Ensino e Pesquisa em Bioquímica

Érica de Melo Azevedo
(Organizadora)

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APRESENTAÇÃO

O livro "Ensino e pesquisa em bioquímica" apresenta artigos de pesquisa na área de microbiologia, bioquímica, processos bioquímicos e análises clínicas. O e-book contem 8 capítulos, que abordam temas sobre processos fermentativos, atividade antibiótica de extratos naturais, bioacumulação de compostos químicos na fauna, estudos de enzimas associadas a patologias, caracterização química de extratos naturais, aproveitamento de produtos naturais na síntese de compostos químicos de interesse industrial e utilização de softwares para gerenciamento de laboratórios científicos.

Os objetivos principais do presente livro são apresentar aos leitores diferentes aspectos das aplicações e pesquisas em processos bioquímicos, microbiologia e análises clínicas de forma prática, objetiva, atualizada e contextualizada.

Os artigos constituintes da coleção podem ser utilizados para o desenvolvimento de projetos de pesquisa, para o ensino dos temas abordados e até mesmo para a atualização do estado da arte nas áreas descritas.

Após esta apresentação, convido os leitores a apreciarem e consultarem, sempre que necessário, a obra "Ensino e pesquisa em bioquímica". Desejo uma excelente leitura!

Érica de Melo Azevedo

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CAPÍTULO 2

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES HERBÁCIA *ZINGIBER OFFICINALE* IN DENTISTRY: A LITERATURE REVIEW

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ABSTRACT: The pathogenic dental biofilm formed by species presents itself as a serious problem, since it contributes to the development of oral and bodily diseases. In this sense, Dentistry stands out for expanding knowledge about the oral ecosystem and performing procedures aimed at reducing its pathogenicity and improving oral health. Thus, technological advances and indiscriminate application of antibiotics have made bacterial strains resistant, with a great search for safer, more natural and effective methods. Therefore, the use of plants for healthy treatments is an area of great study in Dentistry. In the present literature review, we sought to analyze the species *Zingiber officinali* with its antimicrobial and antibiofilm activity. For this study, materials were searched at the BIREME, CINAHL, Cochrane Library, Embase, Google Schoolar, PubMed, Science Direct, published until August 2020. The search for the articles was carried out in August 2020, of the 3,401 studies were refined in 18. The findings showed that the plant *Zingiber officinale* has the capacity to inhibit certain bacteria *in vitro*, such *as Bacillus sp., Escherichia coli, Pseudomonas aeruginosa, Streptococcus mutans* and fungi, like *Candida albicans*. Thus, studies in the area are still needed in order to prove its effectiveness *in vivo*, to analyze the toxicity, drug interactions and side effects of the plant.

KEYWORDS: Antibacterial agents; Antifungal agents; Dental biofilm; *Zingiber officinale.*

ATIVIDADE ANTIBACTERIANA E ANTIFÚNGICA DA HERBÁCIA *ZINGIBER OFFICINALE* EM ODONTOLOGIA: UMA REVISÃO DE LITERATURA

RESUMO: O biofilme dentário patogênico formado por espécies bacterianas e fúngicas e contribui para desenvolvimento doenças orais e corpóreas. Nesse sentido, a odontologia por ampliar o conhecimento sobre o ecossistema oral e realizar procedimentos que visam à reduzir a patogenicidade e melhor a saúde oral. Assim, os avanços tecnológicos e a aplicação indiscriminada de antibióticos tem tornado as cepas bacterianas resistentes, sendo grande a busca por métodos mais seguros, naturais e eficazes. Logo, o uso de plantas aos tratamentos saudáveis é uma área de grande estudo em Odontologia. Na presente revisão de literatura, buscou-se analisar a espécie *Zingiber officinale* e a atividade antimicrobiana e antibiofilme. Para tal estudo, buscaram-se materiais na Biblioteca Regional da Medicina (BIREME), CINAHL, Cochrane Library, Embase, Google Scholar, PubMed e Science Direct publicados até agosto de 2020. A busca dos artigos foi realizada em agosto do mesmo ano, e dos 3.401 estudos foram refinados em 19. Os achados mostraram que a planta *Zingiber officinale* tem capacidade de inibir certas bactérias *in vitro*, como *Bacillus* sp., *Escherichia coli, Pseudomonas aeruginosa, Streptococcus mutans* e fungos, como *Candida albicans*. Dessa forma, ainda são necessários estudos na área, a fim de comprovar sua eficácia *in situ e in vivo,* analisar a toxicidade, interações medicamentosas e efeitos colaterais da planta.

PALAVRAS - CHAVE: Agentes antibacterianos; Agentes antifúngicos; Biofilme dentário; *Zingiber officinale.*

1 I INTRODUTION

Many people are unknow of the importance of the oral cavity for general health. From the mouth, many microorganisms develop and proliferate, reaching the rest of the body. Thus, multiple infectious diseases caused by microbiological dysbiosis can be prevented through daily oral health care, through correct oral hygiene. In this sense, the imbalance of the oral ecosystem as well as the structuring in pathogenic biofilms enable greater bacterial virulence and resistance to antimicrobials (Marsh & Martin, 2018).

Over time, there were many technological changes that aimed at improving drugs, with an increase in the spectrum of action and reduction of side effects, but that maintained the biostatic and biocidal performance. With this perspective, Phytotherapy has presented itself as a viable option, as it provides therapies based on natural compounds, such as plants and their components, seeking to inhibit bacterial virulence mechanisms or cause them to develop more slowly (Grégio et al., 2006; Park et al., 2008; Gull et al., 2012; Kumar et al., 2013; Hasan et al., 2015; Jain et al., 2015; Aghazadeh et al., 2016; Avcioglu et al., 2016; Jami et al., 2017; Lee et al., 2018; Rampogu et al., 2018).

In the present work, the *Zingiber officinale* plant was chosen, which although originate in Asia (Ghasemzadeh et al., 2018) has proliferated in the world, becoming easily accessible in Brazil. In this sense, its effects of therapeutic importance are overlooked, since it is known worldwide for its use in the food industry. It was found that its constituents, such as rhizome extract (stem extension) and phenols (gingerol and shogaol), have pharmacological functions, as they act in addition to antiemetics, anti-inflammatory and thermogenic, such as antibacterials and antifungals, being non-genotoxic (Grégio et al., 2006; Gull et al., 2012; Kumar et al., 2013; Valera et al., 2016; Guo et al., 2017; Cavalcante, 2019).

From this perspective, the objective of this work was to investigate the antibacterial and antifungal activity of *Zingiber officinale* in the existing literature, focusing on activities of interest in Dentistry.

2 | METODOLOGY

The literature review followed the precepts of the integrative study with a qualitative method. This design provides through a bibliographic search in books and scientific articles on the subject, the synthesis of knowledge to show future perspectives and incorporation of the applicability of the results (Pereira et al., 2018). Different searches were carried out in the month of August 2020, including articles that addressed the plant's antibiofilm or antibacterial properties, published in the last 15 years. Literature reviews and case reports were excluded, as well as studies that did not address the theme of the present study.

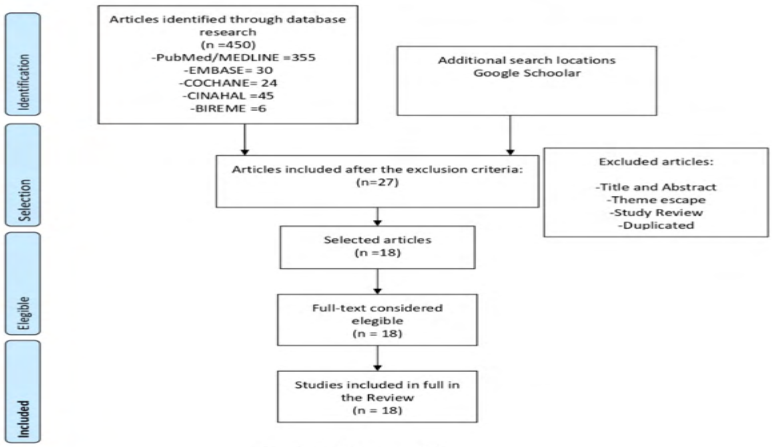
Electronic searches were performed in the period from August and September 2020 in the PubMed / MEDLINE, Embase, Cochrane Library, CINAHL and Science Direct databases for articles published until August 2020, in addition to complementary tracking in Google Schoolar and in the reference lists of the articles included in the review.

In the PUBMED database, the first research was carried out by combining the MeSH descriptors: "Anti infective agents", "Antifungal agents", "Dentistry" and "Periodontal disease" and its derivatives, together with the keyword "Zingiber officinale" and synonyms joined with Boolean operator "AND". In total, 392 articles were found for further analysis of the title and abstract.

In another database, EMBASE, with the Entree descriptors, found 30 articles, in COCHRANE, 24 articles; BIREME, 6 studies and CINAHL 45 articles to be selected later. Finally, the last search was carried out on Google Scholar and references of the selected articles, to complement the study.

The flowchart (Figure 1) presented, describes the number of articles found, how many excluded by the exclusion criteria (escape from the topic, duplicate or papers older than 20 years, case reports and literature review) until reaching the articles included in the review of literature. Following criteria in the selection of studies generates better reliability and generalizability of the study's conclusions.

Figure 1: Flowchart of study selection



Source: Authors (2020)

3 I RESULTS

After a critical reading of titles, abstracts and removal of duplicates, of the 3,401 articles found, 18 studies were selected that met the inclusion criteria. Following up on this screening, their full assessments were made, aiming to define the most considerable points to be analyzed and reflected.

The methodological process of organizing the included articles is shown in Table 1, where the extracts used stand out. All studies were *in vitro* and there are publications in three languages (English, Portuguese and Spanish). In addition, there were tests with various microorganisms as well as with various properties of the plant.

	Title:	Author	Journal	Methodology	Microorganism	Considerations
1	Ação Antimicrobiana do *Zingiber officinalle* frente a microbiota bucal.	GRÉGIO *et al.*, (2006)	Estudos de Biologia	Study *in vitro*	*Candida albicans* , *Escherichia coli*, *Staphylococcus aureus* e *Streptococcus mutans*.	There was antimicrobial activity, with extract (hydroalcoholic and glycolic) of *Zingiber officinale* with the tested bacteria.
2	Antibacterial Activity of [10]-Gingerol and [12]-Gingerol isolated from Ginger Rhizome Against Periodontal Bacteria.	PARK.; BAK.; LEE., (2008)	Phytotherapy Research	Study *in vitro*	*Prevotella intermedia, Porphyromonas endodontalis* e *Porphyromonas gingivalis*.	Ginger presents polyphenolic ketones and alkylated gingols (both in its ethanol extract and in n-hexane), which provided antibacterial activity to the tested gram-negative bactéria.
3	Antibacterial effect *of Allium sativum cloves* and *Zingiber officinale* rhizomes against multiple-drug resistant clinical pathogens.	KARUPPIAH.; RAJARAM., (2012)	Asian Pacific Journal of Tropical Biomedicine	Study *in vitro*	*Bacillus* sp., *Enterobacterium* sp., *Escherichia coli*, *Klebsiella* sp., *Proteus* sp., *Pseudomonas aeruginosa* e *Staphylococcus aureus*.	The ethanolic extract of the rhizome of *Zingiber officinale* act with antibacterial and antifungal functions. This was effective for the bacteria tested, with greater results for Bacillus sp.
4	Antibiofilm effects of *Citrus limonum* and *Zingiber officinale* Oils on biofilm formation of *Klebsiella ornithinolytica*, *Klebsiella oxytoca* and *Klebsiella terrigena species*.	AVCIOGLU .; SAHAL.; BILKAY., (2016)	Africal Journal of Traditional, Complementary and Alternative Medicines	Study *in vitro*	*Klebsiella* (*Klebsiella ornithinolytica*, *Klebsiella oxytoca* e *Klebsiella terrigena*)	The Ginger oil inhibited biofilms formed by the species Klebsiella, because it consists of monoterpenes, causing disruption in the cell membrane of such bacteria. It has ample medicinal potential to fight infectious diseases, but research and testing in vivo are necessary.
5	Antibiofilm and Antivirulence Activities of 6-Gingerol and 6-Shogaol Against *Candida albicans* Due to Hyphal Inhibition.	LEE *et al.*, (2018)	Frontiers in Cellular and Infection Microbiology	Study *in vitro*	*Candida albicans*	Ginger components, such as 6-gingerol and 6-shogoal, have antibiofilm and antivirulence capabilities (such as interaction with genes), thus inhibiting fungal biofilms formed by Candida albicans, resistant to drugs.
6	Action of chlorexidine, zingiber officinale and calcium hydroxide on *candida albicans*, *enterococcus faecalis*, *escherichia coli* AND ENDOTOXIN IN THE ROOT CANALS.	VALERA *et al.*,(2016)	The Journal of Contemporary Dental Practice	Study *in vitro*	*Candida albicans*, *Escherichia coli* e *Enterococcus faecalis*	The extract of *Zingiber officinale* demonstrates good antimicrobial potential. When used, together with Calcium Hydroxide, it presents excellent antimicrobial potential (antibacterial and antifungal), with the tested species. Essential oils of this, present gingerol and shogaol, that function as anti-inflammatory and analgesics.
7	Efecto antimicrobiano del extracto, aceite esencial de gengibre (*zingiber officinale*)	JAMI.; ARAUJO., (2017)	ODONTOLOGIA	Study *in vitro*	*Enterococcus faecalis*	Ginger's antimicrobial action is equivalent to its concentration. Therefore, with the highest concentration used in the study (15% of its hydroalcoholic extract), it was possible to minimize the gram-positive

	sobre cepas de enterococcus faecalis: Estudio in vitro.					*Enterococcus faecalis*, being a possible therapeutic agent for combating biofilm and dental caries.
8	Formation of 6-, 8- and 10-Shogaol in Ginger through Application of Different Drying Methods: Altered Antioxidant and Antimicrobial Activity	GHASEMZADEH *et al.*, (2018)	Molecules	Study *in vitro*	*Aspergillus flavus*, *Bacillus cereus*, *Candida albicans* , *Escherichia coli*, *Fusarium oxysporum*, *Geotrichum candidum*, *Microascus brevicaulis*, *Porphyromonas aeruginosa*, *Trichophyton rubrum*, *Staphylococcus aureus*.	Ginger extract shows better results for gram-positive bacteria, such as Staphylococcus aureus, functioning as an antibacterial and antibiofilm. It works as an antifungal to Candida albicans, having better results than the use of some antimycotics, such as Fluconazole. As essential factors to these performances, the rhizome shogaols stand out.
9	Ginger (*Zingiber officinale*) phytochemicals gingerenone-A and shogaol inhibit SaUPPK: molecular docking, molecular dynamics simulations and in vitro approaches.	RAMPOGU *et al.*, (2018)	Annals of Clinical Microbiology and Antimicrobials	Study *in vitro*	*Staphylococcus aureus*	In vitro tests with gingerone -A and shogaol, derived from Ginger oil, they were able to react (more strongly than some drugs) with the active sites of the aforementioned bacterial enzyme, inhibiting the formation of biofilms.
10	Ginger Extract Inhibits Biofilm Formation by *Pseudomonas aeruginosa* PA14.	KIM.; PARK., (2013)	PLOS ONE	Study *in vitro*	*Pseudomonas aeruginosa* PA14	Ginger extract inhibits the development of biofilms formed by Pseudomonas aeruginosa PA14, affecting bacterial virulence mechanisms. It acts in the transduction of bacterial signals, reduces cellular c-di-GMP and the production of EPS, in addition to promoting bacterial shedding, without affecting its growth.
11	Inhibitory effect of Allium sativum and *Zingiber officinale* extracts on clinically important drug resistant pathogenic bacteria.	GULL *et al.*, (2012)	Annals of Clinical Microbiology and Antimicrobials	Study *in vitro*	*Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus*, *Staphylococcus epidermidis e Shigella sonnei*.	Ginger presents itself as a spice that can be used to fight infectious diseases, but studies in this area are still scarce. Despite this, in this experiment, Escherichia coli and Shigella stood out, when using extract with ethanol and methanol, respectively, verifying that the sesquiterpenoids present in the essential oil of Ginger favor bacterial and fungal inhibition.
12	Inhibitory effect of *zingiber officinale* towards *Streptococcus mutans* virulence and caries development: *in vitro* and *in vivo* studies	HASAN *et al.*, (2015)	BMC Microbiology	Study *in vitro e in vivo*	*Streptococcus mutans*	Zingiber officinale, both in the form of crude extract and methanolic fraction, is able to alter the physiological structure of the dental biofilm formed by Streptococcus mutans. Consequently, it inhibits bacterial growth and virulence mechanisms of this strain, even acting as a possible anticariogenic agent.
13	In vitro activity of essential oils extracted from plants used as spices against fluconazole-resistant and fluconazole-susceptible *Candida* spp.	POZZATI *et al.*, (2008)	Canadian Journal of Research	Study *in vitro*	*Candida* spp (*Candida albicans*, *Candida dublinensis*, *Candida glabrata*, *Canddida krusei* e *Candida tropicalis*)	The essential oil of Ginger has antifungal activity against Candida spp. The main compound of this, responsible for this, is the Zingibereno. However, when compared to Oregano essential oil, it presents less response.
14	Natural products and polysorbates: Potential Inhibitors of biofilm formation in *Pseudomonas aeruginosa*.	MIARI *et al.*, (2020)	The Journal Of Infection in Developing Countries	Study *in vitro*	*Pseudomonas aeruginosa*	Ginger contains phenolic compounds, which block bacterial virulence mechanisms of Pseudomonas aeruginosa.
15	Survey of the Antibiofilm and Antimicrobial Effects of *Zingiber officinale* (*in Vitro* Study).	AGHAZADEH *et al.*, (2016)	Jundishapur Journal of Microbiology	Study *in vitro*	*Acinetobacter baumannii*, *Bacillus cereus*, *Candida sp.*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* e *Staphylococcus aureus*	Ginger extract works as an antifungal to strains, such as *Candida albicans and Candida krusei*, having better results than the use of some antimycotics, such as Fluconazole. In addition, it presented good performance to *Pseudomonas aeruginosa and Staphylococcus aureus*, acting as antibacterial and antibiofilm.
16	Two new monoterpenoid glycosides from the fresh rhizome of Tongling White Ginger (*Zingiber officinale*).	GUO *et* al., (2017)	Natural Product Research	Study *in vitro*	*Staphylococcus aureus* e *Staphylococcus epidermidis*	The monoterpenoids (glycosides 3-6), present in the formation of the rhizome of Zingiber officinale managed to react (as antimicrobials) against the tested bacteria.
17	Use of Traditional Indian Plants in the Inhibition of Caries-Causing Bacteria – *Streptococcus mutans*.	JAIN *et al.*; (2015)	Brazilian Dental Journal	Study *in vitro*	*Streptococcus mutans*	Ginger extract has good activity against the species: Streptococcus mutans, (which is one of the main responsible for dental caries.
18	Zingerone inhibit biofilm formation and improve antibiofilm efficacy of 2 ciprofloxacin against Pseudomonas aeruginosa PAO1.	KUMAR.; CHHIBBER.; HARJAI., (2013)	Fitoterapia	Study *in vitro*	*Pseudomonas aeruginosa*	The use of Zingerone, obtained by Ginger, acts as an antibacterial to Pseudomonas aeruginosas and, consequently, antibiofilm, as it acts on pili type IV and flagella (virulence mechanisms of this strain).

Table 1 - Detailed analysis of publications

Font: Own Authors, 2020

4 | DISCUSSION

The species *Zingiber officinale* Roscoe, coming from the family Zingiberaceae is popularly known as “Ginger”, “Gingivre” or “Mangarataia” and originates in Asia, measuring approximately 80 centimeters (herbaceous) (Karuppiah et al, 2012; Cavalcante, 2019). It is coated with a rough epidermis and has a yellowish color, such tuberous root consisting of the rhizome (underground stem), elongated and flattened, which contains applications in the food and pharmaceutical industry, as it contains essential oils (borneol, camphene, cineole, citral, falandreno, gingerols, shogaols and zingiberene), which give its refreshing essence and carbohydrates. (Cavalcante, 2019). Thus, such a plant is classified as Nutraceutical, as it contains aspects in addition to nutritional, medicinal, with health benefits, without side effects (Rampogu et al., 2018). However, little is known about its application and systemic action, as in the oral cavity, and studies on its uses are essential. Its composition is shown in table 2.

TABLE 2- COMPOSITION OF THE *ZINGIBER OFFICINALE PLANT*

CONSTITUTION:	*Zingiber officinale*
Essencial:	Borneol; cineol; citral; d-canfeno; felandreno; gingerol; zingibereno.
Mucilage	
Essencial oil (Gingerol).	Canfeno; felandreno; zingerona; zingibereno.
***Resin** (almidon).*	
Phenolic substance.	Borneol; cineol; citral; felandreno; limoneno; zingibereno.
Fatty acids.	
Aminoacids.	
Enzime:	*Zingibaína*
Mineral salts	

Basead: CAVALCANTE, R. AS PLANTAS NA ODONTOLOGIA: um guia prático. Rio Branco, Ac: [s.n], 2019.575 p. il.

In this table is possible analyze the plant compounds that are used in research and that have antimicrobial properties, such as gingerol, felandreno, zingibereno presentes in that essential composition of the plant.

In addition to the exposed compounds, ginger is also important because it contains sugars, carbohydrates, proteins, B vitamins and vitamin C, which help the immune system to function properly and, consequently, to prevent diseases (Cavalcante, 2019).

Initially, it came from Southeast Asia, as a spice, and it was only in the 16th century that it was established in South America, based on Portuguese conquerors (Karuppiah and Rajaram, 2012). Although not native to Brazil, it is widely used. Ginger belongs to 66 plants with anti-inflammatory, antiseptic, diuretic, thermogenic, sialogogue and even anti-ulcerogenic activity, based on its compound, (+) - angelicoidenol-2-obD-glucopyranoside, according to ANVISA nº 10 / 2010 (Cavalcante, 2019).

The way of use occurs through poultices, rinses and tinctures, ingestion of mouth lozenges, shavings, teas, syrups and even, through physiological procedures, such as chewing. All the processes listed are aimed at improving oral hygiene, preventing bad breath and oral wounds. In addition, the herbaceous stimulates the Central Nervous, Cardiovascular and Gastrointestinal System, exercising important pharmacological functions when used according to the recommended therapeutic dosages, as there are contraindications such as heart failure patients (Cavalcante, 2019).

The greatest constitution of ginger is made by alcoholic compounds, such as ethanols, phenols and methanols, in addition to sesquiterpenoids in their essential oil (1-3%), such as gingerols, shogaol, proanthocyanins, condensed tannins curcumene, farnesene and zingiberene (volatile or not), which are related to antibacterial, antifungal and antibiofilm and analgesic activity (depending on the plant, which are extracted) (Grégio et al., 2006; Park et al., 2008; Gull et al., 2012; Jain et al ., 2015; Guo et al., 2017; Cavalcante, 2019).

In vitro studies by Gull et al., (2012) and Karuppiah & Rajaram (2012) found an inhibitory effect of the plant on the bacterium *Escherichia coli* (bacteria belonging to the normal intestinal microbiota and causing eventual infections). The (hydro) alcoholic extracts were active (Grégio et al, 2006; Valera et al., 2016), as well as components of the essential oil (zingerone-A and shogaol) that interacted with the active site of the enzyme 6-hydromethyl-7,8 -di-hydropterin pyrophosphokinase (SAHPPK) of the bacteria developing inhibitory activities (Rampogu et al., 2018.). Thus, according to Valera et al. (2016), due to the properties presented, ginger is promising, regarding the possibility of being used to prevent infections caused by this bacterium.

With respect to the bacterium *Pseudomonas aeruginosa*, often associated with pneumonia, the presence of ginger shogaols inhibits it (Gull et al., 2012; Ghazemzadeh et al, 2018). However, according to Lee et al., (2018) the presence of shogaol is almost zero in fresh plants and about 4% of 6-gingerol (by weight). With this perspective, the substances 6-gingerol and 8-gingerol show performance in *P. aeruginosa* for acting on the phenotypes of the second messengers and *quorum sensing,* considered the main bacterial virulence mechanism responsible for interbacterial communication (Lee et al., 2018). Kumar et al., (2013), following the same view, it was found that the zingerone present in the Ginger root reduces the mobile aspects of *P.aeruginosa* (Pili type IV), inhibiting bacterial fixation on surfaces and delaying biofilms.

It regard to *Staphylococcus aureus*, bacteria that cause systemic pathology such as Bacterial Endocarditis and *Staphylococcus epidermidis*; Grégio et al. (2006) and Gull et al. (2012), respectively, demonstrated good performance of ginger in these microorganisms. Polyphenolic ketones, alkylated gingerols, ethanol extract (in the form of n –hexane) showed antibacterial activity (altering cellular c-di-GMP and consequently reducing biofilm) (Park et al., 2008; Kim et al.,2017). Such activity occurs, for example, against gram-negative, responsible for periodontal diseases, such *as Porphyromonas endodontalis, Porphyromonas gingivalis and Prevotella intermedia* (Park et al., 2008).

In essential oil, from Ginger there is its interaction with the active site of the enzyme 6-hydromethyl-7,8-dihydropterin pyrophosphokinase (SAHPPK) from *Staphylococcus aureus* developing inhibitory activities (Rampogu et al., 2018). Whereas, in *Staphylococcus epidermidis* there is interaction between the monoterpenoid glycoside, rans -1,8-cineol-3,6-dihydroxy-3-O- β –D glucopyranoside combined with trans-3-hydroxy-1,8-cineol 3- Ginger's O- β -D-glucopyranoside, thus preventing such bacteria (Guo et al., 2017).

On the other hand, Avcioglu et al. (2016), Gull et al. (2012); Karuppiah & Rajaram (2012) observed that the essential oil of *Zingiber officinale* (such as ethanolic) reduces biofilms formed by the genus *Klebsiella (Klebsiella ornithinolytica, Klebsiella oxytca and Klebsiella terrígena*) varying in terms of the concentration used.

Currently, compounds with potential antibiofilm are used, such as chlorhexidine, although it is known that it can cause side effects such as dental staining and loss of taste. As a result, Ginger in the form of crude extract and methanolic fraction presents itself as a natural option for the control of Streptococcus mutans in dental biofilm and even in tooth decay (Grégio et al., 2006; Hasan et al., 2015; Jain et al., 2015). Both compounds (crude extraction or methanolic fraction) interfere with hydrophobicity, between dental surface-bacterial interactions, through flavonoids, which reduce the enzyme GTFase and AG I / II, during synthesis / adherence, mainly of insoluble and dependent Glucans sucrose. Furthermore, the sites of bacterial binding, pH and integrity of exopolysaccharides are disturbed, in the formation of the climax community, disrupting pathogenicity and the sensing quorum (functioning as an anticariogenic), in addition to the expression of bacterial genes (Hasan et al., 2015; Miari et al., 2020).

On the other hand, *in vitro* studies that initially used 2% Chlorhexidine to eliminate *Enterococcus faecalis* (Valera et al., 2016), this gel by itself, failed to eliminate the bacteria and the performance of Ginger (glycolic extract), proved to be essential to reduce it, (although there was no complete elimination) having its action enhanced, when used with Calcium Hydroxide. Similar to the findings, Jami & Araujo (2017) used 15% hydroalcoholic extract from Zingiber officinale, managing to inhibit the strain, in the same proportion as using 5.25% sodium hypochlorite, and more studies using this extract are promising. Karuppiah & Rajaram. (2012) reached one of the smallest zones of growth inhibition with *Enterobacterium*, using the ethanolic extract of Ginger rhizomes.

In strains *of Bacillus spp*. there was good antimicrobial activity (Karuppiah et al., 2012), due to the presence of shogaols in ginger enzymes (Ghasemzadeh et al., 2018), having according to Gull et al. (2012) better effects through the methanolic extract. With regard to *Salmonella typhi,* Gull et al. (2012) achieved good activities with ethanolic extract, while with Shigella both ethanolic and methanolic extract showed low (and same) results.

As for the antifungal action in species of *Candida spp,* the essential oil of ginger shows activity, due to its main active component zingiberene (Pozzati et al., 2008), in addition to diterpenes and galanolactone (Park, 2008). In addition, hydroalcoholic extract, such as ethanolic (Aghazadeh et al., 2016; Grégio et al. 2012; ValeraA et al., 2016.), through 6-gingerol, 8-gingerol and 6-shogaol these are able to inhibit, effectively *Candida albicans* in sessile format, but 10-gingerol, 8-shogaol and 10-shogaol at 100μg / ml had no effect on it. (Lee et al., 2018). Therefore, it was noticed that Ginger has antifungal mechanisms that act in an improved way, when compared to Fluconazole (Pozzati et al., 2015), Nystatin and Amphotericin B (Aghazadeh et al., 2016). The mechanism of action consists of altering the development of hyphae in colonies (does not act on planktonic forms), repressing the expression of genes (ECE1 and HWP), without causing toxic responses, in the analyzed concentrations (Lee et al., 2018).

When the crude extract of its rhizome is analyzed, it contains antimycobacterial effects (such as 10-gingerol), inhibiting *Mycobacterium species* (responsible for tuberculosis), strains of the respiratory tract and even fungal species (Park et al., 2008).

All authors agree, as for Ginger to present a vast potential for solutions, such as dental products that aim at the disruption of pathogenic dental biofilm and, consequently, fight microbial infections (mainly, in precarious places where there is rapid development of pathogens), through excellent activities in vitro provided by plant compounds. *Zingiber officinale*, in the form of hydroalcoholic fractions or crude extract, contains therapeutic properties and is shown to be antifungal and antibiofilm, as it causes changes in virulence factors (such as the quorum sensing, for example) and thus reduces their pathogenicity (Kumar et al., 2013; Hasan et al., 2015; Avcioglu et al., 2016; Valera et al., 2016; Miari et al., 2020). However, in vitro studies are still insufficient for the development of compounds, since new studies need to be developed in situ and in vivo to prove the reported non-genotoxicity and to analyze the possible drug interactions, in order to also standardize the methodology collection of extracts (Grégio et al., 2006; Park et al., 2008; Gull et al., 2012; Karuppiah et al., 2012; Kumar et al, 2013; Hasan et al., 2015; Jain et al., 2015; Avcioglu et al., 2016; Pozzati et al., 2015; Aghazadeh et al., 2016; Ghasemzadeh et al., 2018; Lee et al., 2018; Rampogu et al., 2018; Miari et al., 2020).

5 I FINAL CONSIDERATIONS

It is concluded that, currently, there is a search for more natural substances that contain antibacterial, antifungal properties and mainly, antibiofilms. The herbaceous *Zingiber officinale* has several active compounds that act on several microorganisms such as *Bacillus sp., Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus mutans and Candida albicans,* which are responsible for infectious diseases (such as Bacterial Endocarditis), being their action still very related to the properties of the compound used.

Although it is known, superficially, about the properties of Ginger, its study and use in whole some media such as Odontology, are still predominantly in vitro. Future research needs to be developed *in situ* and *in vivo,* to analyze toxicity, drug interactions, side effects of the plant and standardization of the extraction collection methodology, so that, in the future, ginger can be used in toothpaste, rinses and ointments for medical and dental purposes.

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ÍNDICE REMISSIVO

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