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Antibacterial, Antifungal and Antiviral Properties of Malpighiaceae Family and Its Potential Impact for Oral Cavity Infectious Diseases

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Authors' contributions

This work was carried out in collaboration among all authors. Author GSVA managed the literature searches. Author MHR designed the study and wrote the first draft of the manuscript. Authors LOSV and LAGC managed the analyses of the study, reviewing and editing. All authors read and approved the final manuscript.

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ABSTRACT

Recently, the impact of oral infections on global human health and their importance in the complications of patients with some chronic conditions have been recognized. Current medical treatments deal with the specificity and resistance of pathogenic strains of the oral cavity made up of by bacteria, fungi and viruses; thus, novel substances are necessary for use as effective drugs. Plants have been a source of active chemical agents since ancient times; however, a number of family plants still remain unstudied. This is the case of Malpighiaceae, a flowering plant family that

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possesses secondary metabolites that have exhibited a variety of pharmacological effects with promising results. This review has as objective to provide an overview of the extracts and active constituents isolated from species belonging to the Malpighiaceae family, to emphasize their activities against bacteria, fungi and viruses during recent years and their potential impact on the pathogens of the oral cavity.

Keywords: Malpighiaceae; bacteria; fungi; viruses; antimicrobial; oral microbiota.

1. INTRODUCTION

Nature remains an essential source of compounds in healthcare, and particularly in the case of plants. It has been calculated that only approximately 15% of the plant species that exist in the world today have been considered for the study of their pharmacological properties [1,2]. Only in recent decades the mechanisms of action of these natural products have been described, encouraging continuing research in the pharmacology of plants [3]. In addition to this, the acceptance of persons on the use of plants as medicine renders plants highly attractive from the economic point of view, since data released by the WHO revealed that between 70% and 95% of individuals use traditional medicines for primary care worldwide. Consequently, the global market for traditional medicines has been estimated at US$ 83 billion annually, with an exponential rate of increase [4]. In this regard, recent estimates disclose that at least 25% of all modern medicines are derived either directly or indirectly from medicinal plants, and, in the case of certain classes of pharmaceuticals, such as antitumoral and antimicrobial medicines, this percentage may be as high as 60% [4,5]. This information results especially interesting when looking at the ongoing explosion of antibiotic-resistant infections that continue to plague global health care [6]. For these reasons, research on plants with potential pharmacological properties, and specifically those that possess antimicrobial activities acquire current relevance in aspects of human health within a global context.

On the other hand, one of the most interesting environments for microbial growth, due to the variety of ecologic niches and the diversity, number of species, and complexity of microbiota, such as fungi, bacteria and viruses is the human oral cavity [7]. Solely for the case of bacteria, some reports refer that over 750 species inhabit the oral cavity, among which more than 50% remain unidentified, and some of these are implicated in a number of oral diseases [8,9]. Interestingly, in that the relationship between humans and their oral microbiota begins more intensely shortly after birth and lasts a lifetime [8], this association results significant for oral and global health in humans. For example, considerable evidence suggests that poor oral health is related with systemic diseases such as rheumatoid arthritis, osteoporosis, cardiovascular diseases, poor glycemic control in diabetics, and preterm low birth weight. Even so, oral infections are also recognized as a problem in patients with some chronic conditions: human immunodeficiency virus, cancer, and pneumonia [10]. Thus, in this respect, it would appear notorious that oral microbes are involved in a number of oral diseases that impact global human health, among dental caries, periodontal disease, and candidiasis are the most common [11]. In addition to this information and especially in developing countries, it has been reported that oro-dental treatments and medicaments are usually expensive for general population; hence, people have been preferred the use of medicinal plants to treat oral afflictions [12]. Therefore, the search for novel drugs against microbes and in particular, for oral diseases, has been intensified during recent years.

Although a variety of medicinal plants has provided new and diverse chemical identities that are potentially useful as drugs, some botanical families remain unstudied. This is the case of the Malpighiaceae family, a flowering plant family which is widely represented in the New World which approximately 75 genera and 1,300 species with tropical and subtropical distributions [13]. However, this is mainly because the Malpighiaceae family possesses a number of conspicuous chemical constituents such as alkaloids, anthocyanins, flavonoids, terpenoids, and tannins that have exhibited a variety of pharmacological effects with promising results when tested as isolated or as part of an extract [14]. Thus, this review has as its objective to provide an overview of the extracts and active constituents isolated from species belonging to the Malpighiaceae family, emphasizing activities against bacteria, fungi, and viruses during recent years and their potential impact on microbes from the oral cavity.

1.1 Malpighiaceae Family: A Brief Panorama

At present, the greatest number of genera and species of Malpighiaceae thrive in South America, which is now considered its center of origin and diversification [13]. In particular, Mexico has been considered as relevant in the diversification process of Malpighiaceae, due the number of lineages that exist now in that country [15]. Thus, today in Mexico, 23 genera and 150 species are registered [16].

Malpighiaceae comprise species of discrete economic importance. A number of Malpighiaceae species are ornamental, among which *Galphimia gracilis* is probably the most common and it is characterized by yellow flowers. Due the pulpous and edible fruits of species of *Byrsonima*, *Bunchosia*, and *Malpighia* these are consumed from Mexico to Brazil [17]. Among these, *Malpighia emarginata* (popularly known as "acerola") has acquired relevance during the last decade, due to that the content of the juices of fruits from different stages of maturity help to reduce oxidative stress and may decrease genotoxicity under obesogenic conditions due the high levels of vitamin C and rutin [18].

Other species of Malpighiaceae are known for their properties exerted on the Central Nervous System (CNS) because of the content of alkaloid types, including: N,N-DiMethylTryptamine (DMT), TetraHydroHarmine (THH), harmaline, and harmine. This is the case of the species *Banisteriopsis caapi*, which is a potent hallucinogen and an ingredient of the popular sacred and psychoactive beverage known as Ayahuasca, which is widely used for prophecy, divination, and as sacrament in South America. Recently, reports indicate the potential benefit of this species for treating Parkinson disease but, at present, there is no conclusive evidence on the effectiveness and efficacy in this disease [19,20]. Diverse species from the genus *Heteropterys* also have been exerting properties on CNS. The ethanolic extract of *H. glabra* possesses anxiolytic/sedative properties [21], while *H. tomentosa* demonstrated a positive effect on memory in aged rats [22]. The methanolic extract of *H. brachiata* showed antidepressant, anxiolytic, and anticonvulsant properties; in this extract, chlorogenic acid and its methyl ester were the majority compounds [23]. The Mexican endemic species *H. cotinifolia* possess antidepressant activities in which chlorogenic acid and rutin are the main content of the extract [24].

The genus *Byrsonima* is probably that most extensively studied in the Malpighiaceae family, due to its traditional uses and its number of species (>100) [25]. Several properties have been investigated for a number of *Byrsonima* species, such as anti-inflammatory, antiulcer, antioxidant, antihyperlipidemic, antihemorrhagic, antidiarrheal, antihyperglycemic, analgesic, and spasmogenic. Some investigations have been focused on their properties against Gram-positive and Gram-negative bacteria, mycobacteria, protozoa, and fungi because of the traditional uses reported [26]. However, information on their possible chemically active compounds remains scarce.

2. SEARCH STRATEGY

Electronic databases PubMed, Reference Manager, Scopus, Web of Science and Google Scholar were systematically reviewed for publications that present data on Malpighiaceae species that exert activities on bacteria, fungi, and viruses. The structured question formulated for this search was as follows: Which species of plants belonging to the Malpighiaceae family exhibit activity on bacteria, fungi, and viruses?. Then, in accordance with the PICO [Patient Problem, (or Population), Intervention, Comparison (or Control), Outcome] strategy for this search, we combined, by using Boolean operators [27], the following keywords (Table 1): "Problem/Population" (5), "Intervention" (6), and "Outcome" (6). The previously mentioned keywords made up the PICO framework, and were the same for the string search in the English and Spanish languages. The resulting articles strictly fulfilled the search inclusion criteria in order to be selected; otherwise, they were excluded.

2.1 Exclusion and Inclusion Criteria

In the present search, the articles eligible for inclusion were those that had in the content of the title or in the abstract, a member of the Malpighiaceae family and the antimicrobial activity. For this purpose, as member of the Malpighiaceae family, we included the names of species and genera, and, in the case of antimicrobial activity, bacteria, fungi, and viruses. Other inclusion criteria were: (i) articles published in the time frame from January 1990 to July 28, 2020; (ii) articles published in English and Spanish, (iii) articles whose research strategy

includes controlled studies. The exclusion criteria were: (i) articles published outside the established time frame, (ii) literature reviews, (iii) and articles that did not include antimicrobial activity of medical interest.

The initial screening of the title and the abstract served to select articles for further reading and analysis, in order to avoid misleading data. Afterward, the articles that were included were classified according to the respective antimicrobial activity.

3. FINDINGS OF THE PICO SEARCH FOR THE MALPIGHIACEAE FAMILY AND ANTIMICROBIAL ACTIVITY

The initial search yielded 57 articles, among which 17 were eliminated due to being duplicates. From the remaining 40 articles, 30 were excluded by criteria described later and only 10 met the inclusive criteria. Fig. 1 presents a PRISMA flow chart to explain this process.

Table 1. PICO strategy. The keywords of each column were combined by "AND" and separated by "OR" for the search

Problem/Population	Intervention	Outcome
Bacteria	Malpighiaceae	Antibacterial
Fungi	Secondary metabolism	Antibiotic
Mycosis	Metabolism	Antimycotic
Virus	Plant extract	Antivirus
Infection	Extract	Fungicide
	Effect	Fungistactic

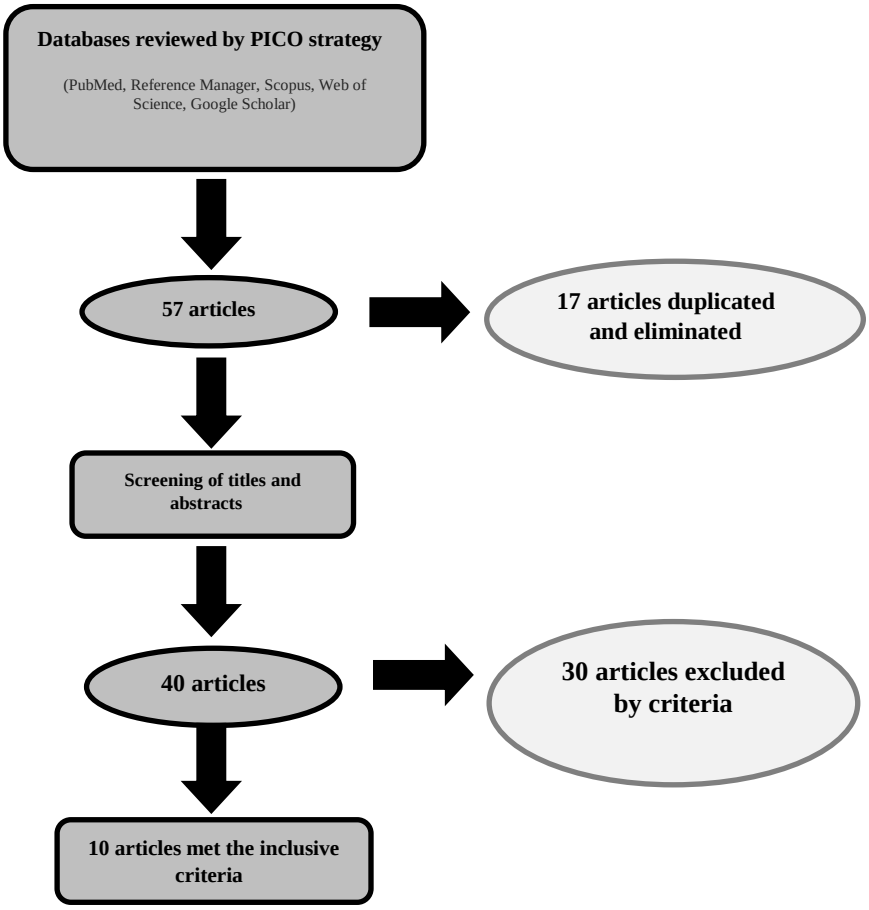

Fig. 1. PRISMA flow chart of exclusion / inclusion criteria. The search yields 17 duplicates from cross results among the groups of bacteria, fungi, and viruses. 10 articles met the inclusive criteria

Table 2. Summary of the articles included according with the criteria of search

Author	Inclusive criteria	Malpighiaceae species	Principal findings	Extract/compound
Bonacorsi et al. 2009 [28]	Antibacterial activity	*Byrsonima crassa* Nied.	*B. crassa* leaves extract possess components against *Helicobacter pylori*	Methanolic and chloroformic extracts
Santos et al. 2012 [29]	Antibacterial activity	*Byrsonima intermedia* A. Juss	*B. intermedia* leaf extract presents gastroprotective, ulcer-healing, antibacterial, and antidiarrheal activities	Methanolic extract contents gallic acid, 3,4-di-*O*-galloylquinic acid, methyl gallate, catechin, epicatechin, 1,3,5-tri-*O*-galloylquinic acid, 1,3,4,5-tetra-*O*-galloylquinic acid, quercetin-3-*O*-β-galactopyranoside, quercetin-3-(2″-*O*-galloyl)-*O*-β-galactopyranoside, quercetin-3-*O*-α-arabinopyranoside, quercetin-3-*O*-(2″-*O*-galloyl)-α-arabinopyranoside and amentoflavone
Olugbuyiro et al. 2010 [30]	Antibacterial activity	*Flabellaria paniculata* Cav.	*F. paniculata* exhibit wound healing properties and antibacterial in vivo activities on *Staphylococcus aureus* and *Pseudomonas aeruginosa*	Chloroform and aqueous fractions of the methanolic extract
Motohashi et al. 2004 [31]	Antibacterial activity	*Malpighia emarginata* DC.	Fractions of acetone and hexane extracts were highly cytotoxic against tumor cell lines such as human oral squamous cell carcinoma (HSC-2) and human submandibular gland carcinoma (HSG). Concerning extracts and fractions of hexane and ethyl acetate, although they showed some relatively higher anti-bacterial activity on Gram-positive *Staphylococcus epidermidis* ATCC 1228, they did not exhibit activity	Acetone, hexane and ethyl acetate extracts and fractions

Author	Inclusive criteria	Malpighiaceae species	Principal findings	Extract/compound
			against Gram-negative species *Escherichia coli* and *Pseudomonas aeruginosa*, *Helicobacter pylori*, two *Candida* species, and HIV. However, hexane fractions exerted higher tumor-specific cytotoxicity and showed higher multidrug resistance (MDR) reversal activity, in which the radical-mediated oxidation is not involved in the induction of tumor-specific cytotoxic activity	
Hussain et al. 2014 [32]	Antifungal activity	*Acridocarpus orientalis* A. Juss	Flavonoids morin and morin-3-*O*-β-D-glucopyranoside were tested for anticancer, allelopathic, antifungal and antioxidant activities. In the case of antifungal properties, both flavonoids inhibited the growth of *Fusarium oxysporum* while they did not show inhibition against *Chaetomium globosum*, *Alternaria alternate* and *Aspergillus niger*. Concerning anticancer activities, only morin tested at the 100 ppm concentration was able to reduce cancer cell viability in HepG2, HT29 and HCT116 cell lines. For allelopathic properties, both flavonoids showed significantly activity on the growth of various pathogenic fungi and phytotoxic activity against lettuce seed at higher concentrations. Finally, both	Morin and morin-3-*O*-β-D-glucopyranoside

Author	Inclusive criteria	Malpighiaceae species	Principal findings	Extract/compound
			flavonoids exhibited strong antioxidant activities	
Oliveira et al. 2018 [33]	Antifungal activity	*Banisteriopsis argyrophylla* (A. Juss.) B. Gates	The ethyl acetate fractions exerted antifungal activities against *Candida* spp. (MIC) between 31.25 and 93.75 µg/ml, while the compound (–)-catechin exhibited a MIC of 2.83 µg/ml against *Candida glabrata*. Different ethyl acetate fractions showed inhibitory activities on the growth of *C. albicans*, *C. glabrata,* and *C. tropicalis* between (5.86–46.87 µg/ml). Although all samples were tested for Vero cells, no significant cytotoxic activities were found	Ethanolic extract, ethyl acetate fraction and compounds (-)-catechin, quercetin-3-*O*-b-D-Glc, quercetin-3-*O*-b-D-Ga, quercetin-3-*O*-b-L-Ara, quercetin-3-*O*-b-D-Xy, quercetin-3-O-a-L-Rha, kaempferol-3-*O*-a-L-Rha, quercetin-3-*O*-(2''- galloyl)-a-L-Rha, quercetin-3-*O*-(3''- galloyl)-a-L-Rha, kaempferol-3-*O*-(2''- galloyl)-a-L-Rha
Barros et al. 2019 [34]	Antifungal activity	*Malpighia emarginata* DC.	The saline extract of *Malpighia emarginata* with high concentration of flavonoids and phenolic acids exhibited antioxidant (through DPPH, ATT, and FRAP assays) and antifungal properties [*Candida albicans* (URM 5901), *C. krusei* (URM 6391), *C. tropicalis* (URM 6551), *C. parapsilosis* (URM 6951), and *C. glabrata* (URM4246)]. Additionally, the saline extract of *Malpighia emarginata* was not cytotoxic against mouse splenocytes (more than 90%), inducing a high proliferation index in these cells, showing the safe use of *M. emarginata*	Saline extract and compounds rhinocerotinoic acid, quinic acid, dimethoxycurcumin, protocatechuic acid, tolypodiol, pauciflorol A, gentisic acid, matricin, gallocatechin, 11a-hidroxi-3,7-dioxo-5a-lanosta-8,24 (E)-dien-26-oic acid, cicutoxin, salicylic acid, 2,5 ihydroxybenzaldehyde, apigenin-7-*O*- glucoside, magnosalicin, apigenin-8-*O*-glucoside, and isotriptophenolide

Author	Inclusive criteria	Malpighiaceae species	Principal findings	Extract/compound
Melo et al. 2008 [35]	Antiviral activity	*Heteropterys aphrodisiaca* O. Mach.	Although the compound 2,3,4,6-tetra-*O*-(3-nitropropanoyl)-*O*-a-D-glucopyranoside exhibited some discrete inhibition on poliovirus type 1 (PV-1) and bovine herpes virus type 1 (BHV-1), this activity was not significant (>50 µg/ml)	2,3,4,6-tetra-*O*-(3-nitropropanoyl)-*O*-a-D-glucopyranoside
Matsuse et al. 1998 [36]	Antiviral activity	*Tetrapteris macrocarpa* Johnst.	A screening of 39 Panamanian medicinal plants against HIV. Extracts of 4 species showed potent inhibition against HIV-RT, among these, the methanolic extract of *Tetrapteris macrocarpa* (Malpighiaceae) (IC_{50}: 8 µg/ml), while 7 species exhibited moderate inhibition on HIV-PR. Additionally, *Jatropha curcas* strongly inhibited the HIV-induced cytopathic effects with low cytotoxicity. Only the compounds corilagin and quercetin 3-*O*-b-D-glucopyranoside, magnesium lithospermate, calcium rosmarinate, and magnesium rosmarinate isolated from *Chamaesyce hyssopifolia* (Euphorbiaceae) exerted potent inhibition on HIV-RT through non-competitive mechanism with respect to the substrate.	Aqueous or methanolic extract. Compounds quercetin, quercetin 3-*O*-a-L-arabinopyranoside, quercetin 3-*O*-bD-xylopyranoside, quercetin 3-*O*-b-D-glucopyranoside, quercetin 3-*O*-b-D-galactopyranoside, apigenin 7-*O*-b-D-glucopyranoside, kaempferol 3-*O*-b-D-glucopyranoside, gallic acid, gallic acid methyl ester, corilagin, and 1,3,4,6-tetra-*O*-galloyl-b-glucopyranose, magnesium lithospermate, calcium rosmarinate and magnesium rosmarinate.
Junior et al. 2005 [37]	Antibacterial and antifungal activity	*Heteropterys aphrodisiaca* O. Mach.	The antibacterial [*Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Bacillus subtilis* (ATCC 6623), *Pseudomonas aeruginosa* (ATCC 15442)], and	2,3,4,6-tetra-*O*-(3-nitropropanoyl)-*O*-β-D-glucopyranoside

Author	Inclusive criteria	Malpighiaceae species	Principal findings	Extract/compound
			the antifungal [(*Candida albicans*, *C. parapsilosis*, *C. krusei*, and *C. tropicalis*) activities were evaluated for the compound 2,3,4,6-tetra-*O*-(3-nitropropanoyl)-*O*-β-D-glucopyranoside]. The antifungal activity was stronger than the antibacterial activity, in which the minimal fungicidal concentration (MCF) was 250 µg/ml against all *Candida* species	

The 30 articles were excluded due to the following reasons: off-topic [not medical interest, biotechnology, medical interest but not according to the antimicrobial activity (18)], data omission [mostly, the articles did not indicate the plant species or the results were not shown (6)], Malpighiaceae was not the subject of study (5), and antimicrobial activity was not in the title nor in the abstract (1).

The 10 articles that met the inclusive criteria are displayed in Table 2 and are classified by antimicrobial activity. In general the articles that studied the antibacterial activity of Malpighiaceae family constituted 50% of the articles included; while antifungal studies constituted 40% of all articles included. The most studied genus was *Candida* spp.

4. DISCUSSION

The present contribution included the literature available on the plant species belonging to the Malpighiaceae family that possess active constituents against bacteria, fungi, and viruses. Antibacterial was the main activity found in the literature reviewed, following by antifungal and antiviral activities. Although a variety of crude extracts, such as methanolic, aqueous, ethanolic, chloroformic, acetonic, hexanic, ethyl acetate, and saline extracts had been prepared and evaluated for antimicrobial activity, in these reviewed papers, the fractions and compounds isolated from these crude active extracts had been identified predominantly as polyphenols, particularly as flavonoids and phenolic acids (Table 2). These findings are in agreement with many other reports in the literature, since the flavan-3-ols and flavonols have been widely recognized as antibacterial, antifungal, and antiviral agents [38]. However, from the literature considered in the present review, the manuscript that stands out due its representing the most extensive phytochemical study of the Malpighiaceae family with antibacterial properties (Table 2), is that concerning the species *Byrsonima intermedia* with activity against *Helicobacter pylori*, *Escherichia coli*, and *Staphylococcus aureus*, in which the antidiarrheal and anti-inflammatory effects observed were attributed to the presence of the oligomeric proanthocyanidins and flavonoids identified by the authors [29].

Regarding antiviral activity, a remarkable manuscript for the present review, was that which exhibited a wide phytochemical analysis carried on the species *Tetrapteris macrocarpa*, in which, in addition to flavonoids and phenolic compounds, tannins were identified as a conspicuous group that previously had revealed inhibitory effects against HIV replicative enzymes such as RT and PR [36].

For the case of antifungal activity, although flavonoids and phenolic acids are the compounds most detected in the Malpighiaceae species cited by authors (Table 2), it results interesting to point out the diversity of the chemical groups detected in addition to flavonoids and phenolic acids as follows: terpenes, ketones, stilbenoids, and polyacetylene hydrocarbons, probably related with the saline extraction [34]. Likewise, the microorganism tested with most frequency for this activity in the literature reviewed in the present contribution was *Candida* spp., due its relevance as a pathogen, since *Candida* species are the most frequently microorganisms recovered from human fungal infection, especially in oral cavity [39,40], and also because recent data has demonstrated that infections caused by *Candida* species have risen significantly worldwide [41,42]. Oral candidiasis is the most common oral infection. Two main clinical forms of oral candidiasis have been described: pseudomembranous and erythematous. In the case of erythematous oral candidiasis, this clinical form has been associated with the use of acrylic dental prostheses (denture stomatitis). Epidemiological studies report a prevalence of prosthetic stomatitis among dental prosthetic users of up to 70%. Denture stomatitis is a common inflammatory reaction generally associated with *Candida* species, particularly *Candida albicans* [43]. Additionally, *Candida albicans* possess high virulence, the ability to adhere to acrylic (denture surfaces) and form biofilms in the oral mucosa. This fact acquires relevance due to the high prevalence of dental prosthesis users throughout the world, and the possibility of developing denture stomatitis. In such case, it is essential to increase phyto-pharmacological anti-candidal drugs, especially due to the increase in *Candida* strains resistant to antifungal agents conventionally used. In the case of pseudomembranous oral candidiasis, this clinical form is more frequent in children and in immunodeficient subjects, such as patients suffering chronic and degenerative diseases, cancer, or HIV infection. In HIV+/AIDS patients the presence of oral pseudomembranous candidiasis has an important diagnostic and prognostic value. Therefore, its control and

treatment is important in HIV+/AIDS patients [44].

Additionally, the emerging and increment of candidemias in hospitals has become more common, contributing mainly to the mortality of immunocompromised patients, such as those with AIDS, cancer, diabetes, chronic kidney disease, and organ transplantation [33]. In contrast to antibiotic-resistant infections, the study and development of antifungal agents have been discrete. This may be due to the mechanism of antifungal resistance, especially in the case of *Candida* spp., in which resistant strains can display a mechanism of inherent or acquired resistance. This may also be because the complex mechanisms of initial colonization of *Candida* spp. where adherence and biofilm formation are crucial. However, these mechanisms have not been fully understood [41,45].

Even when extracts and compounds obtained from Malpighiaceae species have exhibited properties against bacteria, fungi, and viruses, as we previously noted, the oral cavity represents an interesting object-of-study, in that the microorganisms that cause its diseases could be opportunistic and resistant strains. In addition, these could be because these infections are ascending in number and severity of cases worldwide, affecting the general health. For these reasons, searching for novel chemical agents of natural origin seems to be an alternative to explore for future candidates-of-study. In this regard, in the present review, one of the most interesting findings is the recognition of the compound 2,3,4,6-tetra-*O*- (3-nitropropanoyl)-*O*-β-D-glucopyranoside as an antimicrobe isolated from the Malpighiaceae family (Table 2), because of the antibacterial and antifungal activities against microbes that can cause infection in the oral cavity, such as *Candida albicans*, *C. parapsilosis*, *C. krusei*, *C. tropicalis* and *Staphylococcus aureus* [37]. Additionally, another aspect lies in that nitro aliphatic glycoside compounds have been found at present in some high plant families, such as Leguminosae (Fabaceae) [46,47], Malpighiaceae [48] and Corynocarpaceae [49], even more so, the nitro aliphatic compounds were proposed in the past as chemotaxonomic markers of the genus *Heteropterys* (Malpighiaceae) [37]. Thus, further studies of nitro aliphatic glycoside compounds obtained from Malpighiaceae species appear to be attractive for providing potential new pharmacological agents.

Therefore, taking together all the information presented in the present contribution, and to the best of our knowledge, the present study is the first report on the Malpighiaceae family and its pharmacological data for oral diseases. Thus, the Malpighiaceae family could be considered a potential source of secondary metabolites that could provide new therapeutic agents for the treatment of human oral infectious diseases. In addition, the development of dosage forms such as toothpaste, mouthwash and gel appears to comprise a solid possibility because of the recent available technologies that have been used for certain other plant extracts [50].

On the other hand, the present review was conducted following a PICO strategy based on the comprehensiveness that this tool can offer on comparison with others such as SPIDER or PICOS, and also to the feasibility for searching in a variety of databases [51]. Therefore, the present contribution is according with the increasing amount of qualitative state-of-the-art systematic reviews that also employ PICO as an effective search strategy for biomedical research studies [52]; but must of all, the present review pretends to provide knowledge in the area of natural chemical agents against microorganisms, and especially those with antibacterial, antifungal, and antiviral properties, through an exhaustive search of the species of the Malpighiaceae family, in which, these chemicals may be considered as future candidates of studies for pathogens of the oral cavity.

5. CONCLUSION

To the best of our knowledge, the present study is the first report of the Malpighiaceae family and its pharmacological data for oral infectious diseases. The Malpighiaceae family possesses the potential to be considered as a source of secondary metabolites with antibacterial, antifungal, and antiviral properties that could be useful for human oral infectious diseases, maintaining a general good state of health and avoiding complications in patients with chronic diseases. The number of species belonging to the Malpighiaceae that continue to remain unstudied encourages further studies on the development of therapeutic agents.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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