A REVIEW ON VITILIGO WITH ITS HERBAL TREATMENTS

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ABSTRACT
Vitiligo is an acquired cutaneous disorder of pigmentation manifests as white patches on the skin. It is characterized by acquired, idiopathic, progressive, circumscribed hypomelanosis of the skin, hair with absence of melanocytes. Vitiligo is not painful and does not have significant health consequences. The disease may affect any part of the body. And patches may spread to large extent which may affect mucosal membranes also. Vitiligo may be the genetic disorder or it may be associated with medical conditions. Most of the people who have vitiligo will develop the condition prior to the age of 40. Vitiligo may cause emotional, psychological stress and physiological consequences. Some medical treatment can reduce the severity of the condition but it can be difficult to cure. this review explains about classification of vitiligo and its types, diagnosis, symptoms, preventions and different types of treatments majorly the plants extracts of nigella sativa and ginkgo biloba in the treatment of vitiligo.

KEYWORDS: Vitiligo, Types, Nigella Sativa and Ginkgo Biloba.

INTRODUCTION TO VITILIGO
Vitiligo is an acquired, usually asymptomatic pigmentation disorder that results in the loss of functional melanocytes and is often associated with other autoimmune diseases. At the onset of the disease white patches of different sizes appear on different parts of the body.1 Vitiligo usually affects the skin, but it can develop anywhere we have pigment. Patches of hair can turn white. Some people lose color inside their mouths. The affected skin can lighten or turn
Vitiligo affects approximately 1% of the world population of all skin types, usually before the age of 20. Its psychological impact on the quality of life can be disastrous, as dissatisfaction with body image can smother self-esteem and develop a depressive state, especially among darker tan-skinned patients. The Greater Toronto Area (GTA) has significant Caribbean, African, and South Asian populations, which are doubly at risk. The darker skin makes the vitiligo more apparent, and the presence of lesions similar to endemic communicable diseases carries difficult cultural stigma.

Two of the major theories of the pathogenesis of vitiligo are

- The autoimmune theory and
- The autocytotoxicity theory.

The autoimmune theory speculates that patients with vitiligo form auto-antibodies against melanocytes. The existence of anti melanocyte surface antigen antibodies has been demonstrated, and the severity of vitiligo has proven to be related to the amount of antibodies present. Vitiligo has been associated with antibody-mediated autoimmune diseases such as thyroid disease, pernicious anemia, diabetes mellitus, Addison disease, alopecia areata, and myasthenia gravis.

The autocytotoxicity theory postulates that melanocytes are destroyed either by themselves through self generation of melanin precursors (or metabolites) or by keratinocytes, which release chemicals that generate oxidative stresses. It is believed that the normal defense mechanisms of melanocytes against oxidative stress and melanin precursors are defective in vitiligo melanocytes.

The main histopathological finding in vitiligo is the total absence of functioning melanocytes in the lesions. The main inflammatory cells most commonly found on the edges of these lesions are CD4+ and CD8+ T lymphocytes. Based on this principle, commonly used treatment strategies have focused on control of the autoimmune damage as well as stimulation of melanocyte migration from the unaffected edges of the lesions to the affected skin.

Vitiligo can be confused with leprosy, leading to further stigmatization. Vitiligo is not contagious in any approach. The precise reason behind skin disease is not well-understood. It appears to be the results of a mixture of genetic and environmental factors. Some folks have
reported one event, like sunburn or emotional distress to trigger the condition. Heredity could also be an element as a result of there is an accrued incidence of skin disease in some families. However, the additional worldwide analysis is being conducted than ever before, and treatment choices are unit rising. New technologies and analysis are unit ever changing physician's approaches to the condition, and up to date mapping of the human ordering has made-up the approach for advanced genetic analysis. \[6\]

Figure 1. Vitiligo\[20\]

CLASSIFICATION

Classically, vitiligo is divided into segmental and generalized forms. The age of onset of vitiligo is variable, but peaks in the second and third decades. The depigmentation has a predilection for acral areas and around body orifices (mouth, eyes, nose, ano-genital region).

The Vitiligo European Task Force (VETF) was founded in 2003 during the ESPCR meeting in Ghent and formulated the following definition.

“Generalized vitiligo or non-segmental vitiligo (NSV) is an acquired chronic pigmentation disorder characterized by white patches, often symmetrical, which usually increase in size with time, corresponding to a substantial loss of functioning epidermal and sometimes hair follicle melanocytes”. Other unclassified or poorly classified generalized vitiligo conditions like ‘Punctate vitiligo’ refers to pea-sized depigmented macules that may involve any area of the body. When these lesions coexist with classical vitiligo macules, it is best classified as NSV. If not, the term ‘leukoderma punctata’ should be used. Other distinct conditions that may be difficult to distinguish from vitiligo clinically include idiopathic guttate melanosis and progressive macular hypomelanosis. \[4\]

“Segmental vitiligo is an acquired chronic pigmentation disorder characterized by white patches with a unilateral distribution that may totally or partially match a dermatome, but not necessarily. Other distribution patterns can be encountered that cross several dermatomes, or
correspond to large areas delineated by Blaschko’s lines”. Segmental vitiligo typically has a rapidly progressive but limited course, depigmentation spreads within the segment over a period of 6–24 months and then stop; further extension is rare.

TYPES OF VITILIGO

Focal vitiligo
The diagnosis of focal vitiligo should be considered only after having ruled out all other diagnoses and a biopsy may be helpful to exclude other causes of focal hypopigmentation. Focal vitiligo refers to an acquired, small, isolated hypopigmented lesion that does not fit a typical segmental distribution, and which has not evolved into NSV after a period of 1–2 yr.

Mucosal vitiligo
Mucosal vitiligo typically refers to the involvement of the oral and/or genital mucosae. When presenting in isolation, especially for genital involvement, a differential diagnosis of lichen
sclerosis should be addressed by biopsy. Concomitant occurrence of genital lichen sclerosis and vitiligo has been reported suggesting the possibility of a causal link between the two conditions. In fair-skinned individuals, the diagnosis of oral mucosa vitiligo is rarely made. It is unclear whether this is attributable to low incidence or low diagnostic accuracy. It is readily classified as NSV.

Universal vitiligo

Universal vitiligo corresponds to complete or nearly complete depigmentation of the skin. This term is commonly used when NSV gradually progresses to complete depigmentation of the skin and body hair, and sometimes oral/genital mucosae. Scalp hair involvement is also common. However, vitiligo may spare the scalp, pubic, and axillary areas early in the course of disease. Small perifollicular, discrete, or coalescent pigmentation may persist in sun-exposed areas. The distinction between vitiligo universalis (VU) progressing from common NSV versus ‘fulminant’ vitiligo conditions that target skin and non-skin melanocytes (ear, eyes), especially as part of the rare Vogt-Koyanagi Harada syndrome, is not completely clear. Complete skin depigmentation in NSV patients who have undergone therapeutic depigmentation should be excluded from the diagnosis of VU.
Mixed vitiligo
The coexistence of SV and NSV was first reported in a pediatric NSV patient treated with UVB, which left a recalcitrant segmental lesion suggestive of preexisting SV. Additional cases were subsequently reported, with the term ‘mixed vitiligo’ proposed to designate this form of the disease, and a case series subsequently proposed definition criteria. This association may be viewed as an example of a superimposed segmental manifestation of a generalized polygenic disorder, in which segmental involvement precedes disease generalization and is more resistant to therapy. The presence of halo nevi and leukotrichia at onset may be risk factors for developing MV in patients with SV.

Occupational/contact vitiligo
The terms ‘contact’ or ‘occupational vitiligo’ (CV) have been used to describe a distinct form of vitiligo induced by exposure to certain chemicals in the workplace or at home, principally aromatic or aliphatic derivatives of phenols and catechols. However, the precise definition of CV is unclear. Indeed, although the cutaneous depigmentation may be limited to the areas exposed to chemicals, it may extend progressively from the initial site of chemical contact to the whole body, leading to typical NSV. Thus, such chemical agents may serve as uncommon environmental triggers or haptens for the induction of what in fact is typical vitiligo.[4]

<table>
<thead>
<tr>
<th>Type of vitiligo</th>
<th>Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-segmental (NSV)</td>
<td>(focal)⁹, mucosal, acrofacial, generalized, universal</td>
</tr>
<tr>
<td>Segmental vitiligo (SV)</td>
<td>Focal⁹, mucosal, unisegmental, bi- or multisegmental</td>
</tr>
<tr>
<td>Mixed (NSV+SV)</td>
<td>According to severity of SV</td>
</tr>
<tr>
<td>Unclassified</td>
<td>Focal at onset, multifocal asymmetrical non-segmental, mucosal (one site)</td>
</tr>
</tbody>
</table>

EPIDEMIOLOGY
Vitiligo is the most common depigmenting disorder worldwide. Overall, the estimated worldwide prevalence is 0.5% to 2% but peaks of up to 8.8% have been reported in India, possibly relating to the inclusion of chemically induced depigmentation.

Between 15% and 20% of patients have one or more first-degree relatives with vitiligo. Adults and children of both sexes are equally affected. Almost half of all patients present before the age of 20 years, and nearly 70% to 80% before the age of 30 years. Onset before the age of 12 years is common.[8]
VILITIGO GENETICS

Most human diseases result from an interaction between genetic variants and environmental factors, and to establish the actual contribution of genetic factors is the first step of genetic studies that evaluate complex diseases. In general terms, the scrutiny of complex diseases genetic components begins through observational studies, such as: analyzes of pools of familial cases, comparative studies of concordance rates of disease occurrence among monozygotic (MZ) and dizygotic (DZ) twins and complex segregation analyzes (CSA). However, these studies do not provide information on the exact nature of the genetic component in question, as the location and identity of the involved genes. In order to advance it is necessary to perform different studies involving molecular genetic markers, as it is done in linkage and association analysis.

Genetic epidemiological studies have demonstrated that vitiligo can be considered a complex genetic disease because: (i) the disease varies in symptom severity and age of onset, which hinders the definition of the appropriate phenotype and the selection of the optimum study population; early age of onset was associated with familial occurrence of generalized vitiligo. In addition, early onset vitiligo is associated with more severe disease; (ii) the etiological mechanisms of the disease can vary; vitiligo's etiopathogenesis has not yet been fully clarified, and several theories have been proposed; (iii) complex genetic diseases are often oligogenic or even polygenic and each gene contributes to a fraction of the overall relative risk; linkage analysis performed using vitiligo phenotype identified susceptible loci located on chromosomes 1, 4, 6, 7, 8, 17 e 22 co-segregating with the disease.

For these regions, some genes consistently associated with vitiligo have been reported, such as NLRP1 (17p13) and XBP1 (22q12)[9]

DIAGNOSIS OF VITILIGO

Differential diagnosis of vitiligo is very difficult. To diagnose the exact vitiligo one should be able to differentiate between different conditions of the skin like complete depigmentation, hypo pigmentation and normal colour of the skin. Diagnosis of vitiligo is very difficult in patients having light complexion of the skin colour. Wood’s light is very useful to diagnose the vitiligo in the patients having skin type I and II. Pure tone and speech audiometer, Sound treated room, Cochlear Emission Analyzer Madsen, Immittance meter, Evoked Response Audiometer Nickolet Compact four, Wood’s light lamp equipments can be used for the diagnosis of vitiligo.[10]
SYMPTOMS
The most important symptom of vitiligo known is the depigmentation of patches of skin. Initially, the patches are small but they will be enlarged over time. The skin lesions are dominantly observed on the face, hands and wrists\textsuperscript{[11]} or areas where wear or shoes consistently rub on the skin. Less common signs embody pigment loss or greying of hair on the scalp, eyebrows, eyelashes, or totally different affected areas. Some may also experience loss of pigment on the tissues that line the among of the mouth (mucous membranes) and so the membrane of the eye. A number of people with the disease experience intense tactile sensation at the positioning of coloration throughout active stages.\textsuperscript{[6]}

PREVENTION
There is no primary prevention for vitiligo. Heritability explains a minor part of disease development, and environmental triggers are not sufficiently known to warrant or enable primary prevention. Secondary prevention, for example through avoidance of skin stress to limit the Koebner phenomenon is frequently advocated. However, accumulating evidence indicates that mild inflammation at the border of depigmented patches is associated with disease progression or reflects enhanced melanocyte loss caused by mechanical pressure and friction during the inflammatory progressive or acceleration phase of the disease. The concurrent interventions are often used, including oral mini-pulses of corticosteroids, phototherapies or combined approaches, which are aimed at halting inflammation and disease progression.\textsuperscript{[8]}

TREATMENTS
Etiology of the Vitiligo is still unknown. But it involves some theories like Auto immunity, cytotoxicity, triggering, neural, free radicals and genetic. It can be treated by oral or topical formulations of the drug alone in mild cases but in severe case of Vitiligo Light therapy is also given with the consumption of medication to increase the pigmentation of the skin. The treatment of leukoderma or Vitiligo requires not only a deposition of pigment in the areas of depigmentation, but it also requires a redistribution of pigment from hyper pigmented borders, so that the result will be an even distribution of the normal amount of cutaneous colouring. It also depends on the presence of the type of the cell. Possibility of formation of melanocyte in inter-follicular epidermis is decreased by the presence of keratinocyte stem cells in the similar location.
Treatment of vitiligo with herbal medicines from the list of Chinese herbs acting for the treatment of vitiligo decoction of xiaobailing changyee powder and three yellow powders are most effective. These medicines include xanthumstramanum, sophoraflavescens, atractylodes japonica, arisaemaamurense. Some other herbs include carthamustinctorius, eclipta prostrate, pleuroptereesmultiflorees, salvia miltiorrhiza, sesamumindicum, spatholobussuberecutus, rehmaniaglutinosa. Applying these medicines onto skin improves skin coloration and treats the vitiligo. Indian herbs involve cassia accidentalis, eclipta prostrate, curcuma longa, picrorrhizakurroa, psoraleacorylifolia, tribulusterrestris. In this mainly photosensitizers and blood purifiers are used. Photosensitizing agents involve psoraleacorylifolia, semicarpusanacardarium and ficushispida. They are administered locally as well as systemically with the sun exposure. Blood purifiers include curcuma longa, eclipta Alba, tinosporacardifolia, hemiclascusindicis, acasia catechu and acaranthusaspara.

Exact mechanism of the herbs is unclear but it involves some mechanisms like phototoxic reactions, melanocyte proliferation, promoting anti-inflammatory activity and trigger reduction. Traditional Treatment Red clays found by the river side or on hill slopes can also be used for the treatment of vitiligo. It can be given by mixing with ginger juice. Copper in the clay brings skin pigmentation back and ginger facilitates increased blood flow to the spot which helps into the repigmentation of the spots. Radish seeds powdered with the vinegar and paste is formed. This paste can be applied to treat the vitiligo. Mixture of turmeric and mustard oil which is prepared by heating two of them is also helpful in the treatment of white patches.

**Yoga therapy**
Kapalbhati is helpful in the treatment of vitiligo. Because of inhalation and exhalation kapalbhati provides aeration to blood and purifies blood circulation. This is beneficial in different skin diseases like vitiligo, psoriasis and other allergies.

**Homeopathic treatment**
Homeopathy is an alternative medicine originated in germany in 18th century and it is adapted by many countries. Arsach, Bacillinnum, Graphites, Mercasol, Natmurr, nuxvomica, sil, sulph, thuja etc. medicines can be used under homeopathic treatment.
Ayurvedic treatments

In Ayurveda vitiligo is known as Switra and it is mainly caused due to the Pitta Dosha as aggravated Pitta leads to accumulation of toxins (ama) in deep layers of the skin which leads to the condition of Vitiligo. Basic treatment of this disease includes Calming imbalanced body energies, cleansing blood and administering the herbs which restore the skin colour. Poor digestion cause build-up of toxins into the body thus it is a root cause for the disease. Therefore, restoring digestion is the essential part of the body (Jiva Ayurveda). Generally Ayurvedic treatment of Vitiligo involves four steps.

First step is Purification therapies (Shodhana Karma), which includes use of herbal decoction of Psoralea Corylifolia and Euphorbiamerifolia.

Second step includes Oil massage, in which oil is selected on the basis of disease state (roga) and Patient Examination (rogiPariksa).

Third step is exposure of lesions to the sun rays depending on the tolerance of the patient (Sooryapadasanathapam).

And fourth and last step is delivery of decoction (kwatha) made of Ficushispida (malayu), Pterocarpusmarsupium (asana), Callicarpamacrophylla (priyangu), Peusedanumgraveolens (satapuspa), Coleus vettiveroides (ambhasa), and alkaline extract of Buteamonosperma (palasaksara), along with an alcoholic preparation of jaggery (the preparation is called phanitha in Ayurveda) to the patient. The diet should be salt-free and should contain buttermilk during the treatment of decoction.

Lepa (Topical preparations)
Ankollakadi, Avalgujadi, Bakucyadi, Balyadi, Bhallatakadi, Bhringarajadi, Gandhakadi, Grhadhumadi, Gunjadi, Gunjaphaladi, Katukalabvadi, Man asiladi, Maricadi, Panca Nimbava, Pathyadi, Patrakadi, Putikadi, Talakadi, Triphaladi, and Vayasyadi.

Kashaya (Mixtures)
Dhatryadikwata, Kakodumbarika kasaya and Khadiradi kashaya.

Churna (Compound Powder)
Bakucyadya churna, Khadirasaradi churna and Pancanimba churna.
Ghrita (Paste)
Dantyadi ghrita, Mahamarkara ghrita, Mahaneela ghrita, Mahatiktaka ghrita, Mahavajraka ghrita, Neelaka ghrita, Neeli ghrita, Neelinyadi ghrita, Somaraji ghrita and Tiktaka ghrita.

Avaleha (Oral Semisolid preparations)
Bhallatak avaleha and Vidangadileha.

Thaila (Oil preparations)
Aragwadhayadyathaila, Citrakadyathaila, Jyotismatithaila, Kusta Kalanalathaila, Kustaraksasathaila, Laghumaricadyathaila, MahaVajrakathaila, Manasiladyathaila, Maricadyathaila and Vishathaila.

Asava Arista (Fermented preparations)
Kanakabindvarista and Madhwasava.

Vati/Gutika (tablets)
Swayambhuva Gutika, Thripaladi gutika and BrhatSwayambhuva Gutika.

Rasousadha (Formulations containing processed minerals and metallic salts)
Candraprabhavati, Galitakustari rasa, Khageswara rasa, Kustebhakesari rasa, Medanisara rasa, Pittalarasayana, Talakeshwara rasas and Vijayeswara rasa.

Topical allopathic treatments
It involves different topical formulations of steroids and immunomodulators. Steroids applied topically are helpful to treat the patches of vitiligo. Potent corticosteroids like betamethasone, valerate, triaminolone and very potent corticosteroids like alobetasol, fluticasone propionate are helpful to obtain marked or almost complete repigmentation of the skin. Immunomodulators like tacrolimus and pimecrolimus are helpful in the treatment of vitiligo when applied topically. These can also be used to treat the small and difficult areas like eyelids.

Surgical therapies
In surgical therapies white patches are treated with the help of different surgeries. It involves different mechanisms of surgery. In Autologous Skin Grafts technique grafts are implanted into perforations prepared at the recipient sites. Patients with segmental vitiligo are best candidate for this type of grafting. In blister grafting blisters are used. These blisters can be
induced by different ways such as vacuum or liquid nitrogen. At the dermoepidermal junction the mechanical split occurs and the graft is secured on the recipient site. Primarily a cobblestone appearance and limited treatment area per session are the limitations of the above two mechanisms. To overcome these limitations epidermal cell transplantation can be done. This technique involves application of a melanocyte-rich suspension to the affected area and then it is allowed to graft. Only one time treatment is necessary is the main advantage to this technique. Micro pigmentation (Tattooing) technique involves permanent dermal micro pigmentation. It is done by using a non-allergic iron oxide pigment. These pigments provide colour to the skin.

Other alternative treatments
If no treatment works for the treatment than alternative cover-ups can be used. Leukodermic skin easily gets damaged to the sunburn and the effect lasts for very long time. So to avoid the excess exposure to the sunlight and prevent the sunburn sunscreens can be used. To hide the untreated white patches onto the skin cosmetics cover-ups are very useful.

Depigmentation
It is a drastic form of treatment for vitiligo. It involves fading the rest of the skin of the body so the whole body appears in white colour. For that permanent melanocytotoxic agents like monobenzyl ester of hydroquinone cream and 4-methoxyphenol can be used.

Other Drugs used for the treatment
Trioxsalen is given orally. By increasing skin pigmentation, it increases the tolerance of the skin to UV light. This drug sometimes causes cutaneous reaction. Methoxsalen can be given orally as well as topically. In oral dosage form 20mg/day drug is given 2-4 hours before UV exposure. It causes gastric discomfort. In topical dosage form 0.1% to 1% lotion is applied and sun light or UV light exposure is given. It may cause Acute, Vesicular, Cutaneous photosensitivity reaction. Both the formulation of this drug may cause severe sunburn.

Photo chemotherapy
Application of photochemical reaction is an advantageous for the treatment of vitiligo. Photochemotherapy is Traditional therapy for Vitiligo. This therapy is based on ancient Atharva Veda observations. Psoralen is having very good photochemical response to ultraviolet B as well as ultraviolet A. Because of this reason the treatment includes topical/oral psoralen treatment, followed by exposure to ultraviolet light or Sunlight. This
combined treatment is known as PUVA therapy (Psoralen Ultraviolet A therapy). It is based on the observation in Atharva Veda more than 3000 years ago. In this treatment oral psoralen is administered followed by UVA rays exposure. This is FDA approved treatment of Vitiligo and psoriasis. Psoralens are compounds found in many plants. These compounds make the skin temporarily sensitive to UVA. For oral treatment of PUVA, methoxsalen capsules are taken before two hours of the appointment. Topical PUVA is an attempt to limit the area that becomes photosensitized.\cite{12}

PLANT EXTRACTS WHICH IS UESD IN THE TREATMENT OF VITILIGO: NIGELLA SATIVA

INTRODUCTION

The plant Kalonji or Nigella sativa is an annual flowering plant, native to south west Asia and cultivated in countries like Middle Eastern Mediterranean region, South Europe, Syria, Turkey, Saudi Arabia, Pakistan, India. The above plant is a small annual herb distributed all over India. In the religion of Islam, the plant has been given a great importance because of its number of uses. As per the religion it is one of the greatest healing plants. The Islamic prophet Muhammad once stated that the black seed can heal every disease except death. Avicenna, most famous for his volumes called The Canon of Medicine, refers to Nigella as the seed that stimulates the body's energy and helps recovery from fatigue and dispiritedness. It is also included in the list of natural drugs of 'Tibb- e-Nabavi', or "Medicine of the Prophet (Muhammad)"; according to the tradition "holds onto the use of the black seeds for healing all diseases. In the Unani Tibb system of medicine, N. sativa is regarded as a valuable remedy for a number of diseases. In the Indian system of medicine, the seeds are used as astringent, bitter, stimulant, diuretic, emmenagogue, anthelmintic, jaundice, intermittent fever, dyspepsia, paralysis, piles and skin diseases and many more 3-5. The present article is an effort to present out the pharmacology, traditional uses and chemical constituent of the Nigella plant.

Figure 6: NIGELLA SATIVA.
Classification

Kingdom: Plantanae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Ranunculales
Genus: Nigella
Family: Ranunculaceae
Species: N. sativa\[13\]

NIGELLA SATIVA SEEDS\[14\]

Figure 7: Nigella Sativa Seeds.

CHEMICAL COMPOSITION

The chemical composition of Nigella sativa is consists the large variety of organic compounds and that are present in the seeds of Nigella sativa L. The seeds of this herb are used in the Middle East and South Asian countries for the treatment of a large variety of ailments and are accepted as a panacea. For example, the seeds or oil from the seeds have been used to control diabetes, hypertension, cancer (leukeamia, liver, lung, kidney, prostate, breast, cervix, skin), inflammation, hepatic disorder, arthritis, kidney disorder, cardiovascular complications and dermatological conditions. A GC-MS analysis of the seed extract has shown it to be a mixture of 8 fatty acids and 32 volatile terpenes. The major terpenes, thymoquinone (TQ), dithymoquinone (DTQ), trans-anethol, p-cymene, limonine, and carvone have been identified. TQ and DTQ are both cytotoxic for various types of tumors. In addition diterpenes, triterpene and terpene alkaloids have been identified in Nigella sativa seeds. The methanolic extract of the seeds contain two types of alkaloids whilst the major principal active ingredient isolated from the volatile oil of Nigella sativa L. is TQ.
Since Nigella sativa L. acts as a panacea exhibiting a wide variety of pharmacological actions, in the total synthesis of the alkaloids isolated having the isoquinoline and indazole motifs. The isoquinoline alkaloids include nigellicimine (1) and nigellicimine-N-oxide (2), and the indazole alkaloids include niggellidine (3) and nigellicine (4). And several new dolabellane-type diterpene alkaloids, nigellamines A1-A5 (5) have also been isolated from the methanolic extract of the seeds of Nigella sativa L. which have also received synthetic interest.

Figure 8: Structures of alkaloids isolated from Nigella sativa.

Figure 9: Pyrazole and indazole ring systems.

Types of indazole ring compounds
Indazole and pyrazole motifs are embedded in numerous pharmaceuticals and agrochemicals with a broad range of biological activities.
Figure 10: Structures of some pharmaceuticals and agrochemicals with indazole and pyrazole motifs.

Thus multigram quantities of these two alkaloids can now be obtained via their total syntheses that should enable their individual therapeutic evaluation to be possible.\cite{15}

<table>
<thead>
<tr>
<th>Fundamental Oil Composition (1.4%)</th>
<th><em>Nigella sativa</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvone</td>
<td>21.1%</td>
</tr>
<tr>
<td>Alpha-Pinene</td>
<td>7.4%</td>
</tr>
<tr>
<td>Sabine</td>
<td>5.5%</td>
</tr>
<tr>
<td>Beta-Pinene</td>
<td>7.7%</td>
</tr>
<tr>
<td>P-cymene</td>
<td>46.8%</td>
</tr>
<tr>
<td><strong>Fatty Acids</strong></td>
<td></td>
</tr>
<tr>
<td>Myristic Acid (C14:0)</td>
<td>0.5%</td>
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<tr>
<td>Palmitic Acid (C16:0)</td>
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<tr>
<td>Palmitoleic Acid (C16:1)</td>
<td>0.1%</td>
</tr>
<tr>
<td>Stearic Acid (C18:0)</td>
<td>2.6%</td>
</tr>
<tr>
<td>Oleic Acid (C18:1)</td>
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<tr>
<td>Linoleic Acid (C18:2)(Omega-6)</td>
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<td>Linolenic Acid (18:3n-3)(Omega-3)</td>
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<tr>
<td>Arachidic Acid (C20:0)</td>
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<td><strong>Saturated &amp; Unsaturated Fatty Acids</strong></td>
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<tr>
<td>Saturated Acid</td>
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<td>Monounsaturated Acids</td>
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<td>Polyunsaturated Acids</td>
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<td><strong>Nutritional Value</strong></td>
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<tr>
<td>Protein</td>
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<tr>
<td>Thiamin</td>
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<tr>
<td>Fats</td>
<td>35-38%</td>
</tr>
</tbody>
</table>

Chemical constituents of *Nigella sativa*\cite{13}
THYMOQUINONE HELPS IN THE TREATMENT

Oil as well as isolated components, especially on thymoquinone (TQ), isolated from the seed oil of the plant (N. sativa). In N. sativa, among the other chemical moieties, TQ is a foremost concern today as it has been extensively studied for its utmost therapeutic potentials. This review aims to accumulate the findings of TQ up to date with mechanistic descriptions on its therapeutic potentials.
REVIEW OF THYMOQUINONE (TQ)
Thymoquinone (TQ) (2-isopropyl-5-methylbenzo-1, 4-quinone), isolated in 1960s and documented in 1970s is abundantly present in volatile oil as well as fixed oil in N. sativa seeds. It is also found together with its few derivatives such as dithymoquinone, thymohydroquinone and thymol. However, TQ is evident to have in some species of the family Cupressaceae, Lamiaceae and Monarda. TQ exists in keto (~90%) and enol (~10%) forms. The former one is responsible for its pharmacological properties. TQ is a fat soluble molecule. Solubility in aqueous medium at 24-72 h ranges from 0.549-0.740 mg/mL. However, it is unstable in aqueous solution, especially at an alkaline pH. Intravenous (i.v.) administration of TQ followed plasma clearance of 7.19 mL/kg/ min and volume of distribution (steady state) was 700.90 mL/kg; for oral (p.o.) administration that was 12.30 mL/kg/min and 5109.46 mL/kg, respectively. The protein binding nature of TQ in human is 98.99% with a plasma half-life of 217 min. TQ is highly light sensitive and provides UV-vis maximum absorbance at 254-257 nm.

ANTIOXIDANT POTENTIAL OF TQ
The antioxidant potential of TQ is thought to be linked to its conversion of keto form to enol from. The thymohydroquinone/di-hydrothymoquinone is the ultimate molecule which may be obtained by the step-wise reduction of keto-TQ in mammalian microsome by the help of NADPH CYP reductase, NADH CYP-b5 reductase, NADH-ubiquinone oxidoreductase or NADH-quinone oxidoreductase. Thus, during developmental phases, chemotherapy with TQ, is a major concern.[16]
COMPARING NIGELLA SATIVA OIL AND FISH OIL FOR THE TREATMENT OF VITILIGO

After six months, a mean score of (Vitiligo Area Scoring Index) VASI decreased from 4.98 to 3.75 in patients applying topical *Nigella sativa* and from 4.98 to 4.62 in those using topical fish oil. *Nigella sativa* oil and fish oil were effective in reduction the size of patient’s lesions; however, *Nigella sativa* was more effective in comparison to the fish oil. Hence, using *Nigella sativa* with the major drugs in the treatment of vitiligo is recommended.\[17\]

GINKGO BILOBA

INTRODUCTION

The ginkgo tree is having apricot shaped mature, yellow color fruits the name ginkgo comes from the Chinese words sankyo or yin-kuo, which means a hill apricot or silver fruit. So the name ginkgo comes from the Chinese words sankyo or yin-kuo. The family name of ginkgo tree is Ginkgoaceae, which is in the class of Ginkgoatae. Englbert Kaempfer, a German surgeon, first used the term “Ginkgo” in 1712, but it was Linnaeus who termed it Ginkgo biloba.\[19\]

Figure 12: Ginkgo biloba.

Nomenclature

Botanical name: Ginkgo biloba L.
Family: Ginkgoaceae
Genus: Ginkgo
Plant part: Leaf
Common names: Fossil tree; Kew tree; Japanese silver apricot\[18\]
CHEMICAL CONSTITUENTS AND ACTIVE COMPOUNDS

Leaves of the ginkgo tree contain over 40 active components; the two most therapeutic of these are called flavonoids and terpenoids. Gb contains the lipid phosphatidylserine.

<table>
<thead>
<tr>
<th>Class</th>
<th>Major chemical constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terpenoids</td>
<td>Diterpenes: ginkgolides A, B, C, J (J is found in the root)</td>
</tr>
<tr>
<td></td>
<td>Sesquiterpenes: bilobalide, triterpenes: sterols</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>Kaempferol, quercetin, isorhamnetin, rutin, luteolin, delphinidin, myricetin</td>
</tr>
<tr>
<td>Bioflavonoids</td>
<td>Scopoletin, ginkgetin, isoeugenol, quercetin, bilobetin, 5'-methoxybilobetin,</td>
</tr>
<tr>
<td>Organic acids</td>
<td>Benzoic acid derivatives (ginkgolic acid), N-containing acids</td>
</tr>
<tr>
<td>Polyphenols</td>
<td>di:trans-poly-cis-octadecaprenol, wax, steroids, 2-hexenal, cardanol, sugars, catechins, prosthetic acid, phenols, aliphatic acids, rhamnose</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
</tbody>
</table>

The main constituents of Ginkgobiloba leaves

History Folk Use and Pharmacology

The major active components present in Gb along with their biological activities that may be important from the pharmacological point of view. Valued for medicinal properties in China for thousands of years ~2800 BC. The major chemical components include flavonoids and terpenoids, these are antioxidants, flavonol and flavone glycosides, lactone derivatives (ginkgolides), bilobalide, ascorbic acid, catechin, iron-based superoxide, 6-hydroxyquinuetic acid, proteocatechuic acid, shikimic acid, sterols and vanilic acid. The fruits are prepared by fermentation and cooking and are considered a delicacy during weddings and feasts. The nuts are boiled as a tea used to treat lung weakness and congestion (especially asthma), wheezing, coughing, vaginal candidiasis, frequent urination, cloudy urine, and excess mucus in the urinary tract. Ginkgo biloba used to Relieves symptoms of asthma and cough, Used the leaves to treat chilblains (symptoms of frostbite), in the throat pain, Improves circulation to all vital organs, to balanced action on arterial and venous systems, in vasomotor paralysis, in Relaxant effects during vasomotor spasm to enhances oxygen utilization and glucose uptake in the brain. The extract of Gb has been studied for its effectiveness in the treatment of Acrocyanosis, Alzheimer's disease, Cerebral atherosclerosis, Cerebral insufficiencies, Cochlear deafness, Dementia, Depression, Menopause, Peripheral and cerebral circulatory stimulation, Peripheral vascular disease, Raynaud's syndrome, Retinopathy, Senility, Short-term memory loss, Tinnitus, Vascular Diseases, and Vertigo.199
Ginkgo biloba for the treatment of vitiligo vulgaris

60 mg of standardized G. biloba two times per day for 12 weeks. The criteria for feasibility included successful recruitment, 75% or greater retention, effectiveness and lack of serious adverse reactions. Effectiveness was assessed using the Vitiligo Area Scoring Index (VASI) and the Vitiligo European Task Force (VETF). Ingestion of 60 mg of Ginkgo biloba BID was associated with a significant improvement in total VASI vitiligo measures and VETF spread, and a trend towards improvement on VETF measures of vitiligo lesion area and staging.[3]

CONCLUSION

With this I concluded that, vitiligo is a depigmented disease may occur due to hereditary or by sun burn or due to some medications. Till now there is no complete treatment and cure for vitiligo, but people can go with some precautions and herbal treatments to reduce the severity of the white colorless inflammatory patch condition. This review majorly explains about the herbal extracts.

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