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Review Article

Therapeutic applications and antibacterial and antifungal activities of *Syzygium cumini* (L.) Skeels extracts: a systematized literature review focusing on dental applications

Aplicações terapêuticas, atividades antibacteriana e antifúngica de extratos de Syzygium cumini (L.) Skeels: uma revisão sistematizada da literature com ênfase em suas aplicações odontológicas

Aplicaciones terapéuticas, actividades antibacteriana y antifúngica de extractos de Syzygium cumini (L.) Skeels: una revisión sistematizada con énfasis en sus aplicaciones odontológicas

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Abstract

Medicinal plants are an important source of curative substances for the treatment of diseases. Investigations are focusing particularly on medicinal plants used to treat affections of the oral cavity. Among these species, there is evidence of potential applications of *Syzygium cumini* to Dentistry. The objective of this systematized literature review was to synthesize the evidence on the antimicrobial activity of this plant, as well cite some as the traditional uses of its extracts for dental purposes. The data indicate that the extracts prepared from different parts of the plant have antibacterial and antifungal effects on different pathogenic microorganisms of the oral microbiota and/or those that can potentially cause oral diseases, demonstrating a promising therapeutic potential for indication and use in Dentistry to prevent and/or treat oral affections.

Descriptors: Plant Extracts; Medicine, Traditional; Anti-Bacterial Agents; Antifungal Agents; Dentistry.

Resumo

As plantas medicinais representam uma fonte importante para a obtenção de substâncias com fins curativos no tratamento de doenças. Dentre essas, tem se destacado a investigação daquelas voltadas para o tratamento de afecções que acometem a cavidade bucal. Dentre essas espécies, *Syzygium cumini* tem apresentado evidências com potencial aplicação e utilização na Odontologia. Desse modo, o presente trabalho tem como objetivo sintetizar através de uma revisão sistematizada da literatura as evidências acerca da atividade antimicrobiana, bem como dos usos populares de seus extratos com interesse odontológico. As pesquisas foram realizadas nas bases de dados National Library of Medicine National Institutes of Health (PubMed), Scientific Electronic Library Online (Scielo) e Google Scholar. Os dados apontam que os extratos de diferentes partes da planta apresentam efeitos antibacterianos e antifúngicos sobre diversos microrganismos patogênicos presentes e/ou potencialmente causadores de doenças bucais, demonstrando um potencial terapêutico promissor para sua indicação e utilização odontológica na prevenção e/ou o tratamento de afecões bucais.

Descritores: Extratos Vegetais; Medicina Tradicional; Antibacterianos; Antifúngicos; Odontologia.

Resumen

Las plantas medicinales representan una fuente importante para la obtención de sustancias con fines curativos en el tratamiento de enfermedades. Entre ellas, se ha destacado la investigación de aquellas orientadas hacia el tratamiento de afecciones que acomete la cavidad bucal. Entre estas especies, *Syzygium cumini* ha presentado evidencias con potencial aplicación y utilización en la Odontología. De este modo, el presente trabajo tiene como objetivo sintetizar a través de una revisión sistematizada de la literatura las evidencias acerca de la actividad antimicrobiana, así como de algunos de los usos populares de sus extractos con interés odontológico. Los datos apuntan que los extractos de diferentes partes de la planta presentan efectos antibacterianos y antifúngicos sobre diversos microorganismos patógenos presentes y/o potencialmente causantes de enfermedades bucales, demostrando un potencial terapéutico prometedor para su indicación y uso odontológico en la prevención y/o el tratamiento de los afecones la boca.

Descriptores: Extractos Vegetales; Medicina Tradicional; Antibacterianos; Antifúngicos; Odontología.

INTRODUCTION

The use of medicinal plants for curative purposes is intrinsically related to the early days of medicine when they were used as a basis in the treatment of various diseases[1,2]. Medicinal plants have been for a long time the primary source of material for the production and development of drugs[3]. Although medicine is at an advanced technical and scientific stage in most parts of the world, 80% of the population of developing countries continues to primarily rely on traditional resources and practices for basic health care[4-6].

Within this context, given the increasing acceptance of phytotherapy as an alternative therapeutic modality[7,8],research is focusing particularly on medicinal plants with applications to Dentistry because of the large number of species that have been reported for the treatment of affections of the oral cavity[8,9]. Among these species, the plant *Syzygium cumini* (L.) Skeels (Myrtaceae) (synonyms: *Syzygium jambolanum*, *Syzygium jambolana*, *Eugenia jambolana*, *Eugenia cumini*)[1,10-12] commonly known as jambolão, jamun, azeitona, azeitona-roxa and olive[1,10,11,13], is used in folk medicine because of its different pharmacological properties[1,3,10-18].

In this scenario, considering the need for studies investigating medicinal plants with potential application to Dentistry[8,9], the objective of this literature review was to synthesize the biological activities of potential interest for

Dentistry of *S. cumini*, focusing on its antimicrobial and antifungal effects on microorganisms of the oral microbiota.

MATERIAL AND METHOD

This study consists of a literature review and bibliometric study of original articles evaluating the antibacterial and antifungal activities of *S. cumini* extracts on microorganisms of the oral microbiota and/or microorganisms that can potentially cause oral diseases, focusing on some uses and indications of these extracts with potential interest to Dentistry.

- *Search strategy*

For the literature review and bibliometric study, searches were performed in May 2018 using the National Library of Medicine National Institutes of Health (PubMed), Scientific Electronic Library Online (Scielo) and Google Scholar databases. Articles without publication date and language restrictions were selected. The following terms were used: "*Syzygium cumini"*, "antifungal activity", "antimicrobial activity" through the search strategy using Boolean operators "AND" and "OR" as follows: "(*Syzygium cumini*) AND (antimicrobial activity OR antifungal activity)".

- *Inclusion and exclusion criteria*

Only complete literature reviews and experimental studies addressing the topic proposed and that had only used extracts from different parts of *S. cumini* were included for full-text reading. Studies investigating compounds isolated from the plant or synthesized compounds were not considered. Incomplete articles, monographs, master's dissertations, doctoral theses and publications not consistent with the topic were excluded. Articles investigating *S. cumini* extracts combined with other substances were also eliminated.

- *Study selection*

Analysis and selection of the retrieved articles were performed in three steps. In the first step, the title of the articles was read and those whose title indicated studies related to the antimicrobial and antifungal potential of *S. cumini* extracts against oral microorganisms, as well as dental applications, were selected. The second step consisted of reading the abstracts of the selected articles. Finally, the third step consisted of full-text reading of the articles and qualitative analysis of the studies that addressed the topic proposed and met the eligibility criteria. Studies reporting some evidence on the subject of this investigation were selected.

RESULTS

The searches retrieved 5.337 articles, being 260 from PubMed, seven from Scielo and 5.110 from Google Scholar, respectively. After analysis of the title, 1.084 article were excluded and after this step, the abstracts of 174 articles were read and those that addressed the topic proposed and met the eligibility criteria were selected for full-text reading (61 articles). After exclusion of duplicated articles, evaluation and qualitative analysis of the articles retrieved a final sample of 42 articles, including studies related to the antibacterial and antifungal activities of *S. cumini* extracts against microorganisms of the oral microbiota and/or microorganisms that can potentially cause oral diseases (Figure 1).

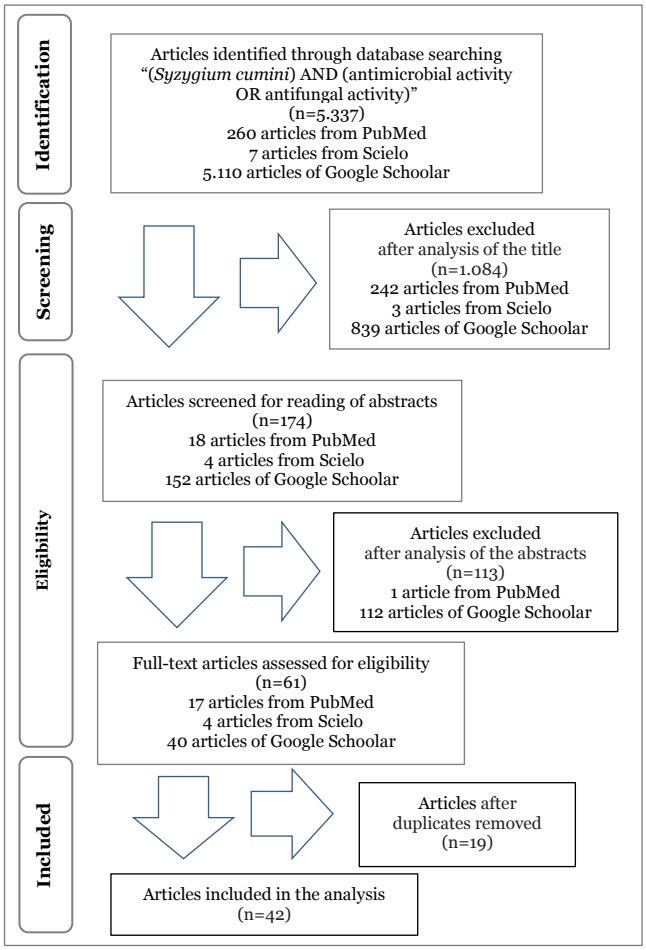

Figure 1: Research data flowchart

Some findings about the popular use of *S. cumini* for therapeutic purposes and application of *S. cumini* extracts to Dentistry is described in Table 1. Evidence available in the literature on the antibacterial and antifungal effects attributed to the *S. cumini* extracts on microorganisms of the oral microbiota and/or microorganisms that can potentially cause diseases of the oral cavity is described in Tables 2 and 3, respectively.

Table 1. Therapeutic use and application of different parts of *Syzygium cumini* to Dentistry

Plant parts	Uses	Therapeutic purposes	References
Fruits	Gargles	Treatment of throat irritation	Migliato *et al.* [1] (2006)
	*NS	Treatment of halitosis	Ayynamar & Subash-Babu [10] (2012)
Leaves	*NS	Strengthening effects on teeth and gingiva	Ayynamar & Subash-Babu [10] (2012); Srivastava & Chandra [11] (2013); Atale *et al.* [14] (2013); Gowri & Vasantha [22] (2010); Borde *et al.* [23] (2013)
	Mouthwash	Treatment of recurrent aphthous ulcers, stomatitis, affections of the throat and other oral diseases	Costa *et al.* [21] (2009)
Seeds	Extract	Treatment of oral eruptions and throat	Ayynamar & Subash-Babu [10] (2012); Chandrasekaran & Venkatesalu [24] (2004)
Stem	*NS	Antiseptic, astringent of oral ulcerations and stomatitis	Migliato *et al.* [1] (2006)
	Decoction as mouthwash	Treatment of recurrent aphthous ulcers, stomatitis and affections of the throat	Loguercio *et al.* [19] (2005)
	Decoction as mouthwash	Astringent effect on oral ulcerations, gingival hyperplasia and stomatitis	Ulla *et al.* [20] (2017)

Legend: *NS= not specified.

Table 2. Evidence of studies demonstrating antibacterial activity of *Syzygium cumini* extracts obtained from different parts of the plant against microorganisms of interest to Dentistry.

Plant parts	Microorganisms	Antimicrobial susceptibility test	References
Fruits	*Bacillus subtilis*	Disk diffusion	Saha *et al.* [25] (2013)
	Escherichia coli	Agar dilution Disk diffusion	Shad *et al.* [26] (2014) Saha *et al.* [25] (2013)
	Pseudomonas aeruginosa	Agar dilution Microdilution	Shad *et al.* [26] (2014) Migliato *et al.* [27] (2010)
	Staphylococcus aureus	Disk diffusion Microdilution	Saha *et al.* [25] (2013) Migliato *et al.* [27] (2010)
Fruit peel	*Enterococcus faecalis; Escherichia coli;Pseudomonas aeruginosa; Staphylococcus aureus*	Disk diffusion; Macrodilution	Priya *et al.* [28] (2013)
Leaves	*Bacillus subtilis*	Agar diffusion Disk diffusion Microdilution	Kaneria *et al.* [5] (2009); Gowri & Vasantha [22] (2010); Shafi *et al.* [29] (2002); Kaneria & Chanda [31] (2011); Tahir *et al.* [33] (2012); Mohamed *et al.* [34](2013); Elfadil *et al.* [35](2015) Bhargava *et al.* [30] (2009); Elansary *et al.* [32] (2012) Elansary *et al.* [32] (2012)
	Enterococcus faecalis	Agar diffusion Microdilution	Oliveira *et al.* [8] (2007); Mohamed *et al.* [34] (2013) Pereira *et al.* [9] (2009)
	Escherichia coli	Agar diffusion Disk diffusion Microdilution	Oliveira *et al.* [8] (2007);Loguercio *et al.* [19] (2005); Gowri & Vasantha [22] (2010); Shafi *et al.* [29] (2002); Tahir *et al.* [33] (2012); Mohamed *et al.* [34] (2013); Elfadil *et al.* [35] (2015); Bajracharya *et al.* [36] (2008) Bhargava *et al.* [30] (2009); Elansary *et al.* [32] (2012) Pereira *et al.* [9] (2009); Elansary *et al.* [32] (2012); Bajracharya *et al.* [36] (2008)
	Klebsiella pneumoniae	Agar diffusion Disk diffusion	Kaneria & Chanda [31] (2011); Bouzada *et al.* [37] (2009) Bhargava *et al.* [30] (2009)
	Neisseria gonorrhoeae	Agar diffusion Disk diffusion Microdilution	Oliveira *et al.* [8] (2007); Jadhav *al.* [38] (2015) Mohamed *et al.* [34] (2013) Jadhav *al.* [38] (2015)
	Pseudomonas aeruginosa	Agar diffusion Disk diffusion; Microdilution	Kaneria *et al.* [5] (2009); Oliveira *et al.* [8] (2007); Loguercio *et al.* [19] (2005); Gowri & Vasantha [22] (2010); Shafi *et al.* [29] (2002); Tahir *et al.* [33] (2012); Mohamed *et al.* [34] (2013); Elfadil *et al.* [35] (2015); Bouzada *et al.* [37] (2009) Elansary *et al.* [32] (2012) Elansary *et al.* [32] (2012)
	Streptococcus mutans	Agar diffusion Macrodilution Microdilution	Tahir *et al.* [33] (2012); Viera *et al.* [39] (2012) Viera *et al.* [39] (2012) Pereira *et al.* [9] (2009)
	Lactobacillus casei; Streptococcus oralis; Streptococcus parasanguis; Streptococcus salivarius	Agar diffusion; Macrodilution	Viera *et al.* [39] (2012)
	Streptococcus viridans	Agar diffusion	Tahir *et al.* [33] (2012)
	Staphylococcus aureus	Agar diffusion Disk diffusion Macrodilution Microdilution	Kaneria *et al.* [5] (2009); Oliveira *et al.* [8] (2007); Loguercio *et al.* [19] (2005); Gowri & Vasantha [22] (2010); Borde *et al.* [23] (2013); Shafi *et al.* [29] (2002); Kaneria & Chanda [31] (2011); Tahir *et al.* [33] (2012); Mohamed *et al.* [34] (2013); Elfadil *et al.* [35] (2015); Bouzada *et al.* [37] (2009) Bhargava *et al.* [30] (2009); Elansary *et al.*[32] (2012); Chanudom *et al.* [40] (2014) Chanudom *et al.* [40] (2014) Pereira *et al.* [9] (2009); Elansary *et al.* [32] (2012); Pereira *et al.* [41] (2017)
	Staphylococcus intermedius	Agar diffusion	Loguercio *et al.* [19] (2005)

Table 2 – Continuation. Evidence of studies demonstrating antibacterial activity of *Syzygium cumini* extracts obtained from different parts of the plant against microorganisms of interest to Dentistry.

Plant parts	Microorganisms	Antimicrobial susceptibility test	References
Seeds	*Bacillus subtilis*	Agar diffusion Disk diffusion; Macrodilution Microdilution	Chandrasekaran & Venkatesalu [24] (2004); Yadav *et al.* [42] (2011); Yadav *et al.* [43] (2017) Duraipandiyan *et al.* [4] (2006);Saha *et al.* [25] (2013) Chandrasekaran & Venkatesalu [24] (2004) Yadav *et al.* [43] (2017)
	Escherichia coli	Agar diffusion Disk diffusion Macrodilution Microdilution	Bag *et al.* [6] (2012);Chandrasekaran & Venkatesalu [24] (2004); Yadav *et al.* [42] (2011); Mariselvam *et al.* [45] (2017) Saha *et al.* [25] (2013); Jasmine *et al.* [44] (2010) Chandrasekaran & Venkatesalu [24] (2004) Bag *et al.* [6] (2012); Jasmine *et al.* [44] (2010)
	Klebsiella pneumoniae	Agar diffusion Disk diffusion Microdilution Macrodilution	Bag *et al.* [6] (2012);Chandrasekaran & Venkatesalu [24] (2004) Duraipandiyan *et al.* [4] (2006); Jasmine *et al.* [44] (2010) Bag *et al.* [6] (2012); Jasmine *et al.* [44] (2010) Chandrasekaran & Venkatesalu [24] (2004)
	Pseudomonas aeruginosa	Agar diffusion Disk diffusion Macrodilution Microdilution	Bag *et al.* [6] (2012); Chandrasekaran & Venkatesalu [24] (2004);Yadav *et al.* [42] (2011); Mariselvam *et al.* [45] (2017) Jasmine *et al.* [44] (2010) Chandrasekaran & Venkatesalu [24] (2004) Bag *et al.* [6] (2012); Jasmine *et al.* [44] (2010)
	Staphylococcus aureus	Agar diffusion Disk diffusion Macrodilution Microdilution	Bag *et al.* [6] (2012); Chandrasekaran & Venkatesalu [24] (2004) ;Yadav *et al.* [42] (2011) ; Duraipandiyan *et al.* [4] (2006) ;Saha *et al.* [25] (2013) Chandrasekaran & Venkatesalu [24] (2004) Bag *et al.* [6] (2012)
	Streptococcus aureus	Agar diffusion	Mariselvam *et al.* [45] (2017)
Stem bark	*Bacillus subtilis; Escherichia coli; Klebsiella pneumonia; Staphylococcus aureus*	Agar diffusion	Prabhakaran *et al.* [46] (2011)
Root	*Streptococcus mutans;Streptococcus oralis*	Microdilution	Cartaxo-Furtado *et al.* [47] (2015)

Table 3. Evidence of studies demonstrating antifungal activity of *Syzygium cumini* extracts obtained from different parts of the plant against fungi of the genus *Candida*.

Plant parts	Microorganisms	Antimicrobial susceptibility test	References
Fruits	*Candida albicans*	Agar dilution Disk diffusion Microdilution	Shad *et al.* [26] (2014) Saha *et al.* [25] (2013) Migliato *et al.* [27] (2010)
	Candida krusei; Candida parapsilosis	Microdilution	Migliato *et al.* [27] (2010)
Fruit peel	*Candida albicans*	Disk diffusion; Macrodilution	Priya *et al.* [28] (2013)
Leaves	*Candida albicans*	Agar diffusion Disk diffusion Microdilution	Oliveira *et al.* [8] (2007); Elfadil *et al.* [35] (2015); Jadhav *et al.* [38] (2015) ; Khan *et al.* [49] (2017) Bhargava *et al.* [30] (2009) Pereira *et al.* [9] (2009); Costa *et al.* [21] (2009); Jadhav *et al.* [38] (2015); Pereira *et al.* [48] (2016); Khan *et al.* [49] (2017)
	Candida glabrata	Agar diffusion Microdilution	Kaneria & Chanda [31] (2011); Khan *et al.* [49] (2017) Costa *et al.* [21] (2009); Khan *et al.* [49] (2017)
	Candida krusei	Agar diffusion Disk diffusion Microdilution	Oliveira *et al.* [8] (2007); Khan *et al.* [49] (2017) Bhargava *et al.* [30] (2009) Khan *et al.* [49] (2017)
	Candida neoformans	Agar diffusion Microdilution	Kaneria & Chanda [31] (2011); Braga *et al.* [50] (2007) Braga *et al.* [50] (2007)
	Candida tropicalis	Agar diffusion Microdilution	Khan *et al.* [49] (2017) Costa *et al.* [21] (2009); Khan *et al.* [49] (2017)
Seeds	*Candida albicans*	Agar diffusion; Macrodilution Disk diffusion Microdilution	Chandrasekaran & Venkatesalu [24] (2004) Saha *et al.* [25] (2013) Höfling *et al.* [2] (2010)
	Candida dubliniensis; Candida glabrata; Candida guilliermondii; Candida krusei;Candida lusitaniae; Candida parapsilosis; Candida rugosa; Candida tropicalis; Candida utilis	Microdilution	Höfling *et al.* [2] (2010)
Stem bark	*Candida albicans*	Disk diffusion Microdilution	Prabhakar *et al.* [51] (2008) Cartaxo-Furtado *et al.* [47] (2015)
	Candida glabrata; Candida guilliermondii; Candida krusei; Candida parapsilosis; Candida tropicalis	Disk diffusion	Prabhakar *et al.* [51] (2008)

DISCUSSION

Native to tropical regions, *Syzygium cumini* is found in several countries of the Asian, African and American continent[1,3,10,27]. The plant has recognized medicinal potential, including antidiabetic activity[10,11,18,27] and different other therapeutic purposes attributed to different pharmacological actions that can be obtained from parts of the plant such as seeds, leaves, stem and fruits[1,3,6,10-13,15-18, 27,31,35,50]. In addition, its medicinal applications also extend to the use of different parts for curative purposes of oral affections[1,10,14,19-22,24], with the demonstration of antibacterial and antifungal effects on oral microorganisms as corroborated by the literature findings mentioned earlier and showing the potencial applications of this plant to prevent and/or treat oral affections.

Within this context, the growing problem of microbial resistance to antibacterial and antifungal drugs [2,4,6,9,21,22,27,31,37,44] highlights the need for identifying alternative sources of antimicrobials [4,6,21,22,27,31,37]. Considering the importance of medicinal plants among these new antimicrobial agents [4,6,21,22,37], the finding of antimicrobial activity of *S. cumini* extracts is therefore an interesting pharmacological property among the various other biological activities associated with its use.

The promising medicinal properties associated with the extracts obtained from different parts of *S. cumini* can be explained by the presence of different groups of bioactive compounds[10-12,16,22,33]. For example, phytochemical compounds such as flavonoids, phenolics, tannins and saponins [46] have been detected in the stem bark of the plant. Furthermore, the leaves contain secondary metabolites such as alkaloids[5,22], anthraquinones[37], flavonoids[10,22,31,37], glycosides[22], phenolics[22,31,46], phlobatannins[5], saponins[5,22,46], steroids[5,22], tannins[5,10,22,37,46], triterpenoids[5,10,37] and terpenoids[22]. The fruits of *S. cumini* contain alkaloids[26], anthocyanins[10], anthocyanidins[28] , flavonoids[25,26], phenolics[25,26], saponins, steroids and tannins[26], while the seeds contain chemical compounds such as alkaloids[6,10,45,46,52], flavonoids[6,10,25,44,46,52], glycosides[6,10,44,52], phenolics[25,44,46,52], proanthocyanidins, reducing monosaccharides[52], reducing sugars[44,45,52], saponins[6,44,52], steroids[44,52], tannins[45,46] and terpenoids[6] . Finally, the roots have been shown to contain alkaloids, flavonoids, phenols and tannins[46]. Hence, since anthocyanins[2], flavonoids[2,11,22,33] , phenolic compounds[11,31,53], saponins[33], steroids[22,54] and tannins[2,11,33,50] have antimicrobial effects and secondary metabolites such as flavonoids[55,56], phenolic compounds[31], saponins[55,57] , tannins[57] and terpenes[55] exert antifungal effects, the existence of antimicrobial and antifungal activities of the extracts obtained from different parts of *S. cumini* can be justified, with these activities being corroborated by the findings of the studies mentioned earlier.

Thus, the antimicrobial effects on pathogenic microorganisms such as *Streptococcus mutans*[9,33], other bacteria of the genus *Streptococcus*[47], fungi of the genus *Candida*[2,9,47] and microorganisms associated with endodontic and periapical infections such as *Enterococcus faecalis*, *Escherichia coli* and *Staphylococcus aureus* [9], as well as microorganisms associated with infections that can potentially affect the oral cavity, such as *Neisseria gonorrhoeae*[38] and *Bacillus subtilis*[9,43], reinforce the promising medicinal effect of the *S. cumini* extract, indicating possible applications to the treatment of affections of the oral cavity like dental caries, periodontal disease, endodontic infections and oral candidiasis[9]. In addition, other biological activities such as anti-inflammatory, antioxidant and anticarcinogenic effects[16] indicate a vast and promising therapeutic potential of the extracts of this plant that go beyond the antibacterial and antifungal effects highlighted here.

CONCLUSION

The present results permit us to state that, in addition to the popular use of different parts of *S. cumini* for therapies of interest and/or for application to Dentistry, the evidence of the antibacterial and antifungal effects of their extracts on different pathogenic oral microorganisms or those that can potentially affect this site, indicates that they present a potential therapeutic activity and may be used in Dentistry for the prevention and/or treatment of oral affections.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interests.

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