SVOA Microbiology

ISSN: 2634-534X

ScienceVolks Open Access

Research Article

Adjuvant Effect of *Crateva tapia* L. (Capparaceae) Extract in Enhancing Antibiotics Against Multidrug-Resistant Bacteria

José Thyálisson da Costa Silva[1], Terezinha Raila Ramos de Sousa[1], João Arthur de Oliveira Borges[1], Talysson Felismino Moura[1], Paula Patrícia Marques Cordeiro[1], Maria Érika de Oliveira Silva[2], Luciene Ferreira de Lima[1], Ademar Maia Filho[1], Maria Aparecida Barbosa Ferreira Gonçalo[1], Daiany Alves Ribeiro[3], Nathallia Correia da Silva[1], João Pereira da Silva-Júnior[1], Emílio Sousa Albuquerque[1], Gabriel de Oliveira Lôbo[4], Henrique Douglas Melo Coutinho[1], José Weverton Almeida-Bezerra[1]*

[1]Regional University of Cariri, Crato – CE, Brazil.

[2]Dr. Leão Sampaio University Center, Juazeiro do Norte – CE, Brazil.

[3]Federal University of Cariri – Crato – CE, Brazil.

[4]CECAPE Faculty - Juazeiro do Norte – CE, Brazil.

***Corresponding Author:** Prof. Dr. Jose Weverton Almeida-Bezerra, Department of Biological Chemistry, Regional University of Cariri, 63105-000, Crato, CE, Brazil.

https://doi.org/10.58624/SVOAMB.2025.06.007

Received: March 15, 2025

Published: April 01, 2025

Citation: da Costa Silva JT, de Sousa TRR, Borges JAO, Moura TF, Cordeiro PPM, Silva MÉO, Lima LF, Maia Filho A, Gonçalo MABF, Ribeiro DA, da Silva NC, da Silva-Júnior JP, Albuquerque ES, Lôbo GO, Coutinho HDM, Almeida-Bezerra JW. Adjuvant Effect of *Crateva tapia* L. (Capparaceae) Extract in Enhancing Antibiotics Against Multidrug-Resistant Bacteria. *SVOA Microbiology 2025,* 6:2, 58-65. doi:10.58624/SVOAMB.2025.06.007

Abstract

Bacterial resistance has become a growing global challenge, highlighting the importance of therapeutic alternatives, such as the use of medicinal plant extracts in inhibiting resistant bacteria. Brazil is one of the most biodiverse countries in the world, including medicinal plants with pharmacological potential and promising biological activities against pathogenic microorganisms. The species *Crateva tapia* L. exhibits significant therapeutic potential in traditional medicine due to its antioxidant and antimicrobial properties. In this context, this study evaluated the antibacterial activity and synergistic potential of the ethanolic extract from *C. tapia* leaves in combination with antibiotics. For this purpose, *C. tapia* leaves were collected, dried, ground, and subjected to ethanol extraction to obtain the ethanolic extract (EECT). Antimicrobial assays were conducted using conventional bacterial strains (ATCC) and multidrug-resistant (MDR) strains. The inhibitory activity was assessed through the Minimum Inhibitory Concentration (MIC). The potentiating capacity of EECT was analyzed at sub-inhibitory concentrations (MIC/8) in combination with the antibiotics gentamicin, ampicillin, and norfloxacin, with results analyzed statistically. The results demonstrated that EECT did not exhibit isolated antibacterial activity (MIC > 512 µg/mL) against ATCC and MDR bacteria. However, it proved to be effective as an antibiotic potentiator, significantly reducing the MIC of gentamicin and norfloxacin against MDR strains of *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. These findings indicate that the ethanolic extract of *C. tapia* has potential for use in combined therapies, representing a promising alternative in addressing bacterial resistance.

Keywords: *"Trapiá"; Microdilution; Antibacterial; Medicinal Plant.*

1. Introduction

Brazil stands out as one of the most biologically diverse countries, encompassing both fauna and flora, and possesses a significant variety of medicinal plants with pharmacological potential and promising biological activities. These characteristics underscore the need for projects focused on scientific research and sustainable development [1,2].

The botanical family Capparaceae includes species with clinical relevance due to their pharmacological and biological activities, such as antiparasitic, antimicrobial (antibacterial and antifungal), anti-inflammatory, and antioxidant properties, being employed in the treatment of various conditions, especially gastrointestinal problems [3-5].

Among the species of this family, the genus *Crateva* exhibits significant therapeutic potential, standing out for its pharmacological and biological activities relevant to public health. These plant species are used in the treatment of sinusitis, stomach pain, cuts, wounds, and have promising applications in combating pathogenic microorganisms [6,7]. Additionally, they have demonstrated antioxidant properties and applications against bacterial infections, suggesting potential for synergistic actions with antibiotics [8-10].

The species *Crateva tapia* L., belonging to the genus *Crateva* (synonyms *Cleome arborea* Schrad. and *Crateva benthamii* Eichler), is popularly known as "trapiá" in the Ceará region, as well as “capança” and “fruto-de-macaco” in the Acre region. It is the only representative of the Capparaceae family in Brazil that has compound leaves and clawed petals [11]. The species *C. tapia* is recognized for its clinically relevant properties, with pharmacological applications and traditional use throughout history, associated with its phytochemical composition [12]. Its notable properties include antioxidant [13] and anti-inflammatory activities [14].

The application of medicinal plants has played an important role in combating and treating various diseases over time, especially in developing effective antibacterial alternatives against pathogenic microorganisms, such as *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) [15-17]. However, a growing adaptation of these microorganisms has been observed, leading to the development of resistance to available drugs, resulting in a global-scale problem [18].

The resistance of microorganisms, especially bacteria, to antimicrobials has become a significant global issue. This resistance can occur through different mechanisms, such as the horizontal transfer of resistance genes via plasmids between the same or different species, drug inactivation, or limitation of drug binding to target sites [18,19]. These adaptive strategies make bacteria resistant to various classes of currently available antibiotics, including tetracyclines, β-lactams, macrolides, fluoroquinolones, aminoglycosides, and quinolones [20]. This phenomenon is often associated with the unregulated use of antibiotics [21].

Given the relevance of bacterial resistance, the biological activity of medicinal plants has emerged as a promising alternative in combating resistant microorganisms. Specifically, the species *Crateva tapia* shows potential as an antimicrobial agent against bacteria. In this context, the present study aimed to evaluate the antibacterial activity and the potentiating effect of antibiotics of the ethanolic extract from *C. tapia* leaves (EECT) against standard and multidrug-resistant bacterial strains.

2. Materials and Methods

2.1 Collecting botanical material

The leaves of *Crateva tapia* (Figure 01) were collected in the morning (09:00 AM) in a Caatinga area in the municipality of Quixelô, state of Ceará, Brazil, at the geographical coordinates 6°15'24.9"S, 39°16'21.5"W, during January 2023. The material was identified in the field by the botanist Dr. José Weverton Almeida Bezerra.

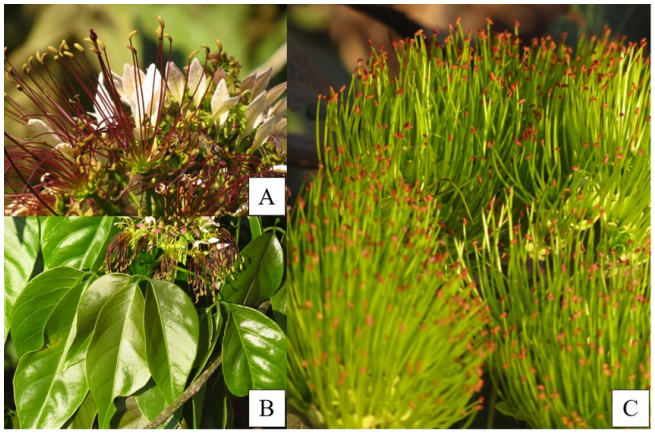

Fig 1. *Individuals of Crateva tapia in the municipality of Quixelô - Ceará.*

2.2 Preparation of ethanolic extract (EE)

The collected leaves were carefully selected, naturally dried, and ground to increase the surface area, making them suitable for the production of the ethanolic extract of *C. tapia* (EECT). The ground material was subjected to a cold extraction process by immersion in analytical-grade ethanol (P.A.) for 96 hours. Afterward, the solution was filtered, and the ethanol was removed using a rotary evaporator operating under reduced pressure, with the temperature maintained between 30 °C and 40 °C to preserve the active compounds [22].

2.3 ***Evaluation of antibacterial activity***

2.3.1 Strains, culture media and drugs

The evaluation of antibacterial activity was performed using conventional and multidrug-resistant (MDR) bacterial strains. The reference strains included *Escherichia coli* (ATCC 25922 and MDR 06), *Pseudomonas aeruginosa* (ATCC 25853 and MDR 24), and *Staphylococcus aureus* (ATCC 25923 and MDR 10). The culture medium used was Brain Heart Infusion (BHI; Merck, Darmstadt, Germany), following the manufacturer's instructions. After incubation in a biological oven, bacterial suspensions were prepared using 3 mL of sterile saline solution (0.9% NaCl), adjusting turbidity to the McFarland 0.5 standard, corresponding to 1.5×10^8 CFU/mL. As control antibiotics for comparison, gentamicin, ampicillin, and norfloxacin were used.

2.3.2 Minimum Inhibitory Concentration (MIC)

The antibacterial capacity of EECT to inhibit bacterial growth was evaluated through the Minimum Inhibitory Concentration (MIC) assay. A total of 100 µL of the bacterial inoculum solution and 900 µL of culture medium (BHI) were distributed into 96-well microtiter plates. The EECT was tested at different concentrations, ranging from 0.5 to 512 µg/mL, using the microdilution technique. The microplates were incubated in a bacteriological incubator at 37 °C for 24 hours. After incubation, liquid resazurin was used as an indicator to detect bacterial growth based on its oxidation-reduction reaction. The color change after one hour of reaction was analyzed: a violet color indicated the absence of bacterial growth, while a light pink color revealed bacterial growth. All tests were performed in triplicate (n = 3) to ensure the reliability of the results.

2.3.3 Antibiotic potentiating activity

After the MIC evaluation, the therapeutic combination potential of EECT with antibiotics was analyzed using subinhibitory concentrations of EECT (MIC/8) in association with the antibiotics gentamicin, ampicillin, and norfloxacin. The assays were performed using the microdilution technique in wells containing antibiotic concentrations ranging from 0.5 to 512 µg/mL, with a volume of 100 µL per well. The microplates were incubated in a bacteriological incubator at 37 ° C for 24 hours. All experiments were conducted in triplicate (n = 3) to ensure the reproducibility of the results [23].

2.4 Statistical analysis

The obtained data were analyzed by calculating the means and their respective standard errors of the mean (± SEM). Subsequently, a one-way analysis of variance (ANOVA) was performed, followed by Tukey's test to determine statistical significance, considering a 95% confidence level. Statistical analyses were conducted using GraphPad Prism software, version 6 (GraphPad Software Inc., San Diego, CA, USA).

3. Results

The evaluation of the antibacterial activity of EECT indicated that the ethanolic extract showed no significant activity against ATCC and MDR bacterial strains when tested alone, with MIC values exceeding 512 µg/mL. However, when assessing the combined ability of EECT to enhance antibiotics, an increase in the efficacy of different drugs, such as gentamicin and norfloxacin, was observed against MDR strains of *E. coli* 06, *S. aureus* 10, and *P. aeruginosa* 24.

As shown in Figure 2, against *E. coli*, a reduction in the MIC of gentamicin was identified, from 20.15 ± 2.88 µg/mL to 2.51 ± 2.88 µg/mL. The potentiating activity of EECT was also observed against *P. aeruginosa* (Figure 3), with a reduction in the MIC of norfloxacin from 32 ± 2 µg/mL to 20.15 ± 2.22 µg/mL. Additionally, against the Gram-positive bacterium *S. aureus* (Figure 4), EECT reduced the MIC of gentamicin (from 40.31 ± 1.49 µg/mL to 10.07 ± 1.49 µg/mL) and norfloxacin (from 128 ± 1 µg/mL to 32 ± 1 µg/mL).

However, it was found that the combination of EECT with ampicillin did not result in a synergistic effect, showing either antagonistic or indifferent activity. This suggests specificity in the interaction with certain antibiotics, possibly associated with the mechanisms of action of these drugs.

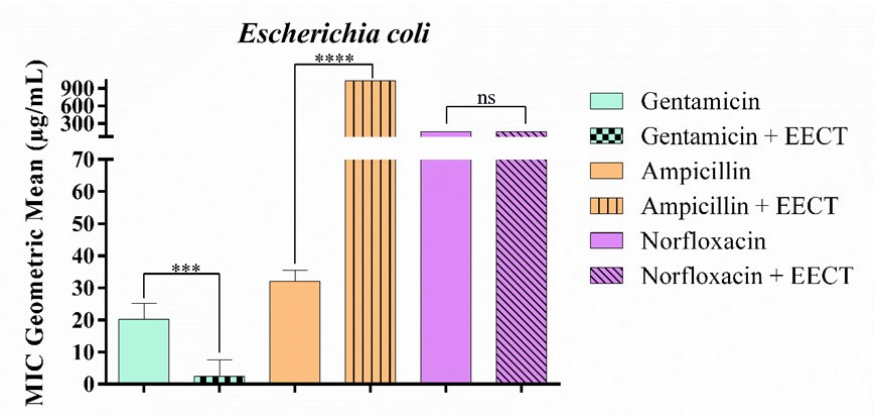

Fig 2. *Determination of the minimum inhibitory concentration (MIC) of the ethanolic extract of Crateva tapia (EECT) in association with antibiotics in the fight against multidrug-resistant strains of Escherichia coli 06; *** = p < 0.001; **** = p < 0.0001; ns: not significant.*

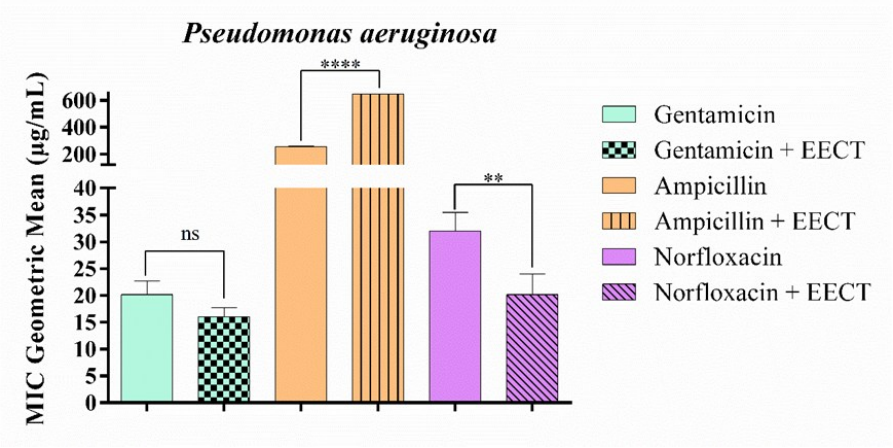

Fig 3. *Determination of the minimum inhibitory concentration (MIC) of the ethanolic extract of Crateva tapia (EECT) in association with antibiotics in the fight against multidrug-resistant strains of Pseudomonas aeruginosa 24; ** = p < 0.01; **** = p < 0.0001; ns: not significant.*

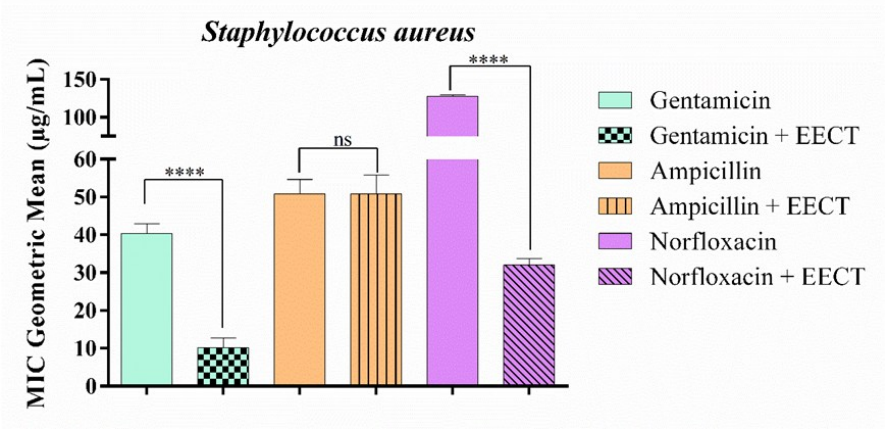

Fig 4. *Determination of the minimum inhibitory concentration (MIC) of the ethanolic extract of Crateva tapia (EECT) in association with antibiotics in the fight against multidrug-resistant strains of Staphylococcus aureus 10; **** = p < 0.0001; ns: not significant.*

4. Discussion

The pharmacological properties identified in *C. tapia* have motivated more detailed studies to investigate the compounds responsible for these activities. Among the highlighted compounds are pectin [24], lignin [25], and lectin [26-29], which are prominent bioactive substances. Lectin isolated from *C. tapia* bark showed a preference for binding to large oligosaccharide chains, which could interfere with the molecular structure [28].

The evaluation of antibacterial activities in the *Crateva* genus has shown relevance for future applications [9]. The literature reports that *Crateva adansonii* DC. extracts demonstrated promising antibacterial action against *S. aureus* ATCC, with the potential to enhance the efficacy of antibiotics and contribute to reversing bacterial resistance. The MIC values for the hydroethanolic extract (0.625 mg/mL), aqueous extract (1.25 mg/mL), and ethanolic extract (1.25 mg/mL) were significant [7,8,30], indicating possible bactericidal activity [31].

A study by Salvat et al. [32] evaluated the methanolic extract of *C. tapia* branches against *P. aeruginosa* ATCC 10031, showing relevant MIC values of 0.5 mg/mL. However, research on the antibacterial activity of *C. tapia* indicated that the hydroethanolic extract did not exhibit significant activity against Gram-positive strains (*S. aureus*) and Gram-negative strains (*E. coli* and *P. aeruginosa*), with MIC values above 1,024 µg/mL. These changes may be associated with the phytochemical composition of these extracts [33].

Phytochemical screening of the ethanolic and methanolic extracts from *C. tapia* leaves revealed the presence of several secondary metabolites known for their pharmacological and biological activities. Among these compounds are phlobaphenic tannins, flavones, flavonols, flavonones, xanthones, steroids, saponins, mono- and sesquiterpenes, and triterpenes [13,33,34], as well as alkaloids, coumarins, glycosides, and saponins [14]. Alkaloids, in particular, have potential antibacterial activity and are considered effective against various bacteria, such as *S. aureus*, *E. coli*, and *Klebsiella pneumoniae* [10].

An important aspect relates to the possible mechanisms of action of the extract in combination with antibiotics. As demonstrated by the results obtained, the combination of the ethanolic extract of *C. tapia* (EECT) with ampicillin showed an antagonistic effect, increasing the MIC of this drug. This antagonism can be partially attributed to competition for the same action site, possibly caused by molecular interaction between the compounds, leading to mutual interference [35,36]. Another potential mechanism involves bacterial resistance, in which changes occur at the drug's targets or action sites [19,37]. This action has been observed in *P. aeruginosa* and *E. coli* when exposed to ampicillin [38].

5. Conclusion

The ethanolic extract of *Crateva tapia* (EECT) did not show clinically significant antibacterial activity against standard and multidrug-resistant pathogenic bacterial strains. However, it demonstrated potential as an enhancer when combined with antibiotic drugs such as gentamicin and norfloxacin, both in Gram-positive and Gram-negative strains. Despite these promising results, the study has limitations, particularly regarding the faithful characterization of the phytochemistry of the extract and the in-depth analysis of the molecular interactions between the extract and antibiotics. Future studies are needed to evaluate the mechanisms of action of these combinations, including approaches like molecular docking, and to assess potential toxic effects.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgement

The authors thank Universidade Regional do Cariri (URCA, Brazil).

References

1. Ferreira, P. M. P.; Arcanjo, D. D. R.; Peron, A. P. Drug development, Brazilian biodiversity and political choices: Where are we heading? *J. Toxicol. Environ. Health, Part B* 2023, *26*, 257–274. https://doi.org/10.1080/10937404.2023.2193762.
2. Antonio Pereira, I.; Silveira, D.; Barros, C.; Santos, V.; Pavan, F. Traditional plants used in southern Brazil as a source to wound healing therapies. *Chem. Biodivers.* 2023, *20*, 1–21. https://doi.org/10.1002/cbdv.202201021.

3. Maroyi, A.; Masika, P. J.; Afolayan, A. J. A synthesis and review of medicinal uses, phytochemistry and pharmacological properties of *Maerua crassifolia* Forssk. (*Capparaceae*). *J. Pharm. Nutr. Sci.* 2020a, *10*, 182–189. https://doi.org/10.29169/1927-5951.2020.10.05.2.
4. Maroyi, A.; Masika, P. J.; Afolayan, A. J. *Maerua angolensis* DC. (*Capparaceae*): A review of its medicinal uses, phytochemistry and pharmacological properties. *J. Pharm. Nutr. Sci.* 2020b, *10*, 247–256. https://doi.org/10.29169/1927-5951.2020.10.05.10.
5. Annaz, H.; Halawani, S. H.; El-Sawi, S. A.; Al-Sobahi, A.; Taha, A.; Al-Qurainy, F.; Khan, S.; Nadeem, M.; Tarroum, M.; Badri, M.; et al. Caper (*Capparis spinosa* L.): An updated review on its phytochemistry, nutritional value, traditional uses, and therapeutic potential. *Front. Pharmacol.* 2022, *13*, 1–30. https://doi.org/10.3389/fphar.2022.878749.
6. Bhattarai, S.; Chaudhary, R. P.; Taylor, R. S. L. Biological activities of some Nepalese medicinal plants used in treating bacterial infections in human beings. *Nepal J. Sci. Technol.* 2009, *10*, 83–90. https://doi.org/10.3126/njst.v10i0.2830.
7. Mignanwandé, Z. F.; Dougnon, T. J.; Yèhouénou, B.; Bankolé, H.; Loko, F.; Baba-Moussa, L. Antibacterial Activities of the Ethanolic Extract of *Crateva adansonii* DC. (*Capparidaceae*) Harvested in Dassa-Zoumè in Central Bénin. *Open J. Med. Microbiol.* 2020, *10*, 46–57. https://doi.org/10.4236/ojmm.2020.102005.
8. Mohammed, N.; Waziri, S. M.; Ahmad, A. M.; Adamu, A. Phytochemical analysis and antibacterial activity of *Crateva adansonii* DC leaves and stem bark extracts against some pathogenic bacteria. *Sci. World J.* 2024, *19*, 403–408. https://doi.org/10.4314/swj.v19i2.16.
9. Srinivas, V.; Giridhar, K.; Kulkarni, M. N.; Naidu, P. A scientific review on *Crateva religiosa*. *Int. J. Adv. Pharm. Biol. Chem.* 2018, *7*, 11–16.
10. Adounkpe, M. F.; Tchetchao, S. A.; Sagbo, I. J.; Gbaguidi, F. A.; Quenum, F.; Dougnon, V. T.; Hounmanou, G. Antibacterial pharmacochemical activity “in vitro” of total alkaloid extracts of *Crateva religiosa* G. Forst. (*Capparidaceae*) versus amoxicillin+clavulanic acid on germs responsible of human common affections. *J. Med. Plants Stud.* 2018, *6*, 175–179.
11. Soares Neto, R.L.; Luber, J. *Capparaceae in* Flora e Funga do Brasil. Jardim Botânico do Rio de Janeiro. Disponível em: <https://floradobrasil.jbrj.gov.br/FB22300>. Acesso em: 03 dez. 2024
12. Sharma, P.; Patil, D.; Patil, A. *Crataeva tapia* Linn.-An important medicinal plant: A review of its traditional uses, phytochemistry and pharmacological properties. *Int. J. Pharm. Sci. Res.* 2013, *4*, 582-589.
13. Xavier, M. E. V.; Borges, F. J. P.; Ferreira, R. A. P.; Bezerra, J. E. C.; Cavalcante, G. F. Potencial antioxidante e alelopático de *Crataeva tapia* L. *Diversitas J.* 2019, *4*, 306–318. https://doi.org/10.17648/diversitas-journal-v4i1.646.
14. Castro, J. P.; Franco, L. A.; Diaz, F. Anti-inflammatory screening of plant species from the Colombian Caribbean Coast. *J. Appl. Pharm. Sci.* 2021, *11*, 106–117. https://doi.org/10.7324/JAPS.2021.110413.
15. Zazharskyi, V. V.; Korotkova, E. I.; Rassokha, O. I.; Sobol, A. V.; Kolomoets, N. S. Antimicrobial activity of 50 plant extracts. *Biosyst. Divers.* 2019, *27*, 163–169. http://dx.doi.org/10.15421/011922.
16. Górniak, I.; Bartoszewski, R.; Króliczewski, J. Comprehensive review of antimicrobial activities of plant flavonoids. *Phytochem. Rev.* 2019, *18*, 241–272. https://doi.org/10.1007/s11101-018-9591-z.
17. Manandhar, S.; Luitel, S.; Dahal, R. K. In vitro antimicrobial activity of some medicinal plants against human pathogenic bacteria. *J. Trop. Med.* 2019, *2019*, 1–5. https://doi.org/10.1155/2019/1895340.
18. Jian, Z.; Yang, Y.; Zhao, L.; Li, Y. Antibiotic resistance genes in bacteria: Occurrence, spread, and control. *J. Basic Microbiol.* 2021, *61*, 1049–1070. https://doi.org/10.1002/jobm.202100201.
19. Gauba, A.; Rahman, K. M. Evaluation of antibiotic resistance mechanisms in gram-negative bacteria. *Antibiotics* 2023, *12*, 1–30. https://doi.org/10.3390/antibiotics12111590.
20. Urban-Chmiel, R.; Wernicki, A.; Puchalski, A.; Kwiecinska-Piróg, J.; Dec, M. Antibiotic resistance in bacteria—A review. *Antibiotics* 2022, *11*, 1–40. https://doi.org/10.3390/antibiotics11081079.
21. Gogry, F. A.; Qureshi, K. A.; Kashoo, Z. A.; Srinivasan, R.; Ahmad, R. T. Current update on intrinsic and acquired colistin resistance mechanisms in bacteria. *Front. Med.* 2021, *8*, 1–19. https://doi.org/10.3389/fmed.2021.677720.

22. Simões, C. M. O.; Schenkel, E. P.; Gosmann, G.; Mello, J. C. P.; Mentz, L. A.; Petrovick, P. R. *Farmacognosia da planta ao medicamento*. 6th ed.; Editora da UFSC, 2010.

23. Coutinho, H. D. M.; Falcão-Silva, V. S.; Gadelha, C. A.; de Almeida, D. A.; de Souza, J. C.; da Costa, J. G. Enhancement of the antibiotic activity against a multiresistant *Escherichia coli* by *Mentha arvensis* L. and chlorpromazine. *Chemotherapy*. 2008, *54*, 328–330. https://doi.org/10.1159/000151267

24. Alves, S. P. L.; Medeiros, C. B.; Alves, R. R.; Vasconcelos, F. G.; Silva, T. H.; Silva, M. L. S.; Souza, M. P.; Albuquerque, A. A.; Albuquerque, J. F. Pectin-like polysaccharide extracted from leaves *Crataeva tapia* promotes antioxidant, immunomodulatory and emulsifiers applied in therapeutic formulations. *3 Biotech* 2023, *13*, 1–19. https://doi.org/10.1007/s13205-023-03509-y.

25. Arruda, M. D. M.; Castro, M. C.; Melo, M. F.; Lima, K. M.; Silva, T. B. P.; Melo, M. E.; Cavalcanti, F. M. Characterization of a lignin from *Crataeva tapia* leaves and potential applications in medicinal and cosmetic formulations. *Int. J. Biol. Macromol.* 2021, *180*, 286–298. https://doi.org/10.1016/j.ijbiomac.2021.03.077.

26. Araújo, R. M. S.; Pereira, V. R. A.; Oliveira, M. C.; Costa, F. L.; Benevides, N. M.; Moura, G. M. Lectin from *Crataeva tapia* bark exerts antitumor, anti-inflammatory and analgesic activities. *Nat. Prod. Bioprospect.* 2011, *1*, 97–100. https://doi.org/10.1007/s13659-011-0014-8.

27. Rocha, A. A.; Assreuy, A. M. S.; Carvalho, A. A.; Ribeiro, A. A.; Morais, C. M.; Vasconcelos, D. F.; Benevides, R. O.; Melo, S. F.; Sampaio, T. B. Lectin from *Crataeva tapia* Bark Improves Tissue Damages and Plasma Hyperglycemia in Alloxan-Induced Diabetic Mice. *Evid.-Based Complement. Altern. Med.* 2013, *2013*, 1–9. http://dx.doi.org/10.1155/2013/869305.

28. Zhang, F.; Yang, B.; Yu, G.; Zhao, J.; Zhu, Z.; Jiang, Z.; Linhardt, R. J. Structural studies of the interaction of *Crataeva tapia* bark protein with heparin and other glycosaminoglycans. *Biochemistry* 2013, *52*, 2148–2156. https://doi.org/10.1021/bi400077b.

29. Nunes, N. N. S.; Lima, J. A.; Araújo, L. G.; Silva, M. C. F.; Souza, M. M.; Melo, M. E. Potential of the lectin/inhibitor isolated from *Crataeva tapia* bark (CrataBL) for controlling *Callosobruchus maculatus* larva development. *J. Agric. Food Chem.* 2015, *63*, 10431–10436. https://doi.org/10.1021/acs.jafc.5b03634.

30. Agbankpe, A. J.; Agbossou, A.; Dougnon, V. T.; Yèhouénou, B.; Fah, L.; Bankolé, H.; Loko, F.; Baba-Moussa, L. In vitro antibacterial effects of *Crateva adansonii*, *Vernonia amygdalina* and *Sesamum radiatum* used for the treatment of infectious diarrhoeas in Benin. *J. Infect. Dis. Ther.* 2016, *4*, 1–7. http://dx.doi.org/10.4172/2332-0877.1000281.

31. Mignanwandé, Z. F. M.; Dougnon, T. J.; Yèhouénou, B.; Bankolé, H.; Loko, F.; Baba-Moussa, L. Antibacterial Properties of *Crateva adansonii* (*Capparidaceae*) on Strains Isolated from Chronic Wounds Diagnosed in the Commune of Ouinhi in 2021. *Pharmacol. Pharm.* 2023, *14*, 449–462. https://doi.org/10.4236/pp.2023.1411029.

32. Salvat, A.; Antonnacci, L.; Fortunato, R.; Suarez, E. Screening of some plants from Northern Argentina for their antimicrobial activity. *Lett. Appl. Microbiol.* 2001, *32*, 293–297. https://doi.org/10.1046/j.1472-765X.2001.00923.x.

33. Cabral, D. L. V.; Santos, A. C.; Alves, M. C.; Andrade, D. H.; Medeiros, R. J.; Oliveira, J. F. Modulatory activity and chemical profile of a hydroalcoholic extract of *Crateva tapia* L. *Afr. J. Microbiol. Res.* 2015, *9*, 326–331. https://doi.org/10.5897/AJMR2014.7039.

34. Magalhães, C. S.; Silva, F. C. L.; Randau, K. P. Morphoanatomy, histochemistry, and phytochemistry of stem and leaves of *Crateva tapia* L. *Microsc. Microanal.* 2023, *29*, 795–801. https://doi.org/10.1093/micmic/ozac035.

35. Goñi, P.; López, P.; Sánchez, C.; Gómez-Lus, R.; Becerril, R.; Nerín, C. Antimicrobial activity in the vapour phase of a combination of cinnamon and clove essential oils. *Food Chem*. 2009, *116*, 982–989. https://doi.org/10.1016/j.foodchem.2009.03.058

36. Almeida-Bezerra, J. W.; Dantas, J. B.; Monteiro, M. T.; Almeida, R. S.; Silva, C. C.; Matias, E. F.; Lima, R. R. Analysis of the Antibiotic-Potentiating Activity, Absorption, Distribution, Metabolism, and Excretion (ADME) and the Molecular Docking Properties of Phytol Against Multi-Drug-Resistant (MDR) Strains. *Antibiotics* 2024, *13*, 1–16. https://doi.org/10.3390/antibiotics13121171.

37. Shariati, A.; Azimi, T.; Safari, H.; Razavi, S.; Safari, S.; Tehrani, A. H. The resistance mechanisms of bacteria against ciprofloxacin and new approaches for enhancing the efficacy of this antibiotic. *Front. Public Health* 2022, *10*, 1–28. https://doi.org/10.3389/fpubh.2022.1025633.

38. Palzkill, T. Structural and mechanistic basis for extended-spectrum drug-resistance mutations in altering the specificity of TEM, CTX-M, and KPC β-lactamases. *Front. Mol. Biosci.* 2018, *5*, 1–19. https://doi.org/10.3389/fmolb.2018.00016.