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Review Article

Medicinal Properties of *Pterodon pubenscens* against Microorganisms and Oral Biofilm. A Review Article

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Abstract

Researches aimed to identify and extracting compounds isolated from plants have been used for many years with the aim of discovering bioactive compounds due to the increased resistance of microorganisms to the antimicrobial commercially used. The action of bioactive compounds present in the seeds, bark, leaves and fruits from plants of the genus *Pterodon spp.*, has been studied in bacteria, yeasts and protozoa, related to antimicrobial, antiinflammatory, antiproliferative and against infection by nematodes. Yeasts of the genus *Candida spp.*, bacteria of the genus *Streptococcus spp.* and *Staphylococcus spp.*, which are associated with biofilm formation in medical devices, has developed a strategy to resist antimicrobial agents and cells of the immune system. This brief review brings a panoramic view concerned to the Medicinal properties of *Peterodon pubescens* against microorganisms and oral biofilm studies in the field of microbiology.

INTRODUCTION

Infectious diseases are a more cause of death in the world [1]. Fungal infections infect billions of people worldwide every year [2]. The spread of resistant microorganisms, leading to untreatable infections, has become a public health problem and the discovery of new antibiotics has been decreased [3].

Yeasts of the genus *Candida* are commensal microorganisms that colonize the microbial flora of the oral cavity, skin, gastrointestinal and urogenital tract of healthy individuals [4,5]. However, in immunocompromised patients or people submitted to an antimicrobial therapy for a long time, these yeasts may become pathogenic, causing diseases known as candidiasis [6,7]. The majority of the population is asymptomatically colonized by *C. albicans* and *C. glabrata*, or by only one of it [8].

Candida albicans plays an important role in the development of oral infections, but pathogenic species such as *C. kefir*, *C. krusei* and *C. tropicalis* have been identified in oral candidiasis, especially in immunocompromised patients [9-11]. *C. albicans* diseases are often associated with biofilm formation, which are well-structured communities with the ability to resist antimicrobial agents and immune system cells [12,13]. *Candida krusei* have innate resistance to many azole-based drugs such as fluconazole, voriconazole, miconazole, itraconazole, ketoconazole and ravuconazole [14].

Considered the main etiological agent of dental caries, *Streptococcus mutans*is found in the biofilm adhered to the surface of the teeth [15-17]. Other species of *Streptococcus* belonging to the *mutans* group are *S. sobrinus* and *S. downei* [18].

Actually, the general picture of infectious diseases and the use of antimicrobial therapy is more complicated, with multi-drug resistant bacteria posing a threat and a source of worldwide concern. Microorganisms have shown an enormous capacity to evolve towards resistance [19].

The problems of resistance to antibiotics and antifungals produced commercially, leads alternatively to the development of researches from plants showing antimicrobial and antifungal activity beside the reduction of side effects and the resistance of the microorganisms.

Popularly, medicinal plants have been used for therapeutic purposes; however, since the 1970s, the World Health Organization (WHO) has encouraged the scientific study of these plants, aiming to know the benefits of these medicinal agents and the risks when consumed of exaggerated form. Several factors have contributed to the development of health practices that include medicinal plants, mainly low cost and easy handling [20]. In Brazil, a large number of plants have been used in the form of crude extract, infusions or patches to treat common infections [21-23].

Several studies have been carried out with the *Pterodon* genotype, with different purposes such as antiproliferative activity tests [24], anti-inflammatory activity [25] and chemoprophylaxis [26,27]. The genus *Pterodon* comprises five species native from

Brazil: *P. pubescens* Benth, *P. appariciori* Pedersoli, *P. abruptus* Benth, *P.polygalaeflorus* Benth and *P. emarginatus* Vog. [28]. The species *Pterodon pubescens* is a tree native from Brazil, located mainly in the cerrado region, popularly known as sucupira, faveiro or sucupira-lisa. The antimicrobial properties of the substances present in extracts and essential oils produced by plants have been recognized through research for many years [29].

Alcoholic extracts of the *Pterodon* fruit are used in folk medicine as anti-rheumatic, anti-inflammatory (sore throat) and as analgesic [30]. Phytochemical studies with the genus *Pterodon* demonstrated the presence of isoflavones [31], diterpenoids in seed oil [32] and compounds as alkaloids [33]. Only 10% of the bioactive compounds are isolated from the plants [34,35], and further studies are needed.

Therefore, researches demonstrating the antimicrobial activity of *Pterodon pubescens* is an important tool to enable the development of new drug sources that can be used to combat microorganisms, many of which are already resistant to commercial antimicrobials in use.

Yeasts of the Genus *Candida*

Yeasts of the genus *Candida* are opportunistic pathogens frequently found in humans and can be isolated between 50 and 60% of the oral cavity of healthy adults, and colonize the surfaces of the vaginal and intestinal epithelium [36].

Candida albicans is the main cause of two types of infection: superficial infections of the skin and mucosa, and invasive infections, where the fungus can spread through the bloodstream and infect the internal organs [37]. The overall incidence and prevalence of oral candidiasis can be attributed to immunosuppressed individuals in the population [38].

The *C. albicans* species is the most commonly found in the oral cavity, being responsible for superficial and systemic fungal infections [39]. This is due to tolerance to commonly used azole antifungals, such as ketoconazole and fluconazole [40,41]. However, *Candida* non-albicans species such as *C. glabrata, C. tropicalis, C. parapsilosis*, *C. guilliermondii, C. dubliniensis* and *C. krusei* are also isolated from infectious sites [42]. The isolates from the bloodstream of *Candida* species are 18.3% *C. glabrata* [43]. Among the species of *Candida*, *C. albicans* and *C. glabrata* are the first and second most isolated species, respectively, and both account for 65-75% of systemic candidiasis cases, followed by *C. parapsilosis* and *C. tropicalis* [44].

Fungi use various strategies to trigger disease and resist host defense mechanisms, including adherence to specific tissues, resistance to host defense mechanisms, and proliferation to a certain extent [45]. To survive and colonize the host, fungi have mechanisms of sensitivity and response to changes in pH, oxidation, osmotic stress, and nutritional limitations [46]. The virulence of *Candida albicans*is attributed, among others, to the ability to grow from different vegetative forms, which may be yeast-like, hyphae and pseudohyphas. Studies on the ability of hyphae to escape phagocytic cells and to diffuse into tissues and blood suggest that morphology is a contributing factor for the survival of *C. albicans* at different sites and conditions [47].

Yeasts of the species *Candida spp*. shows mechanisms of virulence that are important during infection. Adhesion to host cells is mediated by adhesion factors such as Als, Hwp1 and Eap1 family proteins expressed on the cell wall known as adhesins [48]. Adhesins such as Als3 and Hwp1 are expressed during the formation of hyphae which is important in *Candida'*s adhesion to host cells [49]. According to Hoyer et al. (2008) [50], the ALs3 proteins in *Candida albicans* have many functions, as adhesion at epithelial cells, ferritin acquisition and fungal biofilm [51,52].

After *C. albicans* adheres to epithelial cells, the next step is penetration that can be accomplished through two mechanisms: by induction of endocytosis by host cells, through proteins that are expressed on the fungal cell surface that bind to the receptors present In the host cell, such as E-cadherin in epithelial cells and N-cadherin in endothelial cells, which trigger fungus embolization [53,54], or through active penetration through Hyphae [55]. In active penetration, it is believed that the hyphae penetrates the tissue through the combination of physical forces exerted by the filament extension and the secretion of hydrolytic enzymes [55].

Many microorganisms have hydrolytic enzymes that are related to virulence [56]. Proteinases catalyze the hydrolysis of peptide bonds in host proteins [57]. The secreted aspartyl proteinase, known as SAP, is an extracellular hydrolytic enzyme produced by *Candida spp*. [58], which is important in mucosal infections, and SAP production is associated with other virulence attributes such as hypha formation, adhesion and phenotypic change [56].

Mechanisms of quorum sensing are used for communication between microorganisms. In *C. albicans* the main molecules of the quorum sensing are farnesol, tyrosol and dodecanol, and when there is a high cell density, they promote the growth in the yeast form [59], and the yeast-rich virus for dissemination in host tissues [60,61] through histological analysis have observed that quorum sensing also regulates the depth of tissue invasion by controlling the alteration between yeast and hyphae morphologies.

Some micronutrients are required for *C. albicans* to infect the host, such as iron, which requires acquisition systems [62]. Iron is an essential element for both the host and *C. albicans*. Iron uptake during the infection process is considered a virulence factor, and colonization and proliferation occur only if it has enough iron [63]. Iron uptake can be in several ways: through a reducing system, siderophores or by a heme iron uptake system [62]. In the reducing system, the acquisition of iron is obtained through ferritin, transferrin or the environment, by the adhesin Als3, which has a receptor for ferritin [51]. Iron uptake through the siderophore is performed by *C. albicans* through these components produced by other microorganisms [64]. In the heme system of iron uptake, iron acquisition is obtained from hemoglobin and heme proteins [62,65].

Another important factor is the adaptation to the metabolic changes for the survival and growth of *Candida spp*. living organisms. During the candidiasis, the fungus that is in the bloodstream uses glucose as a source of nutrients, however within macrophages and neutrophils, phagocytic *C. albicans* passes from the glycolysis pathway to gluconeogenesis [66]. In

tissues with low glucose concentration, alternative metabolic pathways are required to obtain host proteins, amino acids, phospholipids and lipids [67].

Phagocytic cells of the immune system produce reactive species of oxygen and nitrogen. According to works by Wysong et al. [68], and [69], *C. albicans* uses catalase Cta1 and superoxide dismutase for the detoxification of reactive oxygen species (ROS) in systemic candidiasis models in rats. Mühlschlegel & Fonzi [70] affirms that *C. albicans* has cell wall β-glycosidases, important factor of regulation on pH changes, such as Phr1 and Phr2, being expressed in alkaline-neutral pH and acid pH, respectively.

Slutsky et al. [71], observed the importance of epigenetic change in the morphology of *C. albicans* in pathogenicity. It may present white cells, which are round, and opaque cells, which are ellipsoids. White cells are more virulent in systemic infections than opaque cells [72], and less susceptible to phagocytosis by macrophages [73].

Candida Biofilm

Candida species are able to form biofilms in many implanted medical devices [13]. Since *Candida spp.* [74], one can avoid the immune response to the patient [74], can colonize internal organs and implants such as prostheses and pacemakers. According to Hawser et al. [75], the biofilm of *Candida albicans* consists of a dense chain of yeasts, hyphae and pseudohifas, joined in a matrix which is synthesized.

Candida spp. make contact with inerts materials through the cell wall, which is constituted by polysaccharides, chitin, mannoproteins, and two types of covalently linked proteins, called GPI (Glycosylphosphatidylinositol) and proteins Pir (Proteins with internal replicates) [76,77].

Donlan and Consterton [78] relates of cells that form biofilms are phenotypically distinct from planktonic cells, being less susceptible to antimicrobial agents. The matrix formed in the biofilm is three-dimensional, giving rise to a highly hydrated and charged environment in which the microorganisms are immobilized [79]. The microcolonies are surrounded by the matrix, separated by water channels, where the circulation of nutrients to the biofilm [78].

During the formation of the *C. albicans* biofilm, the cells communicate by *quorum sensing*, which modulates cell development, growth and dispersion (Hogan, 2006) [80]. According to Hogan (2006) [80] and Hornby et al. (2001) [81], two signaling molecules are characterized in biofilm, tyrosol and farnesol. Tirosol promotes the formation of hyphae in the early stage of biofilm formation, while farnesol inhibits the formation of hyphae, preventing the overgrowth of biofilm.

The extracellular matrix of the biofilm of *C. albicans* is composed of β 1,3 glucans that sequester azole and polyenes from the antifungal, preventing the access of the antifungal to the biofilm cells [82], besides protecting *Candida spp*., of the phagocytic cells and promote the maintenance of nutrients [83]. Studies have shown that the niche within the *C. albicans* biofilm is a hypoxic environment, and this adaptation is an important feature for biofilm formation [84]. Hyphal morphology is required for the formation of a biofilm, as well as cell-substrate, cell-cell and extracellular matrix production, which are important steps in biofilm formation [85,86].

According to Budtz and Jorgensen (1990) [87], biofilms cause problems in dentistry, on the surface of acrylic prostheses, the formation of a mixed biofilm of species with a large number of bacteria, particularly streptococci and yeasts, is a form to expressed resistance of microorganisms. Furthermore, studies have shown that the development of resistance to antifungal agents such as fluconazole in *Candida* strains isolated from AIDS patients [88] occurs during treatment [89,90], where high doses are given with prolonged use of this antifungals [91,92]. It is probably due to the fact that they all have the same mechanism of action [93,94], and the reduction of the sensitivity of *C. albicans* and other species to azole antifungals.

Streptococcus mutans

The oral cavity is an environment that exhibits many fluctuations, such as nutrient supply, temperature, pH and saliva flow, selecting microorganisms that can adapt to these changes through biofilm formation. *Streptococcus mutans* is considered the etiological agent Primary at the onset of human dental caries [95]. The different anatomical sites of the oral cavity present distinct microenvironments [96]. The prevalence of *S. mutans*is not only found in people with moderate or high caries, but also in populations with absence or low incidence of caries [17]. *Streptococcus mutans* produces acids that cause the structure to dissolve in the presence of fermentable carbohydrates such as sucrose, fructose and glucose (Kleinberg, 2002) [97].

Streptococcus mutans produces the glycosyl transferases that allow the sucrose to be broken down into glucose monomers, being this sugar important in the formation of caries [98]. Other diseases, in addition to caries, are related to *S. mutans*. Endocarditis is a disease associated with biofilm in cardiac valves, induced by streptococci and buccal staphylococci [99]. The persistence of biofilm induces inflammation and may contribute to chronic bacteremia and thrombol events. Nomura et al. (2004) [100] and Teng et al. (1998) [101], report the presence of *S. mutans* in patients with infective endocarditis and with serious pyogenic infections.

RESISTANCE TO COMMERCIAL ANTIMICROBIALS

Increasing levels of microorganism resistance to the available antimicrobials has led to an increase in studies taking in account the molecular mechanisms of resistance acquisition and transmission among microorganisms, including the way bacteria recruit and mobilize antibiotic resistance genes [19]

Several antimicrobial resistance mechanisms exist, among which we can mention: the inactivation of antimicrobial drugs, through enzymes that modify the drug making it inactive or less active in therapeutic concentrations; and modifications in the target of the antibiotic, that result in the diminution of the affinity by the molecular structures generating a mechanism of resistance. Some targets of antibiotics are intracellular, meaning they need to reach the cytoplasm. Thus, a mechanism of bacteria resistance is the loss of the porins present in the cell wall that limits the entry of these molecules in the bacterial cell and also the pumps of extrusion exerted by proteins that promote

the efflux of the molecules of the antibiotic to the extracellular environment [19].

Bacteria and fungi have developed mechanisms of resistance to commercial antimicrobials. In recent years an increase in resistance to antimicrobial and antifungal agents has been observed. Emerging strains with intermediate or high resistance to penicillin are growing and being recognized worldwide [101]. However, this resistance is not only to beta-lactams, but also to many other antimicrobial agents, such as vancomycin [102-104].

Strains of many bacterials resistant to methicillin (MRSA) express several virulence factors, among them, surface proteins that aid in tissue adhesion and evasion of the host immune system [105], toxins and superantigens that cause damage epithelial [106]. MRSA strains are often isolated in hospitals, and the spread can be considered clinically significant. Krebes et al. (2011) [107] verified that 2% of patients were colonized by MRSA during hospitalization. The increase in transmission among hospitalized patients occurs due to the prescription of antibiotics such as fluoroquinolones and β-lactams that select resistant MRSA [108].

Studies have shown that in recent years infections in the bloodstream caused by *Candida glabrata* resistant to multiple triazoles and echinocandins have increased [14]. Triazoles inhibit the enzyme 14-α-demethylase responsible for the conversion of lanosterol to ergosterol, limiting the pathway of ergosterol biosynthesis, resulting in abnormalities in membrane fluidity and function, preventing the growth of fungal cells. Among the resistance mechanisms of *Candida spp*., species associated with triazoles, are the mutations in the ERG11 gene that is the target of the drugs, by altering the binding domain of some triazoles, causing a decrease in their potency [109,14].

In this context, as increased resistance by fungi and bacteria is a major public health problem, it is necessary to develop new effective drugs in the fight against these resistant microorganisms, making infection therapy quicker and simpler caused by these agents, and the medicinal plants is one alternative for this to happen.

MEDICINAL PLANTS

In developing countries, infectious diseases are the leading cause of death [110]. The treatment of infectious diseases faces a major problem, due to the resistance development of the microorganisms to the widely used antibiotics and antivirals [111]. Medicinal plants have played an important role in the discovery and development of drugs and are widely known as the source of active antimicrobial metabolites [112].

The plants represent valuable sources of products for the maintenance of human health, and their use has become more widespread especially in recent years, after numerous studies with medicinal products from medicinal plants, becoming the focus of scientific research aimed to determine their pharmacological effects. However, the official use of these therapeutic sources in the health services requires the scientific knowledge for the transformation of these plants into a therapeutic source of safe, rational and beneficial use [113,22].

According to the World Health Organization [114], a large part of the population uses traditional medicines, mainly derived from medicinal plants. In developing countries, 65-80% of the population depends exclusively on medicinal plants for basic health [115]. In 1990, interest in drugs derived from higher plants, especially phytotherapics, increased significantly. Shu (1998) [116] found that about 25% of all medicines were derived from medicinal plants either directly or indirectly.

Thus, essential oils and their components are becoming popular as antimicrobial agents for use in a wide variety of purposes, including food preservation in complementary medicine and natural therapies [117].

ISOLATED COMPOUNDS OF THE PLANT OF THE GENUS PTERODON

The literature reports a variety of studies on the medicinal properties of plants, including seed, fruit, leaf and stem research of the *Pterodon* plant, being considered one of the most representative genera of the *Fabaceae* family. This species is found in the cerrado biome [118,119]. In general, the native trees of this species are aromatic, about 5 to 10 meters high, distributed throughout central Brazil (Dutra et al., 2008) [120]. Its active principles are concentrated in the bark (alkaloids), in the stem (isoflavones and triterpenes) and seeds (diterpenos and isoflavones) [121], which can be used as the basis for the production of essential oil. The hexane extract shows the presence of compounds such as fatty acids, sesquiterpenes (α-caryophyllene, β-caryophyllene, mycene, α-pinene, farnesene) and diterpenes (6α, 7β-diacetoxyivouacapan-17β- (Lopes et al., 2005)[122]. In the bark, were found, tripterpenos (lupeol and betulina), flavonoids and saponins [123,124].

Santos et al., 2009 [24], found sesquiterpene compounds in oil extracted from *Pterodon emarginatus* seeds, being α-pinene, myrene, methyl eugenol, ethyl eugenol, eugenol geraniol, and caryophyllene. According to Suarez and Engleman (1980) [125], the mature seeds of some species have a distinct characteristic, which is the presence of phenolic compounds in the tegument, which contribute to the hardness, permeability to water and resistance to attack by pathogens.

The chemical diversity of plant metabolites is due to the pressures of nature, including abiotic stress, fauna and microorganisms that live in the environment, being relevant factors in the production of these metabolites [126]. The chemical constituents present in the plants may vary in relation to some factors that influence the content of the secondary metabolites, such as the time of collection, known as seasonal variations and may alter the quantity and nature of the active constituents, such as terpenics compounds [127,128], saponins [129], and the presence of the essential oils [130,127], sesquiterpene lactones [131] and tannins [132]. Another factor associated with the production of metabolites is the age and the development stage of the plant, since newer tissues have a higher biosynthetic rate of metabolites [133], such as essential oils [134] and alkaloids [135]. According to Evans (1996) [136] at elevated temperatures, the formation of volatile oils increases. Certain periods appear to be important in the concentration of metabolites, depending on the degree of stress and the period in which it occurs, and in the short term there is an increased production and, in the long term,

there is a decrease in the production of secondary metabolites [137]. The same population of morphologically and sexually undifferentiated plants may present essential oil yields with different chemical composition [138,139].

The genus *Pterodon* is popularly known for its antirheumatic, analgesic, antimicrobial, anticerviral and anti-inflammatory activities. Some authors have studied the chemoprophylactic action for schistosomiasis of compounds isolated from the *Pterodon* plant. Mors et al. (1967) [28] isolated 14.15-epoxigeranilgeraniol from the essential oil of the fruit of *P. pubescens*, observing that it showed chemoprophylactic activity in *Schistosoma mansoni* and Santos Filho et al. (1972) [140] isolated 14-15-dihydrogeranylgeraniol founding that it was responsible for inhibiting the penetration of cercariae into the skin. Subsequently, Santos Filho et al. (1972) [140] developed a soap containing essential oil of *Pterodon pubescens* and found that if applied 24 hours earlier, it shows a protective action against schistosomiasis infection.

Other isolated compounds such as diterpenoids obtained from *P. emarginatus* fruit oil [26], later two new diterpenoids with vouacapane skeleton of *P. emarginatus* [27] and two terpenes of *Pterodon pubescens* [32] also had activity against cercariae.

According to Menna-Barreto et al. (2008) [141], the compound extracted from the *P. pubescens* seed, geranilgeraniol inhibited the intracellular proliferation of amastigote forms of *Trypanosoma cruzi* at concentrations that do not affect mammalian cells.

Silva-Santos et al. (2016) [142] in studies with nanoemulsions produced from the fruits of *Pterodon pubescens* proved effective in combating *Leishmania amazonensis* in its amastigote and promastigote form. Nanoemulsions have also been tested against larvae of *Aedes aegypti* if it is effective in controlling larvae of this vector, which is responsible for transmitting diseases such as Dengue, Zika and Chickungunya [143]. Another study by Omena et al. (2006) [144] also demonstrated larvicidal characteristics of the ethanolic extract of *P. polygalaeflorus* in larvae of the mosquito *Aedes aegypti*.

Studies on the hexanic crude extract from the fruit of the species *Pterodon emarginatus* Vog, described antinociceptive action [145] and anti-inflammatory action of diterpene vouacapane 6α, 7β-dihydroxyivouacapane 17 oate (Carvalho et al.,1999; Coelho et al., 2001) [25,146]. Sabino et al. (1999) [147] studied the action of the hydroalcoholic extract of *Pterodon pubescens* seeds and observed a significant reduction of collagen-induced arthritis after prolonged oral preventive treatment.

Nunan et al. (1982) [148] observed a decrease in rat paw edema induced by carrageenan, histamine and serotonin caused by the furoditerpenes of *P. poygalaeflorus* Benth.

The antiproliferative activity of non-lactone 5-voucapanoids was studied by Spindola et al. (2009) [149], in which the oil of the *P. pubescens* seed was isolated, and three of them showed good results for prostate cancer cell lines. According to Menna-Barreto et al. (2008) [141], the compound extracted from the *P. pubescens* seed, geranilgeraniol inhibited the intracellular proliferation of *Trypanosoma cruzi* amastigotes, at concentrations that do not affect mammalian cells.

Euzébio et al. (2009) [24] also verified the antiproliferative activity of compound 2-furoditerpene in ovarian cancer cells. On the other hand, Cardoso et al. (2008) [150] showed that *P. pubescens* oil has an effect on the exacerbated humoral and cellular immune response of patients with autoimmune diseases and chronic inflammatory diseases, suppressing B and T lymphocytes.

Study of Assunção et al. (2014) [151] involving toxicity of *P. emarginatus* revealed that sucupira oil was not cytotoxic, genotoxic or antigenotoxic. Sabino et al. (1999) [147] showed that the 50% CI of *P. pubescens* seed oil in peripheral blood mononuclear cells was 2 and 1 microg PPSO / ml after 24 and 48 h of exposure to oil. Mutagenic tests did not show mutagenic activity, and no death of rats or signs of acute toxicity was observed. No macroscopic changes were found in the organs, nor was there any change in histopathological examination. Concluding, therefore, that *P. pubecens* oil is not cytotoxic, is not mutagenic, and does not cause acute toxicity when used.

Coelho et al. (2001) [146] verified that there was no subacute toxic effect of the hydroalcoholic extract in histopathological, hematological and clinical studies performed through the mouse arthritis model. Dutra et al. (2008) [120] showed that the phenolic constituents present in *P. emarginatus* seeds have antioxidant activity.

Martino et al. (2014) [152] showed that isolated fractions of *Pterodon pubescens* showed high cytotoxicity for low and no lymphocytic leukemia cells for solid tumor cells without toxicity to peripheral mononuclear cells of healthy humans. Evidence for its antitumor and selective activity for cells with altered cell chylia. This fraction led to mitochondrial pathway-induced apoptosis, similar to traditional antineoplastic chemotherapeutic drugs [152].

Moraes et al. (2012) [153] *in vivo* tests of inhibition to anti-inflammatory effects pointed out the compounds lupeol and betulina as responsible for the anti-inflammatory activity of the ethanolic extract of *P. emarginatus*. Vieira et al. (2008) [154] affirmed that an isolated fraction of *P. pubescens*, which appears to be the compound Voucapano, caused apoptotic nuclear alterations in SK MEL 37 (human melanoma) cancer cells.

Studies of Bustamante et al. (2010) [155], in which the crude ethanolic extract of the *Pterodon emarginatus* bark was used, reported that the presence of flavonoids, saponin heterosides, resins and traces of steroids and triterpenoids in bark powder showed antimicrobial activity against sporulated gram-positive bacteria and Non-spores, gram-negative and yeast against *Candida albicans*.

Santos et al. (2010) [119] tested the antimicrobial activity of *P. emarginatus* leaves and found moderate antimicrobial activity in Gram-positive bacteria *Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus roseus, Micrococcus luteus, Bacillus atropheus, Bacillus cereus, Bacillus stearothermophylus* with minimal inhibitory concentration ranging from 0.72 to 50 mg/mL.

These studies evidence the potential of antimicrobial, antiparisitary and non-cytotoxic activity of *Pterodon spp*.

CONCLUSION

Knowing that different virulence factors, such as biofilm formation, can be expressed by microorganisms that cause disease, leading to persistence of infection and resistance to conventional antimicrobial therapies, it is necessary to develop studies in the search of new antimicrobial molecules for the treatment of these infectious diseases.

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