

The Antibacterial properties of *psidium guava* to eliminate *Helicobacter pylori*: Preventing Gastric Cancer

Forough Heydari¹, Behrouz Motamedi Zadeh², Abbas Ganjali^{3*}, Gholamreza Haghighi⁴

¹ Department of Toxicology and Pharmacology, Faculty of Pharmacy, Zabol University of Medical Sciences, Zabol, Iran

² Department of Epidemiology, Zabol University of Medical Sciences, Iran

³ Food and Drug Deputy, Zabol University of Medical Sciences, Zabol, Iran

⁴ Department of Internal Medicine, School of Medicine Zabol University of Medical Sciences, Zabol, Iran

***Corresponding Author:** Abbas Ganjali, Food and Drug Deputy, Zabol University of Medical Sciences, Zabol, Iran. E-mail: a.ganjali@zbmu.ac.ir

Submitted: 30 June 2024

Revised: 02 September 2024

Accepted: 29 August 2024

e-Published: 10 October 2024

Keywords:

Psidium guava

Medicinal plants

Helicobacter pylori

Cancer

Antibiotic treatment has often failed due to the increased biological resistance of *Helicobacter pylori* (*H. pylori*). Therefore, medicinal plants have become necessary to combat this bacteria. This study aims to investigate the antibacterial properties of *psidium guava* and focus on the effect of the properties of this plant on *H. pylori* infection to prevent gastric cancer. This study systematically followed the PRISMA guide and searched various international and national databases such as SciELO, PubMed, ProQuest, Google Scholar, Ovid, SID, MediLib, IranDoc, and Cochrane. The search was conducted for articles published in Farsi and English from 2003 to 2023, covering two decades. The search was performed using Persian keywords such as "antibacterial activity," "*Psidium guava*," and "*Helicobacter pylori*", as well as their English equivalents and various combinations of these words. The articles were evaluated based on their relevance to the study's purpose without statistical analysis. Out of the 368 selected articles, only nine were deemed final. The results showed that most research was focused on the leaves and fruits of *Psidium guava* L (*PGL*). It can be stated that the essential oil of *PGL* leaves exhibits the most biological activity, and the compounds present in this plant make it a promising candidate for producing drugs with antibacterial activity. *PGL* plant extracts have appropriate antimicrobial substances that can be used as a pharmaceutical base or a suitable herbal medicine to fight against *H. pylori*, heal stomach ulcers, and ultimately prevent gastric cancer (GC).

Copyright © 2024 Pirkani et al. Published by Breast Cancer Research Center, ACECR. This work is licensed under a Creative Commons Attribution - NonCommercial 4.0 International License (<https://creativecommons.org/licenses/by-nc/4.0/>) non-commercial uses are permitted, provided the original work is properly cited.

INTRODUCTION

One of the main challenges of treating bacterial infections is the increase in antibiotic resistance. One of these infections is stomach infection caused by *Helicobacter pylori* (*H. pylori*), which causes approximately 90% of gastric cancers [1]. *H. pylori* is

a prevalent bacterial infection that is crucial in causing gastrointestinal ulcers. It is also a leading cause of chronic and progressive inflammation that can ultimately lead to gastric cancer [2]. *H. pylori* is a gram-negative bacterium found on the stomach's epithelial lining, which usually affects individuals in

their early years and persists indefinitely if not treated. *H. pylori* infection is the main cause of three important upper gastrointestinal tract diseases. Among them are duodenal ulcers or gastric ulcers, reported in 1 to 10 percent of affected patients, and GC, which occurs in 0.1 to 3 percent of cases. Additionally, Mucosa-Associated Lymphoid-Tissue (MALT) is another rare disease caused by *H. pylori* infection, affecting just 0.01 percent of individuals [3]. Current treatments with a combination of at least three antibiotics fail in 40% of patients, which is one of the most important challenges in the health field [1].

In recent years, *H. pylori* has become increasingly difficult to treat due to its high antibiotic resistance. *H. pylori* eradication is the first choice for treatment due to the various complications associated with this bacterium. There are different drugs to treat and destroy this bacteria, and clarithromycin is a key component of some of these drugs [4]. In a study conducted in China, the resistance levels of *H. pylori* to clarithromycin, metronidazole, and levofloxacin were 37%, 77%, and 33%, respectively [5]. Recently, the World Health Organization has recognized clarithromycin-resistant *H. pylori* as a "high priority" for which more effective drugs are needed [6]. Researchers are exploring various methods to address this issue, including developing new antibiotics, immunotherapy, probiotics, and medicinal plants. Consequently, there is a growing focus on finding more effective ways to treat and eradicate *H. pylori*, increasing the importance of exploring the potential of medicinal plants.

Psidium guava plant (PGL) is a subfamily of Myrtaceae found in tropical and subtropical countries. This plant is native to Central and Latin America and adapts well to soil use. In Iran, it is cultivated in Sistan –Baluchistan, and Hormozgan. PGL is a plant with great diversity that is used as food and a therapeutic

agent.[7]. PGL is used to treat symptoms related to the problems and diseases caused by the action of pathogenic/opportunistic microorganisms [8]. In the ongoing battle against bacterial infections, discovering new sources of antimicrobial compounds is crucial. To advance this goal, the present review study was conducted to investigate the antibacterial properties of the PGL plant and determine its effect on *H. pylori*. Researching the antibacterial properties of medicinal plants, such as *psidium guava*, could provide insights into potential alternative treatment options for *H. pylori* infection.

METHODS

This study aimed to conduct a systematic review following the PRISMA guide and searching in various international and national databases such as SciELO, PubMed, ProQuest, Google Scholar, Ovid, SID, MediLib, IranDoc, and Cochrane. The search was conducted for articles published in Farsi and English from 2003 to 2023, covering two decades. The search was performed using Persian keywords such as "antibacterial activity," "*Psidium guava*," and "*Helicobacter pylori*", as well as their English equivalents and various combinations of these words. The articles were evaluated based on their relevance to the study's purpose without statistical analysis (Table 1).

Two authors checked the articles to ensure the work was carried out and there was a significant match. The Irandoc database was also used to check the theses and dissertations, but no case was found that matched the purpose of the present study.

The inclusion criteria were articles that only dealt with the antibacterial effects of the *Psidium guava* plant and were related to the study's objectives. Exclusion criteria included articles whose full text was unavailable or presented as a poster, speech, or letter to the editor. Also, the authors qualitatively evaluated

Table 1. Search strategy for articles in PubMed database.

Row	Boolean operators	Result
1	AND OR	"antibacterial activity"[Title] AND (("psidium"[MeSH Terms] OR "psidium"[All Fields]) AND "guava"[Title]) AND "helicobacter pylori"[Title]

the validity of the selected articles in terms of their originality, credibility, and the Journal that published them. The final articles were reviewed according to study type using the PRISMA guidelines in the next step (Figure 1).

In the initial search strategy, articles containing the keywords in the title and abstract were selected based on the research's purpose, and there were 368 articles. Finally, considering the entry and exit criteria of the articles in the research, nine articles, considering all the criteria, were included in the study for review.

RESULTS

The summary of the results of the reviewed studies was classified in the tables in the text of this research. The antibacterial activity of the PGL plant is listed in (Table 2). The study findings suggest that guava

leaves and bark possess antibacterial properties.

PGL leaf extract contains high amounts of gallic acid and quercetin, which greatly influence antioxidant activity. 70% ethanol extract of this plant causes high inhibition for *H. Pylori*. After the phytochemical screening, the multi-herb suspension (combination of guava with herbs of similar function) showed the presence of terpenoids, flavonoids, and tannins that have anti-ulcer activity (Table 3).

The leaves of the PGL plant are used in India as an anti-fever, anti-spasm, and rheumatism. It is used in Colombia, Mexico, Maya, USA, and Mozambique to treat diarrhea and stomachache. In the United States, the leaves are used as an antibiotic [27]. Many of the biological activities of PGL are related to the active chemical compounds of this plant, which are mentioned in Table 4. It has been reported that the

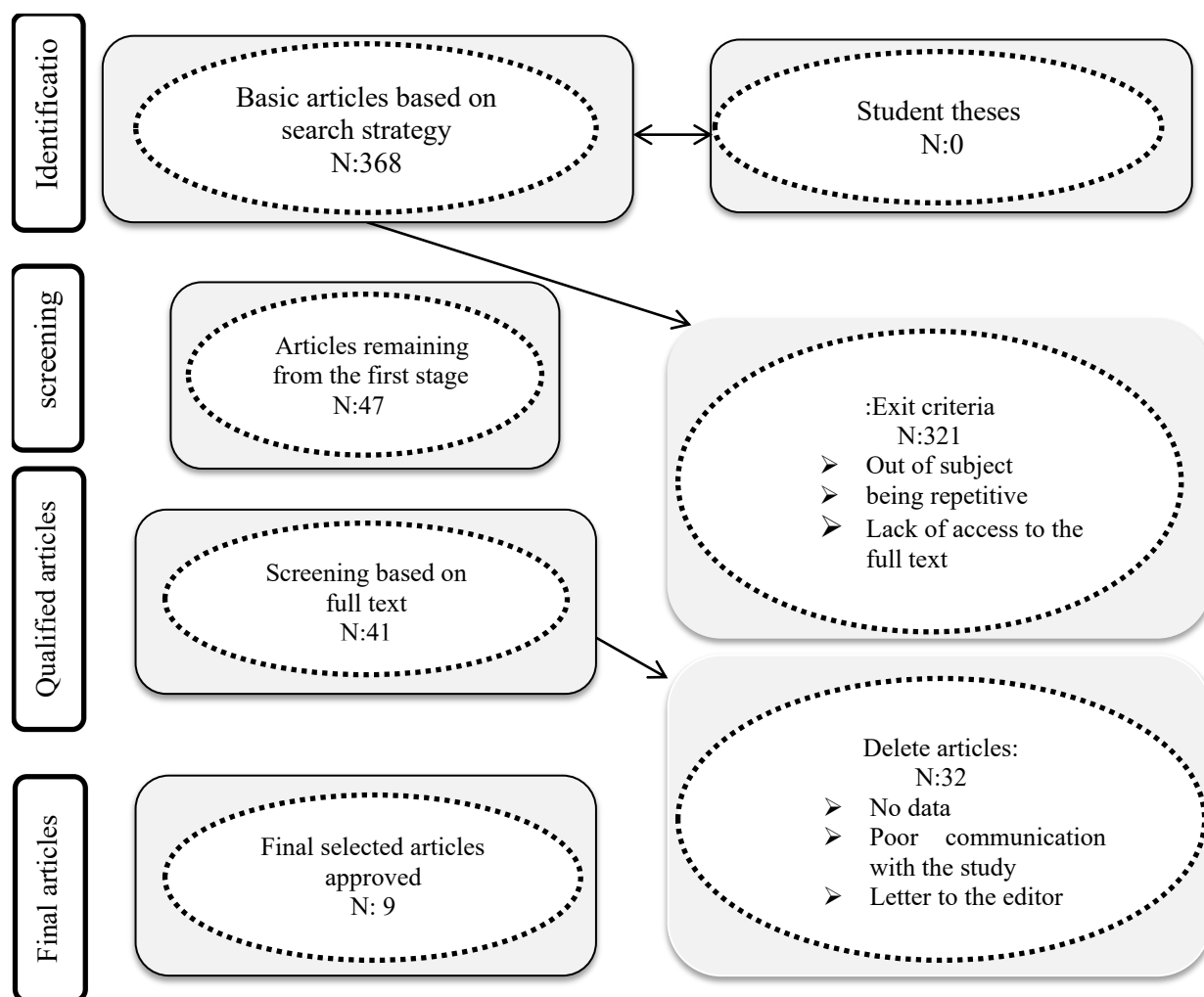


Figure 1. Flowchart of the process of selecting articles and entering the study.

Table 2. Antibacterial activity of *PGL* (In vivo and In vitro).

Row	Plant/part used	bacteria	Results	Ref.
1	<i>PGL</i> / leaf bark, fruit	<i>Helicobacter pylori</i> <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Streptococcus mitis</i> ,	This study demonstrated that the leaf extract of <i>P. guajava</i> is effective in treating diseases caused by protozoa, fungi, bacteria, and viruses.	[8]
2	<i>PGL</i> / leaf	<i>Staphylococcus aureus</i>	In the study, a concentration of 5 mg/ml of the extract was effective against MDR bacteria within 10 hours.	[9]
3	<i>PGL</i> / leaf	<i>Enterococcus faecalis</i> , <i>Staphylococcus aureus</i>), <i>freundii</i> , <i>Escherichia coli</i> and <i>Pseudomonas sp</i>	Based on the findings, the <i>PGL</i> leaf extract exhibits excellent antioxidant activity, while the <i>PGL</i> essential oil contains the highest amount of polyphenols. Interestingly, a significant negative linear correlation exists between total polyphenol content (TPC) and antioxidant capacity, as evidenced by the Pearson correlation coefficients. Moreover, the <i>PGL</i> essential oil shows remarkable antibacterial and antifungal activity against all the bacteria and fungi tested in the study.	[10]
4	<i>PGL</i> / leaf	<i>Candida albicans</i> and <i>Streptococcus mutans</i>	The study found that <i>PGLEO</i> exhibited potent anticancer activity of 45.89% at 200 µg/mL, with an IC ₅₀ value of 188.98 µg/mL, which was significant ($p < 0.001$) when compared to doxorubicin (47.87%). Additionally, the results suggest that <i>PGLEO</i> has antimicrobial properties and holds promise as a potential anticancer agent.	[11]
5	<i>PGL</i> / leaves and bark	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Bacillus cereus</i> , and <i>Staphylococcus aureus</i> .	The study findings suggest that guava leaves and bark possess antibacterial properties and may have the potential as alternative treatment options in traditional herbal medicine.	[12]
6	<i>PGL</i> / leaves and bark	<i>V. cholerae</i>	The researchers determined that the crude aqueous mixture and water-soluble methanolic extract had a minimum inhibitory concentration of 1250 µg/mL and 850 µg/mL, respectively, against 10 ⁷ CFU/mL <i>V. cholerae</i> in laboratory conditions.	[13]
7	<i>PGL</i> / leaf	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> and <i>Bacillus subtilis</i>	According to the findings, it was observed that the hydroalcoholic extracts of <i>psidium guajava</i> leaves, administered at a dosage of 400 mg/kg, exhibited notable anti-ulcer properties in comparison to the standard medication.	[14]
8	<i>PGL</i> / leaf	<i>S.aureaus</i> and <i>E.Coli</i>	The results show that the plant extract alone can have antimicrobial activity experimentally.	[15]
9	<i>PGL</i> / leaf	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> ,	Aqueous and ethanol extracts of <i>PGL</i> have been suggested as a potential alternative to common antibiotics.	[16]

10	PGL / leaf	<i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> <i>Salmonella typhi</i> and <i>Escherichia coli</i>	The study found that the antimicrobial activity of guava's methanol extract was the highest against <i>Bacillus cereus</i> , while it was the highest against <i>Salmonella typhi</i> in the ethanolic extract. On the other hand, the lowest antimicrobial activity was observed against <i>Staphylococcus aureus</i> in the ethanolic extract.	[17]
11	PGL / leaf	<i>S. sanguinis</i> , <i>S. mitis</i> and <i>Actinomyces</i> sp	The results of both extracts were promising as they exhibited positive anti-adhesion activity and decreased the hydrophobicity of the bacteria's cell surface. This could potentially lead to a reduction in their adhesion to the tooth surface during the initial stages of plaque formation. Additionally, both extracts were found to have the ability to suppress the growth of these bacteria.	11[18]

Table 3. Articles included in the study with the effect of guava leaf extract on *H. pylori*.

Row	plant/plants	The part to be tested	Method Extraction	Results	Ref.
1	PGL	leaf	Ethanol	The inhibitory effect of the PGL extract was evaluated, and the results indicated that PGL had significantly higher effective concentrations (125 µg/mg) and MIC90 (26.6) compared to clarithromycin (1.95 µg/mg) and MIC90 (0.7) against <i>H. pylori</i> .	[19]
2	32 types of plants of which PGL was a part.	leaf	chloroform , Petroleum ether, and methanol	The antimicrobial activity of 32 medicinal plants in Malaysia against <i>Helicobacter pylori</i> was evaluated using disk diffusion and agar dilution methods. <i>Psidium guajava</i> showed significant antibacterial activity.	[20]
3	50 types of plants of which PGL was a part.	Leaf/stem/root/flower (PGL)	Ethanol	Based on this research, PGL was classified as moderate against <i>Helicobacter pylori</i> among 26 plants tested.	[21]
4	Two types of plants: Terminalia catappa and PGL	leaf	Ethanol	The study confirms that PGL and T. catappa leaves have a strong antioxidant potential.	[2]
5	16 types of plants of which PGL was a part	leaf	Ethanol	As per the study, most of the tested medicinal plant extracts were found to have cytotoxicity, with PGL being classified as moderate against <i>H. pylori</i> .	[22]
6	PGL and Chinese Coptis	leaf	Hydroalcoholic	Both extracts obtained from the early hours of incubation showed the ability to inhibit the growth of <i>H. pylori</i> strains in culture.	[23]
7	6 types of plants, of which PGL was a part	leaf/bark	Ethanol	In addition to its inhibitory effect, the extract of PGL contained the highest amount of polyphenols and effectively inhibited tumor necrosis factor, interleukin-1, and interleukin-6 at both mRNA and protein levels. The extract also exhibited high antioxidant potential, making it a promising candidate for treating gastric ulcers caused by <i>H. pylori</i> .	[24]
8	12 types of plants, of	leaf	Hydroalcoholic	After phytochemical screening, the multi-plant suspension showed the presence of terpenoids,	[25]

which PGL was a part				flavonoids, and tannins that have anti-ulcer activity. The anti-ulcer activity in the model induced by ethanol showed a significant decrease of P<0.05 from the wound.	
9	PGL	leaf	chloroform	The results indicate that phytochemicals in guava leaf extract cause apoptosis in SNU-16 cells, suggesting potential for new strategies in treating human gastric cancer.	[26]

Table 4. Biological activity of some PGL compounds

Plant components/ country	Active chemical compounds	Biological activity	Ref.
guava peel, flesh, and seed /China	catechin, galangin, homogentisic acid, gallic acid, kaempferol and cyanidin 3-glucoside	Anticancer and Antioxidant	[29]
Leaf / Taiwan	Ferulic acid, gallic acid, quercetin	Anticoagulant, anti-inflammatory, anti-glucose	[30]
Leaf / India	Main compounds α -terpinyl acetate, trans-caryophyllene, nerolidol, α -cadinol, α -copene and identified minor components of α -humulene.	Pain reliever, anti-inflammatory, antibacterial	[28]
Stem and leaf / Tunisia	The main compounds identified in the stem oil were alpha-humulene, germacrene D, and valenrol, whereas vein florol and trans-caryophyllene were predominant in the leaf oil.	Anti-inflammatory, anti-spasmodic	[31]
Leaf/Egypt	b- Caryophyllene, transnerolidol, global and d-limonene.	Antimicrobial, antidiarrheal, antipyretic, antihypertensive	[32]
Leaf / Thailand	The most active quercetin compound and two flavonoid compounds, quercetin-3-O-glucopyranoside and murine, were found.	Antioxidant	[33]
Leaf / Oman	Most of the leaf oil contains caryophyllene, veiniflorene, farnesin, and limonene.	Antimicrobial, cytotoxic	[34]
Leaf / Korea	The research reveals that guava leaves contain around 60 plant compounds, including phytol, β -eodesmol, α -copene, These compounds have the potential to disrupt various signaling pathways associated with the formation of tumors, making them promising candidates for developing cancer prevention and treatment therapies.	Anticancer	[35]

chemical composition of PGL varies by geographic region (seasonal changes and climatic conditions) [28]. Findings show that guava leaves contain many compounds, including phytol, beta-desmol, α -copene, etc. These compounds can potentially disrupt various signaling pathways associated with tumorigenesis, making it a promising candidate for cancer prevention and treatment.

DISCUSSION

One of the most common and critical causes of death in modern society is gastrointestinal cancer, one of the main causes of which is *H. pylori* infection [36]. As previously stated, *H. pylori* is considered to be a primary risk factor for the development of gastric cancer [37]. Antibiotics have been very effective in managing microbial infections. However, they are

expensive and have many side effects. In addition, the threat of antimicrobial resistance has led to the inactivity of various conventional antibiotics. Medicinal plants are used in traditional medicine to control microbial infections since they are affordable and have shown fewer side effects [38]. PGL, commonly known as guava, contains tannins, phenols, saponins, vitamins, fibers, flavonoids, essential oils, fatty acids, etc [39]. Many pharmacological studies with PGL have shown that this plant has anticancer, antioxidant, antimicrobial, analgesic, and antitussive properties [40].

In a 2015 study comparing two plants PGL and *Coptis chinensis* Franch, for their effect on AGS human gastric cancer cells, the synergy of the mixture of these two plants can prevent chronic gastritis caused by *H. pylori* [23].

In a 2014 study, most plant extracts demonstrated cytotoxic effects. PGL was categorized as a moderate inhibitor against *H. pylori*, indicating that combining this plant with others possessing similar antibacterial properties could yield inhibitory effects. Nevertheless, further investigation is warranted [22]. Notably, most of the PGL extracts in the articles reviewed in the above tables contain phenolic compounds that could be involved in the antibacterial activities observed in this study, some showing antibacterial properties together. The amount of phenolic compounds inside the plant is [41]. In another article, the anti-disease activity of the methanol extract of guava was mentioned due to the percentage of avoided, especially murine glycosides, quercetin glycosides, and quercetin [42]. In this study, the example mentioned in Table No. 2 has been considered as one of the chemical compounds against *H. pylori*.

In many articles, the chemical composition of the obtained extract was of great importance, and in a way, the extract that contained that compound in question showed antibacterial and anti-inflammatory effects. PGL extracts contain chemical compounds of gallic acid and catechin, which may be related to the antimicrobial, anti-inflammatory, and analgesic activities of these extracts [41]. In a study in 2013, researchers investigated the antimicrobial effect of gallic acid and catechin on *H. pylori* culture. Both

polyphenols demonstrated strong inhibitory effects on two strains of *H. pylori* [43]. Histochemical or chemical compounds of PGL leaf or fruit extract can treat gastric ulcers. This disease is caused by one of the important causes, *H. pylori* [44].

In a 2019 study, PGL leaves were found to contain high amounts of gallic acid, quercetin, and corilagin based on HPLC analysis. These compounds have demonstrated significant anti-*H. pylori* activities [19]. It is clear from the findings that this plant's main use is in treating digestive disorders, and it has also been used to treat several microbial diseases caused by protozoa, fungi, bacteria, and viruses. A significant gap is that more research should be done on different parts (leaves, stems, roots, fruits, etc) of plants native to Iran and can be used as medicine.

CONCLUSION

The high prevalence of *H. pylori* in the population must be considered, as it often goes undetected unless symptoms require diagnostic tests. This review serves as a good reference for those researching *H. pylori* and inspires further research to improve diagnostic and therapeutic methods to reduce the impact of this common gastrointestinal pathogen. The results of this study show that PGL plant extracts have appropriate antimicrobial substances that can be used as a pharmaceutical base or a suitable herbal medicine to fight against microorganisms such as *H. pylori*. It was found that the good antimicrobial activity of this plant against *H. pylori* is related to its phenolic compounds. However, more research is necessary for efficacy studies in animal models and determining the effective methods of PGL plant extracts (including urease inhibition) for *H. pylori* bacteria to access more comprehensive and practical information in the future.

ACKNOWLEDGMENTS

I appreciate and thank all my Zabol University of Medical Sciences colleagues who helped us in this research.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS APPROVAL

Not applicable.

REFERENCES

- Fonseca DR, Chitas R, Parreira P, Martins MCL. How to manage *Helicobacter pylori* infection beyond antibiotics: The bioengineering quest. *Applied Materials Today*. 2024;37:102123. DOI: [10.1016/j.apmt.2024.102123](https://doi.org/10.1016/j.apmt.2024.102123).
- Timothy O, Ugwu G. Antioxidant activities of ethanol leaf extracts of *Psidium guajava* L., *terminalia cattapa* L. and their combined formulation. *Fudma journal of sciences*. 2022;6(3):301-6. DOI: [10.33003/fjs-2022-0603-986](https://doi.org/10.33003/fjs-2022-0603-986).
- Crowe SE. *Helicobacter pylori* infection. *New England Journal of Medicine*. 2019;380(12):1158-65. DOI: 10.1056/NEJMra020542.
- Ahmadzadeh A, Eftekhari Z, Mohsenifar Z, Rezaei Tavarani M. Investigating the prevalence of clarithromycin resistance among *Helicobacter pylori* strains isolated from patients with digestive problems. *Pars Journal of Medical Sciences*. 2023;21(4):62-70.
- Zhang Y, Feng X, Bian L, Zhang Y, Li Q, Xu Y, et al. Antibiotic Resistance of *Helicobacter pylori* and Related Risk Factors in Yangzhou, China: A Cross-Sectional Study. *Journal of Clinical Medicine*. 2023;12(3):816. DOI: [10.3390/jcm12030816](https://doi.org/10.3390/jcm12030816).
- Alba C, Blanco A, Alarcón T. Antibiotic resistance in *Helicobacter pylori*. *Current opinion in infectious diseases*. 2017;30(5):489-97.
- Khanpara P, Mavani P. A review on herbal plants used in peptic ulcer. *Journal of Medicinal Plants*. 2022;10(5):122-30.
- Morais-Braga MFB, Carneiro JNP, Machado AJT, Dos Santos ATL, Sales DL, Lima LF, et al. *Psidium guajava* L., from ethnobiology to scientific evaluation: Elucidating bioactivity against pathogenic microorganisms. *Journal of Ethnopharmacology*. 2016;194:1140-52. DOI: [10.1016/j.jep.2016.11.017](https://doi.org/10.1016/j.jep.2016.11.017).
- Nsofor OU, Ogochukwu AP, Chigozie U-uJ, Emmanuel E, Chinemelu OJ, Okwuchukwu AJ, et al. In vitro Antimicrobial Activities of Methanol Crude Leaf Extract of *Psidium guajava* L. on Clinical Isolates of Multidrug Resistant *Staphylococcus aureus*. *Asian Journal of Biotechnology and Genetic Engineering*. 2023;6(1):39-45.
- Lahlou J, Amraoui B, El-Wahidi M, Bamhaoud T. Chemical composition, antioxidant and antimicrobial activities of Moroccan species of *Psidium guajava* extracts. *Roczniki Państwowego Zakładu Higieny*. 2022;73(1):65-77. DOI: [10.32394/rpzh.2022.0199](https://doi.org/10.32394/rpzh.2022.0199).
- Alam A, Jawaid T, Alsanad SM, Kamal M, Balaha MF. Composition, Antibacterial Efficacy, and Anticancer Activity of Essential Oil Extracted from *Psidium guajava* (L.) Leaves. *Plants*. 2023;12(2):246. DOI: [10.3390/plants12020246](https://doi.org/10.3390/plants12020246).
- Ndako JA, Oludipe EO, Dojumo VT, Fajobi VO, Echemita RF, Ndako PJ, et al., editors. Optimizing Antibacterial Activity of *Psidium guajava* Extracts using Solvent Fractionation method and its Efficacy against Foodborne Pathogens. 2023 International Conference on Science, Engineering and Business for Sustainable Development Goals (SEB-SDG); 2023: IEEE. DOI: [10.1109/SEB-SDG57117.2023.10124522](https://doi.org/10.1109/SEB-SDG57117.2023.10124522).
- Rahim N, Gomes DJ, Watanabe H, Rahman SR, Chomvarin C, Endtz HP, et al. Antibacterial activity of *Psidium guajava* leaf and bark against multidrug-resistant *Vibrio cholerae*: implication for cholera control. *Japanese journal of infectious diseases*. 2010;63(4):271-4. DOI: [10.7883/yoken.63.271](https://doi.org/10.7883/yoken.63.271).
- Divyaprabha M, Chitra P, Rameshwari KS. Antiulcer activity of *Psidium guajava* on pylorus ligation induced gastric ulcer in albino rats. *Int J Pharm Sci Res*. 2021;12(1):443-9. DOI: [10.13040/IJPSR.0975-8232.12\(1\).443-49](https://doi.org/10.13040/IJPSR.0975-8232.12(1).443-49).
- Gideon M. Novel Optimization of *Psidium guajava* Antibacterial Activity for Drug Discovery and Development. 2023. DOI: [10.26434/chemrxiv-2023-1z7nk-v2](https://doi.org/10.26434/chemrxiv-2023-1z7nk-v2).
- Evbuomwan L, Jacob IB, Ebiala FI, Chukwuka EP. Antibacterial activity of aqueous and ethanolic leaves extract of *Psidium guajava*. 2018.
- Moses AS, Singh SN, Pratap D, Salam S. Determination and comparison of antimicrobial activity of *Psidium guajava* and *Embllica officinalis* against MDR bacteria. *Journal of Pharmacognosy and Phytochemistry*. 2019;8(1):2169-72.
- Fathilah A. Piper betle L. and *Psidium guajava* L. in oral health maintenance. *Journal of Medicinal Plants Research*. 2011;5(2):156-63.
- Taha TF, Elakkad HA, Gendy AS, Abdelkader MA, Hussein S. In vitro bio-medical studies on *Psidium guajava* leaves. *Plant Arch*. 2019;19(1):199-207.
- Uyub AM, Nwachukwu IN, Azlan AA, Fariza SS. In-vitro antibacterial activity and cytotoxicity of selected medicinal plant extracts from Penang Island Malaysia on metronidazole-resistant-*Helicobacter pylori* and some pathogenic bacteria. 2010.
- Wang Y-C, Huang T-L. Screening of anti-*Helicobacter pylori* herbs deriving from Taiwanese folk medicinal plants. *FEMS Immunology & Medical Microbiology*. 2005;43(2):295-300. DOI: [10.1016/j.femsim.2004.09.008](https://doi.org/10.1016/j.femsim.2004.09.008).
- Masadeh MM, Alkofahi AS, Alzoubi KH, Tumah HN, Bani-Hani K. Anti-*Helicobacter pylori* activity of some Jordanian

- medicinal plants. *Pharmaceutical biology*. 2014;52(5):566-9. DOI:[10.3109/13880209.2013.853811](https://doi.org/10.3109/13880209.2013.853811).
23. Lozoya X, Agüero Agüero J, Gascón Muro M, Torres J, Camorlinga M, Vázquez Jimenez FE. Propiedades anti-*Helicobacter pylori* de los extractos de *Psidium guajava* y *Coptis chinensis*. *Rev fitoter*. 2015;149-56.
 24. Phromnoi K, Sinchaiyakij P, Khanaree C, Nuntaboon P, Chanwikrai Y, Chaiwangsi T, et al. Anti-inflammatory and antioxidant activities of medicinal plants used by traditional healers for antiulcer treatment. *Scientia Pharmaceutica*. 2019;87(3):22 DOI:[10.3390/scipharm87030022](https://doi.org/10.3390/scipharm87030022).
 25. Kumar AP, Jonnalagadda VG, Joy JM, Lakshmi M. Pharmacognostical, Phytochemical and Pharmacological evaluation for the antiulcer activity of Polyherbal suspension. *Journal of Pharmacognosy and Phytochemistry*. 2013;2(3):128-35.
 26. Moon JY, Mosaddik A, Kim H, Cho M, Choi H-K, Kim YS, et al. The chloroform fraction of guava (*Psidium cattleianum* Sabine) leaf extract inhibits human gastric cancer cell proliferation via induction of apoptosis. *Food chemistry*. 2011;125(2):369-75.
 27. Gupta GK, Chahal J, Arora D. *Psidium guajava* Linn.: Current research and future prospects. *J Pharm Res*. 2011;4(1):42-6.
 28. Borah A, Pandey SK, Haldar S, Lal M. Chemical composition of leaf essential oil of *Psidium guajava* L. from North East India. *Journal of Essential Oil Bearing Plants*. 2019;22(1):248-53.
 29. Chen Y, Zhou T, Zhang Y, Zou Z, Wang F, Xu D. Evaluation of antioxidant and anticancer activities of guava. *International Journal of Food Nutrition and Safety*. 2015;6(1):1-9.
 30. Hsieh C-L, Lin Y-C, Yen G-C, Chen H-Y. Preventive effects of guava (*Psidium guajava* L.) leaves and its active compounds against α -dicarbonyl compounds-induced blood coagulation. *Food chemistry*. 2007;103(2):528-35.
 31. Khadhri A, El Mokni R, Almeida C, Nogueira J, Araújo MEM. Chemical composition of essential oil of *Psidium guajava* L. growing in Tunisia. *Industrial Crops and Products*. 2014;52:29-31.
 32. Hassan EM, El Gendy AE-NG, Abd-ElGawad AM, Elshamy AI, Farag MA, Alamery SF, et al. Comparative chemical profiles of the essential oils from different varieties of *Psidium guajava* L. *Molecules*. 2020;26(1):119.
 33. Tachakittirungrod S, Ikegami F, Okonogi S. Antioxidant active principles isolated from *Psidium guajava* grown in Thailand. *Scientia pharmaceutica*. 2007;75(4):179-93.
 34. Weli A, Al-Kaabi A, Al-Sabahi J, Said S, Hossain MA, Al-Riyami S. Chemical composition and biological activities of the essential oils of *Psidium guajava* leaf. *Journal of King Saud University-Science*. 2019;31(4):993-8. DOI:[10.1016/j.jksus.2018.07.021](https://doi.org/10.1016/j.jksus.2018.07.021).
 35. Ryu NH, Park K-R, Kim S-M, Yun H-M, Nam D, Lee S-G, et al. A hexane fraction of guava leaves (*Psidium guajava* L.) induces anticancer activity by suppressing AKT/mammalian target of rapamycin/ribosomal p70 S6 kinase in human prostate cancer cells. *Journal of medicinal food*. 2012;15(3):231-41.
 36. Ganjali A, Fakheri BA, Bahari A, Fahmideh L, Valadan R. The Role of Cytokines and Pattern Recognition Receptors in Inflammation Caused by *Helicobacter pylori* Infection in Gastric Cancer. *International Journal of Basic Science in Medicine*. 2022;7(1):3-10 DOI: [10.34172/ijbsm.2022.02](https://doi.org/10.34172/ijbsm.2022.02).
 37. Ganjali A, fakheri Ba ,Bahari A, fahmideh l, valadan r. The Role of *Helicobacter Pylori* Virulence Factors in Gastric Cancer. *Multidisciplinary Cancer Investigation*. 2022;6(3):1-7. DOI:10.30699/mci.6.3.598-1.
 38. Kerubo AC. Antibacterial activity of dichloromethane: methanolic leaf and stem bark extracts of *Psidium guajava* Linn against selected bacteria: Kenyatta University; 2019.
 39. Mandal SK, Dawn S, Bose A. Antiulcer agents: A pharmacological update of the past ten years. *Asian J Pharm Clin Res*. 2019;12(8):37-41.
 40. Gutiérrez RMP, Mitchell S, Solis RV. *Psidium guajava*: a review of its traditional uses, phytochemistry and pharmacology. *Journal of ethnopharmacology*. 2008;117(1):1-27.
 41. de Araújo AA, Soares LAL, Ferreira MRA, de Souza Neto MA, da Silva GR, de Araújo Jr RF, et al. Quantification of polyphenols and evaluation of antimicrobial, analgesic and anti-inflammatory activities of aqueous and acetone–water extracts of *Libidibia ferrea*, *Parapiptadenia rigida* and *Psidium guajava*. *Journal of ethnopharmacology*. 2014;156:88-96.
 42. Arima H, Danno G-i. Isolation of antimicrobial compounds from guava (*Psidium guajava* L.) and their structural elucidation. *Bioscience, biotechnology, and biochemistry*. 2002;66(8):1727-30. DOI: [10.1271/bbb.66.1727](https://doi.org/10.1271/bbb.66.1727).
 43. Díaz-Gómez R, López-Solís R, Obreque-Slier E, Toledo-Araya H. Comparative antibacterial effect of gallic acid and catechin against *Helicobacter pylori*. *LWT-Food Science and Technology*. 2013;54(2):331-5. DOI:[10.1016/j.lwt.2013.07.012](https://doi.org/10.1016/j.lwt.2013.07.012).
 44. Nayak B, Mishra L, Pusty P, Prakash K, Bhattacharyay D. Efficacy of Phytochemicals from guava (*Psidium guajava*) leaf against *Helicobacter pylori* causing ulcer: an In silico analysis. *plant cell biotechnology and molecular biology*. 2020:134-7