Somraji, Soma, Indulekha, Chandralekha, Shashilekha, Somvalli, Kalameshi, Kushthanashini, Durgandha, Kushthahantri, Suparnika.
Table no:1 *Rasapanchaka* attributed to *Bakuchi* in various Nighantu

Sr. No	Nighantu	*Rasa*	*Guna*	*Virya*	*Vipak*	*Dosaghnata*
1	Dhanvantari Nighantu [15]	*Tikta*	-	*Shita*	*Katu*	K alleviating
2	Madanpala Nighantu [16]	*Madhura, Tikta*	*Ruksha*	*Shita*	*Katu*	K alleviating; Phala-P Aggravating; VK alleviating
3	Kaiyadeva Nighantu [17]	*Tikta, Madhura*	*Laghu, Ruksha*	*Shita*	*Katu*	RPK alleviating
4	Bhava Prakasa Nighantu [18]	*Madhura, Tikta*	*Ruksha*	-	*Katu*	KRP alleviating; Phala-P Aggravating; KV alleviating
5	Raja Nighantu [19]	*Tikta*	-	*Ushna*	*Katu*	K alleviating
6	Shaligrama Nighantu [20]	*Tikta*	*Ruksha*	*Shita*	*Katu*	K alleviating
7	Dravya Guna Sangraha [21]	*Tikta*	-	*Shita*	*Katu*	PK alleviating

Karma- *Kushthaghna*,[22] *Jantughna*, *Twakdoshaghna, Vranashodhan, Vranaropan, Keshya*[22], *Aamdoshanashak, Pandurognashak, Pramehaghn*[22], *Uttejak, Vajikaran, Mutral, Swedal, Mridu Virechak.*
Usefull Part – Beeja, Beejtail
Chemical Constituents - **Psoralen**, Psoralidin, Isopsoralen, Isopsoralidin and Bakuchiol, Corylifolin. Metroterpenes, Flavonoid, Coumarins,

2.MOLECULAR MECHANISM

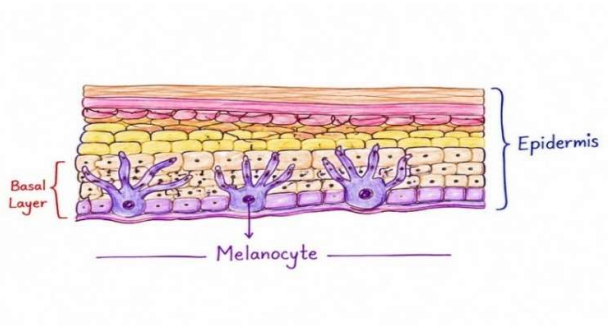


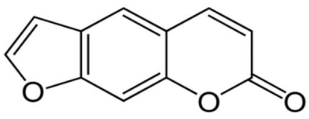
Fig. 2 Structure of epidermis showing basal layer and melanocytes.

Bakuchi(Psoralea corylifolia) includes more than 163 phytochemicals. Psoralen, isopsoralen, bakuchiol, bavachin and bavachalcone are thought to be most relevant in vitiligo therapy. These chemicals have photosensitising, antioxidant, anti-inflammatory and immunomodulatory properties. Photostimulation by psoralen promotes melanocyte activity, while bakuchiol, bavachin, and bavachalcone protect melanocytes from oxidative and inflammatory damage. Together, these mechanisms may enhance survival of melanocytes and repigmentation in vitiligo. *Bakuchi* primarily targets the melanocytes concealed in the basal layer of the epidermis and the hair follicles. It activates new melanocytes on basal layer which assists in repairing pigmentation.

S.No.	**Chemical Constituent**	**Chemical Class**	**Major Molecular target**	**Gene/protein Expression**	**Effect on melanocyte**
1.	**psoralen**	Linear furocoumarin	MITF Pathway DNA Photoadduct Formation (PUVA)	TYR↑ Indirect activation of melanogenic genes	Proliferation and differentiation of melanocytes Stimulates melanocyte activity after UVA exposure
2.	**Bakuchiol**	Meroterpene phenol	Antioxidant Axis Nrf2–HO-1 NF-κB Pathway	HO-1↑, SOD↑, Nrf2↑, Catalase↑ IL-6 ↓, TNF-α↓, COX-2↓	Protects melanocytes from oxidative injury Reduces inflammatory damage to melanocytes

Table no:-2

2.1.Psoralen: -



Poralen (C_{11} H_6 O_3)
Mol wt.186.16

Fig. 3 Chemical structure of psoralen from PCL

Bakuchi → Psoralen, Topical Absorption Psoralen is a photoactive furocoumarin that is activated by ultraviolet A (UVA) radiation. Upon UVA irradiation, psoralen absorbs photons and forms photoadducts with pyrimidine bases of DNA, leading to the activation of DNA damage response pathways and the alteration of cellular signalling systems.[23,24]These photobiological effects are not only beyond photosensitisation but also directly contribute to the repair of melanocytes in vitiligo.

Activated psoralen prevents autoimmune responses against melanocytes by inducing death of activated T lymphocytes and reducing the generation of pro-inflammatory cytokines such as interferon-γ (IFN-γ), tumour necrosis factor-α (TNF-α) and interleukin-2 (IL-2).[25,26]This immunomodulatory effect decreases immune-mediated death of melanocytes and creates a favourable milieu for melanocyte survival.[25,26] Simultaneously, psoralen induces activation, proliferation and migration of the remaining epidermal melanocytes and melanocyte stem cells in the hair follicles.[27,28]Activated follicular melanocyte stem cells differentiate into mature melanocytes and migrate to depigmented epidermis, resulting in perifollicular repigmentation.[27,28] The interaction of Psoralen and UVA also increases melanogenesis by upregulating the expression and activity of tyrosinase, the rate limiting enzyme of melanin production. enhanced activity of tyrosinase stimulates the conversion of tyrosine to L-DOPA and subsequently to dopaquinone, which leads to enhanced melanin synthesis.[29] Furthermore, photoactivated psoralen-treated melanocytes exhibit increased dendricity and accelerated melanosome transfer to neighbouring keratinocytes, enabling restoration of epidermal pigmentation.[27,29]

In addition, photoactivated psoralen induces keratinocytes and dermal fibroblasts to release melanocyte-supporting growth factors such as stem cell factor (SCF), basic fibroblast growth factor (bFGF), endothelin-1 and hepatocyte growth factor (HGF).[26,30] These growth factors promote the proliferation, differentiation, migration and melanogenic activity of melanocytes. Altogether, the combined effect of immunomodulation, activation of melanocyte stem cells, increased melanogenesis and growth factor mediated support lead to repigmentation in vitiligo.[23-30]

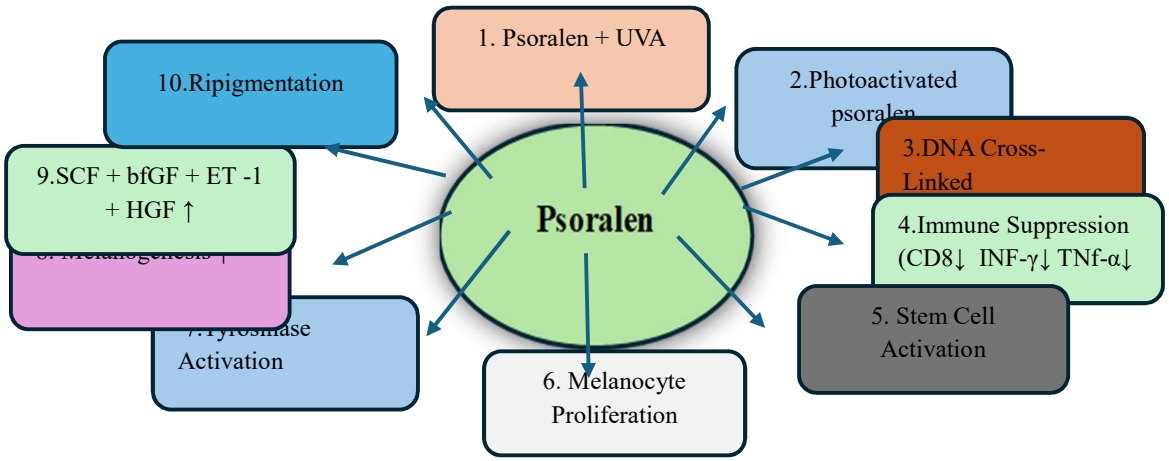
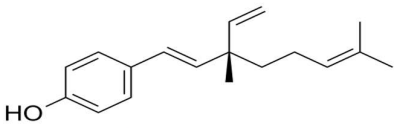


Fig.4 Mechanism or action of psoralen in vitiligo.

2.2. Bakuchiol: -



Bakuchiol ($C_{18}H_{24}O$)
Mol wt.256.38

Fig. 5 Chemical structure of Bakuchiol from PCL

The prenylated meroterpene, bakuchiol, isolated from Psoralea corylifolia L., is being acknowledged as a multifunctional bioactive component with antioxidant, anti-inflammatory and cytoprotective activities. Although there is little direct evidence of Bakuchiol activation of melanogenic enzymes, increasing experimental investigations suggest that it promotes repigmentation mainly by maintaining melanocyte viability and creating a favourable milieu for melanogenesis.[31-33]

Oxidative stress is a major initiator factor in the development of vitiligo, which results in excessive accumulation of reactive oxygen species (ROS), mitochondrial dysfunction and melanocyte death. Bakuchiol effectively scavenges ROS, reduces lipid peroxidation and stimulates the SIRT1/Nrf2 antioxidant signalling pathway, leading to the over-expression of endogenous antioxidant enzymes such as superoxide dismutase and glutathione peroxidase. These effects reduce oxidative damage and maintain redox homeostasis in melanocytes.[33-35]

Bakuchiol also maintains mitochondrial integrity by reducing mitochondrial oxidative damage and preventing ROS-induced activation of apoptotic pathways. Higher production of the anti-apoptotic protein Bcl-2 and

inhibition of Bax and cleaved caspase-3 has been shown to enhance melanocyte survival in oxidative circumstances in experimental research.[34,35]

Bakuchiol downregulates the inflammatory responses that are involved in melanocyte death by inhibiting NF-κB signalling and downregulating pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6. In addition, the downregulation of p38 MAPK and ERK signalling pathways reduces cellular stress responses and production of inflammatory mediators.[36-38]

Together, these antioxidant, anti-inflammatory, mitochondrial protective and anti-apoptotic effects may protect residual melanocytes and melanocyte stem cells in hair follicles, and facilitate their survival, migration and functional recovery. Therefore, Bakuchiol may indirectly stimulate melanogenesis and repigmentation by providing the conditions favourable to the regeneration of melanocytes and melanin synthesis in the vitiliginous skin.[31-35]

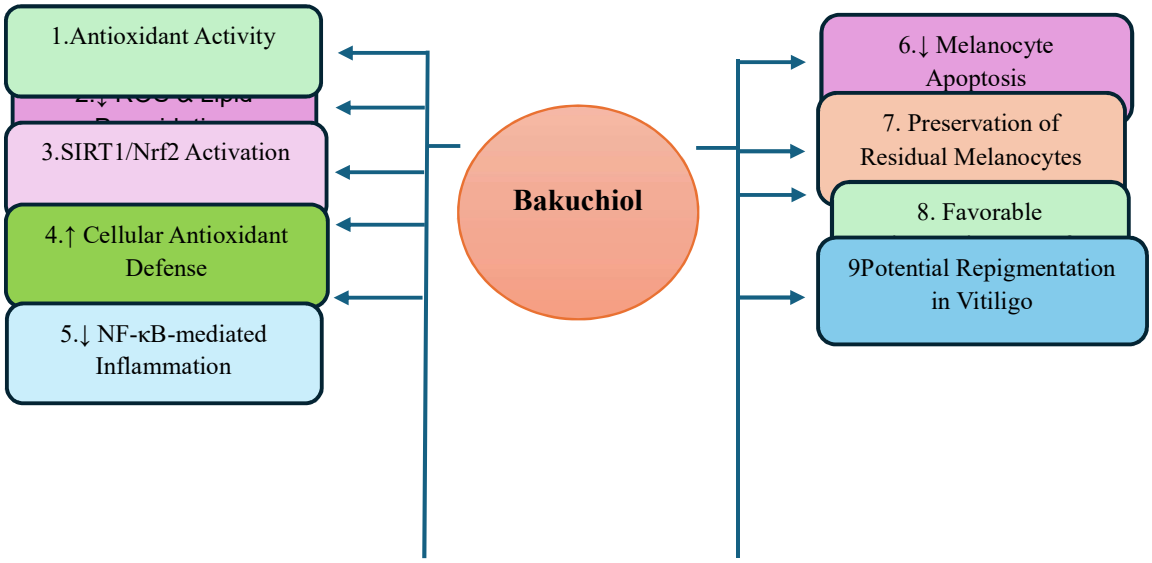


Fig.6 Proposed mechanism of bakuchiol in promoting repigmentation in vitiligo through antioxidant, anti-inflammatory and anti-apoptotic pathways leading to preservation of melanocytes and a favorable microenvironment for melanogenesis

DISCUSSION: -

Vitiligo is a chronic acquired depigmenting illness characterised by selective destruction of epidermal melanocytes that results in depigmented macules and patches. At now, it is thought to be a multifaceted disease, with a complex interaction of genetic predisposition, environmental factors, oxidative stress, immune system dysregulation, mitochondrial dysfunction and epigenetic changes.

Oxidative stress has been proposed as one of the key pathogenic mechanisms involved with vitiligo. Melanocytes are highly susceptible to oxidative injury because melanin synthesis yields reactive oxygen species (ROS). Excessive accumulation of ROS causes melanogenesis problems, degradation of cellular macromolecules, alteration of mitochondrial activity and finally apoptosis of melanocytes.

The antioxidant defence system is substantially weakened in vitiligo. Decreased activity of nuclear factor erythroid 2-related factor 2 (NRF2) and its downstream antioxidant enzymes, such as catalase, superoxide dismutase (SOD), glutathione peroxidase (GPx), heme oxygenase-1 (HO-1), and NAD(P)H quinone oxidoreductase-1 (NQO1), results in oxidative damage and increased vulnerability of melanocytes to cellular stress.

It also causes production of inflammatory mediators and activation of immunological responses. Elevated levels of interferon-gamma (IFN-γ), interleukin-15 (IL-15), interleukin-17 (IL-17) and interleukin-1β (IL-1β) have been reported in vitiligo lesions and in the peripheral circulation. The

activation of the IFN-γ/CXCL9/CXCL10 chemokine axis leads to the recruitment of autoreactive CD8+ T cells into the skin, followed by specific death of melanocytes and the development of the illness. Recent research has highlighted the involvement of mitochondrial dysfunction in the aetiology of vitiligo. In vitiligo melanocytes there are aberrant mitochondrial respiratory chain complexes, disturbed oxidative phosphorylation, reduced ATP synthesis and increased ROS generation. These modifications begin a vicious cycle of oxidative stress that results in the destruction and depletion of melanocytes.

However, the melanocyte defects are not the only mechanism contributing to disease progression. The poor cellular interaction within the epidermal milieu is also significant. Downregulation of E-cadherin leads to reduced adherence of melanocytes to keratinocytes and increased susceptibility of melanocytes to mechanical and oxidative stress. Aberrant production of melanocyte-supporting factors such as stem cell factor (SCF), basic fibroblast growth factor (bFGF), endothelin-1 and granulocyte-macrophage colony-stimulating factor (GM-CSF) also negatively affect melanocyte survival and melanogenesis.

Epigenetic dysregulation has been shown to play a significant role in vitiligo. Dysregulation of microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs) affects genes associated with melanocyte formation, pigmentation, oxidative stress response and immunological regulation. Multiple miRNAs have been identified as direct targets of MITF, the master regulator of melanocyte development and melanogenesis. These miRNAs are associated with the melanocyte malfunction and depigmentation.

In summary, the available data support the concept that vitiligo is a multifactorial systemic disease in which oxidative stress, mitochondrial dysfunction, immune mediated destruction of melanocytes, defective cellular communication in the epidermis and epigenetic modifications are interacting to cause progressive loss of melanocytes and depigmentation.

MOLECULAR MACHNISM

1.PSORALEN

PUVA (Psoralen plus Ultra Violet A) therapy is a complicated treatment method in vitiligo, which acts beyond simple photosensitisation. UVA radiation activates psoralens, which then initiate photochemical processes that affect numerous cellular and molecular pathways. PUVA stimulates proliferation, migration and differentiation of melanocytes by activation of residual melanocytes and follicular melanocyte stem cell.It also stimulates melanogenesis by promoting melanogenic pathways and tyrosinase activity. Moreover, PUVA has immunomodulatory effects by suppressing autoreactive immune responses and altering the local cytokine milieu. Together, these effects result in repigmentation of vitiligo lesions.

1.1. Photochemical activation of psoralen

Psoralens are naturally occuring furocoumarins that intercalate between the base pairs of DNA, especially the pyrimidine bases, such as thymine. The psoralen absorbs the photons of the UVA light (320-400 nm) and becomes photochemically active in an excited state (triplet). Once activated, the psoralen molecule covalently bonds to thymine residues. These are called monoadducts. Interstrand DNA crosslinks are formed by absorption of a second UVA photon. These photoadducts cross-link DNA strands and initiate a series of biological events that mediate the therapeutic benefits of PUVA.

1.2. DNA Damage Response and Cellular Signalling

Psoralen-DNA crosslinks activate DNA damage response mechanisms in cells. Recognition of these damages leads to p53-dependent signalling and subsequent induction of p21-mediated cell cycle arrest.

In fast proliferating cells, particularly activated lymphocytes, critical DNA damage induces death by intrinsic or extrinsic pathways. The selective sensitivity of activated immune cells forms the basis for the immunosuppressive activity of PUVA therapy.

1.3. Immunomodulatory Activities in Vitiligo

Current data indicate that autoreactive CD8+ cytotoxic T cells are key effectors of melanocyte destruction in vitiligo. [5] PUVA therapy induces apoptosis of activated T cells by forming DNA crosslinks and activating DNA damage pathways. This decreases the number of melanocyte-specific cytotoxic T lymphocytes that enter vitiliginous skin.PUVA also suppresses the production of pro-inflammatory cytokines, including IFN-γ, TNF-α and IL-2, resulting in a reduction of immune responses directed against melanocytes.Through these processes, PUVA generates a local immune environment that promotes melanocyte survival and repigmentation.

1.4. Induction of melanocyte proliferation

Histologic studies have demonstrated that PUVA therapy induces melanocyte proliferation and enhances melanocyte survival in vitiliginous lesions. PUVA-treated melanocytes show increased dendricity and increased melanosome transfer to neighbouring keratinocytes, which contributes to pigment restoration.

1.5. Melanocyte stem cell pools activation

Hair follicles are the major reservoir of melanocyte stem cells in vitiligo.PUVA causes activation and proliferation of these hidden melanocyte stem cells located within the bulge region and outer root sheath of hair follicles. the activated stem cells proliferate

to mature melanocytes and migrate to depigmented epidermis, resulting in characteristic perifollicular repigmentation.

1.6. Induction of Melanogenesis

PUVA not only increases the number of melanocytes, but also directly stimulates melanin synthesis. Experimental investigations have demonstrated a significant increase in melanogenesis when psoralen and UVA are given together rather than either treatment alone.This increased melanin synthesis is mediated by activation of melanogenic pathways and increased expression of enzymes involved in melanin production.

1.7. Activation of Tyrosinase and Synthesis of Melanin

Tyrosinase is the rate limiting enzyme in melanin synthesis. The mechanism of PUVA-induced melanogenesis is an increase in tyrosinase activity which leads to an increased conversion of tyrosine to L-DOPA, then to dopaquinone, and finally to increased production of eumelanin and pheomelanin. Tyrosinase inhibition shows strong inhibition of PUVA-induced pigmentation and underlines the vital participation of this enzyme in the process of repigmentation.

1.8. Melanocyte Growth Factor Support

PUVA induces the production of growth factors supporting melanocyte function, such as the basic fibroblast growth factor (bFGF), stem cell factor (SCF), endothelin-1, and hepatocyte growth factor (HGF), by keratinocytes and dermal fibroblasts.These growth factors stimulate melanocyte proliferation, migration, differentiation and melanogenesis and thus help in sustained repigmentation.

1.9. Receptor Tyrosine Kinase and Cell Surface Receptor Signalling

There is also evidence that photoactivated psoralen may interact with growth factor signalling pathways and membrane associated receptors, in addition to DNA mediated mechanisms. Altered epidermal growth factor receptor (EGFR) signalling and tyrosine kinase activity may play a role in the regulation of melanocyte proliferation and differentiation.These results demonstrate that PUVA exerts both DNA dependent and DNA independent biological effects.

1.10. Combined mechanism of PUVA-induced repigmentation

The mechanisms of PUVA-induced repigmentation involve several overlapping pathways including DNA photoadduct formation, apoptosis of autoreactive T cells, downregulation of inflammatory cytokines, stimulation of melanocyte stem cells, stimulation of proliferation of melanocytes, stimulation of melanogenesis and increased production of factors supporting melanocytes.Collectively, these effects ultimately lead to the restoration of melanocytic function and repigmentation of vitiliginous skin.

2. BAKUCHIOL

Bakuchiol is a biologically active meroterpene mainly distributed in seeds and leaves of Psoralea corylifolia L. It has good antioxidant, anti-inflammatory and cytoprotective properties. Although the exact molecular mechanism of Bakuchiol in vitiligo is unknown, the existing experimental data indicate the potential protective effects of Bakuchiol against melanocytes destruction by modulating oxidative stress, mitochondrial dysfunction, inflammatory signalling and apoptosis pathways. Such biological activities are of special interest in the present understanding of the pathophysiology of vitiligo.

2.1. Antioxidant activity and reduction of oxidative stress

One of the early events in the pathophysiology of vitiligo is considered to be oxidative stress. Overproduction of reactive oxygen species (ROS) such as superoxide anions, hydroxyl radicals and hydrogen peroxide leads to the malfunction and death of melanocytes. Melanocytes are especially susceptible to oxidative stress due to the generation of ROS as byproducts of melanin synthesis. Bakuchiol has strong antioxidant activity by directly scavenging free radicals and inhibiting lipid peroxidation. Experimental studies further show that Bakuchiol inhibits mitochondrial lipid peroxidation and reduces the intracellular accumulation of ROS. Bakuchiol may reduce the oxidative load to protect melanocytes from ROS-induced cellular damage and maintain the cellular redox balance.

2.2. SIRT1/Nrf2 Antioxidant Signalling Pathway Activation

The Nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is the primary endogenous antioxidant defence system to oxidative stress. Activation of Nrf2 leads to the transcription of antioxidant and cytoprotective genes and protects cells from oxidative damage.

In vitro, bakuchiol has been shown to induce the SIRT1/Nrf2 signalling pathway. Activation of this pathway leads to an increase in the activity of the endogenous antioxidant enzymes responsible for the detoxification of ROS, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). Improved antioxidant defence system may be involved in the protection of melanocytes from oxidative stress-induced degeneration in vitiligo.

2.3. Inhibition of Lipid Peroxidation

Lipid peroxidation is a major consequence of oxidative stress and a key function in melanocyte damage. Oxidative membrane damage has been described in vitiligo patients in the form of elevated levels of malondialdehyde (MDA), 4-hydroxynonenal (4-HNE) and other lipid peroxidation products.

Bakuchiol inhibits lipid peroxidation and reduces oxidative markers such as MDA, 4-HNE and 3-nitrotyrosine. Lipid peroxidation inhibition might extend the lifespan and functional stability of melanocytes through the preservation of the integrity of the membrane.

2.4. Protection against mitochondrial dysfunction

Mitochondrial abnormalities have recently been implicated in the pathogenesis of vitiligo. Mitochondrial dysfunction causes overproduction of ROS, depletion of ATP and activation of cell death pathways.

Bakuchiol has been shown to decrease mitochondrial oxidative damage, enhance mitochondrial antioxidant defence, and preserve mitochondrial function by modulating SIRT1-dependent pathways. These responses may decrease mitochondrial ROS formation and protect melanocytes against mitochondrial injury by oxidative stress.

2.5. Suppression of NF-κB-mediated inflammatory responses

Vitiligo is a disease in which melanocytes are destroyed, and it is believed that oxidative stress triggers inflammatory pathways that lead to this process. Nuclear factor-kappa B (NF-κB) is a major transcription factor controlling the expression of inflammatory mediators like TNF-a, IL-6, IL-1b and inducible nitric oxide synthase (iNOS).

Bakuchiol inhibits the activation of NF-κB and suppresses the production of several pro-inflammatory cytokines. Experimental trials have shown that bakuchiol therapy could significantly reduce the expression of TNF-α, IL-6, IL-1β and iNOS. Bakuchiol has potential to attenuate inflammatory signalling and therefore the inflammatory milieu that causes increasing melanocyte loss in vitiligo.

2.6. Regulation of the MAPK pathway

Mitogen-activated protein kinase (MAPK) signalling pathways including p38 MAPK and ERK pathways are involved in oxidative stress-induced inflammatory responses and apoptosis. This enhanced activation of these pathways contributes to melanocyte destruction under oxidative stress settings.

Bakuchiol inhibits phosphorylation of the signal molecules p38 MAPK and ERK. Inhibition of these pathways results in decreased production of inflammatory mediators and cellular stress responses, thus helping cellular protection.

2.7. Anti-Apoptotic Effects

Melanocyte loss in vitiligo is largely due to apoptosis. Oxidative stress induces apoptosis by mitochondrial mechanisms including alterations of Bcl-2 family proteins and activation of caspases.

Bakuchiol exhibits anti-apoptotic activity by increasing the expression of anti-apoptotic protein Bcl-2 and decreasing the expression of pro-apoptotic Bax and cleaved caspase-3. These effects inhibit apoptosis caused by oxidative stress and extend the cells' life span. Inhibition of apoptosis and maintenance of melanocyte survival may play a role in the maintenance of pigmentation.

2.8. Melanogenesis and potential effects

We reported earlier that bakuchiol and other prenylated phenolic compounds from Psoralea corylifolia modulated the melanin synthesis in melanocytic cells. However, there is no direct evidence showing activation of MITF, tyrosinase (TYR), TYRP1 or TYRP2 by Bakuchiol in vitiligo melanocytes.

Therefore, the beneficial effect of Bakuchiol on pigmentation is more likely related to the protection of melanocytes from oxidative stress and inflammatory damage rather than direct stimulation of the melanogenic enzymes.

3. ANGELICINE OR ISOPSORALEN

Isopsoralen (Angelicin), an angular furocoumarin constituent of Psoralea corylifolia has been implicated in pigment promoting and melanogenic effects. Experimental studies show that isopsoralen can stimulate the production of melanin and activity of melanocytes in the process of repigmentation. It also possesses antioxidant activity that protects melanocytes from oxidative stress, which is one of the major pathogenic factors of vitiligo. Isopsoralen protects melanocyte survival and pigment-producing activity, and thus may serve as a bioactive aid for the treatment of vitiligo. But more research is needed to understand the exact chemical pathways that cause its effects.

4 BAVACHIN-

4.1 Activation of MITF-Tyrosinase Signalling Pathway

Prenylated flavonoid, Bavachin from Psoralea corylifolia Linn. *Bakuchi*) has been reported to accelerate melanogenesis by activation of the microphthalmia-associated transcription factor (MITF), the master regulator of melanocyte differentiation and pigment synthesis. MITF is then up-regulated, enhancing the expression of the main melanogenic enzymes, tyrosinase (TYR), tyrosinase-related protein-1 (TRP-1) and tyrosinase-related protein-2 (TRP-2), resulting in the increased production of melanin. This pathway could be implicated in the repigmentation of vitiligo lesions through the re-establishment of melanocyte functional activity.

4.2. Induction of melanocyte proliferation and survival

Experimental data have demonstrated that Bavachin improves the viability and proliferation of melanocytes and inhibits the apoptosis induced by oxidative or inflammatory stress. A characteristic of

vitiligo is the progressive loss of melanocytes. Thus, the cytoprotective activity of Bavachin may be useful in protecting the remnant populations of melanocytes in the depigmented skin and hair follicles, allowing subsequent repigmentation.

4.3. Oxidative stress and antioxidant defence

Vitiligo is predominantly caused by overproduction of reactive oxygen species (ROS) leading to melanocyte dysfunction and death. Bavachin scavenges free radicals, reduces intracellular ROS formation and enhances the endogenous antioxidant defence systems, thus exhibiting strong antioxidant properties. Bavachin may reduce oxidative damage, and create a favourable environment for melanocyte repair and melanogenesis**.**

4.4 Regulation of MAPK and cAMP-Dependent Signalling Pathways

Molecular data where available, suggests the possibility of flavonoids of Psoralea corylifolia such as Bavachin, to have an effect on MAPK/ERK and cAMP-based pathways for melanocyte differentiation and pigment production. These signalling pathways activate MITF transcriptional activity and synthesis of melanogenic proteins, which ultimately results in increased melanin formation.

4.5. Anti-Inflammatory and Immunomodulatory Activities

Vitiligo is increasingly recognised as an autoimmune disease in which cytotoxic T-cells destroy melanocytes. Bavachin has anti-inflammatory effect and inhibits synthesis of pro-inflammatory mediators and cytokines, which are involved in damage of melanocytes. Reduction of local inflammatory responses may alleviate the autoimmune-mediated damages of melanocytes and promote the restoration of pigmentation.

4.6. Potential Synergism with Other Constituents of *Bakuchi*

Bavachin is not considered to be active per se in *Bakuchi* preparations. It can act in synergy with psoralen, isopsoralen, bakuchiol, bavachalcone and other similar prenylated flavonoids instead. These phytochemicals synergistically induce melanogenesis, have antioxidant activity and modify immunological responses, which are important for the therapeutic effect of Psoralea corylifolia in vitiligo.

CONCLUSION

Vitiligo is a multifactorial depigmentary condition, marked by the complex interplay of oxidative stress, immunological dysregulation, mitochondrial dysfunction, melanocyte survival impairment, faulty epidermal cellular communication and epigenetic changes. Recent research suggests that successful repigmentation requires not only stimulation of melanogenesis but also protection, restoration and maintenance of functional melanocytes within the cutaneous microenvironment.

One of the classical medicinal plants which are commonly utilised in the management of *Shwitra* (Vitiligo) is Psoralea corylifolia (*Bakuchi*). It contains bioactive phytoconstituents such as psoralen, bakuchiol, isopsoralen, and bavachin that act on several pathogenic pathways involved in vitiligo. The therapeutic potential of *Bakuchi* seems to extend beyond its usual photosensitising actions and include antioxidant, immunomodulatory, cytoprotective and melanogenesis-promoting activities.

Psoralen, especially combined with ultraviolet A radiation (PUVA), induces repigmentation by activation of residual melanocytes and follicular melanocyte stem cells, enhancement of melanogenesis, stimulation of melanocyte proliferation and migration and suppression of melanocyte-directed immune responses. Bakuchiol demonstrates potent antioxidant and anti-inflammatory activities through the modification of the SIRT1/Nrf2 axis, attenuation of oxidative stress, maintenance of mitochondrial function, suppression of NF-κB-driven inflammatory signalling, and apoptosis inhibition. Moreover, there is some experimental evidence that isopsoralen may be involved in the maintenance of melanocyte survival and restoration of pigment, but its precise molecular mechanisms are not entirely understood. Bavachin is said to enhance melanogenesis through the activation of MITF-dependent signalling and upregulation of melanogenic enzymes, and to give antioxidant and immunomodulatory support that may benefit the survival of melanocytes.

Overall, the available evidence suggests that the therapeutic actions of P. corylifolia are mediated through orchestrated control of oxidative stress, inflammatory and autoimmune responses, melanocyte survival pathways and melanogenic signalling networks. The biological rationale for its age-old therapeutic use in vitiligo and reported repigmenting effects may lie in the synergistic action of its abundant phytoconstituents.

Despite promising experimental and pharmacological data, many mechanistic aspects are still ill-defined, in particular the direct molecular targets of individual phytoconstituents, their impact on melanocyte stem-cell biology and their interaction with immune and pigmentary signalling pathways in human vitiligo. Therefore, more mechanistic research, omics-based studies and well-designed clinical trials are needed to confirm these discoveries and to establish evidence-based therapeutic applications.

In conclusion, the current evidence suggests that Psoralea corylifolia is a promising multi-target candidate for the treatment of vitiligo. Its ability to simultaneously modulate oxidative stress, immune dysregulation, melanocyte survival and

melanogenesis provides a sound scientific basis for its traditional use and calls for its future investigation as a supplemental method of promoting repigmentation in vitiligo patients.

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