

Action of Propolis on Microorganisms of the Oral Cavity: an Integrative Review

REVIEW

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Abstract

Introduction: In the mouth there are several microorganisms, including bacteria and fungi, which, under favorable conditions, can cause oral health problems. In combating these diseases there are several antibiotics and antifungals, synthetic drugs and also natural.

Objective: Identifying the action of propolis on microorganisms in the oral cavity.

Method: We opted for the integrative literature review, using the descriptors: oral cavity, propolis, anti-inflammatory activity, antimicrobial activity, endodontics, antimicrobial, propolis, saliva, metabolism, microbiology, antimicrobial activity and mouth; the consulted databases were PubMed, LILACS and SciELO, published between 1999 and 2014. The results were obtained through the selection of 09 articles, through close reading, critical and reflective texts, and then the organization of summary frames of data.

Results: Evidence was gathered and synthesized, pointing to the antibacterial action (*Gram-positive and Gram-negative*) and antifungal (*C. albicans and C. tropicalis*) of propolis. The methodological designs of the studies analyzed were in majority, of weak evidence, for evidence-based practice. Therefore, the findings may be questioned.

Conclusion: It needs that are carried out research studies in a systematic review and randomized clinical studies with humans, because they are considered major force evidence and are defined therapeutic parameters and minimum chemical composition, the different types of propolis, so having the appropriate/desired therapeutic properties.

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Introduction

In the mouth there are several microorganisms, including bacteria and fungi, which, under favorable conditions, can cause oral health problems. Therefore, the oral microbiota is one of the main objects of study in order to understand mechanisms that cause dental caries, mouth ulcers, gingivitis, periodontitis and alveolitis, as well as the treatment of these, as they are considered infectious diseases [1].

In combating these diseases there are several antibiotics and antifungals, synthetic drugs and also natural. With therapeutic purpose in vivo, the products of natural extracts base have been used.

Most of products of vegetable origin shows antibacterial substances, in its composition, capable of reducing the growth of bacteria in the mouth, and inhibit glucan synthesis from sucrose by the glycosyltransferase [2].

Among the natural compounds, propolis has been propagated in dentistry, for the treatment of the aforementioned diseases, due to its anti-inflammatory and efficiency in the removal of the oral microbial flora.

Propolis is a complex mixture, formed by resinous and balsamic material and is collected by bees in the branches, flowers, pollen, shoots and exudates of trees. This resin, mixed with salivary secretions of bees is used for the core protection against the proliferation of microorganisms, including fungi and bacteria [3].

In many countries, various components of propolis have been analyzed, and caffeic acid, phenethyl ester of caffeic acid (PECA) and flavonoids mainly responsible for the antibiotic power of this resin [4].

Thus, it has been demonstrated antibacterial activity of propolis, especially against gram-positive bacteria, and cariogenic involved in periodontal pathogenic process, highlighting the *Streptococcus mutans*, *Lactobacillus casei*, *Prevotella intermedia*/ *Prevotella nigrescens*, *Porphyromonas gingivalis*. Moreover, they highlight their potential antifungal

and anti-inflammatory because it stimulates cell mediated immunity and enhances the phagocytic activity and the inhibition of prostaglandin synthesis [5].

Accordingly, the objective was to identify what is the action of propolis on the microorganisms present in the oral cavity, through the analysis of scientific production.

Method

It is an integrative literature review, an approach that allows, from the analysis of the data, having a support helps in decision-making and improve clinical practice. The integrative review process includes six distinct stages, similar to conventional research stages of development [6]:

1st) identification of the theme and selecting the search issue. It begins with the definition of a problem and the formulation of a hypothesis of research that has relevance for health. In this sense, when you think of the mouth, their invasion by microbial agents and action of propolis on top of these, the central question of this study was: What is the action of propolis on microbial oral cavity?

2nd) Criteria for the selection of the sample. The survey was conducted on 2014 September 24th, by searching in the databases of the Virtual Health Library (BVS): LILACS (Latin American and Caribbean Health Sciences) and SciELO (Scientific Electronic Library Online) and international database PubMed (Medical Published-serve of the US National Library of Medicine).

The descriptors were used: oral cavity, propolis, anti-inflammatory activity, antimicrobial activity, and endodontics, antimicrobial (85 articles in PubMed); In LILACS database, using the descriptors propolis, antibiotics and mouth was found only one article. In order to find more articles was decided to use two descriptors by search. Thus, the descriptors were used propolis and saliva (5 articles), propolis and metabolism (1 article), propolis and microbiology (3 articles), which referred to the oral cavity. Similarly

it was proceeded in PubMed and SciELO, with no addition to the articles.

In Scielo, the descriptors with propolis, antimicrobial activity and mouth, totaled 4 articles, of which 2 contained in the LILACS database. Exclusion criteria were literature review articles of the narrative type and preliminary study. Articles published in Portuguese were included, English and Spanish, with abstracts and full text available on the selected databases; It referred to the action of propolis on microorganisms of the oral cavity, which method adopted allow to obtain strong evidence (levels 1, 2, 3 and 4), i.e., a systematic review and meta-analysis or not, randomized clinical trial (RCT) with 1000 patients, RCT with less than 1000 patients and cohort study [7].

These evidences were adopted considering the question that guided this review, because it is clinical question [7]. However, given the lack of systematic review and cohort study, and the minimum publication of clinical trials, and that most of the studies found in the bases was accessed *in vitro* (evidence level 8), it was decided to include them. The strategies used to fetch the articles in the databases were adapted, because such bases present specific characteristics.

Thus, the research was guided by the question and inclusion and exclusion criteria, to maintain consistency in the search for articles and avoid possible biases. To refine your search, in addition to those descriptors were added to the filters: humans, free full text, languages (English, Spanish, and Portuguese). Thus, in PubMed and LILACS, the search amounted to ten articles in each; In SciELO, two articles.

3rd) Identification of pre-selected and selected studies. Was held at first reading the summaries, being preselected five articles - PUBMED, ten - LILACS and two - SciELO. It was later performed in full, a close reading of the pre-selected articles and verified their suitability for inclusion criteria of the study. That done, there were obtained the bibliogra-

phic material and the consolidation of the findings, to facilitating reflection and conclusion of the study. In reading found repeated articles in LILACS and SciELO databases. Finally, they selected nine articles, as follows: one - SciELO, two - PubMed, four - LILACS and two - LILACS and SciELO.

4th) Categorization of studies. An analogous phase to collecting the conventional survey data. For data collection of articles it was used a validated instrument containing the following items: identification of the original article, methodological characteristics of the study, assessment of the methodological rigor of measured interventions and results found [8].

Through data collection instrument it was possible an individual assessment of the studies included, both methodologically and in relation to the synthesis of the results, keeping in mind the issue problem, the findings were listed by reading and the inclusion criteria previously mentioned.

5th) Analysis and interpretation of results. For the analysis and subsequent synthesis of the articles that met the inclusion criteria was used a summary frame specially built for this purpose, which included the following aspects considered relevant: Name of the research, authors' names for article, level of evidence and the action of propolis on microbial oral cavity. Finally, there was analyzed descriptively in the light of scientific evidence.

6th) Presentation of synthesis of knowledge. The evidence was gathered and synthesized and conclusions of studies questioned because of their limitations.

Results

Table 1 shows the characterization of the analyzed publications. Regarding the articles published by publication year, stand out: in 2013 and 2007 with two articles per year [9-10, 13-14]; 2011 [11], 2008 [12], 2006 [15], 2002 [16] and 1999 [17] with one (1) article per year.

Table 1. Characterization of the analyzed publications.

Article	Title/Language/Journal	Objective	Study type	Evidence Level
[9]	Effects of typified propolis on <i>mutans streptococci</i> and <i>lactobacilli</i> : a randomized clinical trial. English/Braz Dent Sci	Determining, in a randomized, double-blind, placebo-controlled the effects of propolis typified and chlorhexidine on salivary levels of group a <i>Streptococci mutans</i> (SM) and <i>Lactobacilli</i> (LACT)	Clinical essay randomized 60 patients: 20 – propolis typified; 20 – chlorhexidine; 20 – placebo.	3
[10]	Effect of Zingiber officinale and propolis on microorganisms and endotoxins in root canals English/J Appl Oral Sci	Evaluating the action of glycolic acid Propolis (PRO) and Ginger extracts (GIN), calcium hydroxide (CH), chlorhexidine gel (CLX) and their combinations used as irrigation intracanal against <i>C. albicans</i> , <i>E. faecalis</i> and <i>Escherichia coli</i> endotoxin.	<i>In vitro</i> study – fill intracanal	8
[11]	Antimicrobial activity of natural products in front of the dental biofilm-forming bacteria Portuguese/ Odontoped Clin Integr.	Assessing the sensitivity of bacterial species found in the oral cavity: <i>Streptococcus mutans</i> , <i>Streptococcus salivarius</i> , <i>Streptococcus mitis</i> and <i>Lactobacillus casei</i> front of propolis extracts and aqueous alcohol, diluted respectively in alcohol and distilled water and diluted pollen in alcohol, at concentrations of 5% and 50%.	<i>In vitro</i> study – by determining the Maximum Inhibitory Dilution	8
[12]	<i>In vitro</i> and <i>ex vivo</i> study of the action of different concentrations of extracts of propolis against the microorganisms present in human saliva Portuguese/Rev. Bras. Farmacogn	In phase 1, were evaluated <i>in vitro</i> , the action of three different concentrations of propolis extract compared to industrialized products Periogard®, Listerine®, Malvatricin® and Parodontax®, while in phase 2 was evaluated the action, <i>ex vivo</i> , propolis extract in the same concentrations used in phase 1, front of microorganisms that occur in saliva.	<i>In vitro</i> study (lab) e <i>ex vivo</i> (experimental)	8
[13]	Effect of a propolis extract on <i>Streptococcus mutans</i> counts in vivo English/J Appl Oral Sci	Evaluating <i>in vivo</i> antimicrobial activity of the extract prepared with propolis produced by bees <i>Melipona compressipes fasciculata</i> (Ministry of agriculture, registration number 0005/731) and used as mouthwash on <i>S. Mutans</i> concentration present in the oral cavity of young individuals.	Experimental clinical study	3

Article	Title/Language/Journal	Objective	Study type	Evidence Level
[14]	Microbial activity of essential oils and extracts of propolis on cariogenic bacteria Portuguese/Rev. Sciences Farm. Basic Apl.	Assessing the susceptibility profile of ethanolic extracts of propolis from the States of Paraná, Minas Gerais and São Paulo and essential oils, front cariogenic bacteria <i>Streptococcus mutans</i> and <i>Lactobacillus casei</i> using the agar diffusion method, for possible incorporation into formulations of infant dental folders.	<i>In vitro</i> study of agar diffusion bioassay	8
[15]	Clinic Effects of Anti Septic solution based on Propolis in children with Active Caries Portuguese/ Research Bras. Odontoped. Clin. Intgr	Checking the performance of an antiseptic solution based on propolis on clinical indexes of accumulation of biofilm and gum disease as well as the salivary levels of <i>S. mutans</i> in children active caries	Clinical trial Cross (15 children) with propolis and chlorhexidine Mouthwash	3
[16]	Propolis antimicrobial activity against periodontopathic bacteria English/Braz. J. Microbiology	Investigating the <i>in vitro</i> antimicrobial action of a propolis extract (with a previously determined composition) against the bacteria periodontopathic, as well as against superinfectants.	<i>In vitro</i> study of agar diffusion bioassay	8
[17]	<i>Candida</i> sp in the oral cavity with and without lesions: maximal inhibitory dilution of Propolis and Periogard English/ Revista de Microbiologia	Isolating, identifying and determining the prevalence of yeasts in the oral cavity of individuals with and without lesions; and test the minimum inhibitory dilution of propolis and Periogard against yeasts isolated.	Saliva collection of 50 adult patients, for <i>in vitro</i> research. Antifungal activity of the tested products was determined by dilution technique in solid medium.	8

Source: PubMed, LILACS e SciELO, 2014 sept 24.

Regarding the language found were 05 articles in English and four in Portuguese. All publications were made in Brazil, highlighting the South Region, with 4 articles [9, 10, 16-17]; Northeast Region, with 4 articles [11-13, 15]; and only 1 in the Midwest Region [14].

Journals that published the articles were: Brazilian Dental Science [9], Journal of Applied Oral Science [10, 13], Pesq Bras Odontopediatria Clinica Integrada [11, 15], Revista Brasileira de Farmacognosia [12], Rev. Ciência Farmacêutica Básica Aplicada [14], Brazilian Journal of Microbiology [16], Revista de Microbiologia [17].

In the analysis of the journals subject of publications, stood out periodic dental area [9, 10-11, 13, 15], magazines pharmacy area [12, 14] and microbiology area [16-17].

The method of six articles [10-12, 14, 16-17] The *in vitro* study was considered weak evidence, one of them being combined with the experimentally [17]; and three clinical trials [9, 13, 15], with evidence level 3, as were a few patients.

Evidence about the action of propolis on oral cavity microorganisms

In response to the main question of this integrative review: "What is the action of propolis on the microorganisms of the oral cavity", **table 2** presents a summary of the analyzed articles.

After reviewing the research, the action of propolis on the microorganisms of the oral cavity referred to by the authors was: antibacterial action, with reports in 8 articles [9-16]; and antifungal action in three articles [10, 16-17].

Discussion

The interest in propolis in Brazil happened in the 80s of the twentieth century, with record of pioneering work of Ernesto Ulrich Breyer. In his writing, "Bees and health," demonstrated the therapeutic properties of propolis and its use as a natural antibiotic [18].

However, despite this elapsed time, are few and incipient research involving propolis, as evidenced by the quantitative research that this literature review and years of publication.

When the language of the reports analyzed, it is noticed that while English is considered a frontier language serving as a key point for the construction, reconstruction and improvement of research [19], it was found almost the same number of articles published in Portuguese.

The highlight in knowledge identified in the revised publications is due to the fact that propolis has different types of biological activity and applications in various therapies, especially in the dental field [2].

Although most studies have applied analytical statistics with reliable statistical tests, casts doubt on generalizations about the studied object, because besides the methodological designs were of weak evidence (level 8), the sample size was small, which does not reveal representation. In turn, *in vitro* studies are lower Evidence strength, because they mimic biological conditions in the laboratory and are used to test new materials or therapeutic or preventive methods. Such studies "do not establish guidelines for clinical management, nor do they provide priority information for clinical decision making" [20].

In addition, the above authors analyzed published research in Brazilian dental journals and concluded that the small number of research publications with higher level of evidence points to the importance of an expanded knowledge among Brazilian researchers on evidence-based clinical practice.

It is observed that the oral rinsing of alcohol-free propolis had a more effective action than chlorhexidine. However, statistical significance was the same for both products ($p < 0.05$) compared to *Streptococcus mutans* and *lactobacilli* [9].

A clinical study found that propolis reduced the plaque index by about 44.7% after treatment compared to placebo. In addition, the used mouthwash propolis decreased to 61.7%, the concentration of

Table 2. Action of propolis on oral cavity microorganisms, as revised publications.

Article	Concentration of propolis	Region	Antibacterial action	Antifungal action
[9]	PROP-alcohol-free rinse of Propolis 2% typified (n = 20)	Florianopolis-SC	Treatment effect analysis of covariance revealed significant effects of treatment, after 28 and 45 days of use, for reduction of salivary levels of <i>S. mutans</i> , both for the group using typed Propolis (p < 0.05), as for chlorhexidine Group (p < 0.05). The mouthwash was superior to propolis chlorhexidine rinses and placebo in 7 days, 14 days and 28 days visits (effects of treatment) in suppressing the salivary levels of (<i>S. mutans</i>) Residual effect-after 4 weeks use of propolis rinse, there was a significant suppression of salivary levels of <i>Lactobacilli</i> , when compared to chlorhexidine and placebo	
[10]	12% glycolic extract of propolis	<i>Apis Flora</i> , Ribeirão Preto, SP, Brazil	Completely eliminate the <i>E. Coli</i> and reduced <i>E. faecalis</i> endotoxin of root canals. (p < 0.05)	Reduced <i>C. albicans</i> (p < 0.05)
	0.1 g of calcium hydroxide + 100 µl of Propolis containing 5.63 mg/mL of flavonoids	Biodinamics, Chemistry and Pharmaceutical Ltda., Ibiporã, PR, Brazil	Reduced the <i>E. faecalis</i> and <i>Escherichia coli</i> endotoxin of root canals	
[11]	Propolis extracts with and without alcohol, has been diluted in alcohol 70 and distilled water at concentrations of 1: 1 and reaching 1: 64, as was also tested in their pure forms.	<i>APIs Flora</i> Ind. com. Ltda. was acquired on homeopathic pharmacy of reference in the city of João Pessoa/PB.	All dilutions of propolis alcohol inhibited bacterial growth. The minimum inhibitory Dilution recorded for the strains of <i>S. mutans</i> , <i>s. salivarius</i> and <i>s. mitis</i> was 1:64 while the observed for <i>L. casei</i> has been 1:32	
[12]	Dry extract of propolis to 11%	Salvador-BA NaturApi Natural products and Beekeeping Ltda (11%).	<i>In vitro</i> - there was no glucose consumption– the product has antimicrobial activity against oral pathogens. <i>Ex vivo</i> - from the 11% concentration of extracts of propolis has antimicrobial action.	
	Dry extracts of propolis to 20%	<i>APIs-Flora</i> Ind. e Com. Ltda (20%).	The extracts of propolis to 11%, 20% and 30% showed inhibition of the glucose consumption, similar to Listerine® industrial products, Malvatricin®, Periogard® Parodontax® and widely used as an oral antiseptic.	
	Dry extract of propolis to 30%	<i>Herbarium</i> Botanic Lab Ltda (30%)		

Article	Concentration of propolis	Region	Antibacterial action	Antifungal action
[13]	Extract prepared with propolis produced by bees <i>Melipona compressipes fasciculata</i> (Ministry of Agriculture, registration number 0005/731)	Maranhão	Reduction in the number of <i>S. mutans</i> after the beginning and end of treatment.	
[14]	The extraction was performed by maceration with ethyl alcohol 96 GL, for a period of fifteen days, then made the filtration and concentration of macerated in evaporator route, obtaining thus alcoholic extracts the 25%.	Paraná	<i>Paraná - showed no bactericidal action on microorganisms tested, even at the highest concentrations tested.</i>	
		Minas Gerais	Propolis from Minas Gerais was the one that proved most active of all, with the formation of inhibition halos slightly larger in relation to the propolis of São Paulo.	
		São Paulo	Minas Gerais and São Paulo - showed antimicrobial activity for the microorganism <i>S. mutans</i> from concentration equivalent to 0.6 µg/L.	
[15]	The propolis extract was sprayed and macerated in hydroalcoholic, obtaining a propolis solution to 60% and determined the antimicrobial activity of strain of <i>S. mutans</i> in solid medium for determining the Minimum Inhibitory Concentration (MIC).	Southern Region of the State of São Paulo	Propolis solution to 6.25% interfered significantly on growth of microorganisms ($p < 0.001$), being observed similar reduction when the use of chlorhexidine solution to 0.12% ($p < 0.01$).	
[16]	Ethanolic extract of Propolis (70% ethanol)	UNESP-Botucatu-Department of Production Animal – Brazil	The propolis extract showed antimicrobial activity against all strains tested-periodontal pathogens: <i>A. actinomycetemcomitans</i> , <i>P. intermedia</i> , <i>P. melaninogenica</i> , <i>P. gingivalis</i> , <i>C. gingivalis</i> e <i>F. Nucleatum</i> , <i>Pseudomonas aeruginosas</i> , <i>Escherichia colie</i> , <i>Staphylococcus aureus</i> . And also against some microorganisms capable of causing superinfection (<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>Escherichia coli</i>).	<i>Candida albicans</i>
[17]	Propolis tested was in the form of an alcohol extract containing quantities corresponding to 10 g% soluble solids present.	<i>Apis-Flora</i> (Ribeirão Preto/SP)		Most strains 67/70 (95.71%) was sensitive to two antimicrobials (antiseptics Periogard® and propolis). The dilution of propolis 01:20 inhibited 77.1% of strains in your mouth healthy; The <i>C. albicans</i> and <i>C. tropicalis</i> were sensitive to the same concentrations (01:20 ou 01:40)

Source: PubMed, LILACS e SciELO, 2014 sept 24

insoluble polysaccharides, plate, compared to placebo suggesting that had an effect on the oral microflora. However, the study did not specify what concentration or solute treatment was performed [21].

The glycolic extract of propolis reduced *C. albicans* and *E. coli* completely eliminated, while the calcium hydroxide reduced growth, demonstrating resistance against this bacterium used product [11]. However, the actual mechanism of the antimicrobial properties of propolis appears to be complex and not fully understood. In this sense, some authors attribute to the highest antimicrobial activity flavonoids present in propolis extract [22]. Using alcoholic extract of propolis, a study obtained better results in relation to the strains of *S. mutans*, *S. salivarius*, *S. mitis* and *L. casei*, compared to aqueous extract [11]. *In vitro* research, developed using as antimicrobial agent propolis extracts (not specified where concentration nor solute), isolated fractions and purified compounds showed reductions in *Streptococcus mutans* count, as well as interference with its adhesion capacity and activity glycosyltransferase, which are considered large properties in the establishment of cariogenic process [23].

Research *In vitro* followed by *ex-alive*, it used dry extract of propolis at low concentrations (11%, 20% and 30%), comparing the results to those of industrialized products Listerine®, Malvatricin®, Parodontax® and Periogard® and found that there was inhibition of glucose consumption, similarly to those products [12]. In this regard, a survey showed antibacterial inhibitory effect of propolis in concentration reduced front of *Staphylococcus aureus*, a gram-positive species with broad-spectrum oral pathogenicity [24].

In an experiment with 41 young people who did not alter the oral hygiene, or eating habits during the experiment, it was used propolis extract mouthwash (without solute information or concentration) three times daily for seven days. Saliva was collected from participants before the first use and

after an hour and seven days after the first rinse. The results showed that in 49% of all samples collected after the use of the extract, a reduction of the concentration of *S. mutans*. However, 26% of the samples there was no change, and 25% noted an increase of *S. mutans* [13]. This phenomenon can happen because of caries be a mixed infection and oral microflora is highly diversified. Furthermore, *S. mutans* may be present in the oral cavity in three different serotypes C, E and F [25].

Using the propolis of three distinct regions, they observed that the Paraná (even in higher concentrations) showed no bactericidal activity on the tested microorganisms, unlike the propolis of Minas Gerais, which showed antimicrobial property to the *S. mutans*, from equivalent concentration to 0.6 µg/L, and introduced more active regarding that of Paraná and São Paulo. [14]

Referring to the propolis by regions of Brazil, points out research in the Japanese market, the propolis produced in Minas Gerais State is considered the world's best, according to the Beekeepers Federation of Minas Gerais [2].

The fact of the biological properties of propolis are directly related to its chemical composition, which varies with the type of vegetation in the area, the time of collection, the technique employed, the species of bee and the level of Africanization of *Apis mellifera* in Brazil suggests that the antimicrobial action is closely related to the concentration of flavonoids and caffeic acid [2, 26].

In crossover trial (15 children) analyzing the effects of mouthwash with propolis and chlorhexidine, showed that, similar to the 0.12% chlorhexidine mouthwash, the hydroalcoholic extract of propolis to 6.25% significantly reduced levels of *S. mutans*, bacteria that act on the conditions of gum disease and dental plaque accumulation, suggesting that propolis mouthwash may be indicated as therapeutic chemical agent [15].

Another study showed that the ethanol extract of propolis has antimicrobial activity against all tes-

ted periodontal bacteria, and also capable of causing about superinfection (*S. aureus*, *P. aeruginosa*, *Escherichia coli*); and antifungal activity against *C. albicans* [16]. Moreover, other research inhibitory results obtained with *gram-negative anaerobes*, such as *Prevotella intermedia*, *Prevotella nigrescens* and *Porphyromonas gingivalis*, which have been associated with periodontal disease, confirmed the antibacterial activity of the compound of propolis [27].

Authors tested the minimum inhibitory dilution of propolis and Periogard® against yeasts oral cavity, lesions and healthy, and found that most strains were sensitive to both antimicrobials. However, they observed that propolis 50% inhibited 77.1% of the strains, most of *C. albicans* (96.5%). Noting that *C. albicans* and *C. tropicalis* were sensitive to the same concentrations (01:20 ou 01:40), while the other species are sensitive to the concentration of 01:20. Interestingly, the isolated species of oral injury, *C. albicans*, *C. tropicalis* and *C. glabrata* were resistant to all Propolis dilutions tested [17].

The resistance of *C. albicans* may be related to its ability to adapt to different environmental conditions, since this fungus is able to survive as a dinner in adaptation to acidic or basic pH. Furthermore, the *C. albicans* has the ability to undergo morphological transition, hyphae yeast change for representing a change of state pathogenicity for dinner, being able to invade host tissues and escaping phagocytosis by macrophages; this yeast also form biofilms on different surfaces [28].

In the analysis of all studies we noticed the use of propolis in different concentrations and solutes, resulting in some regions of Brazil, once identified. In the early twenty-first century, Brazil was responsible for 10-15% of world production of propolis, and that Japan has preference for Brazilian propolis, due to its pharmacological properties, its organoleptic characteristics and the lowest content of heavy metals and other pollutants environmental [2].

These facts have been confirmed, since the studies analyzed showed the antimicrobial activi-

ty of propolis in the oral cavity, enhancing their inhibitory character on *gram-negative* and *gram-positive*, anaerobic and aerobic, as well as antifungal activity on *Candida albicans*; excepting to the fact that most research revised result from in vitro studies and some did not specify what type of extract, if alcoholic, aqueous or glycolic, either concentrations.

Synthesis of knowledge about the action of propolis on the microorganisms of the oral cavity

Several species, from bacteria and fungi naturally colonize the oral cavity, which, in favorable conditions, can cause diseases, highlighting caries, periodontitis and others. In this sense, propolis is a natural alternative substance to be used in the control and prevention of such diseases.

Thus, this review showed that researchers testing of low concentrations propolis, with prevalence used alcohol as a solvent, being effective against *gram-positive bacteria Staphylococcus mutans*, *S. salivarius* and *S. mitis*; and *gram-negative* (periodontal pathogens), as follows: *Actinobacillus actinomycetemcomitans*, *pseudomonas intermedia*, *Pseudomonas melanogenic*, *Pseudomonas gingivalis* and *Fusobacterium nucleatum*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* (particularly those last three species are also capable of causing superinfection).

Used in typed form, free of alcohol, propolis was able to reduce the salivary levels of *S. mutans*, demonstrating preventive against caries treatment effect and residual compared to chlorhexidine, widely used as a mouthwash.

However, the aqueous propolis, in pure form and in dilutions 1:1 to 1:4, showed an effect only on *S. mitis*. It was found also that glycolic extract of propolis and 12%, and propolis containing 5.63 mg/mL flavonoids, associated with calcium hydroxide, were able to completely eliminate *E. coli* and *E. faecalis* reduce and endotoxins and *C. albicans* root canal.

The antifungal activity of propolis in the oral cavity has been demonstrated when used glycolic extract of propolis 12% and the ethanol extract of propolis (70% ethanol) causing efficacy in reducing *C. albicans*. In addition, it was found that the *C. albicans* and *C. tropicalis*, in clinically healthy mouths, were sensitive to the alcoholic propolis extract concentrations at 01:20 or 01:40.

Moreover, to safely say the effectiveness of propolis on the microorganism in the oral cavity would require evidence from studies of systematic reviews and randomized clinical trials with humans, because they are considered major evidence force; since the results presented in this study derived in most part from in vitro studies, evidence of which strength is weak. In addition, some studies do not make clear which the solvent of the propolis extract or concentration is.

Otherwise, this literature indicates the need for therapeutic parameters are defined and the minimum chemical composition, the different types of propolis, so that they have the appropriate/desired therapeutic properties.

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