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Pityriasis versicolor: Causes and new active ingredients as a potential treatment

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ABSTRACT

Pityriasis versicolor is caused by Malassezia spp. It's characterized by a superficial fungal infection that affects both sexes, mostly tennagers and young adults, accounting for 40% of the population in tropical regions. Malassezia proliferates in organisms with intense sweating with the use of oily and occlusive cosmetics, or with occlusive clothing, triggering an imbalance in the skin microbiota system. The clinical manifestations are discrete oval or confluent, scaly, dark or depigmented macules on seborrheic regions of the body. Essential oils (EOs), including Oregano (Origanum vulgare) and Melaleuca (Melaleuca alternifolia) contain compounds, such as carvacrol, thymol and terpenes, which demonstrate antimicrobial and antifungal properties. Silver nanoparticles (AgNPs) have an inhibitory and fungicidal effect, which can combat resistance biofilm forming species, such as Candida spp, Malassezia spp. Therefore, the association between EOs and AgNPs suggests great potential in the treatment of Pityriasis versicolor.

Keywords: Pityriasis versicolor, *Malassezia* spp., Silver nanoparticles, *Origanum vulgare*, *Melaleuca alternifolia*.

1 INTRODUCTION

Pityriasis versicolor (PV), popularly known as white cloth, is considered a superficial fungal infection, characterized by a skin pigmentation disorder, caused by lipophilic yeast species of *the genus Malassezia* spp. (Santana; Azevedo; Campos Filho, 2013; Gharehbolagh *et al*., 2019). It occurs worldwide, being more incident in tropical regions (warmer and more humid regions), reaching up to 50%, compared to Scandinavian countries, which corresponds to 1%. (Rodoplu *et al*., 2014; Chebil *et al*., 2022). It affects people of both sexes and of all age groups, especially in adolescents and young adults due to the high production of sebum at this age (Fariña-González *et al*., 2019; Khattab; Omran, 2020; Chebil *et al*., 2022).

PV is classically manifested by irregular macules (round to oval), thin and scaly, which can be hyperpigmented, hypopigmented or erythematous (hence "versicolor" in the name). The diagnosis of PV is usually made by physical examination of the skin, where it is possible to observe the exposure of the yeast by the scaly appearance of the skin. Microscopic observation of shaved portions of the skin in potassium hydroxide (KOH) can be used to confirm the presence of spherical hyphae and blastoconidia characteristic of *Malassezia* spp. Generally, the spots are distributed over the neck, face, upper part of the trunk and proximal upper extremities, since these are areas with a greater number of sebaceous glands (Hudson; Sturgeon; Peiris, 2018; Alberdi; Gómez, 2020; Li *et al*., 2021; M; Freitas, 2021; Chebil *et al*., 2022; Varsha *et al*., 2023).

There are several endogenous and exogenous factors responsible for the occurrence of PV. Endogenous factors include genetic predisposition, endocrine disorders, use of corticosteroids, use of oral contraceptives, pregnancy, and acquired immune deficiency syndrome. Exogenous factors, on the other hand, are hot weather and humidity, causing hyperoiliness, in addition to occlusion of the skin by inappropriate clothing or cosmetics that alter the skin's microflora and pH. Above all, hyperhidrosis is the most important predisposing factor for the manifestation of PV (Lima *et al*., 2002; Alberdi; Gómez, 2020).

PV is usually asymptomatic, although some people may experience mild and recurrent itching. The greatest concern and questioning of patients is the unpleasant aesthetic appearance of the skin, directly impacting their quality of life, both for their physical and mental health . (Gupta; Foley, 2015; Renati; Cukras; Bigby, 2015; Wang *et al*., 2020). Response to treatment is variable. Although most patients have a good response, recurrence of PV is frequent. The major concern of the disease is hypopigmentation or hyperpigmentation associated with frequent eruption, even after treatment independent of immunity (Renati; Cukras; Bigby, 2015; Romero-Sandoval *et al*., 2017).

Usually, PV responds well to the application of topical antifungal agents, lasting between 1 to 4 weeks. The usual topical treatment is through creams, gels, lotions, shampoos, and sprays containing azole antifungals such as miconazole, ketoconazole, clotrimazole, or oxyconazole (Gupta; Lyons, 2014; Telesaúde RS-UFRGS, 2019), or by active ingredients such as selenium sulfide and zinc pyrithione (Hudson; Sturgeon; Peiris, 2018). In cases of recurrence of the infection, the use of systemic (oral) antifungals can be used, as well as ketoconazole, itraconazole, or fluconazole (Li *et al*., 2021).

However, it is common to have failure in the treatment of PV due to occasional skin irritation, multiple applications of topical agents for weeks or months, costly treatments, and resistance to antifungals, resulting in poor patient adherence and, consequently, recurrence of PV. Side effects of systemic antifungals may occur, as well as risk of liver toxicity from long-term use of ketoconazole and interactions with numerous other drugs. Due to these considerations, it is necessary to find new alternative antifungal strategies for the future treatment of PV (Gupta; Lyons, 2014; Alberdi; Gómez, 2020).

A new alternative for PV may be to use essential oils (EOs) extracted from plants, which have compounds with antimicrobial properties, such as phenols and terpenes (Kalemba; Kunicka, 2003), and metallic nanoparticles with antimicrobial properties, such as silver (Morandi, 2023; Scandorieiro *et al*., 2023).

EOs are widely used in the cosmetic, perfumery, and aromatherapy industries, due to their antioxidant, anti-inflammatory, antibacterial, antiviral, antifungal, antiseptic, antimycotic, antitumor, antispasmodic, and immunostimulant properties (Arámbula *et al*., 2019; Srivastava *et al*., 2019; Ebani *et al*., 2020). Two EOs with antimicrobial properties proven by the literature are those of the species *Origanum vulgare* (OEO) and the species *Melaleuca alternifólia* (OEM) (Souza *et al*., 2013).

Metal nanoparticles (NPs) have also been gaining prominence for being an efficient biotechnological tool in medicine, cosmetics, pharmaceuticals, and food (Nakazato *et al*., 2020; Ziotti, 2023). It has attracted great attention for its antimicrobial properties, and has been widely exploited by the nanotechnology industry. In addition, it is an innovative and sustainable input, since it is produced by ecological and low-cost methods (Scandorieiro *et al*., 2022). AgNPs can be an alternative to antibiotics, as they have the ability to overcome the resistance that bacteria have to antibiotics. Because they have this action against microorganisms, AgNPs are also used in the healing of burns and wounds (Cadinoiu *et al*., 2022).

Considering the causes and occurrences of PV, along with the difficulty of treating it, this review aims to describe the potential applications of OEO and OEM essential oils, and AgNPs, as treatment suggestions for this dermatitis.

2 SKIN MICROBIOME

The skin microbiome is the combination of microorganisms and the surrounding environment. As an epithelial barrier to the external environment, the skin also supports a diverse microbiota (bacteria, fungi, viruses, and microeukaryotes). The human body is fully interconnected with the communities of microorganisms that inhabit the surfaces of the body and the external environment, so that the skin microbiota becomes a unique niche, adapted to life in the micro-habitats that define the environmental and nutritional conditions of this ecosystem. The commensal microbiome is essential for maintaining the protective function of the internal organism, where microorganisms from the normal skin microbiota participate in essential physiological processes. In particular, the microbiome is present in the physical, chemical, microbiological, and immunological reactions that maintain the skin's barrier function system (Jo; Kennedy; Kong, 2017; Flowers; Grice, 2020; Lee; Kim, 2022).

The skin surface is usually considered an acidic, high-salt, dry and aerobic environment. The relationships between extrinsic and intrinsic factors generate a well-controlled and delicately balanced microbiome (Lee; Kim, 2022).

The various communities of microorganisms are susceptible to colonize on the skin according to their physiological specificities. With joint and mutualistic or commensal interaction with mammalian host cells, the skin microbiota promotes immune defense and responses, inhibits colonization and infection by opportunistic microorganisms (pathogens), promotes tissue repair and skin barrier (Flowers; Grice, 2020). According to Safady (2021), studies of the diversity, taxonomy, and functional potential of a microbial community coexisting in an environment, i.e., metagenomic analyses, have shown that most of the readings obtained from skin regions are bacterial, but also relatively high proportions of fungi or viral sequences (Jo; Kennedy; Kong, 2017).

Several skin diseases, such as seborrheic dermatitis, atopic dermatitis, and dermatophytosis, originate from the interactions between extrinsic and intrinsic factors. The imbalance of the cutaneous microbiota system can lead to pathophysiological problems, as well as induce inflammation, infections, allergic diseases and autoimmune diseases (Jo; Kennedy; Kong, 2017; Lee; Kim, 2022). Areas such as the face, scalp, thorax and back are commonly colonized by *Malassezia* and *Propionibacterium* species, which metabolize sebum lipids, present in the epidermis, into free fatty acids (Grice; Dawson, 2017).

2.1 SPECIES OF *MALASSEZIA* SPP.

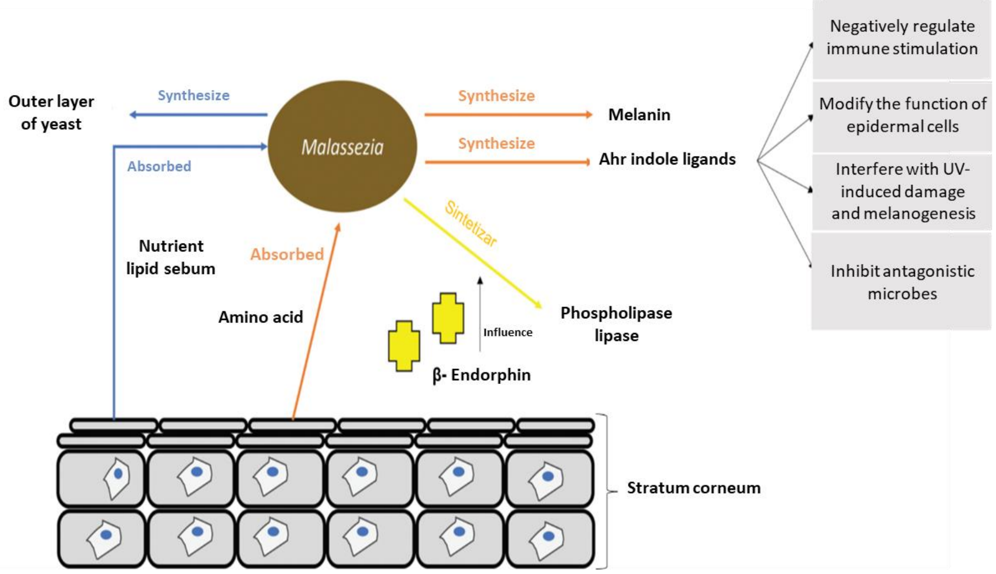
Yeasts of the genus *Malassezia, formally known as* Pityrosporum*, are lipophilic yeasts belonging to the phylum* Basidiomycota *(class* Malasseziomycetes*), and* integral members of the skin microbiome of humans and warm-blooded animals. Based on morphology, structure, physiology and molecular biology, eighteen species of the genus have currently been identified, namely: M. furfur, M. *pachydermatis*, M. sympodialis*, M. globosa, M. restricta*, M. obtusa*, M. slooffiae*, M. dermatis*, M.* japonica*,* M. yamatoensis*, M.* nana*, M. caprae*, M. equina*, M. cuniculi*, M. arunalokei*, M. brasiliensis*, M. psittaci *, and* M. vespertilionis. The species predominantly isolated from PV lesions worldwide were M. *globosa*, *M. furfur* and *M. sympodialis* (Saunte; Gaitanis; Hay, 2020; Chandra *et al*., 2021; Chebil *et al*., 2022; Hamdino *et al*., 2022).

Malassezia *species* are the agents that often cause skin infections in humans and animals, especially in tropical and subtropical areas. In humans, Malassezia species *account for 75%, up to 98%, of the skin microflora and can cause various skin infections, as well as PV*, Malassezia folliculitis, seborrheic dermatitis (SD), and atopic dermatitis (AD) (FAR; Al-Obaidi; Desa, 2018; Hamdino *et al*., 2022).

It is an opportunistic polymorphic lipophilic microorganism that is distinguished from other genera by its multilayered and thick cell wall. According to the conditions in which they are found, *Malassezia* yeasts vary from the saprophytic form to the pathogenic mycelial form, causing various infections in the host (Far; Al-Obaidi; Desa, 2018). There is controversy as to whether *Malassezia* yeasts are benign commensals or pathogens. According to the different circumstances, both are acceptable, as they can potentially interact with almost all cells of the epidermis, such as keratinocytes, melanocytes, Langerhans cells, and the immune system. The interaction between fungi and human hosts is complex, and the pathogenicity of such a genus is not only defined by the presence or absence of the microbe, but also by the interaction of the environment and susceptibility of the host (Hamdino *et al*., 2022).

The occurrence of dermatological disorders associated with *Malassezia* spp. yeast is still unclear. Physiologically, it is possible that *Malassezia* uses the nutrients available in the skin for its growth and still the skin remains healthy. Only with a disturbance in this physiological interaction does the yeast adapt and modify the expression of enzymes involved in the acquisition of energy such as lipase and phospholipase. At the same time, yeast is able to synthesize indole ligands of the aryl hydrocarbon receptor (AhR) (present in almost all epidermal cells). Therefore, *Malassezia* is able to modify AhR-expressing cells, such as inducing melanocyte apoptosis and inhibiting neutrophil activity. Figure 1 shows a representative schematic of how indoles are associated with a deficient immune system and features associated with skin lesions caused by *Malassezia* (Kurniadi *et al*., 2022).

Figure 1 – Physiological interaction diagram between *Malassezia* spp. yeasts and the skin.



Legend: Ahr = Aryla Hydrocarbon Receiver.
Source: Adapted from Kurniadi *et al*., 2022.

The schematic of interaction between *Malassezia* yeast and skin (Figure 1) occurs when yeasts acquire the sebaceous lipids to form their outer surface, and the amino acids to synthesize melanin and AhR indole ligands. With the influence of the enzyme β-endorphin, yeasts are also able to synthesize and excrete the enzymes lipase and phospholipase. The formation of AhR indole ligands can cause epidermal cell damage, as well as interfere with immune response, melanogenesis, and UV-induced damage, modify epidermal cell function, and inhibit antagonist microbes (Kurniadi *et al*., 2022).

In recent years, reports of systemic infections caused by *Malassezia* have gradually increased, with a high incidence rate, generating a great impact on the physical and mental health of patients. According to different regions and countries, the species isolated from *Malassezia* vary, in addition to showing differences between healthy individuals and patients with various skin diseases (Wang *et al*., 2020).

2.2 PITYRIASIS VERSICOLOR: CAUSES AND EPIDEMIOLOGY

PV is a mild, superficial and chronic infection that is quite recurrent in fungal infections, caused by the overgrowth of yeasts belonging to the genus *Malassezia*, a normal component of the cutaneous flora. The largest cases of PV occur in the species *Malassezia furfur (formerly* Pityrosporum ovale*), Malassezia globosa* and *Malassezia sympodialis*. Other species also described as occurrence of PV are: *Malassezia pachydermatis, Malassezia obtusa, Malassezia stricta, Malassezia slooffiae*, Malassezia dermatis, Malassezia yamatoensis*, Malassezia nana and* Malassezia *japonica* (Macedo; Freitas, 2021; Saunte; Gaitanis; Hay, 2020; Krueger *et al*., 2021).

PV has a universal distribution, with a high incidence in tropical regions, in view of warmer environments. It can affect up to 40% of the population, with no gender or race pattern, but adolescents and young adults are usually more affected due to hormonal variations. The pathogenesis of PV is designated by a genetic predisposition, as well as an imbalance in the host-fungus interaction. Because they are usually lipophilic yeasts, *Malassezia* species proliferate preferably in organisms with intense sweating, with the use of oily and occlusive cosmetics, or even with occlusive clothing, causing an imbalance in the skin microbiota system. Other risk factors for PV are diabetes, Cushing's disease, the use of long-term corticosteroids, the use of oral contraceptives, and pregnancy (Macedo; Freitas, 2021; Saunte; Gaitanis; Hay, 2020).

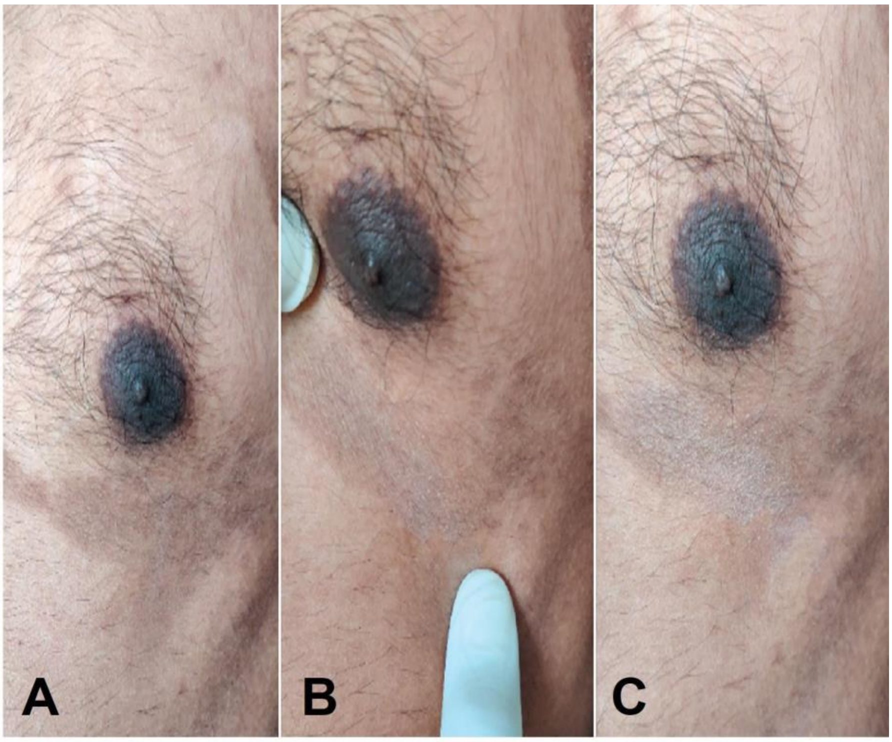
PV affects the stratum corneum, characterized by discrete or confluent oval macules, squamous, dark (hyperpigmented) or depigmented (hypopigmented), as shown in Figure 2. The lesions appear mainly in seborrheic regions of the body, as well as in the upper part of the trunk, and may extend to the neck, shoulders, abdomen, back, and proximal extremities. PV scales are thin and overlapping, merging into larger patches (Macedo; Freitas, 2021; Saunte; Gaitanis; Hay, 2020; Krueger *et al*., 2021; Karray; McKinney, 2022).

Figure 2 - Pityriasis versicolor. A) Hyperpigmented macules on the back, and B) Hypopigmented macules.

Source: Adapted from Saunte, Gaitanis, and Hay (2020).

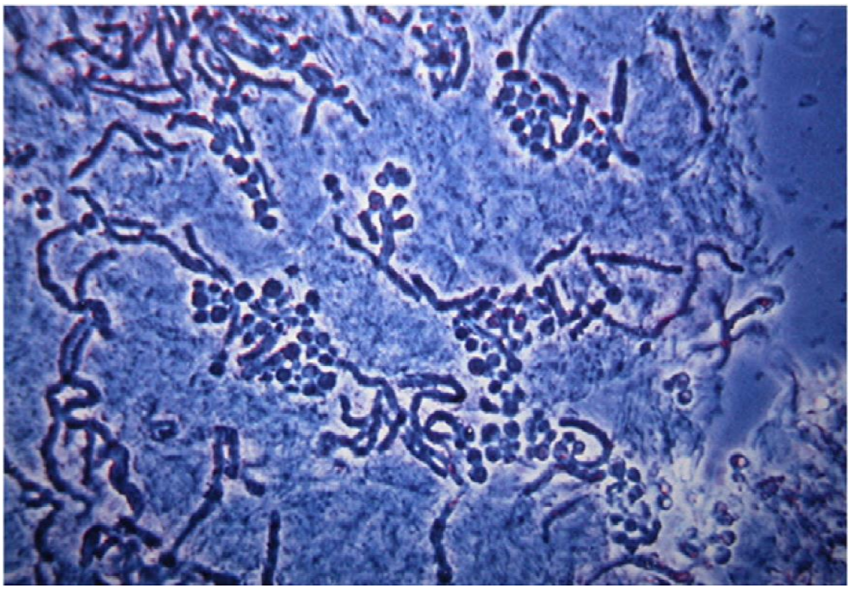
The diagnosis of PV is clinical, usually by visually observing the spots that have a scaly characteristic (Figure 3), i.e., the peeling of the skin is evaluated when stretching it, positioning the fingers at an angle of 180°, also called "evoked-skin" or Zireli's sign, so that the *Malassezia* yeast is exposed (Macedo; Freitas, 2021; Varsha *et al*., 2023). Ultraviolet black light and microscopic examination of scales embedded in potassium hydroxide (KOH), as depicted in Figure 4, can be used in case of doubtful diagnosis. In cases of lack of sensitivity and specificity in the diagnosis of PV with variable interpretation associated with KOH (Potassium Hydroxide) preparations, it is necessary to use auxiliary diagnostic tools, such as dermoscopy. PV responds well to treatment with antifungals, however, long-term treatment is often required due to the high recurrence rate (Krueger *et al*., 2021; Karray; McKinney, 2022).

Figure 3 - Zireli's sign examination in a patient with PV. A) PV before, B) during the evoked-skin exam, and C) After the exam.



Source: Adapted from VARSHA *et al*., 2023.

Figure 4 - Malassezia species seen under a microscope, where a portion of skin scraping containing PV was inserted into KOH solution.

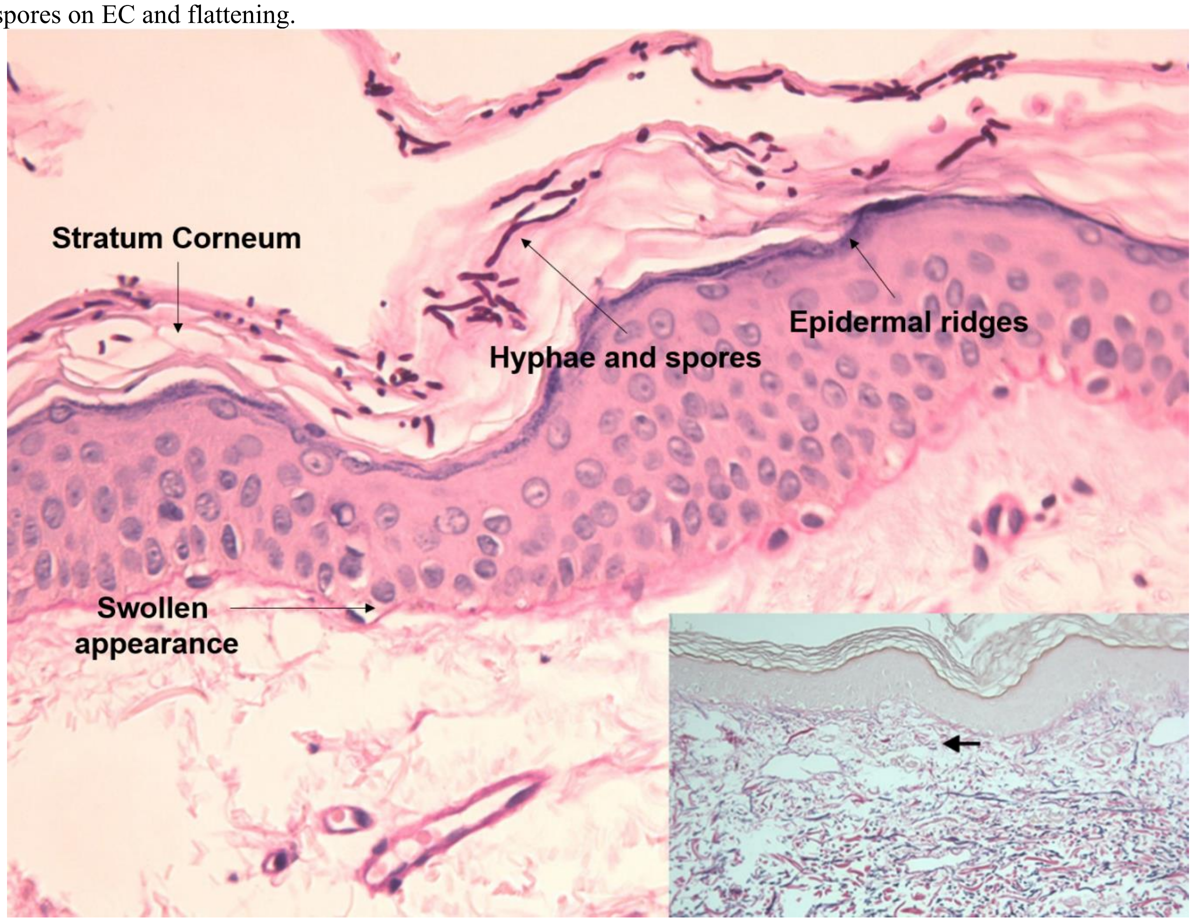


Source: Macedo; Freitas, 2020.

PV occurs when the fungus invades keratinized cells of the superficial layers of the skin, and some fungal metabolites are associated with the clinical presentation of mycosis. Hypo- or hyperpigmented plaques appear because the fungus causes alterations in the production of melanin in the regions where they are colonizing due to the presence of azelaic acid, which interferes with melanogenesis. Fragments of curved, septate hyphae and thick-walled, usually without branches, are observed on the skin scales (Figure 4). The yeast-like characteristics are observed: Spherical, thick-walled blastoconidia, isolated or in groups, close to the hyphae, some felid shoots also observed, typical of the genus *Malassezia* (Andrade, 2016; M; Freitas, 2021).

In a case study conducted by a patient with suspected PV, a skin biopsy was performed (Figure 5). It was possible to observe laminate hyperkeratosis in the epidermis, with flattening of the epidermal ridges and vascular dilatations, with a swollen appearance with the papillary dermis. With Periodic Acid Schiff (PAS) staining, it revealed abundant short and septate hyphae (dark violet) and spores between the keratin layers, indicating the presence of yeast-like species. Orcein staining revealed a decrease in elastic fibers in the papillary dermis and fragmentation of elastic fibers in the superficial reticular dermis.

Figure 5 - Papillary dermis with thin and decreased elastic fibers (arrow) and reticular dermis with fragmented elastic fibers, as well as vascular ectasia (orcein staining, with 100X magnification - Figure A). Epidermis with abundant hyphae and spores on EC and flattening.



Source: Adapted from Allegue *et al*., 2018.

3 NEW ANTIFUNGAL POTENTIALS

3.1 ESSENTIAL OILS

EOs are mixtures of volatile components extracted from aromatic plants, which produce their active ingredients in essential oils, and the composition varies with the place of growth, the climate and the part of the plant's extraction. Some of the EOs are widely used in the cosmetics, perfumery, and aromatherapy industries, due to their antioxidant, anti-inflammatory, antibacterial, antiviral, antifungal, antiseptic, antimycotic, antitumor, antispasmodic, and immunostimulant properties (Arámbula *et al*., 2019; Srivastava *et al*., 2019; Ebani *et al*., 2020).

Regarding the essential oils aimed at the treatment of PV, oregano essential oil and tea tree essential oil can be options, which will be discussed below.

3.1.1 Oregano essential oil

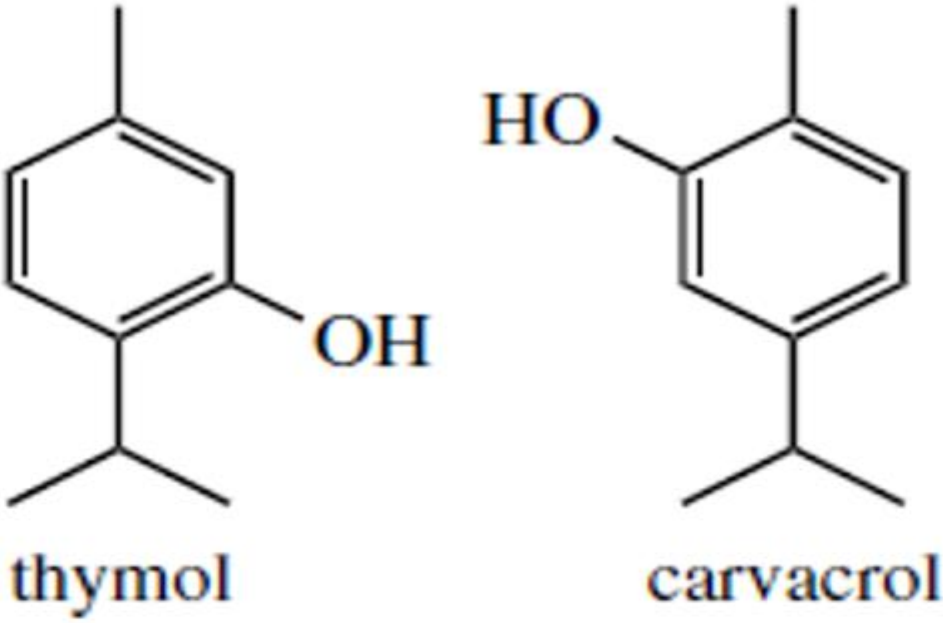
Oregano essential oil (OEO) of the species *Origanum vulgare* (Figure 9), is a plant native to Europe and North America, and belongs to the Lamiaceae family. The genus *Origanum* is present in several areas of the planet, especially in the Mediterranean region with approximately 45 species, 6 subspecies and 3 varieties. It is an aromatic, herbaceous and perennial plant, woody at the base and stem approximately 90 cm high. The types of extracts used for OEO therapy are extracted from parts of the air plant, such as leaves, flowers, and seeds (Alexander, 2020; Bora *et al*., 2022).

Figure 6 - Representation of the species *Origanum vulgare*.

Cast iron: <https://www.ferquima.com.br/novo/index_novo.html>, 2023.

The main activities of oregano EOs are related to the phenolic monoterpenes carvacrol and thymol (Figure 10), which are biosynthesized through the process of aromatization and hydroxylation of p-cymene. However, the volatile chemical compounds present in OEO can vary according to geographic location, plant development, or because of structural or physiological modification of the plant caused by specific environmental factors (phenotypic plasticity), as well as the method of extraction. The chemical composition of OEO is diverse including acyclic, monocyclic, and bicyclic monoterpenes (γ-terpinene, p-cymene, linalool, geraniol, -myrcene, trans-sabinene, -pinene, and terpinen-4-ol), sesquiterpenes (1,8-cineole, -caryophyllene and germacrene-D, -citronellol), flavonoids (luteolin, apigenin, and quercetin), phenolic acids (rosmarinic and chlorogenic acids), and tannins (Alexander, 2020; Bora *et al*., 2022).

Figure 7 - Chemical structures of the monoterpenes present in the essential oil of oregano (*Origanum vulgare*).



Source: Adapted from Dewick, 2002.

Due to its components, OEO has been used in the pharmaceutical, cosmetic, and agrifood industries, due to its antioxidant, anti-inflammatory, antimicrobial, and cytotoxic effects against several human cancer cell lines, but mainly for its antioxidant and antimicrobial activity (Alexaneer, 2020; Cid-Chevecich *et al*., 2022; Kryeziu *et al*., 2022).

According to Scandorieiro et al. (2022), the main bioactive components of OEO (carvacrol and thymol) stand out among EOs as excellent bactericidal agents against several strains, including multidrug-resistant microorganisms. In the study by Naqvi et al. (2019), *O. vulgare* showed antifungal activity against *Aspergillus flavus*, A. parasiticus*, A. fumigatus*, A. terreus, *and* A. ochraceus*; Candida albicans*; species *Penicillium* (*P. aurantiogriseum, P. glabrum and P. brevicompactum, P. chrysogen*);

Fusarium proliferatum, F. oxysporum, F. verticillioides, F. subglutinans, and against human pathogens *Malassezia furfur, Trichophyton rubrum and Trichosporon Beigelii*. A similar result was also observed by Carvalho, Oliveira and Cavalcante (2021), where *O. vulgare* had antifungal action against several fungi, especially for yeasts of the genus *Candida*. For Santin et al. (2014), *O. vulgare* was sensitive to the yeast *Malassezia pachydermatis* at low concentrations of the active ingredient, making it promising in the bioprospecting of new drugs.

3.1.2 Tea tree essential oil

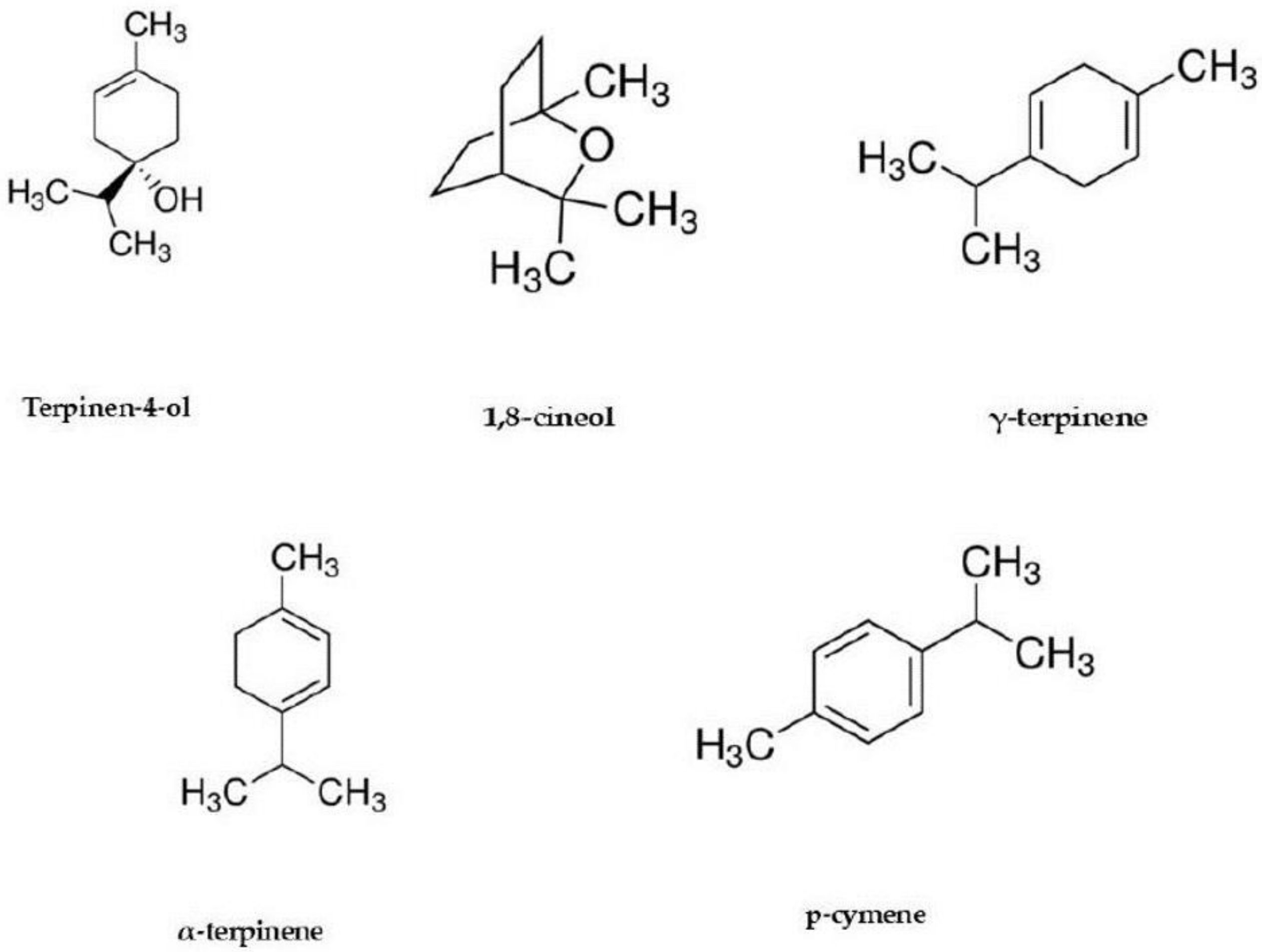
Melaleuca essential oil (OEM) is extracted from the fresh leaves and wood of *the Melaleuca alternifolia* tree (Figure 11), a tree species native to Australia and belonging to the Myrtaceae family. It is considered a tall shrub up to 15 meters tall, with a thick, thin-barked crown, with a characteristic odor of terpene, conifer and camphor-mint. It is found in more than 80% of the Brazilian national territory. It has 140 genera, ranging from 3,500 to 5,800 species, whose fruits grow under adverse environmental conditions of drought, flood and heat. They are a rich source of secondary metabolites involved in plant defense, especially polyphenols (Srivastava *et al*., 2019; Assis *et al*., 2020; Santos *et al*., 2021).

Figure 8 - Representation of the leaves of the *Melaleuca alternofolia tree*.

Cast iron: <https://www.ferquima.com.br/novo/index_novo.html>, 2023.

OEM is extracted by steam distillation from the leaves and terminal branches of the *M. alternifolia* tree. In its composition are present more than 100 components, mainly sesquiterpenes, monoterpenes, hydrocarbons and their related alcohols, as well as terpinen-4-ol, γ- and α-terpinene, p-cymene and 1,8 cineole. The most abundant components are terpinen-4-ol comprising approximately 40% of the oil composition, and γ-terpinene comprising approximately 20% (Figure 12). However, the concentration of the components is in accordance with the variety of *M. alternifolia,* methods and time of extraction, climate, and age of the leaf. The chemical composition of commercial oil is regulated by the International Organization for Standardization (ISO 4730:2017) which has defined the cut-off values for 15 main components: terpinel-4-ol (30-48%), γ-terpinene (10-28%), 1.8-cineole (traces-15%), α-terpinene (5-13%), α-terpineol (1.5-8%), p-cymene (0.5-8%), α-pinene (1-6%), terpine- 3%), δ-cadinene (traces-3%), ledeno (traces-3%), limonene (0.5-1.5%), globulol (traces-1%) and viridiflorol (traces-1%) (Srivastava *et al*., 2019; Assis *et al*., 2020; Roana *et al*., 2021; Santos *et al*, 2021; Ferquima, 2023).

Figure 9 - Chemical structure of the main components isolated from tea tree essential oil (*Melaleuca alternifolia*).



Source: Adapted from Roana *et al*., 2021.

These components are responsible for several activities reported in the literature, as well as analgesic, antiviral, antibacterial, antifungal, antiprotozoal, anti-inflammatory, antioxidant, anticancer, insecticide, acaricide, (Yadav *et al*., 2016; Assis *et al*., 2020; Santos *et al*, 2021). The multiple biological activities of MSP make it an immense potential for dermatological treatments, especially for facial treatments, highlighting for the treatment of acne due to its broad-spectrum antimicrobial properties (Yadav *et al*., 2016; Santos *et al*, 2021). Yadav et al. (2016) report that OEM overcomes the development of resistance by bacterial species to conventional drugs. However, due to its hydrophobicity, volatility, and sensitivity to light, air, and temperature, it is challenging to incorporate the oil into the formulation effectively to maintain stability and active properties, with minimal adverse effects (Yadav *et al*., 2016; Battisti; Caon; Campos, 2021).

According to Brun et al. (2019) and Pazyar et al. (2013), terpinen-4-ol, abundant in the composition of OEM, is responsible for the antimicrobial and anti-inflammatory properties. Other uses of OEM are seen in oral health and treatment of periodontal disease, treatment of wounds, scarring, eczema, psoriasis, onychomycosis, fungal skin infections, and cancer (Srivastava *et al*., 2019).

3.2 SILVER NANOPARTICLES

Nanotechnology is a booming area that is intrinsically associated with contemporary life. There are more than 1800 products containing nanomaterials distributed in various areas of daily life, as well as in the agricultural, food, textile, environmental, pharmaceutical, and electronics sectors (Silva, 2019; Ziotti, 2023). Among nanomaterials, metallic nanoparticles (NPs) have been gaining prominence for being an efficient biotechnological tool in medicine, cosmetics, pharmaceuticals, and food (Nakazato *et al*., 2020; Ziotti, 2023).

Silver nanoparticles (AgNPs), since ancient times, have been known as effective antimicrobial agents, possessing inhibitory and fungicidal effects (Nakazato *et al*., 2020). AgNPs exhibit broad-spectrum antimicrobial activity against bacteria and fungi, being a good alternative to combat resistant biofilm-forming species, such as *Candida spp.,* Malassezia *spp., Cryptococcus* spp ., among others (Figueredo; Cafarchia; Otranto, 2013; Nakazato *et al*., 2020; Fonseca *et al*., 2022).

Silver nanoparticles (AgNPs) is a nanotechnology with particle sizes ranging from 1 to 100 nm. Because it has various physicochemical properties (optical, thermal, magnetic, and electrical), it can be applied in various industry sectors, from textiles to health sectors (Sun, 2016; Masimen *et al*., 2022).

It has attracted great attention for its antimicrobial properties, and has been widely exploited by the nanotechnology industry. In addition, it is an innovative and sustainable input, since it is produced by ecological and low-cost methods (Scandorieiro *et al*., 2022).

AgNPs are obtained by reducing silver salts (Ag+) into metallic silver (Ag0), which can occur by chemical, physical, electrochemical, or biological synthetic methods. Biomolecules present in fungi, algae and plants can reduce Ag+ to Ag0 in order to obtain biogenic AgNPs (Ziotti, 2023).

AgNPs can be an alternative to antibiotics, as they could overcome the resistance that bacteria have to antibiotics. Because they have this action against microorganisms, AgNPs are also used in the healing of burns and wounds (Cadinoiu *et al*., 2022).

AgNPs have many mechanisms of action related to their antimicrobial action. One of these mechanisms is the binding that AgNPs make to the surface of the microorganism where it acts, altering the integrity of the membrane. AgNPs also act by penetrating the interior of the microorganism and interacts with its intracellular components, damaging these microorganisms until it can no longer perform its functions. AgNPs can induce oxygen species reactions and free radical generation. In addition, they can modify the signal transduction required for the cell's life cycle (Masimen *et al*., 2022).

According to Nakazato et al. (2020), nanometals in general have great potential in medicine due to their applications in skin infections, acne vulgaris, mycoses, cutaneous leishmaniasis, and wounds. Thus, AgNPs are excellent antifungal actives for incorporation into pharmaceutical formulations for the treatment of PV.

4 CONCLUSION AND FUTURE PROSPECTS

Based on the literature review described, it is possible to conclude that the bioactive silver nanoparticles and essential oils of *Origanum vulgare* and *Melaleuca alternifolia*, can be incorporated into pharmaceutical formulations as potential antifungals for the treatment of pityriasis versicolor. In addition to being natural compounds that enable the development of "eco-friendly" products, they are powerful alternatives to solve antifungal resistance in cases of PV.

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