



Review Article

Exploring antibacterial & antiulcer activity of aegle marmelos linn. : A review

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ABSTRACT

Antimicrobial drugs are those drugs which are used to treat diseases caused by microorganisms. To treat the diseases caused by pathogenic microorganisms antibiotic, antiviral, antifungal and antiparasitic medicines are used. These microbes produces diseases in humans, animals and plants. According to World Health Organization (WHO). The cases of Antimicrobial resistance (AMR) is increasing day by day and it threatens the effective treatment and prevention of infections caused by bacteria, viruses, fungi and parasites. AMR occurs when these microbes gets resistance against the effects of medications, which makes common infections difficult to treat and hence increases the risk of severe illness, disease spread and death. As a result, the medicines becomes ineffective, infections remains in the body and increases the probability of spread to others. WHO recommends that decreased use of synthetic antibiotics and increased use of herbal antimicrobial drugs are the only ways by which the AMR can be controlled or eliminated. Herbal drugs are considered to be effective and free from side effects. In the present article we discussed about Aegle Marmelos Linn. (Bael) which is useful in treating many health ailments. It possess many pharmacological activities like anticonvulsant, antioxidant, antihyperglycemic, anxiolytic, antidepressant, antihistaminic, antimicrobial, hepatoprotective, analgesic, immune modulatory, cardio protective and antithyroid activity. Due to its antibacterial activity it is used to treat many infections caused by bacteria and also have antiulcer activity due to which it is used to treat ulcer patients. The bacteria, Helicobacter pylori is one of the cause of peptic ulcer. This review article discusses about the effect of Aegle Marmelos on this bacteria.

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1. Introduction

1.1. Antimicrobial resistance (AMR)

Pathogenic microorganisms causes infection and which leads to many diseases in human, animals and plants. To those diseases antimicrobial drugs are used like antibacterial, antifungal antiviral and antiparasitic drugs. Due to excessive use of the antimicrobial drugs, microbes are getting resistance towards these drugs which means that the medications are becoming ineffective. This is called antimicrobial resistance (AMR). WHO says it's a global problem and recommends to decrease the synthetic antimicrobial drugs and in place of that herbal antimicrobial

drugs should be used.¹ These are the ways by which AMR can be controlled or eliminated.

1.2. Peptic ulcer

The common causes of peptic ulcer are infection due to bacteria known as Helicobacter pylori (H.pylori) and Non-steroidal anti-inflammatory drugs (NSAID) use. Exposure of acid-pepsin secretions to the regions of the upper gastrointestinal tract (GIT) leads to peptic ulcer.¹ It affects stomach either one or all layers or duodenum. Gastric ulcer and duodenal ulcer are the two most common types of peptic ulcer. Duodenal ulcer is 2-4 times more usual than gastric ulcer.² Gastric ulcers occurs in the stomach which is characterized by pain and are common in persons of older age. Other symptoms of gastric ulcers are nausea, vomiting

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and weight loss. Although there is normal or diminished acid production in patients with gastric ulcers, it may occur even in absence of acid also.³ At the beginning of small intestine duodenal ulcers are found which is characterized by burning sensation in upper abdomen with severe pain that awakens patients from sleep. Generally, pain occurs in empty stomach and relieves after eating. In younger individuals duodenal ulcer is more common and mostly affects males.⁴

1.3. Global and national status of peptic ulcer

If we talk about the GIT disorders in the world, peptic ulcer is the major one. 10% of the world population is effected by peptic ulcer.⁵ As we know duodenal ulcer is more common and about 19 out of 20 peptic ulcer patients are suffering from duodenal ulcer. It is estimated that due to peptic ulcer 15000 deaths occurs every year. It is also estimated that the annual incidence of peptic ulcer hemorrhage was 19.4-57 per 100,000 individuals and peptic ulcer perforation was 3.8-14 per 100,000 individuals. On an average the rate of recurrence of hemorrhage in seven days and long term perforation were 13.9% and 12.2% respectively.⁶ WHO latest data published in 2017 says that deaths in India due to peptic ulcer disease reached 57,658 or 0.66% of total deaths in the country. The India ranks 53 in the world in age adjusted death rate which is 5.79 per 100,000 of population.⁷ Antacids and antiulcer drugs in the Indian pharmaceutical industry shares 6.2 billion rupees and which is about 4.3% of the market share.⁸ Aggressive and protective factors are probably responsible for the occurrence of peptic ulcer due to the disturbance in balance between these two in the stomach.⁹ Aggressive factors includes *Helicobacter pylori*, hydrochloric acid, pepsins, Non-steroidal anti-inflammatory drugs, bile acids, ischemia, hypoxia, smoking and alcohol and on the other hand protective factors includes bicarbonate, mucus layer, mucosal blood flows, prostaglandins and growth factors.¹⁰

1.4. *Helicobacter Pylori*

Helicobacter pylori is a common bacterial human pathogen and can transmit from one person to another person. The bacteria infects the upper GIT which causes progressive acute and chronic gastroduodenal inflammation. Gastritis, gastric atrophy, duodenal ulcer disease, gastric ulcer disease, primary gastric B-cell lymphoma, gastric adenocarcinoma, iron deficiency anaemia, and vitamin B12 deficiency are the manifestations of *H.pylori* infection. Overall sanitary conditions and exposure to infected humans are the factors which are inversely related to the risk of infection. Contaminated water is one of the mode of transmission in rural areas. However, in urban areas the risk of infection depends on the level of household hygiene.¹¹ *H. pylori* is a bacteria found in almost 50% of the global population. The

relation between peptic ulcer disease and *H. pylori* infection has been found over the last few decades and documented studies says that *H. pylori* infection causes 90% of duodenal ulcers and up to 70% of gastric ulcers. If not treated, peptic ulcer disease creates complications in 20 to 25% of the patients.¹²

Natural products became the most attractive source of new drug and relatively less expensive, safe to use even at higher doses for the treatment and prevention of many diseases, these are the reasons why it is continuously expanding all over the world.¹³ According to WHO, medicinal plants would be the best source to obtain a variety of drugs. Therefore, these should be properly investigated to better understand their properties, safety and efficacy.¹⁴ Number of antibacterial drugs are available in India like *Azadirachta indica* (Neem), *Ficus religiosa* (Peepal) etc. In this review article we tried to collect all information about *Aegle marmelos* which is potent antibacterials and antiulcer.

2. Antibacterial Activity of *Aegle Marmelos*

Srikala Ganapathy & Karpagam S. (2016) told that increase of antibiotic resistant bacteria gives rise to limited options for treatment of bacterial diseases. *Escherichia coli*, Gram negative bacteria causing community and hospital acquired infections. Herbal drugs are the alternative source of useful antibacterial agents. They carried out their studies by extracting the constituents of leaves and fruits of *Aegle marmelos* using water, hexane and ethanol and tested it against MDR *Escherichia coli*. It was concluded that the ethanol extract showed highest antibacterial activity as compared to hexane and water extracts. Tannins, flavonoids, saponins and alkaloids were the antibacterial compounds found in leaf and fruit.¹⁵

Padmanav Behera et al. (2014) evaluated the fruit pulps of *Aegle marmelos* (Linn.) Correa and they found Reducing Sugars, Saponins, Tannis, Flavonoids and Phenols present in it. They tested the crude extract for antimicrobial activity against two gram positive strains and found that a different concentration range of the ethanolic, aqueous and petroleum ether extracts were effective to inhibit the growth of the above strain.¹⁶

S. K. Gangai Abirami et al. (2014) performed antibacterial screening of three extracts of leaves of *Aegle marmelos* on five bacterial strains and three fungal strains. They found that the Chloroform extract showed good antibacterial activity and antifungal activity against *E.coli* and *Fusarium oxysporum* respectively.¹⁷

Subramanian Ramya et al. (2012) performed the antimicrobial screening of ethanolic leaf extracts of *Aegle marmelos* (L) Corr. on six bacterial strains like *B. subtilis*, *E. coli*, *S. aureus*, *P. aeruginosa* and *K. pneumonia* and found that ethanolic leaf extracts of *A. marmelos* exhibit significant antibacterial activity towards all the selected bacterial strains. *B. subtilis* and *E. coli* were more

sensitive as compared to *S. aureus*, *P. aeruginosa* and *K. pneumonia*.¹⁸

Saroj Kothari et al. (2011) investigated in vitro antimicrobial activity of leaves of *Aegle marmelos* against different species of bacteria and fungus. Extraction was done by using petroleum ether, chloroform and methanol. All the extracts exhibited antimicrobial activity. It also revealed that petroleum ether extract was more effective against bacteria like *Staphylococcus aureus*, β *Streptococcus haemolyticus* group A, *Pseudomonas aeruginosa* and *Escherichia coli*. chloroform extract was effective against *Proteus mirabilis*, *Klebsiella pneumonia* and methanolic extract was effective against *Salmonella typhi*. Petroleum ether extract exhibited the highest antifungal efficacy against all tested fungal species. Phenols, sterols were found in petroleum ether and chloroform extracts whereas tannins, flavonoids, coumarins, saponins and triterpenoids were found in methanolic extract.¹⁹

Rajamurugan R. et al. (2013) performed phytochemical screening, antioxidant and antibacterial activities of ethanolic extracts on leaves of five medicinal plants including *Aegle marmelos*. Phytochemical screening revealed the presence of terpenoids, phenols, flavonoids, tannins, alkaloids, cardiac glycosides and steroids in all extracts. All extracts showed considerable antioxidant activity. Antibacterial activity was performed against *E. coli*, *Pr. Mirabilis* & *S. aureus*. All the extracts were found effective against all three species.²⁰

K. Suresh et al. (2009) performed antimicrobial screening of methanol extracts of leaves and flowers of *Aegle marmelos*. They showed effective inhibitory effect against *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Salmonella typhi*, *Staphylococcus aureus* and came to the conclusion that Methanolic extracts of *Aegle marmelos* has great antimicrobial potential.²¹

Rijamol K. Ulahannan et al. (2008) performed phytochemical and antibacterial studies of various extracts on leaves of *Aegle marmelos*. *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Serratia marcescens* & *Klebsiella pneumonia* are the bacterial strains used to check antibacterial activity. The methanolic extract showed antibacterial activity. Phenols, alkaloids, flavanoids were found in phytochemical analysis of methanol extract and considered as one of the reasons for antibacterial property.²²

C. Rajasekaran et al. (2008) carried out evaluation of the antimicrobial activity of leaf extracts from *Aegle marmelos* (L.) Corr. Different extracts of the leaves, eight Gram positive and two Gram negative bacteria were used for investigation. Results depict that ethanol and chloroform extracts were found more effective towards the bacterial species tested. The leaf extracts were capable to inhibit the growth of both Gram positive and Gram negative bacterial species.²³

Surender S. Yadav et al (2015) investigated the antibacterial property of *Aegle marmelos* (L.) Correa leaf extracts. Two Gram-positive and three Gram-negative bacteria were used for the study. The zone of inhibitions showed that methanolic and chloroform leaf extracts exhibited higher activity against *P. aeruginosa* and *S. aureus* as compared to *B. subtilis* and *K. pneumonia*.²⁴

M. Poonkothai & M. Saravanan (2008) studied the antibacterial activity of the leaves, bark and fruit of *A. marmelos* against different Gram positive and Gram negative bacterial strains. Results suggested that the methanolic extract has significant antibacterial activity against both Gram positive and Gram negative bacteria.²⁵

Biresh K Sarkar & Shailendra Singh Solanki (2011) isolated phytoconstituents responsible for antibacterial activity of leaves of *Aegle marmelos*. They tested it on four bacterias i.e. *Staphylococcus aureus*, *Solmonella typhi*, *Bacillus subtilis* and *Escherichia coli* which showed that it had a high efficiency of destroying bacteria.²⁶

Sandeep Dhankhar et al (2011) isolated Coumarins, alkaloids, Tannins, Carotenoids and seed oils and other miscellaneous compounds from *Aegle marmelos* and reported its properties like antidiabetic, antiulcer, antioxidant, antimalarial, antiinflammatory, anticancer, radioprotective, antihyperlipidaemic, antifungal, antibacterial and antiviral activities.²⁷

Rabi Ranjan Chattopadhyay et al (2009) carried out a comparative in vitro antibacterial study to find out the potential of aqueous extracts and ethanolic extract of five important medicinal plants including *Aegle marmelos* against common pathogenic bacteria. The ethanolic extract of *Aegle marmelos* showed higher antibacterial activity compared to aqueous extract. *T. chebula* and *A. marmelos* had the strongest antibacterial activity.²⁸

Manandhar B. et al (2018) told that leaves, bark, stem, fruits and seeds of *Aegle marmelos* Linn have been used for many medicinal purposes. Bael fruits are very effective in the treatment of chronic diarrhoea, dysentery and peptic ulcers, laxative and respiratory infections. Pharmacological studies states that it is antibacterial, antiviral, antidiarrhoeal, gastroprotective, antiulcerative colitis, hepatoprotective, antidiabetic, cardioprotective, radioprotective effects and anticancer agent.²⁹

Mujeeb F. et al (2014) carried out study on phytochemical screening of aqueous and methanolic leaf extracts of 18 varieties of *A. marmelos* and found highest quantity of alkaloids, flavonoids, and phenols in Pant Aparna variety. The antibacterial efficacy was obtained in aqueous extract against *S. epidermidis*, whereas methanolic extract was found potent against *S. aureus*. However, in aqueous:ethanol, the best results were observed against *E. aerogenes*. Bioactive compounds like flavonoids, alcohols, aldehydes, aromatic compounds, fatty acid methyl esters, terpenoids, phenolics, and steroids that can be considered

as responsible for antibacterial activity.³⁰

Manoharan Sivananthan (2013) told that years ago, the medicinal plants were just used as a treatment without knowing the active compound/s responsible for curing the disease and listed 50 medicinal plants having antibacterial property proved by modern research.³¹

Rehnuma Sharmeen et al. (2012) carried out a study to evaluate antibacterial activity of 35 aqueous herbal extracts against 20 clinical *Klebsiella* sp. isolates. The maximum antibacterial activity was found in leaf of *Syzygium aromaticum* and fruit of *Citrus limon* L. followed by leaf of *Spondias pinnata*. When sensitivity of these isolates was tested for eight commercial antibiotic discs like Chloramphenicol, Erythromycin, sulfamethoxazole, Cephadrine, Gentamycin, Streptomycin, Ciprofloxacin and Azithromycin. Out of 35 herbal extracts tested, 19 herbal extracts showed antimicrobial activity in all multi-drug resistant isolates.³²

3. Antiulcer Activity of Aegle Marmelos

J. Ilavarasan et al (2002) studied efficacy of *Aegle marmelos* against gastric ulcer. A daily dose of 1 gm/kg body weight of the aqueous extract of leaves of *Aegle marmelos* was administered orally for 21 days. The volume of the gastric secretion, ulcer lesion count, pepsin content, PH, total acidity, hexose and hexosamine content were the parameters to estimate. The observation indicated a significant reduction in the ulcer lesion count, volume of gastric juice, acidity (increase in pH) and hexosamine after treatment with aqueous extract. However there was no significant alteration in pepsin and hexose content.³³

Samanta Sifat Lamia et al (2018) collected and compiled all the pharmacological and phytochemical studies done on *Aegle marmelos* (L.). Extensive scientific studies show that this plant have antifungal, antioxidant, antibacterial, antiprotozoal, antispermatic, antiinflammatory, anthelmintic, antidiabetic, laxative and expectorant, chemopreventive, antipyretic, ulcer healing, antigenotoxic, and diuretic activities.³⁴

Dr. Sharmin Rahman et al (2016) carried out a work to investigate the antiulcer activity of *Aegle marmelos*. By ethanol induced gastric ulcer method, the ethanolic extract at 400mg/kg body weight was studied for ulcer protective activity. Ethanolic extract exhibited significant antiulcer activity.³⁵

Ashoka M. Shenoy et al (2012) evaluated the antiulcer activity of methanolic extract of leaves of *Aegle marmelos* on gastric ulcer induced rats by aspirin plus pylorus ligation. Indomethacin induced ulcer in rats, water immersion stress test induced ulcer in rats. In aspirin plus pylorus ligation model, *Aegle Marmelos* when given in doses of 200 and 400 mg/kg produced significant reduction in gastric volume, free acidity and ulcer index compared to control. Severity of ulceration was significantly reduced In Indomethacin and

water immersion stress test induced ulcer models when administered doses of 200mg/kg & 400mg/kg of *Aegle marmelos* extract. *Aegle marmelos* leaves extract possesses potential antiulcer activity was the conclusion obtained after the study.³⁶

V. Ramamurthy & S. Thirumeni (2015) evaluated antiulcer activity of ethanolic extract of *Aegle marmelos* against aspirin induced gastric ulcer in albino rats. Gastric volume, pH of gastric content, free acidity and total acidity, total carbohydrate content such as total protein, hexoses, hexosamine, fucose and sialic acid were the various biochemical parameters which were estimated in alcoholic precipitate of gastric juice and examined on the test and control group of animals. A protective effect on ulcer induced models was exhibited by the extract in a dose dependent manner and was comparable with the standard drug Lansprazole. As a result gastric volume, free and total acidity and ulcer index were significantly reduced due to the extract of *Aegle marmelos*. When compared with the standard drug, it was concluded that the extracts possess significant gastroprotective activity.³⁷

Sharmin Rahman et al (2018) evaluated the efficacy of *A. marmelos* leaf to prevent ethanol induced gastric ulcer in a rat model. Thirty two Wister albino rats were administered dose of 200 mg/kg or 400 mg/kg aqueous extract of *A. marmelos* leaves. The animals were sacrificed after one hour and then ulcer scores, index and Percentage protection of ulcer were determined. They concluded that extracts of *A. marmelos* leaves have potential ability to prevent experimentally induced peptic ulcer formation.³⁸

Yarasi Gayathri et al (2015) evaluated the antioxidative and antiulcer effect of methanolic extract of unripe fruit of *Aegle marmelos* against *Helicobacter pylori*-Lipopolysaccharide induced gastric ulcer in Sprague Dawley rats. Volume of gastric juice, free and total acidity, acid output, pepsin concentration were analyzed and activities of enzymatic antioxidants, non-enzymatic antioxidants and the levels of lipid peroxidation products were also measured. Oral administration of methanolic extract of *Aegle marmelos* fruit reduced the gastric ulcer compared to standard drug sucralfate and significantly inhibited the increase in gastric secretory parameters in ulcerated rats It was concluded that antioxidant properties of *Aegle marmelos* contributes to the gastroprotective effect in *Helicobacter pylori*-Lipopolysaccharide induced gastric ulcer model.³⁹

G. Vimala & F. Gricilda Shoba (2014) discussed some medicinal plants which are mentioned in Ayurveda and also in modern science for the treatment or prevention of peptic ulcer.⁸

Pushpendra K. Patel et al (2012) summarizes the pharmacological activity of *Aegle marmelos* based on scientific information. This plant is used to cure many disease like diabetes, cholesterol, peptic ulcer,

inflammation, diarrhea and dysentery, anticancer, cardio protective, antibacterial, antifungal, radioprotective, antipyretic, analgesic, constipation, respiratory infection, antioxidant, hepatoprotective, wound healing and many more.⁴⁰

Purnima Singh & Debjani Guha (2012) conducted a study on aspirin-induced ulcerogenesis in cannulated free-moving rats to evaluate the gastroprotective effect of *Aegle marmelos* extract. NSAIDs including aspirin cause gastric ulcer. Lesion index, gastric secretions glycoprotein levels and mucosal histopathology were the parameters to determine the possible antiulcer effect of *Aegle marmelos* which were determined in aspirin induced gastric mucosal injury in cannulated free-moving rats. As a result, pretreatment significantly prevented the development of gastric mucosal lesion and decreased the gastric toxicity produced by ulcerogen. *Aegle marmelos* exhibits antisecretory and cytoprotective property that protects the gastric mucosa against ulceration.⁴¹

Saranya, Sumitha, Padmavathi, Dhananjay S Kotasthane, Manimekalai et al (2019) conducted a study to find out the ulceroprotective property of ethanolic extract of *Aegle marmelos* leaves in wistar albino rats using indomethacin induced ulcer model. Mean ulcer index and histopathological examination confirmed the ulceroprotective activity of the extract and also concluded pretreatment of the ethanolic extract have the ability to prevent gastric ulcer.⁴²

Jincy J et al (2019) listed evidence-based information on plants available in Kerala reported with antiulcer property. Secondary metabolites like alkaloids, flavanoids, terpenoids, tannins, glycosides, terpenes and resins acts in relieving ulcers due to its antisecretory, antioxidant, and cytoprotective properties.⁴³

Kausik Bhar et al (2019) prepared a complete profile of *Aegle marmelos* L. Traditionally it is used in abdominal disorders, ulcer, cholera, diarrhea, nerve disorders, gonorrhoea, heart disorders, dog bite, jaundice, snake bite etc. Phytocompounds It contains are Alkaloids, Terpenoids, Vitamins, Coumarins, Tannins, Carbohydrates, Flavonoids, Fatty Acids, Essential Oils and other. It possesses pharmacological activities like Antioxidant, Antimicrobial, Antidiarrhoeal, Antidiabetic, Antiproliferative, Cytoprotective, Hepatoprotective, Antifertility, Analgesic, Antiarthritis, Contractile, Antihyperlipidemic, Cardioprotective, Radioprotective, Anticancer, Antiviral, Anti ulcer, Immunomodulatory and Wound Healing properties.⁴⁴

Rahul Swarnkar et al (2019) focused to explored the different phytochemicals and pharmacological activity of *A. marmelos*. Phytochemicals i.e. alkaloids, cardiac glycoside, saponin, steroids, coumarines terpenoids, phenylpropanoids, tannins, polysaccharides and flavonoids are present in the plant that exhibits pharmacological

activity used to treat diseases like cancer, cardiovascular disease, immunosuppressive disease, gastrointestinal disorder and have properties like anticonvulsant, antioxidant, antihyperglycemic, anxiolytic, antidepressant, antihistaminic, antimicrobial, hepatoprotective, analgesic, immune modulatory, cardio protective and antithyroid activity.⁴⁵

4. Conclusion

In modern medicine system, four synthetic drugs are used to treat peptic ulcer 1. drugs to inhibit gastric acid secretion 2. Antacids to neutralize gastric acid 3. Ulcer protective agents and 4. Antibacterial drugs. These synthetic drugs causes lot of side effects and also produces AMR. WHO also recommends the use of herbal drugs to reduce AMR. *Aegle marmelos* Linn. is a potent antibacterial and used as antiulcer drug for the treatment of peptic ulcer. To reduce AMR, treatment with herbal drugs is need of hour and *Aegle marmelos* Linn. is one good option because it possess both antibacterial and antiulcer activities proved scientifically. The bacteria *H.pylori* is responsible for causing peptic ulcer. No or less literatures are available on effect of *Aegle marmelos* on *Helicobacter pylori*, hence research is needed in this field to know its effect on *H.pylori*. If it shows positive effect, to reduce AMR it will be a nice herbal drug to treat Peptic ulcer without any side effect.

5. Source of Funding

None.

6. Conflict of Interest

None.

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