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A Review on medicinal plants with antimicrobial activity

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ABSTRACT

Plants have been used for thousands of years to flavour and conserve food, to treat health disorders and to prevent diseases including epidemics. The knowledge of their healing properties has been transmitted over the centuries within and among human communities. Active compounds produced during secondary vegetal metabolism are usually responsible for the biological properties of some plant species used throughout the globe for various purposes, including treatment of infectious diseases. Currently, data on the antimicrobial activity of numerous plants, so far considered empirical, have been scientifically confirmed, concomitantly with the increasing number of reports on pathogenic microorganisms resistant to antimicrobials. Products derived from plants may potentially control microbial growth in diverse situations and in the specific case of disease treatment, numerous studies have aimed to describe the chemical composition of these plant antimicrobials and the mechanisms involved in microbial growth inhibition, either separately or associated with conventional antimicrobials. Thus, in the present work, medicinal plants with emphasis on their antimicrobial properties are reviewed.

INTRODUCTION

The use of plants for treating diseases is as old as the human species. Popular observations on the use and efficacy of medicinal plants significantly contribute to the disclosure of their therapeutic properties, so that they are frequently prescribed, even if their chemical constituents are not always completely known. All over the globe, especially in South American countries, the use of medicinal plants has significantly supported primary health care (1). From 250 to 500 thousand plant species are estimated to exist on the planet, and only between 1 and 10% are used as food by humans and other animals (2). Brazil has the world's highest biodiversity, accounting for over 20% of the total number of known species. This country presents the most diverse flora, with more than 55 thousand described species, which corresponds to 22% of the global total. Such biodiversity is followed by a wide acceptance of the medicinal plant use (3). Most of the Brazilian population (80%) consumes only 37% of the commercially available drugs and depend almost exclusively on medicines of natural origin (4).

Thus, phytotherapics entered the market promising a shorter and cheaper production, since basic requirements to use medicinal plants do not involve strict quality control regarding safety and efficacy compared to the other types

of drugs (5). Infectious diseases represent an important cause of morbidity and mortality among the general population, particularly in developing countries.

Therefore, pharmaceutical companies have been motivated to develop new antimicrobial drugs in recent years, especially due to the Biological properties of medicinal plants: a review of their antimicrobial activity Silva NCC (1), Fernandes Júnior A (1) (1) Department of Microbiology and Immunology, Botucatu Biosciences Institute, São Paulo State University (UNESP – Univ Estadual Paulista), Botucatu, São Paulo State, Brazil.

ANTIMICROBIAL PROPERTIES OF MEDICINAL PLANTS

The antimicrobial actions of "carqueja" (Baccharis trimera Less.) decoction on grampositive (Staphylococcus aureus and Streptococcus uberis) and gram-negative (Salmonella gallinarum and Escherichia coli) bacterial strains were evaluated and it was found that the former microorganisms are more sensitive to this herb than the latter, which corroborates previous studies (9).

The substances that demonstrated inhibitory activity were ethanol extract and its fractions (n-hexane, water, chloroform, dichloromethane, ethyl acetate and n-butanol) from Punica granatum fruit (pomegranate) and parts of T. avellanedae wood (purple trumpet tree). The greatest activities were found in the ethyl acetate fraction from P. granatum and hexane and chloroform fractions from T. avellanedae.

As to the common yarrow (Achillea millefolium), its essential oil (obtained from stem and leaves) presents higher antimicrobial activity than its respective extracts (methanol extract separated by chloroform into parts that were not all soluble). The oils prevented the growth of Streptococcus pneumoniae, Clostridium perfringes and Candida albicans and slightly inhibited Mycobacterium smegmatis, Acinetobacter lwoffii and Candida krussei (12)

A study evaluated the effects of some plant extracts (aqueous and 40% hydroalcoholic) against bacteria found in the oral cavity of dogs (13). It found that standard S. aureus strain and isolated Streptococcus oralis and Streptococcus mitis strains were sensitive to extracts from garlic (Allium sativum), "espinheira santa" (Maytenus ilicifolia) and guava tree leaves (Psidium guajava). Similarly, antibacterial properties against Staphylococcus aureus were found in chamomile.

The phenolic compounds present in its ethanol extract are responsible for this activity (14). It was also reported that the aqueous extract from the artichoke (Cynara scolymus) and the ethanol extracts (80%) from both artichoke and "macela" (Achyrocline satureioides) inhibited the growth of Bacillus cereus, B. subtilis, Pseudomonas aeruginosa and S. aureus (14). In Argentina, terpene compounds (eugenol, geraniol, thymol and carvacrol) derived from essential oils of native plants showed inhibitory effects on MRSA (15).

cyclohexane extract of Monodora myristica fruit and the ethyl acetate extract from the stem bark of Albizia gummifera were effective in inhibiting C. albicans and Candida krusei (36). As in previous studies, the antimicrobial activity of essential oils from oregano (Origanum vulgare), thyme (Thymus vulgaris), marjoram (Origanum majorana) and basil (Ocimun basilicum) was evaluated in meat products against strains of L. monocytogenes and Salmonella Enteritidis (37). It was reported that all oils showed antibacterial activity and that,

particularly, gram-positive bacteria were more susceptive to them. Based on the aforementioned data, it is possible to conclude that the literature on testing antimicrobial activity of plant products is broad, including an increasing number of publications per year. Therefore, it is difficult to integrate all those numerous studies on the antimicrobial action of plant products into the present review; a multidisciplinary approach to this theme is increasingly required.

There areCytotoxicity and antibacterial activities of *Euphorbia schimperiana* total extract, fractions, and isolated secondary metabolites were investigated. The cytotoxicity assays were assessed against four human cancer cell lines HCT116, MCF7, HePG2, and PC3 as well as against normal cell line RPE1. The plant total extract, fractions, and pure compounds were more effective against PC3 and HepG2 cell lines than HCT116 and MCF7. Significant results were observed for ethyl acetate and *n*-hexane fractions against PC3 with IC_{50} of 4.7 µg/ml for ethyl acetate, however, *n*-hexane exhibited 100% cytotoxicity up to 6.25 µg/ml. The antibacterial potential activity was achieved on four pathogenic Gram-positive and four Gram-negative bacteria. The results showed that ethyl acetate and *n*-butanol fractions had more valuable results ($p < 0.05$) against the tested pathogenic bacteria than total extract and *n*-hexane fraction. The major components of *n*-hexane were determined by GCMS analysis and 14 compounds were tentatively identified. Chromatographic isolation of ethyl acetate and *n*-butanol afforded 7 secondary metabolites: Quercetin **(1)**, quercetin-3-*O*-*α*-glucuronide **(2)**, quercetin-3-*O*-*β*-*D*-glucuronide-methyl ester **(3)**, quercetin-3-*O*- *α*-*L*-rhamnoside **(4)**, 3,3′-di-*O*-methylellagic acid **(5)**, *3,3′-di-O*-methyl-ellagic acid-4-*β*-*D*-xylopyrnoside **(6)** and 4-*O*-ethylgallic acid **(7)**. Structures of the obtained compounds were elucidated by nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry. The inhibition zones of pure compounds revealed that compounds **4,6** and **7** exhibited antibacterial efficiency against all tested strains. A significant inhibition for 4-*O*-ethylgallic acid (**7)** was recorded against *Listeria monocytogenes* (LM) and *Staphylococcus aureus* (SA). Promising cytotoxicity of pure compounds was observed for 3,3′-di-*O*-methylellagic acid (**5)** against PC3 with IC_{50} of 5.5 µg/ml.

There are variety of medicinal plants like *Euphorbia schimperiana* ,calotropus prucera , ***Cordia gilletii*** , *Thymus vulgaris* and *Pimpinella anisum* etc, have wide range of activity including antimicrobial avtivity like antifungal ,antibacterial,antiviral and so on hence these plants find application as an anti-inflammatory agents. This study provides an evidence that these plants have antimicrobial properties.

Literature review

1. **Roshina et, al (2009)** Suggested that antimicrobial activities of the crude ethanolic extracts of five plants were screened against multidrug resistant (MDR) strains of Escherichia coli, Klebsiella pneumoniae and Candida albicans. ATCC strains of Streptococcus mutans, Staphylococcus aureus, Enterococcus faecalis, Streptococcus bovis, Pseudimonas aeruginosa, Salmonella typhimurium, Escherichia coli, Klebsiella pneumoniae and Candida albicans were also tested. The strains that showed resistance against the maximum number of antibiotics tested were selected for an antibacterial assay. The MDR strains were sensitive to the antimicrobial activity of Acacia nilotica, Syzygium aromaticum and Cinnamum zeylanicum, whereas they exhibited strong resistance to the extracts

of Terminalia arjuna and Eucalyptus globulus. Community-acquired infections showed higher sensitivity than the nosocomial infections against these extracts. The most potent antimicrobial plant was A. nilotica (MIC range 9.75-313µg/ml), whereas other crude plant extracts studied in this report were found to exhibit higher MIC values than A. nilotica against community acquired as well as nosocomial infection. This study concludes that A. nilotica, C. zeylanicum and S. aromaticum can be used against multidrug resistant microbes causing nosocomial and community acquired infections.

2. **Balchew dasta et, al ()** Performed an experiment on A total of 315 extracts/fractions from 63 traditionally used Ethiopian plants were subjected to antimicrobial screening using known strains of *Staphylococcus aureus, Salmonella gallinarum, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Candida albicans*. The agar plate well-diffusion method was used at a sample concentration of 1000 µgml; it was found that all of the plants showed activity against one or more of the microorganism(s). Direct aqueous extracts from six plants were found to be active against all of the test organisms. These findings confirm traditional therapeutic claims for aqueous dosage forms of these herbs. The relative susceptibility of the test organisms to the five types of extracts/fractions indicated a decreasing rank order of: *S. aureus P. aeruginosa C. albicans S. gallinarum E. coli K. pneumoniae* and *P. vulgaris*.

3. **Mohhamad H. et,al (2009)Suggested that** *alotropis procera* (family Apocynaceae) is a valuable medicinal plant as it contains many valuable phytochemicals such as glycosides (mostly cardenolides), flavonoids, triterpenes, alkaloids, steroids, saponins, proteins and enzymes. Multiparous biological activities such as anti-inflammatory, antioxidant, anticancer, wound healing and wideranging antimicrobial activities of *C. procera* have been well investigated and reported. The main aim of this review was to present the encompassing information regarding antimicrobial activities of *C. procera* latex, different crude extracts and some isolated compounds which have been tested for antimicrobial property. Comprehensive data extracted from earlier as well as recently published original articles regarding antibacterial, antifungal, anti-protozoal and antiviral properties of *C. procera* were discussed and summarised in tabular forms. The compiled data comprised of plant parts, geographical origin, type of tested extracts/fractions, test model, used doses, tested microorganisms, obtained results and relevant references. In addition, the isolated antimicrobial pure compounds of *C. procera* are also discussed in a separate section. The analysis and information presented in this review identified the existing critical knowledge gaps in the research and also explored the future perspectives and further research opportunities of *C. procera*.

4. **Amini M.H et, al (2021)** *Suggested that Calotropis procera* (family Apocynaceae) is a valuable medicinal plant as it contains many valuable phytochemicals such as glycosides (mostly cardenolides), flavonoids, triterpenes, alkaloids, steroids, saponins, proteins and enzymes. Multiparous biological activities such as anti-inflammatory, antioxidant, anticancer, wound healing and wide ranging antimicrobial activities of *C. procera* have been well investigated and reported. The main aim of this

review was to present the encompassing information regarding antimicrobial activities of *C. procera* latex, different crude extracts and some isolated compounds which have been tested for antimicrobial property. Comprehensive data extracted from earlier as well as recently published original articles regarding antibacterial, antifungal, anti-protozoal and antiviral properties of *C. procera* were discussed and summarised in tabular forms. The compiled data comprised of plant parts, geographical origin, type of tested extracts/fractions, test model, used doses, tested microorganisms, obtained results and relevant references. In addition, the isolated antimicrobial pure compounds of *C. procera* are also discussed in a separate section. The analysis and information presented in this review identified the existing critical knowledge gaps in the research and also explored the future perspectives and further research opportunities of *C. procera*. Amini, M. H(12)

5. **Jermeie ngezehayo et, al (2015)** Surveyed in different markets and herbal shops in Bujumbura city, medicinal plants sold to treat microbial infections, with particular emphasis on the different practices of traditional healers (THs) regarding plant parts used, methods of preparation and administration, dosage and treatment duration. The ethnobotanical survey was conducted by interviewing, using a pre-set questionnaire, sixty representative healers, belonging to different associations of THs approved and recognised by the Ministry of Health. Each interviewed herbalist also participated in the collection of samples and the determination of the common names of plants. The plausibility of recorded uses has been verified through an extensive literature search.

6. **O.N Okusa et,al (2005)** ***Cordia gilletii*** De Wild (Boraginaceae) root bark is traditionally used in Democratic Republic of Congo (DRC) for the treatment of various disorders, including malaria, diarrhoea, wounds and skin diseases; part of these activities may rely on antimicrobial and antioxidant properties. Successive extracts of root barks powder with *n*-hexane, dichloromethane, ethyl acetate, methanol and water were tested for antimicrobial activity, both direct and indirect (antibiotic resistance reversal), against 10 strains of bacteria and 1 strain of fungi by broth microdilution and agar diffusion methods. The eventual synergy between plant extracts and antibiotics was investigated by the determination of the fractional inhibitory concentration index (FIC index). The methanol extract showed direct antimicrobial activity against all tested microorganisms with minimum inhibitory concentrations (MIC) ranging between 125 and 1000 µg/ml, whereas the ethyl acetate and the dichloromethane extracts showed activity on four and three strains, respectively. 200 µg/ml of *n*-hexane and dichloromethane extracts decreased the MICs of penicillin and streptomycin 4–64-fold for methicillin-resistant *Staphylococcus aureus*. A synergistic effect was found between the methanol extract and tetracycline, whereas additive effects were observed for the other combinations tested. The methanol and dichloromethane extracts showed the greater antioxidant activity by scavenging the free radical DPPH with IC_{50} values of 3.2 and 8.1 µg/ml, respectively. These results support the use of the plant in the treatment of infectious diseases and wounds; they warrant further studies as to the nature of active compounds.

7. **Salha al jubiri et , al (2021)** Suggested that cytotoxicity and antibacterial activities of *Euphorbia schimperiana* total extract, fractions, and isolated secondary metabolites were investigated. The cytotoxicity assays were assessed against four human cancer cell lines HCT116, MCF7, HePG2, and PC3 as well as against normal cell line RPE1. The plant total extract, fractions, and pure compounds were more effective against PC3 and HepG2 cell lines than HCT116 and MCF7. Significant results were observed for ethyl acetate and *n*-hexane fractions against PC3 with IC_{50} of 4.7 µg/ml for ethyl acetate, however, *n*-hexane exhibited 100% cytotoxicity up to 6.25 µg/ml. The antibacterial potential activity was achieved on four pathogenic Gram-positive and four Gram-negative bacteria. The results showed that ethyl acetate and *n*-butanol fractions had more valuable results ($p < 0.05$) against the tested pathogenic bacteria than total extract and *n*-hexane fraction. The major components of *n*-hexane were determined by GCMS analysis and 14 compounds were tentatively identified. Chromatographic isolation of ethyl acetate and *n*-butanol afforded 7 secondary metabolites: Quercetin **(1)**, quercetin-3-*O*-*α*-glucuronide **(2)**, quercetin-3-*O*-*β*-*D*-glucuronide-methyl ester **(3)**, quercetin-3-*O*- *α*-*L*-rhamnoside **(4)**, 3,3′-di-*O*-methylellagic acid **(5)**, *3,3′-di-O*-methyl-ellagic acid-4-*β*-*D*-xylopyrnoside **(6)** and 4-*O*-ethylgallic acid **(7)**. Structures of the obtained compounds were elucidated by nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry. The inhibition zones of pure compounds revealed that compounds **4,6** and **7** exhibited antibacterial efficiency against all tested strains. A significant inhibition for 4-*O*-ethylgallic acid (**7)** was recorded against *Listeria monocytogenes* (LM) and *Staphylococcus aureus* (SA). Promising cytotoxicity of pure compounds was observed for 3,3′-di-*O*-methylellagic acid (**5)** against PC3 with IC_{50} of 5.5 µg/ml.

8. **Hseih P.C et , al (2000)** Performed an experiment on the combined extracts of corni fructus, cinnamon and Chinese chive were used to evaluate its antimicrobial activity on common foodborne micro-organisms, including bacteria, yeasts and moulds. The combined extract (8:1:1, v/v/v) showed an entire antimicrobial spectrum and outstanding inhibitory effect. The combined extract was very stable under heat treatment. The inhibitory effect of the combined extract was greater with more acidic pH values but lowered with increased pH values. With addition of metal ions, the antimicrobial activity of the combined extract was slightly affected. With addition of food additives, its antimicrobial activity was slightly enhanced, except for citric acid. When the combined extract used in food products, the expected antimicrobial effect in dumplings, guava juice and green and black tea was observed. Conclusively, in addition to be used as seasoning, the combined extract is suitable for incorporating in various food products where a naturally antimicrobial additive is desired.

9. **Firas A al et,al (2007)** Performed an experiment on Essential oils (EOs) and methanol extracts obtained from aerial parts of *Thymus vulgaris* and *Pimpinella anisum* seeds were evaluated for their single and combined antibacterial activities against nine Gram-positive and Gram-negative pathogenic bacteria: Staphylococcus aureus, Bacillus cereus, *Escherichia coli*, Proteus vulgaris, Proteus mirabilis, Salmonella typhi, Salmonella typhimurium, Klebsiella pneumoniae and Pseudomonas aeruginosa. The essential oils and methanol extracts revealed promising antibacterial activities against most pathogens using broth microdilution method. Maximum activity of *Thymus vulgaris* and *Pimpinella*

anisum essential oils and methanol extracts (MIC 15.6 and 62.5 µg/ml) were observed against *Staphylococcus aureus*, *Bacillus cereus* and *Proteus vulgaris*. Combinations of essential oils and methanol extracts showed an additive action against most tested pathogens especially *Pseudomonas aeruginosa*.

10. **Zorica Radic et, al (2011)** *Carlinae radix* is an herbal drug, commonly used by the locals in southeastern Serbia for the treatment of respiratory and urogenital diseases and, externally, for various skin conditions. There still seems to be no detailed studies correlating the chemical composition of this drug and its ethnopharmacological uses. antimicrobial activity and mode of action of *C. radix* essential oil, isolated from commercial samples (confirmation of whose true biological identity was also the aim of this work) were analyzed. Antimicrobial potential of decoctions (extracts prepared by boiling plant material in a given solvent), used in ethnomedicine preferentially to the pure essential oil, was also investigated.

Discussion and conclusions

Some general considerations must be established for the study of the antimicrobial activity of plant extracts, essential oils and the compounds isolated from them. Of utmost relevance is the definition of common parameters, such as plant material, techniques employed, growth medium and microorganisms tested. Scientific criteria should be used in the selection of the plant material. Moreover, to avoid the use of random criteria, the selection of plants should be made from an ethnopharmacological perspective. All the species tested should be J.L. R´ıos, M.C. Recio / Journal of Ethnopharmacology 100 (2005) 80–84 83 perfectly described and identified; this must include the specifics of collection including location, season, date and time of day. The use of commercial samples should be limited to cases of standardized extracts or defined phytomedicines.

The solvent and the extraction system may both modify the final results. The most appropriate method would be that in which the extract were the same as that used in folk medicine or phytotherapy, although in the lab the use of methanol or ethanol extract is much more common, sometimes making room for the essential oil. The results are notably affected. Thus, in the in vitro test carried out by Ross et al. (2001) with garlic, the activity of garlic powder against most bacteria was higher than for the plant or crude drug; however, these authors specify that garlic oil offers even greater therapeutic potential. For their part, Nostro et al. (2000) demonstrated that species such Helichrysum italicum or Phytolacca dodecandra showed moderate activity against Escherichia coli when the diethyl extract obtained after extraction of the aqueous suspension of the drug powder was used, but that there were no active extracts or fractions against this bacteria when a sequential extraction with petroleum ether, dichloromethane, dichloromethane–methanol (9:1) and methanol were used. In contrast, all the extracts were active against Propionibacterium acnes. The pH of compounds in dilutions also modifies the results, as can sometimes be observed when phenolic or carboxylic compounds are present in the extract. Not only do ionisable compounds change the activity; indeed, it has been reported that the different effects of neutral essential oil depend on the pH.

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