Antimicrobial activity of *Achyrocline satureioides* (Lam.) DC. extract in a potentizing solution

Mariana Faccini Pinheiro[1,*]
Amanda Keller Siqueira[2]
Meire Christina Seki[2]
Adriano de Oliveira Torres Carrasco[2]
Margarete Dulce Bagatini[3]
Ricardo Key Yamazaki[1]

[1]Federal University of Fronteira Sul, Rodovia BR 158, 85319-899, Laranjeiras do Sul, Brazil
[2]Midwestern State University, Alameda Elio Antônio Dalla Vecchia, 85040-167, Guarapuava, Brazil
[3]Federal University of Fronteira Sul, Rodovia SC 484, 89815-899, Chapecó, Brazil
**Corresponding author: marianafp48@gmail.com*

ABSTRACT

Achyrocline satureioides (Lam.) DC. is a medicinal plant traditionally used in Brazilian ethnomedicine through infusion and decoction for various therapeutic purposes. The objectives were to determine the antimicrobial activity of the *A. satureioides* extract against *Pseudomonas aeruginosa* and to describe a novel technique using iron dextran solution to enhance the activity of bioactive compounds and antimicrobial agents. The extract was characterized for phytochemical composition, antioxidant activity *in vitro*, and antimicrobial activity. The extract exhibited a high content of phenolic compounds and considerable antioxidant activity. Concerning the antimicrobial activity, it inhibited the development of the strain at low concentrations, with a minimum inhibitory concentration (MIC) of 0.0390 mg/ml for the pure extract and 0.0195 mg/ml for the extract diluted in iron dextran, thus presenting bacteriostatic activity at these concentrations. It showed a bactericidal activity from 10 mg/ml, with inhibition halo of 2.11±0.19 and 2.22±0.50 mm for the pure extract and 2.55±0.19 and 2.66±0.33 mm for the extract diluted in iron dextran in the disk diffusion and punch hole methods, respectively. *A. satureioides* has an important antimicrobial activity, and the iron dextran solution enhanced the effect of bioactive compounds and antimicrobial agents.

Keywords: Iron dextran, *Macela* infusion, Traditional medicine, Medicinal plant, *Pseudomonas aeruginosa*.

INTRODUCTION

Infectious diseases have emerged, and microorganisms have developed resistance to the usual treatments, leading to a critical therapeutic scenario that urgently requires new antimicrobial agents (WHO 2019). In this context, traditional medicinal plants can be a rich source of compounds for these purposes.

Brazil is a megadiverse country (Abranches 2020) with rich biological and cultural diversity. Among the various medicinal plants found in Brazil and used in local ethnomedicine, *Achyrocline satureioides* (Lam.) DC. stands out in folk medicine with various therapeutic purposes, including digestive problems, muscle pain, treatment of infections, and sleep promoters in insomniacs, among others (Lorenzi and Matos 2021).

The *A. satureioides* species belongs to the Asteraceae family and is popularly called *macela*. It is an herbaceous plant native to South America, rich in bioactive compounds that confer different therapeutic properties, especially antimicrobial activity. Several studies have shown this effect on different microorganisms, such as *Enterococcus faecalis*, *Salmonella enteritidis*, *Escherichia coli* (Mota et al. 2011), *Bacillus cereus,* and *Staphylococcus aureus* (Moresco et al. 2017).

Therefore, knowledge about the potential

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of this herb contributes to its biological conservation and the preservation of traditional knowledge. This study aimed to evaluate the antimicrobial activity of *A. satureioides* extract against *P. aeruginosa* and to describe an unprecedented methodology with the use of iron dextran solution as a potentiator of the activity of bioactive compounds.

MATERIAL AND METHODS

Plant raw material and extract preparation

The *A. satureioides* samples (inflorescences) were collected in the fall, in the morning (before sunrise), in Nova Laranjeiras city in the state of Parana, in an area belonging to the Atlantic Forest biome (25°18'22'' S; 52°32'3'' W, 756 m). The plant's name was confirmed on *Flora e Funga do Brasil* (https://floradobrasil.jbrj.gov.br - accessed March 26, 2024). The plant sample is deposited in the Coleção Biológica Realeza, Herbarium of the Federal University of Fronteira Sul (REAL), however the collection number is not yet available, nor is the computerization of the sample data. After botanical confirmation of the species, the inflorescences associated with up to three centimeters of brancheswere weighed and dried in an oven with forced air circulation at 25 ºC, then stored in plastic packaging in a light-protected environment.

The plant extract was obtained by infusion in sterile distilled water at 80 ºC, with a contact time of 15 min, in the ratio of 1 g of *A. satureioides* (inflorescence branches < 3 cm) to 100 ml of water, as described by Salgueiro et al. (2016). The extract was freeze-dried as described by Flor et al. (2011), with modifications, and stored until use.

Phytochemical characterization

Standards, reagent and solvents

The standards, reagents and solvents used in this study were purchased from Sigma-Aldrich, Merck, Darmstadt, Germany.

Content of total phenolic compounds and flavonoids

The polyphenol content was determined using the Folin-Ciocalteau method according to Bucic-Kojic et al. (2007), and the flavonoid content was determined as described by Zhishen et al. (1999). Standard curves of gallic acid and quercetin were used to determine total phenolic compounds and flavonoid equivalents in the extract, respectively.

High-performance liquid chromatography with diode array detector (HPLC-DAD)

The analysis was performed as described by Loescher et al. (2014). The freeze-dried extract was dissolved in methanol, homogenized, and filtered through PTFE syringe filters 0.22 µm diameter. Then, 1 µl of the sample was evaluated in a liquid phase chromatograph coupled to a diode array detector.

The chromatographic peaks were confirmed by comparing the retention times of the compounds in the sample with the retention times of the reference standards for quercetin, myricetin, kaempferol, epicatechin, epigallocatechin, flavone, *p*-coumaric acid, pyrocatechol, syringic acid, caffeic acid, and gallic acid.

Antioxidant activity

The results of the antioxidant analysis were expressed in µg of Trolox per gram of *A. satureioides*, using a Trolox standard curve.

DPPH• assay

The antioxidant activity of the extract against the DPPH radical (1,1-diphenyl-2-picrylhydrazyl) was determined according to the methodology described by Katalinic et al. (2006).

ABTS•+ assay

The antioxidant potential of the extract was also measured by its ability to capture the ABTS radical (2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonic acid), as described by Re et al. (1999).

FRAP assay

The ferric-reducing antioxidant power of the extract was determined according to the Benzie and Strain´s method (1996).

Selection of the microorganism

The gram-negative bacteria *Pseudomonas aeruginosa* (Schroeter) Migula (ATCC® 27853) was selected for this study because the resistant strains of this species are on the WHO priority list of antibiotic-resistant bacteria (WHO, 2017). This choice also considered the fact that bacteria of the genus *Pseudomonas* are one of the main opportunistic pathogens that affect cancer patients undergoing treatment, and in parallel to the present study, research was also carried out on the antineoplastic effect of *macela*(Paprocka et al. 2022).

Culture medium

BHI broth and blood agar were used to reactivate the strain and confirm the macroscopic aspects of the colony. Mueller-Hinton agar and Mueller-Hinton broth were used in the antimicrobial susceptibility tests. All culture media were purchased from Newprov Ltd.

Antimicrobial susceptibility testing

All procedures used in the study were carried out for pure and iron dextran-added extracts.

The freeze-dried extract was reconstituted in distilled water, comprising the pure extract and the iron dextran-based extract of known molarity for the treatment called iron dextran-added extract.

The antimicrobials ceftazidime and imipenem were used as the control group for all tests. The extract diluents (water and iron dextran solution) were also investigated for their inert nature.

In addition to the control treatments, a positive control (inoculum not exposed to either the antimicrobial or the extracts) and a negative control as an indicator of sterility (Mueller-Hinton broth without inoculum) were used to determine the minimum inhibitory concentration and minimum bactericidal concentration.

Minimum inhibitory concentration (MIC)

This test was carried out according to the methodology established by the Clinical and Laboratory Standards Institute (2015). The analysis was carried out in a microplate by exposing the standardized bacterial inoculum to the *A. satureioides* extract, starting with the mother solution (10 mg/ml) followed by 9 sequential dilutions, corresponding to 5, 2.5 1.25, 0.625, 0.3125, 0.15625, 0.07815, 0.0390, and 0.0195 mg/ml.

The inhibition of microbial growth was determined by spectrophotometry (spectrophotometer Thermo Scientific™ Multiskan FC Microplate), comparing the absorbance at time zero and the absorbance after 24 h of incubation.

Minimum bactericidal concentration (MBC)

After determining the MIC, the concentration of the pure extract and the extract diluted in iron dextran capable of inducing bacterial death was determined as described by Araújo et al. (2009).

Agar diffusion methods

Disk diffusion test

The disk diffusion test was carried out according to the methodology described by the Clinical and Laboratory Standards Institute (2015) to determine the diameter of the inhibition halo promoted by the pure extract and the extract diluted in iron dextran at the concentrations that led to growth inhibition of the targeted microorganism.

Punch hole method

The diameter of the inhibition halo provided by the pure extract and the extract diluted in iron dextran at the minimum inhibitory concentrations previously determined was also evaluated using the Kondo methodology (1976). This method is suitable for aqueous compounds deposited in standardized perforations in the inoculated agar.

Experimental design and statistical analysis

Three replicates were carried out, in triplicate, for all determinations. Data were analyzed by analysis of variance (One-Way ANOVA) followed by Tukey's test at a significance level of $p<0.05$, using Past 4® statistical software. All data were expressed as mean ± standard deviation.

RESULTS

Phytochemical characterization

Concentration of total phenolic compounds and flavonoids

The phenolic compounds content of the extract was 131.29±3.32 mg gallic acid equivalent per gram of *A. satureioides*. In turn, the flavonoids concentration was 50.25±1.09 mg of quercetin equivalent per gram.

High-performance liquid chromatography with diode array detector (HPLC-DAD)

Table 1 shows the compounds that were quantified in the *A. satureioides* extract.

Table 1. Phenolic compounds of *Achyrocline satureioides*.

Compounds	mg per gram of dry plant
Gallic acid	38.62±4.53
Caffeic acid	12.78±1.19
p-Coumaric acid	2.85±0.09

Although retention signals compatible with quercetin and kaempferol were also detected in the sample studied, it was not possible to quantify the concentration of these compounds.

Antioxidant activity

The results of the antioxidant activity of the extract are shown in Table 2.

Table 2. IC_{50} values of *Achyrocline satureioides*.

Antioxidant activity assay	IC_{50} in µg Trolox per ml of extract
ABTS •+	60.07±1.16
DPPH •	102.14±1.59
FRAP	79.24±1.44

Antimicrobial susceptibility tests

Minimum inhibitory concentration (MIC)

Bacterial growth was inhibited from the penultimate dilution of the pure extract (0.0390 mg/ml water) and the last dilution of the extract diluted in iron dextran (0.0195 mg/ml iron dextran solution).

There was growth in the positive control, while the sterility control remained sterile throughout the test. No growth inhibition was observed for the control groups with distilled water and iron dextran solution.

Minimum bactericidal concentration (MBC)

Bacterial death was induced at the highest concentration studied, which was 10 mg/ml for both the pure extract and the extract diluted in iron dextran. No bacterial death was observed for the inoculum treated with distilled water and the iron dextran solution.

Agar diffusion methods

Disk diffusion test and punch hole method

The diameter (mm) of the inhibition halos observed for the agar diffusion methods is shown in Table 3.

DISCUSSION

Bacterial growth was inhibited at a concentration of 0.039 mg/ml of the pure extract, which was potentiated at 0.0195 mg/ml of iron dextran. In turn, Joray et al. (2011) observed a higher MIC (0.500 mg/ml) than that observed in the present study for the antimicrobial activity of the ethanolic extract of *A. satureoides* against the ATCC 27853 *P. aeruginosa* strain, which was the same strain used in this study. These differences may be due to the great variation in the phytochemical composition of different *A. satureioides* samples since the biosynthesis of secondary metabolites with biological activity can be influenced by various factors such as the stage of plant development and the environmental conditions during growth (Trindade et al. 2018).

The results of minimum inhibitory concentrations were used to determine the minimum bactericidal concentration. The bacterial death occurred only in the treatment with the highest concentration (10 mg/ml) for both the pure extract and the extract diluted in iron dextran. Different results were reported by Mostafa et al. (2018), who evaluated the antimicrobial activity of *Syzygium aromaticum* (L.) Merr. & L.M.Perry and *Punica granatum* L. extracts and observed an MBC of 12.5 mg/ml for the *P. aeruginosa* strains, while the concentration of 10 mg/ml presented only a bacteriostatic effect. Those authors stated that the *P. aeruginosa strain* was the least susceptible to the extracts and had the highest MBC among the five bacterial species tested.

Concerning the disk-diffusion and Punch Hole tests, slightly smaller inhibition halos were observed for both the disks and wells containing pure *macela* extract when compared to the disk/well inoculated with *macela* extract diluted in iron dextran. However, this difference was not significant since both discs/wells were inoculated at the minimum concentration for inhibition. Although both treatments used the extract concentration that promoted similar growth inhibition, it is worth noting that the concentration of pure extract required for inhibition was double that required for the iron dextran-added extract. Anaya Muñoz et al. (2020) evaluated the effect of *A. satureioides* extract on *P. aeruginosa* using the disk diffusion test and also reported an inhibition halo when compared to the disks soaked in the plant extract. However, the authors did not mention the diameter of the inhibition halo and only reported the presence or absence of a halo.

The antimicrobial effect of *macela* against *P. aeruginosa* found in this study may be due to the high concentration of phenolic compounds present in the plant. As reported by several authors, gallic acid, para-coumaric acid, and caffeic acid were found to be antibacterial agents against gram-negative bacteria (Park and Kang 2011; Lou et al. 2012; Coelho et al. 2016; Khatkar et al. 2017).

In addition to its action against gram-negative bacteria, para-coumaric acid has a bacteriostatic effect by interfering with DNA and bactericidal activity with irreversible membrane damage, capable of attenuating pulmonary inflammation promoted by lipopolysaccharide membrane (LPS), characteristic of gram-negative bacteria (Kheiry et al. 2019; Souza et al. 2021). Gallic acid can also minimize inflammation promoted by LPS and

Table 3. Diameters of the inhibition halos (mm) of the treatments against *Pseudomonas aeruginosa.*

Method	Pure extract	Extract diluted in iron dextran	Ceftazidime	Imipenem	Distilled water	Iron Dextran solution
Disk Diffusion	2.11 ± 0.19	2.55 ± 0.19	23.11 ± 0.50	24.88 ± 0.38	0	0
Punch Hole	2.22 ± 0.50	2.66 ± 0.33	23.11 ± 0.38	25 ± 0.33	0	0

has been tested against *P. aeruginosa*, showing a bactericidal effect and potent antibiofilm activity (Borges et al. 2012; Tanaka et al. 2018; Lin et al. 2022). Concerning caffeic acid, Khan et al. (2021) reported a marked antipseudomonal effect due to the induction of bacterial death by irreversible damage to cell structures. Other bioactive components of this plant species also have antimicrobial activity, such as quercetin (Nguyen and Bhattacharya 2022), epicatechin, and catechin (Nakayama et al. 2013; Wu and Castanho 2021).

This study is the first to report the potentiating effect of bioactive compounds in iron dextran solution on antimicrobial activity. To date, no similar studies have been found in the literature, as the methodology was developed by the research team of the present study.

The difference in the results observed for the treatment diluted in iron dextran compared to the pure extract may be due to a multifactorial aspect, including the interaction between iron and the bioactive compounds, bacterial iron metabolism, and specifically, the mutual influence between these factors.

The activity of bioactive compounds can be affected by various chemical and physical elements that exist and act in a living being, such as minerals like iron (Gfeller et al. 2013; Pradhan et al. 2013; Wang et al. 2021). Iron interacts with phenols and flavonoids forming stable chelated complexes, which can minimize the degradation of these compounds and accentuate their antioxidant activity (Wu et al. 2019), and this behavior is complex and still poorly elucidated (Kejík et al. 2021).

Almost all living beings depend on iron for good metabolic reactions, leading to complex mechanisms for capturing this element. This characteristic leads some authors to believe in the possibility of using iron as an antimicrobial carrier, a strategy known as the “Trojan Horse Antibiotic” (Tillotson, 2016; Breijyeh et al. 2020; Klebba et al. 2021). *P. aeruginosa* has a considerable demand for iron, expressing various absorption mechanisms, often related to increased virulence. Studies have shown that the use of antimicrobials in formulations associated with substances related to iron absorption can guarantee greater efficiency in inactivating or killing gram-negative pathogens, especially *P. aeruginosa* (Wiener & Horanyi et al. 2011; Cheng et al. 2012; Cama et al. 2019; Bonneau et al. 2020). Therefore, the antimicrobial agents in *A. satureioides* may interact with iron and form metal complexes, thus contributing to better absorption of the compounds by the bacteria.

CONCLUSION

The *A. satureioides* extract showed high antipseudomonal activity, even at low concentrations, with a potential effect associated with iron dextran. This is the first study to demonstrate these findings. The present results suggest that this medicinal plant can be used either pure or diluted in iron dextran in therapeutic approaches against *P. aeruginosa* infections. Future studies on other microorganisms are required to elucidate the role of iron dextran in potentiating the effects of bioactive compounds and antimicrobial activity

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AUTHORS’ CONTRIBUTIONS

Conceptualization: MFP, RKY, MDB, AKS, AOTC, and MCS; methodology: MFP, AKS, and MCS; formal analysis: MFP; investigation: MFP; data curation: MFP; writing - original draft preparation: MFP; writing - review and editing: MFP, RKY, MDB, AKS, AOTC, and MCS; project administration: MFP, RKY, and MDB. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES

Abranches S Biological (2020) Megadiversity as a tool of soft power and development for Brazil. Bras Political Sci Rev 14(2):1–18. https://doi.org/10.1590/1981-3821202000020006

Anaya Muñoz SF, Calvo Orellana EE, Ramallo MAV, Santa Cruz RAC (2020) Actividade antimicrobiana de wira wira y cerraja contra Estafilococo, Enterococo, *Pseudomonas* y *Escherichia*. Rev Cientif Cienc Med 23(1):15–21

Araújo CRF, Pereira JV, Pereira MSV, Alves PM, Higino JS, Martins AB (2009) Concentração mínima bactericida do extrato do cajueiro sobre bactérias do biofilme dental. Pesq Bras Odontoped Clin Int 9(2):187–191. https://doi.org/10.4034/1519.0501.2009.0092.0009

Benzie IF, Strain JJ (1996) The ferric reducing ability of plasma (FRAP) as a measure of “antioxidant power”: The FRAP assay. Anal Biochem 239(1):70–76. https://doi.org/10.1006/abio.1996.0292

Bonneau A, Roche B, Schalk IJ (2010) Iron acquisition in *Pseudomonas aeruginosa* by the siderophore

pyoverdine: An intricate interacting network including periplasmic and membrane proteins. Sci Rep 10:120. https://doi.org/10.1038/s41598-019-56913-x

Borges A, Saavedra MJ, Simões M (2012) The activity of ferulic and gallic acids in biofilm prevention and control of pathogenic bacteria. Biofouling 28(7):755–67. https://doi.org/10.1080/08927014.2012.706751

Breijyeh Z, Jubeh B, Karaman R (2020) Resistance of gram-negative bacteria to current antibacterial agents and approaches to resolve it. Molecules 25(6):1340—1360. https://doi.org/10.3390/molecules25061340

Bucić-Kojić A, Planinić M, Tomas S, Bilić M, Velić D (2007) Study of solid-liquid extraction kinetics of total polyphenols from grape seeds. J Food Eng 81(1):236–242. https://doi.org/10.1016/j.jfoodeng.2006.10.027

Cama J, Henney AM, Winterhalter M (2019) Breaching the barrier: Quantifying antibiotic permeability across gram-negative bacterial membranes. J Mol Biol 431(18):3531–3546. https://doi.org/10.1016/j.jmb.2019.03.031

Coelho HA, Silveira LHC, Araújo, JHB, Kwiatkowski A (2016) Antioxidant and antimicrobial potential of phenolic compounds extracted from leaves and flowers of *Allamanda cathartica* L. Rev Bras Plantas Med 18(3):650-656.

Cheng J, Miller PA, Miller MJ (2012) Iron transport-mediated drug delivery: practical syntheses and in vitro antibacterial studies of tris-catecholate siderophore-aminopenicillin conjugates reveals selectively potent antipseudomonal activity. J Am Chem Soc 134(24):9898–901. https://doi.org/10.1021/ja303446w

Clinical and Laboratory Standards Institute (2015) Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, twelfth ed. CLSI, Wayne.

Clinical and Laboratory Standards Institute (2015) Performance standards for antimicrobial disk susceptibility tests, twelfth ed. CLSI, Wayne.

Flor RV, Campos MAA, Solano AGR, Jokl L, Dantas-Barros AM (2011) Drying of *Echinodorus macrophyllus* and autoclaving and lyophilization of the fluid-extract: Effects on the pharmacochemical composition. Rev Bras Farmacogn 21(3):518–524. https://doi.org/10.1590/S0102-695X2011005000075

Gfeller D, Michielin O, Zoete V (2013) Shaping the interaction landscape of bioactive molecules. Bioinform 29(23):3073–3079. https://doi.org/10.1093/bioinformatics/btt540

Joray M, Del Rollán M, Ruiz G, Palacios S, Carpinella M (2010) Antibacterial activity of extracts from plants of central Argentina: Isolation of an active principle from *Achyrocline satureioides*. Plan Med 77(1):95–100. https://doi.org/10.1055/s-0030-1250133

Katalinic V, Milos M, Kulisic T, Jukic M (2006) Screening of 70 medicinal plant extracts for antioxidant capacity and total phenols. Food Chem 94(4):550–557. https://doi.org/10.1016/j.foodchem.2004.12.004

Kejík Z, Kaplánek R, Masařík M, Babula P, Matkowski A, Filipenský P, Veselá K, Gburek J, Sýkora D, Martásek P, Jakubek M (2021) Iron complexes of flavonoids-antioxidant capacity and beyond. Int J Mol Sci 22(2):636–646. https://doi.org/10.3390/ijms22020646

Khan F, Bamunuarachchi NI, Tabassum N, Kim YM (2021) Caffeic acid and its derivatives: Antimicrobial drugs toward microbial pathogens. J Agric Food Chem 69(10):2979-3004. https://doi.org/10.1021/acs.jafc.0c07579

Khatkar A, Nanda A, Kumar P, Narasimhan B (2017) Synthesis, antimicrobial evaluation and QSAR studies of *p*-coumaric acid derivatives. Arab J Chem 10(2):3804–3815.

Kheiry M, Dianat M, Badavi M, Mard SA, Bayati V (2019) *p*-Coumaric acid attenuates lipopolysaccharide-induced lung inflammation in rats by scavenging ROS production: An *in vivo* and *in vitro* study. J Inflamm 42(6):1939–1950. https://doi.org/10.1007/s10753-019-01054-6

Klebba PE, Newton SMC, Six DA, Kumar A, Yang T, Nairn B, Munger C, Chakravorty S (2021) Iron acquisition systems of gram-negative bacterial pathogens define TonB-dependent pathways to novel antibiotics. Chem Rev 121(9):5193–5239. https://doi.org/10.1021/acs.chemrev.0c01005

Kondo S (1976) Punch Hole Method. A Simplified Bio-Assay Technique of Antibiotic Concentrations, in: Williams, J.D., Geddes, A.M. Chemotherapy: Laboratory Aspects of Infections, 2.ed. Springer, Boston, p.155–158. https://doi.org/10.1007/978-1-4684-7653-8_24

Lin TH, Wu CC, Tseng CY, Fang JH (2022) Effects of gallic acid on capsular polysaccharide biosynthesis in *Klebsiella pneumoniae*. J Microbiol Immunol Infect 55(6):1255–1262.

Loescher CM, Morton DW, Razic S, Agatonovic-Kustrin S (2014) High performance thin layer chromatography (HPTLC) and high performance liquid chromatography (HPLC) for the qualitative and quantitative analysis of *Calendula officinalis* - Advantages and limitations. J Pharm Biomed Anal 98:52-59. https://doi.org/10.1016/j.jpba.2014.04.023

Lorenzi H, Matos FJA (2021) Plantas medicinais no Brasil: nativas e exóticas, 4.ed. Instituto Plantarum de Estudos da Flora, Nova Odessa.

Lou Z, Wang H, Rao S, Sun J, Ma C, Li J (2012) *p*-Coumaric acid kills bacteria through dual damage mechanisms. Food Control 25(2):550–554.

Moresco KS, Silveira AK, Zeidán-Chuliá F, Correa APF, Oliveria RR, Borges AG, Grun L, Barbé-Tuana F, Zmozinski A, Brandelli A, Vale MGR, Gelain D, Bassani VL, Moreira JCF (2017) Effects of *Achyrocline satureioides* inflorescence extracts against pathogenic intestinal bacteria: Chemical characterization, *in vitro* tests, and *in vivo* evaluation evidence-based. Evid Based Complement Alternat Med 2017(7):1–10.

Mostafa AA, Al-Askar AA, Almaary KS, Dawoud TM, Sholkamy EN, Bakri MM (2018) Antimicrobial activity of some plant extracts against bacterial strains causing food poisoning diseases. Saudi J Biol Sci 25(2):361–366.

https://doi.org/10.1016/j.sjbs.2017.02.004

Mota FM, Carvalho HHC, Wiest JM (2011) Atividade antibacteriana *in vitro* de inflorescências de *Achyrocline satureioides* (Lam.) DC. - Asteraceae ("macela", "marcela") sobre agentes bacterianos de interesse em alimentos. Rev Bras Plantas Med 13(3):298–304.

Nakayama M, Shimatani K, Ozawa T, Shigemune N, Tsugukuni T, Tomiyama D, Kurahachi M, Nonaka A, Miyamoto T (2013) A study of the antibacterial mechanism of catechins: Isolation and identification of *Escherichia coli* cell surface proteins that interact with epigallocatechin gallate. Food Control 33(2):433–439. https://doi.org/10.1016/j.foodcont.2013.03.016

Nguyen AT, Oglesby-Sherrouse AG (2015) Spoils of war: iron at the crux of clinical and ecological fitness of *Pseudomonas aeruginosa*. Biometals 28(3):433–443. https://doi.org/10.1007/s10534-015-9848-6

Nguyen TLA, Bhattacharya D (2022) Antimicrobial activity of quercetin: An approach to its mechanistic principle. Molecules 27(8):2494(1–13). https://doi.org/10.3390/molecules27082494

Paprocka P, Durnaś B, Mańkowska A, Król G, Wollny T, Bucki R (2022) *Pseudomonas aeruginosa* infections in cancer patients. Pathogens 11(6):679(1–17). https://doi.org/10.3390/pathogens11060679

Park MY, Kang DH (2021) Antibacterial activity of caffeic acid combined with UV-A light against *Escherichia coli* O157:H7, *Salmonella enterica* Serovar *Typhimurium*, and *Listeria monocytogenes*. Appl Environ Microbiol 87(15):e00631–21. https://doi.org/10.1128/AEM.00631-21

Pradhan AC, Nanda B, Parida KM, Das M (2013) Quick photo-Fenton degradation of phenolic compounds by Cu/Al2O3–MCM-41 under visible light irradiation: small particle size, stabilization of copper, easy reducibility of Cu and visible light active material. Dalton Trans 42(2):558–556. https://doi.org/10.1039/c2dt32050a

Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C (1999) Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free Radic Biol Med 26(9–10):1231–1237. https://doi.org/10.1016/S0891-5849(98)00315-3

Salgueiro ACF, Folmer V, Da Rosa HS, Costa MT, Boligon AA, Paula FR, Roos DH, Puntel GO (2016) *In vitro* and *in silico* antioxidant and toxicological activities of *Achyrocline satureioides*. J Ethnopharmacol 194:6–14. https://doi.org/10.1016/j.jep.2016.08.048

Souza TN, Santos FM, Alves PR, Ferro JN, Correia ACC, Melo TS, Soares WR, Andrade BS, Lagente V, Barreto E (2021) Local administration of *p*-coumaric acid decreases lipopolysaccharide-induced acute lung injury in mice: In vitro and in silico studies. Eur J Pharmacol 897:173929. https://doi.org/10.1016/j.ejphar.2021.173929

Tanaka M, Kishimoto Y, Sasaki M, Sato A, Kamiya T, Kondo K, Lida K (2018) *Terminalia bellirica* (Gaertn.) Roxb. extract and gallic acid attenuate LPS-induced inflammation and oxidative stress via MAPK/NF-κB and Akt/AMPK/Nrf2 pathways. Oxid Med Cell Longev 8:1–15. https://doi.org/10.1155/2018/9364364

Tillotson GS (2016) Trojan horse antibiotics - A novel way to circumvent gram-negative bacterial resistance? Infect Dis (Auckl) 11(9):45–52. https://doi.org/10.4137/IDRT.S31567

Wang X, Li Y, Li J, Liu C, Sun C (2021) Role of flavonoids in the treatment of iron overload. front. Cell Dev Biol 9:1–12. https://doi.org/10.3389/fcell.2021.685364

World Health Organization (2017) WHO publishes list of bacteria for which new antibiotics are urgently needed. http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/ . Accessed on: 01 Aug. 2022.

World Health Organization (2019) New report calls for urgent action to avert antimicrobial resistance crisis. https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis. Accessed on: 01 Aug. 2022.

Wu M, Brown AC (2021) Applications of catechins in the treatment of bacterial infections. pathogens 10(5):1–17. https://doi.org/10.3390/pathogens10050546

Wu Y, Xiang W, Fu X, Sen Y (2016) Geochemical interactions between iron and phenolics originated from peatland in Hani, China: Implications for effective transport of iron from terrestrial systems to marine. Environ Earth Sci 75:336. https://doi.org/10.1007/s12665-015-5189-6

Zhishen J, Mengcheng T, Jianming W (1999) The Determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. Food Chem 64(4):555–559. https://doi.org/10.1016/S0308-8146(98)00102-2