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Developing Novel Approaches to The Management of Vitiligo

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ABSTRACT
The worldwide prevalence of vitiligo, a widespread depigmenting skin condition, is believed to be between 0.5 and 2% of the population. The condition is typified by the non-scaly, chalky-white macules that are the result of a selective loss of melanocytes. Our understanding of the pathophysiology of vitiligo, which is now unmistakably characterized as an autoimmune disease, has advanced significantly in recent years. Vitiligo is sometimes written off as a cosmetic issue, even though it can have terrible psychological impacts and significantly interfere with daily living. An international consensus in 2011 defined vitiligo as all nonsegmental vitiligo types, and classed segmental vitiligo as distinct from all other kinds of vitiligo. This review aims to provide an overview of the future of vitiligo treatment while summarizing the state of the art in the field.
Keywords: *Vitiligo, Melanocytes, Skin disorder, Repigmentation Treatment.*

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INTRODUCTION

The skin disease known as vitiligo, which causes dilution of pigment in the affected areas of the skin, is typified by a selective loss of melanocytes. The acquired pigmentary skin illness known as vitiligo, which is brought on by the lack of pigment-producing cells in the epidermis, causes the body to produce white macules and patches. The signature lesion is a chalky-white, fully amelanotic, and nonscaly macule with distinct edges [1]. Recent advances in our understanding of the etiology of vitiligo have led to the definitive recognition of the condition as an autoimmune illness, impacted by a combination of genetic and environmental factors, as well as issues with metabolism, oxidative stress, and cell detachment [2]. An international consensus in 2011 separated vitiligo into two primary categories: no segmental vitiligo (NSV) and segmental vitiligo (SV) [3]. It is officially acknowledged now as an autoimmune disease associated with metabolic abnormalities, oxidative stress, cellular detachment problems, genetics, and environmental factors. In 2020, Bergqvist and Ezzedine Vitiligo is still often seen and diagnosed by dermatologists, most clinicians, and certain well-informed members of the general public. Typically, the fingers, knuckles, and area around the lips, eyes, toes, and reproductive organs are the first places to notice hypo pigmented patches, the hallmark feature of the disease organs [4]. A Critical Appraisal of Vitiligo Etiologic theories is Melanocyte Loss called as melanocytorrhagy [5]. There are two main primary methods by which the skin can become white [6]. The melanin produced by the melanocytes within the melanosomes is then transferred to the nearby keratinocytes. From the basal layer of the epidermis to the stratum corneum, where they are desquamated and released into the environment, the melanin and melanosomes are transported by the keratinocytes. Skin that lacks pigmentation is a result of some disorders that stop or reduce melanin production. The epidermis has normal numbers of melanocytes, yet in several disorders, melanin production is reduced. The hypopigmentation on the skin is usually modest to obvious [7].

Types of Vitiligo

There are three major types of vitiligo are as follows:

- Segmental Vitiligo
- Non-Segmental Vitiligo
- Mixed Vitiligo

Segmental Vitiligo

Partial vitiligo affects only one side of the body in segments. It is an autoimmune condition. It is more noticeable in younger age groups, affecting about 30% of children with vitiligo. It reacts well to topical treatment.

Non-Segmental Vitiligo

Due to its autoimmune nature, it often manifests on both sides of the body. This most common kind accounts for 90% of cases with vitiligo. They commonly appear on areas of skin, such as the hands, neck, and face that are frequently exposed to the sun. Not just vitiligo vulgaris, but also sporadic, extensive, acrofacial, neck and facial, and mucosal subtypes are also included in the classification of NSV. The appearance of depigmented macules in more than two sites is associated with a severity score of 1-3 for sporadic vitiligo. Generalized vitiligo (grade 4) is defined as depigmented macules encompassing more than 50% of the BSA [7].

Mixed Vitiligo

In the rare instances where segmental vitiligo intersects with non-segmental vitiligo [8].

SYMPTOM AND CAUSES

Loss of skin colour is the primary indicator of vitiligo. Discoloration initially appears on the hands, lips, arms, cheeks, and other exposed areas [9]. Vitiligo may be the outcome of an immune system disorder when your skin's melanocytes are attacked and killed.

- Hereditary heritage from the family.
- A catalyst, which includes burns, stress, or contact with industrial chemicals.
- Intense circumstances
- Contact is not the way vitiligo is transmitted. One individual cannot secure it by themselves [10].

DIAGNOSIS

Skin Biopsy and Blood Draw

a) Take a little sample of the skin that is affected.
b) Draw blood for laboratory tests to rule out autoimmune diseases such as diabetes or anemia.
c) An important diagnostic tool for vitiligo is the Wood's light.

Medical History and Exam

The physician will ask you about your medical history, perform a thorough examination, and attempt to rule out any other disorders you might have, such as dermatitis or psoriasis, if you are diagnosed with vitiligo. He or she can use a special lamp to shine ultraviolet light into your skin to determine if you have vitiligo [11].

Etiology of Vitiligo

Several theories have been proposed to elucidate the pathophysiology of vitiligo. Innervation, micro vascular anomalies, oxidative stress-induced melanocyte degeneration, issues with melanocyte adhesion, autoimmune, somatic mosaicism, and genetic variables are all taken into consideration in these ideas.

Neural Theory

The "neural hypothesis," which postulates that depigmentation is influenced by innervation, is typically predicated on a small number of incredibly speculative observations: 1) because segmental vitiligo is unilateral, it is mistakenly classified as a dermatomal disorder; nevertheless, the disease seldom affects only one dermatome and often crosses many dermatomes [12-13]. 2) According to Lerner, vitiligo is caused by an increase in the neuropeptides that neurons release, which in turn decreases the synthesis of melanin by melanocytes [14-15]. High catecholamine levels in the urine of vitiligo patients have also been seen, which has prompted some to hypothesize that this is caused by malfunctioning neurons [16-17].

Autoimmunity Theory

The immune system's destruction of melanocytes is strongly supported by the available data. Patients with melanoma who have hypopigmentation have better prognoses, which implies that both hypopigmentation and tumor control are products of the immune system's reaction to melanocytes [18-19]. New-onset vitiligo has been linked to bone marrow or lymphocyte infusions used to treat lymphomas and leukemia's [20-21].

Melanocyte Adhesion Theory

Melanocytes are easily removed or lost in other ways because, according to the melanocyte adhesion theory, they lose or have diminished adherence to the skin when they are subjected to oxidative stress or mechanical strain, such as friction from clothing. Tenascin, a protein, may help lower melanocyte adhesion in vitiligo, according to Le Poole et al. Tested controls did not express this protein as much as vitiligo patients did [22].

Biochemical Theory

According to the hypothesis of oxidative stress, the reduction-oxidation balance of vitiliginous skin is out of equilibrium. Reactive oxygen species (ROS) like H2O2 are consequently created in astounding quantities. Melanocyte death and the formation of depigmented macules are caused by ROS-oxidizing cell components [23]. This theory states that dysregulation of biopterin pathways predisposes vitiligo and melanocyte cytotoxicity. Both (6R)-L-erythro tetrahydrobiopterin (6BH4) and (7R)-L-erythro tertahydropterin (7BH4) had increased teridine levels in vitiligo. 6BH4 is a cofactor for phenylalanine hydroxylase, the enzyme that converts dietary phenylalanine into tyrosine. An accumulation of byproducts like 7BH4 and H2O2 results from the metabolic pathway being driven forward by increased 6BH4, which can be caused by either decreased activity of the enzyme responsible for recycling it, 4a-hydroxy BH4 dehydratase, or increased activity of the enzyme responsible for producing it, GTP cyclohydrolase I [24].

Micro vascular Theory

The micro vascular theory states that increased blood flow into the skin lesions causes segmental vitiligo. Lesional skin from segmental vitiligo patients had up to triple the blood flow of healthy skin, while non-segmental lesional skin did not, according to isotophoresis and laser Doppler flowmetry [25]. It was proposed that the auto-reactive T cells in the local lymph nodes had grown and activated before departing and entering the bloodstream, which is why the presentation was unilateral. Increased blood flow may hasten lymphocyte migration to the lesion for melanocyte death due to the formation of cutaneous homing receptors on melanocyte-specific cytotoxic T cells [26].

Decreased melanocyte survival hypothesis

Another theory asks whether melanocyte apoptosis is caused by a deficiency of survival signals. The keratinocyte-derived stem cell factor regulates melanocyte survival and proliferation via binding to the membrane tyrosine kinase receptor c-kit. The much lower expression of stem cell factor from surrounding keratinocytes and the drastically decreased number of c-kit receptors in perilesional melanocytes may have an impact on the etiology of vitiligo [27].

Neurohumoral hypothesis

Nervous system dysregulation may be the cause of melanocyte demise in vitiligo, either locally or systemically. Neural crest cells are the source of both melanocytes and nerves. Segmental vitiligo follows the path of nerves, and changes in sweating patterns coincide with anatomical changes in nerves [28]. Immunohistochemical staining demonstrates an increase in neuropeptide Y levels intra- and perilesionally. The increased neurotransmitters may damage the cells directly or indirectly by localized vasoconstriction, which results in hypoxia and the production of hydrogen peroxide (H2O2) under stressful conditions. Antibodies to intracellular pigment cell antigens, cell surface pigment cell antigens, and nonpigment cell antigens (common tissue antigens) are present in the sera of vitiligo patients. The first antigens identified were cell surface antigens with molecular weights of 35, 40–45, 75, 90, and 150 kDa. The prevalence of VIT 40/75/90 antigens is higher than that of antibodies to 35- and 150-kDa molecules. In 83% of patients with vitiligo, the former is present, compared to 7% of controls. While VIT 90 is only found on pigment cells, VIT 40 and VIT 75 are recognized as common tissue antigens since they are found on both pigment and non-pigment cells. Compared to keratinocytes or fibroblasts, melanocytes are significantly more susceptible to immune- or toxic-mediated injury. As a result, even mild damage from nonspecific antibodies can be fatal to melanocytes but not to nearby cells [29].

Apoptosis and accelerated cell senescence

Melanocytes from vitiligo patients without skin lesions show abnormalities like detachment, loss of dendrites, rough endoplasmic reticulum dilatation, cytoplasm vacuolization, and DNA marginalization in the nucleus [30]. Keratinocytes undergo apoptosis, at least in the skin of patients with vitiligo who have experienced damage. The depigmented and normally colored skin exhibits degeneration of the basal and suprabasal epidermal cells due to the enlargement of the membrane-bound organelles, formation of vacuoles, and condensation of the cytoplasm [31]. Melanocytes' epidermal melanin unit is where epidermal melanocytes manufacture growth factors (GF). Its destruction therefore has a major effect on melanocyte survival. Therefore, keratinocyte death may occur before melanocyte apoptosis due to low levels of growth factors (GF) like SCF or endothelin-1 (ET-1) or high levels of cytokines that hinder melanocyte growth like TNF- and IL-6. The lifespan of lesional keratinocytes is significantly lower than that of normal, non-lesional vitiligo keratinocytes. It also shows different expressions of proliferation and senescence markers (p16, p53, and p21) when compared to keratinocytes from skin that are not clinically impacted.

Degenerative Theory

The degenerative theory states that melanocytes have a defect that makes them disappear from the skin, leading to depigmentation. The idea for this theory came from autoimmune inflammation. For example,

autoimmunity may arise from a large release of auto antigens, or reduced adherence may arise from innate abnormalities in the body's response to stress or an autoimmune attack [32].

Current Approaches for the treatment of Vitiligo

The medicinal treatments corticosteroids, psoralens, and depigmenting medicines are the well-researched and often utilized.

Corticosteroids

Topical steroids are commonly used as the first line of treatment, particularly for localized diseases or in youngsters. Topical corticosteroids of potent to moderate potency are used. For vitiligo, however, these drugs must be used continuously, often for much longer than the usual "safe" recommended durations of treatment for inflammatory dermatoses. The result is significant unfavorable effects that are limited by the therapy, such as atrophy, hypertrichosis, and peri-lesional hypopigmentation [33]. The main goals of using systemic corticosteroids (SCS) are to lessen the immunological response, stabilize the disease, and encourage repigmentation. SCS is used to treat actively developing, quickly worsening vitiligo. Pulse treatment with SCS is recommended to lessen the chance of adverse effects. Short-term therapy has been linked to a few mild adverse effects, such as headache, acne, weight gain, agitation, increased appetite, fatigue, and hypertrichosis. Additionally, corticosteroids have a propensity to weaken children's immune systems, making them more susceptible to infections, when administered to them for longer than two weeks. The most common side effects in children have been reported to include vomiting, behavioral issues, sleep disturbances, and a higher risk of fractures. In rare cases, signs of hypothalamus-pituitary axis (HPA) axis suppression, including joint pain, myalgia, hypoglycemia, and electrolyte abnormalities, may even show up after a 2-week course of steroid therapy [34].

Calcipotriol

A synthetic vitamin D3 analog called calcipotriol has been shown to induce perilesional hyperpigmentation in psoriasis patients. The use of this discovery in vitiligo was initiated. Its effects on immunomodulation and melanocyte upregulation are widely acknowledged. 18 pediatric vitiligo patients participated in a trial and were given topical calcipotriol at a dose of 50 g/g twice a day. Of these patients, 77.8% showed signs of repigmentation, and 21.4% showed complete repigmentation [35].

Phototherapy

Phototherapy was among the first therapies for vitiligo, and it remains the mainstay of vitiligo care to this day. Of the three types of psoralen, the most commonly used is 8-MOP (methoxsalen), 5-MOP (bergapten), and 4, 5, and 8-trimethylpsoralen (TMP). Topical psoralen photochemotherapy (PUVA) is often used for people with mild disease. Children with localized vitiligo patches 12 years of age and older are also treated with it. Topical PUVA therapy may cause severe sunburn, blisters, and very dark repigmentation as major side effects. Psoralen's uncontrollably strong photoreaction with UV light is the cause of this. Because the medication is readily available in the dosage formulations that are now on the market, topical application of the medication results in an irradiation of the skin [36].

Calcium modulators

Recently, tacalcitol and calcipotriol—which are vitamin D3 mimics—have also been investigated as potential therapies for vitiligo. (M R. M., 2009). Defective calcium transport has been reported in the collected melanocytes and keratinocytes of vitiligo patients. It has also been shown that vitamin D3 increases the synthesis of melanin. .Their efficacy in treating vitiligo, either in isolation or in conjunction with PUVA and NB-UVB phototherapy, is inconsistent. When calcipotriol is administered in doses greater than 100 mg per week, the most common adverse effects include lesional pain and possibly hypercalcemia. Therefore, by altering the current dosage formulations, regulated distribution may be able to yield better outcomes by lowering both systemic absorption and local irritation [37].

Flavonoids

Bioflavonoids, also known as flavonoids, are polyphenolic compounds that possess antioxidant, anti-inflammatory, and anti-microbial properties. Numerous dietary items and plants, including dark chocolate, wine, beer, tea, onions, blueberries, bananas, and all citrus fruits, contain them. Because flavonoids have antioxidant properties, they have been recommended as supplements for the treatment of vitiligo. One flavonoid that merits specific attention is quercetin, which has been investigated for the treatment of pigmentary diseases both in vivo and in vitro. Quercetin has been shown in numerous trials to protect melanocytes and keratinocytes from oxidative damage, indicating that it may be a useful adjuvant oral therapy for vitiligo sufferers. Furthermore, it has been observed that topical use of quercetin can protect cells from UV rays [38].

Vitamin D3 analogues

The two primary sources of vitamin D are diet and UVB light-induced skin production of 7-dehydrocholesterol. According to AT endogenously produced non-classical vitamin D hydroxy metabolites function as inverse agonists on RRR alpha and ROR Gamma and biassed agonists on VDR. The conventional

process for getting hormonally active vitamin D involves hydroxylation, mostly in the liver, to 25-hydroxyvitamin D3, which is subsequently converted to 1, 25-hydroxyvitamin D3, the active form of the vitamin, in the kidney. One possible mechanism of vitamin D3 activation is the production of physiologically active metabolites by cytochrome P450 family 11 subfamily A member 1 (CYP11A1). The hydroxysterol derivatives and vitamin D have photo protective properties. Topical vitamin D analogues may improve the efficacy of NB-UVB phototherapy. Vitamin D's antiapoptotic and antioxidant qualities are beneficial to vitiligo patients who are at risk of vitamin D deficiency. The administration of vitamin D has been beneficial for kids with normal or low vitamin D levels. It can also be used in conjunction with topical tacrolimus. The Indian Academy of Paediatrics advises supplementing 400 and 600 IU of vitamin D, respectively, for infants and kids with normal vitamin D levels [39].

Use of TCIs (Tacrolimus ointment and Pimecrolimus cream)

Treating vitiligo on the face and neck with TCIs (pomecrolimus cream and tartaricus ointment) is very successful. TCI may be applied as periorbital vitiligo's initial treatment. TCI is also applicable to sensitive anatomic regions, such as the vaginal region and the mucosa of the labial mucosa.Topical calcineurin inhibitor therapy, when applied sporadically, is usually required for three to six months or more. Unlike steroids, TCI do not have significant adverse effects. On the other hand, TCI can result in or exacerbate skin disorders like herpes simplex, folliculitis, and acne. TCI can be applied either on its own or in combination with other therapies. Ebrahim et al. conducted a trial. Patients with locally isolated, stable vitiligo received a 0.1% tacrolimus injection either by itself or in conjunction with microneedling, which entails puncturing the skin with minuscule needles. In addition to taking tacrolimus every day, the combo group had up to 12 sessions of microneedling every two weeks. According to the results, compared to 29.92% of patients in the monotherapy group, 50.00% of patients in the combination group exhibited early pigmentation and a pigmentation level of 75% (HM, 2020). Moderate daily sun exposure is recommended during treatment. TCI can also be used in conjunction with TCS's intermittent treatment plans, in order to continue a treatment plan on days when TCS is not used [40].

Use of depigmentation agents

If depigmented macules affect more than 95% of the BSA and traditional therapy do not result in repigmentation, depigmentation should be considered. Depigmented skin requires a strict sunscreen regimen to prevent sunburn and the repigmentation of the treated remaining normal skin after sun exposure.

Topical Depigmenting Substances

Topical depigmenting medications, 20% 4-methoxyphenol (mequinol, monomethyl ether of hydroquinone) and 20% monobenzone (monobenzyl ether of hydroquinone), are both recommended to be applied twice daily for three to six months. Initially, 10% of mequinol is added; this amount is then progressively raised every one to two months until the desired degree of depigmentation is attained. Prior to treating the unexposed pigmented macules, the remaining exposed macules are treated [41].

Novel Drug Delivery Systems for Vitiligo

When opposed to the traditional oral form of administration, topical medication treatment for vitiligo offers several advantages. By leaving out the major organ systems like the GIT, liver, kidney, etc., it avoids several issues with side effects, bioavailability, etc. Nevertheless, applying topical medication is not a simple process. Current dosage forms, such as gels, lotions, creams, and ointments, are not able to serve or deliver what is needed, where it is needed, which is the primary barrier to attaining the intended therapeutic impact. The complex lipid and cellular structure of the cornified layer of the intra-follicular epidermis, composed of free fatty acids, cholesterol, and ceramides, renders the skin impermeable. Because of these characteristics, many potential treatment candidates with primary cutaneous symptoms have been treated systemically when a topical route would have been a more appropriate course of action. Systemic oral administration of potentially harmful drugs such as psoralen and corticosteroids has been utilized for vitiligo and many other skin disorders [42].

Topical drug delivery systems

Because improved profiles (pharmacokinetic and pharmacodynamics) of the chosen drug molecules for various skin diseases were observed when using these phospholipid-structured carrier systems for optimized topical delivery, phospholipid-structured carriers would be the preferred method of topical delivery for vitiligo [43]. The following list of causes will discuss some of them:

Skin-friendly

Research has demonstrated that phospholipid-based carrier systems, like lecithin, help to retain moisture in the skin while being safe and non-irritating. One naturally occurring substance that is thought to be an excellent skin conditioner and skin barrier restorer is lecithin.

Super solvent effect

Because of their amphiphilicity and supramolecular association, phospholipid-based carrier systems provide a super solvent effect that helps transfer through the skin while maintaining the active drug in a molecularly dispersed state. These can be used to administer medications that are lipophilic or hydrophilic. Methoxsalen typically has a crystalline structure, however, carriers can keep it distributed, creating the appearance of a super-solvent.

Pronounced action

Beyond a prolonged presence, another benefit that might be associated with the therapeutic molecules' ability to stay at or near the target region is enhanced pharmacological activity. There's a chance that the medication in the recommended carrier will produce better drug-target interactions. Methoxsalen will only react with UV radiation at or near melanocytes not on the skin's surface when the medication is administered via a carrier, which lessens the harmful effects of photo toxicity in vitiligo patients.

Phospholipid-structured carriers

Vesicular approaches

Liposomes and Niosomes

Liposomes are lipid-based particles that have a double layer that mimics the structure of a normal cell membrane around an aqueous center. Biodegradable and non-toxic components. The most promising properties are believed to be present in liposomes. Delivering medication topically using a nanocarrier. Liposome development could result from the apparent success of lipid vesicles. The deeper layers of the skin are penetrated by the therapy to reach the stratum corneum [44]. One study examined the effects of co-loading resveratrol and psoralen onto ultra-deformable liposomes (UDL) to treat vitiligo. Psoralen, a naturally occurring furanocoumarin derivative, is used with UV or PUVA to treat a range of skin disorders. The presence of a surfactant allows the vesicle to adjust to external conditions. It has been demonstrated that resveratrol stimulates mitogen-activated protein kinase signaling and possesses antioxidant qualities. To show how well these substances might be utilized as adjuvants in the treatment of vitiligo, one team produced samples of baicalin and berberine that were also co-loaded with ultra-deformable vesicles. Baicalin and berberine were selected as therapeutic agents due to their proliferative, antioxidant, and anti-inflammatory qualities. Studies conducted in vitro showed that preparation enhanced the absorption of drugs and antioxidants Tyrosinase and melanin activities were increased by co-loaded vesicles, according to assessments of the photoprotective effects [45].

Microemulsions

Transparent colloidal entities that exhibit thermodynamic stability are known as micro emulsions. Micro emulsions usually consist of water and oil stabilized by a surfactant, sometimes supplemented with a cosurfactant. One group's clobetasol propionate-loaded micro emulsion-based gel effectively overcame the drug's poor solubility. The effectiveness of the preparation indicated that the stratum corneum thickened due to water retention caused by the gel formulation, facilitating the absorption of clobetasol propionate into the skin. A clinical trial found that repigmentation occurred more quickly and in greater amounts in patients treated with a micro emulsion-based gel containing clobetasol propionate than in control groups. Because of a significant increase in penetration rate, anti-inflammatory medication (NSAID) transdermal delivery utilizing micro emulsions has shown potential [46].

Transferosomes

Cevc et al. originally reported on the first generation of elastic vesicles, often known as transferosomes. These self-optimized aggregates, which have an incredibly flexible membrane, can distribute the medication through or into the skin very effectively and consistently. The greater ability of these elastic vesicles to penetrate skin than liposomes has been demonstrated by numerous investigations [47].

Ethosomes

Ethosomes are lipid-based, elastic vesicular networks that hold ethanol and enhance the administration of topical medications. They have a comparatively high ethanol content. The presence of ethanol increases the physical stability of ethosomes concerning liposomes. The enhanced distribution of the ethosomes' active components is caused by interactions between ethosomes and skin lipids (Table 2). This may open up new avenues for medication delivery because of the ethosome's malleability and ability to fuse with skin lipids, which permits the drug to reach deeper skin layers [48].

Non-vesicular approaches

Lipid emulsion

Lipid emulsions are low-viscosity, isotropic colloidal dispersions stabilized by an interfacial layer of alternating surfactant and cosurfactant molecules. They contain micro-domains of water or oil. Thermodynamic stability applies to them. Lipids improve the physical stability of the emulsion by forming a mono- or multi-layer around the dispersed liquid droplets that reduce interfacial tension or increase droplet-droplet repulsion. Topical vehicles such as lipid emulsions [Table 2] can enhance penetration and create local cargo or micro-reservoirs in the deeper layers of the skin to enable targeted action [49].

Lecithin organogels (LOs)

LOs are micro-structured biocompatible gels that work well with phospholipids (lecithins) and organic liquids. Many medicinal ingredients have been added to LOs to improve their treatments and make them easier to distribute across the skin. The commercial availability of a particular class of LOs, called PLOs (Pluronic lecithin Organogels), as a template vehicle for the topical delivery of several medications, has increased the importance of research in this field [50].

Clinical trial report on the vitiligo

To better understand the efficacy of drugs in human health, suitably planned clinical studies combat the vitiligo. We have talked about a few clinical trials (Table 2.) that are pertinent to the therapy of vitiligo.

Drug-Carriers Used For Drug Delivery in vitiligo			
Phospholipid-Structured Carriers	**Polymeric Carriers**	**Proteinases Carriers**	**Cellular Carriers**
Liposomes Transferosomes Ethosomes Lipid emulsion Micro particles Organogels	Resealed Erythrocytes Antibodies Platelets Leukocytes Serum albumin	Soluble synthetic polymeric Biodegradable Signal sensitive Bio erodible Bio adhesive	Lecithin and Polysaccharides Proteins Glycosylated Immunotoxin Soluble Polymers Monoclonal antibodies

Table 1: List of various drug-carriers used for drug delivery

Sr.No.	Study	Year	Intervention/ Treatment	No. of subjects	Result Obtained
1.	Effect of Micro needling, Bimatoprost and Excimer in Vitiligo Treatment	2022	Device: Excimer laser & Micro needling with a dermaroller	4 participants	Percentage of skin repigmentation after 12 weeks
2.	Role of Tofacitinib in Vitiligo Patients (ETV)	2022	Interventional	80 participants	Change in Vitiligo at 6th week by Vitiligo European Task Force scoring
3.	Pilot Study Assessing the Effect of Tildrakizumab in Vitiligo (TILDVIT-1227)	2022	Interventional (Clinical Trial)	12 participants	Percentage repigmentation: Vitiligo Area Scoring Index (VASI)
4.	To Study the Efficacy of Therapeutic Pulsed Ultrasound in the Treatment of Vitiligo: a Randomized, Intra-individual, Left-right Comparison Study	2019	Device: HGM	30 Patients with Vitiligo	The HGM system will be combined to provide the non-invasive microscopic images in Vitiligo sites during each follow-up for pathological diagnosis.
5.	Effects of Camouflage on the Life Quality of Patients With Vitiligo	2018	Interventional (Clinical Trial)	400 participants	Chinese version of the vitiligo life quality index, VLQI-C
6.	Autologous Cell Suspension Grafting Using ReCell in Vitiligo and Piebaldism Patients	2017	Device :Full surface CO2 laser 200 mJ,150 mJ Device: Fractional CO2 laser 7.5 mJ, 20%	10 participants	Repigmentation
7.	Botulinum Toxin Treatment for Localized Vitiligo	2010	Interventional (Clinical Trial)	10 participants	The percentage of repigmentation in the previously depigmented patch, in form of colour or size changes and folliculocentric repigmentation, of the treated and the control patches.

Table 2. Recent clinical trials for the treatment of vitiligo

Sr. No.	Title	Type And Patent numbers
1.	Therapy For Vitiligo	US9801924B2 United States [51]
2.	One treats leukodermic Chinese medicine composition and	China CN106074778A [52]
3.	Methods and systems for treating vitiligo using phloroglucinol and related compositions	United States US20210260001 [53]
4.	Phytotherapeutic formulation for vitiligo treatment Brazil	Brazil WO2016123682A1 [54]

Table 3. Patents on the vitiligo

Sr. No.	Marketed formulation for vitiligo
1.	Melanomax Tablets
2.	Aarogyam Curcumin Capsules
3.	Nutrova Formula V
4.	Aarogyam Leucoderma Skin Pack
5.	Dermaceutic Mela Cream
6.	Vitcure Repigmentation Oil
7.	Barphani VitliGon
8.	Leukoderma care
9.	Bella Aurora Repigment12
10.	Viti-Nutrient
11.	Vitix Gel
12.	Vitix Tablet
13.	MDHL Vitiligo cream
14.	Tijara Herbal white care

PATENTS

The number of patents has increased 30% annually since 2000, keeping pace with the recent surge in interest in nanotechnology. A list of pertinent patents for the treatment of vitiligo that were published between 2010 and 2021 has been presented. Modern inventions offer a medicinal solution for skin diseases related to dermatology. Some of the patents relevant to vitiligo are briefly outlined in Table 3.

CONCLUSION

Vitiligo is a pigmentary disorder that primarily affects melanocytes in the epidermis and mucosal membranes. It is a widespread ailment that affects approximately 1.0% of people worldwide. It is the outcome of the dynamic interaction between environmental and genetic factors that lead to autoimmune illness. Eliminating melanocytes using a few natural chemicals could be considered a viable treatment for vitiligo. We talked about opportunities for the future. Clinical trials and patents for vitiligo are currently ongoing to have a deeper understanding of natural therapies' effectiveness. To combat vitiligo, well-designed clinical trials need to be carried out. This article aims to provide a succinct overview of the current state of vesicle formulations used to treat vitiligo. In the upcoming years, nano-fibrous material combined with plant-based components will surely realize the benefits of the current medication delivery technology. It has the potential to significantly improve the absorption and stability of synthetic and natural medications, hence increasing their efficacy. In the future, nano-fibre medicine will greatly enhance people's health. The authors are confident that Nano fibrous system medicine will be reasonably priced and accessible on the market soon. This overview discusses the different vesicular formulations that have been and will be used to treat vitiligo.

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