



## Phytochemistry, Pharmacological and Traditional Uses of *Aegle marmelos*

Yogita Choudhary, Abhishek Saxena\*, Yatendra Kumar, Sagar Kumar, Vijay Pratap

Department of Pharmacy, Brahmanand Group of Institution, Bulanshahr (UP), India

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Corresponding Author:

E-mail: [abhiclinical@rediffmail.com](mailto:abhiclinical@rediffmail.com)

Mob.: +917520921727

### Abstract

Since ancient times, plants are used as source of medicine. *Aegle marmelos* is a pharmacologically varied medicinal plant. The various parts of *Aegle marmelos*, precisely fruit, have an immense range of medicinal uses in folk medicine and used for the healing of different disease. The numerous phytochemical constituents of this plant have been exposed namely, marmeline, Agelin, aegelenine, marmeline, dictamine, fragrine, inulin, proteins, carbohydrates, alkaloids, cardiac glycosides and flavonoids. Researchers reported pharmacological potential of various parts such as fruits, leaves, and stems of *Aegle marmelos* as antioxidant, antimicrobial, hypoglycemic, anti-inflammatory, analgesic, nephroprotective, hepatoprotective etc. We performed PUBMED, EMBASE, Google scholar searches for medicinal values along with other uses of *Aegle marmelos*. In present review, comprehensive study focused on knowledge regarding several traditional, chemical and pharmacological activities of *Aegle marmelos* has been described.

### 1 Introduction

Ayurveda is a medical system primarily skillful in India that has been recognized for almost 5000 years. It includes food and herbal remedies, while emphasizes the organization and brain in sickness prevention and management<sup>1</sup>. Flora and their secondary metabolite components have an extended history of use in contemporary medicine and in certain systems of conventional medicine and are the sources of significant drugs. The World Health Organization (WHO) estimates that four billion people, 80% of the world's population presently use herbs for some aspect of primary care. The chemical components present in plant are a part of the physiological functions of living plant life and hence they are whispered to have better compatibility with the human body<sup>2</sup>.

*Aegle marmelos* is commonly known as wood apple or Bael/Bilva, and belongs to Rutaceae family. This herb has great medicinal, spiritual and religious significance. Its fruits and leaves are considered sacred and used as offerings to the Hindu Gods like Lord Shiva. This is why it is also known as "Shiva druma" or the tree of Shiva in ancient scriptures. The leaves, bark, roots, fruits and seeds are used extensively in the

Indian traditional system of medicine the Ayurveda and in various folk medicine to treat myriad ailments. Although this plant is native to Northern India it is also widely found throughout the Indian peninsula and in Ceylon, Burma, Thailand and Indo-China<sup>3,4</sup>.

Bael fruits are of dietary use and the fruit pulp is used to prepare delicacies like murabba, puddings and juice. Bael fruits are also used in the treatment of chronic diarrhea, dysentery, and peptic ulcers, as a laxative and to recuperate from respiratory affections in various folk medicines. Leaves of this plant used to cause infertility/abortion in women.

The fruit possesses broad range of therapeutic effects that includes free radical scavenging, antioxidant, inhibition of lipid peroxidation, antibacterial, antiviral, anti-diarrheal, gastroprotective, anti-ulcerative colitis, hepatoprotective, anti-diabetic, cardioprotective and radioprotective effects<sup>5</sup>.

### 2 Chemical constituents of *Aegle marmelos*

Different organic extracts of the leaves of *A. marmelos* have been reported to possess alkaloids (halfordino, ethylcinnamamide, marmeline, Agelin, aegelenine, marmeline, dictamine, fragrine, O-methylhalfordinine, Oisopentanylhalford

iniosyl, N-4-methoxy styryl cinnamide), cardiac glycosides, terpenoids ( $\alpha$ -Phellandrene,  $\beta$ -Phellandrene, p-cymene, Limonene), saponins, tannins (skimmianine, Carotenoids, umbelliferone), Coumarin (Marmelosin, marmesin, imperatorin, marmin, alloimperatorin, methylether, xanthotoxol, scoparone, scopoletin, umbelliferone, psoralen and marmelide), Polysaccharide (Galactose, arabinose, uronic acid and L-rhamnose), flavonoids and steroids. *Aegle marmelos* fruit pulp reported for the availability of steroids, terpenoids, flavonoids, phenolic compounds, lignin, fat and oil, inulin, proteins, carbohydrates, alkaloids, cardiac glycosides and flavonoids. Various phytoconstituents have been isolated from the various parts of *Aegle marmelos* and given below (Fig 1).

Leaf contains Skimmianine, Aegeline, Lupeol, Cineol, Citral, Citronella, Cuminaldehyde, Eugenol, Marmesinine,  $\alpha$ -Phellandrene, p-cymene.

Bark consist Skimmianine, Fagarine, Marmin.

Fruit consist of Marmelosin, Luvangetin, Auraptin, Psoralen, Marmelide, Tannin,  $\alpha$ -Phellandrene, p-cymene<sup>9,10</sup>.

Seed oil Composed of palmitic, Stearic, oleic, linoleic and linolenic acid. The percentage content of some of theminerals, viz. phosphorus, potassium, calcium, magnesium and iron is 0.137, 0.746, 0.188, 0.127 and 0.007 respectively.

### 3 Traditional uses of *Aegle marmelos*

*Aegle marmelos* has been used as a herbal medicine for the management of *diabetes mellitus* in Ayurvedic, Unani and Siddha systems of medicine in India. *Aegle marmelos* is traditionally used to treat jaundice, constipation, chronic diarrhea, dysentery, stomachache, stomachic, fever, asthma, inflammations, febrile delirium, acute bronchitis, snakebite, abdominal discomfort, acidity, burning sensation, epilepsy, indigestion, leprosy, myalgia, smallpox, spermatorrhoea, leucoderma, eye disorders, ulcers, mental illnesses, nausea, sores, swelling, thirst, thyroid disorders, tumors, ulcers and upper respiratory tract infections. It is also used to treat Anaemia, Fractures, Healing of Wounds, Swollen Joints, High Blood Pressure, Diarrhoea, Healthy Mind and Brain Typhoid Troubles during Pregnancy.

Sweet drink prepared from the pulp of fruits produce a soothing effect on the patients who have just recovered from bacillary dysentery. The pulp of unripe fruit is soaked in gingelly oil for a week and this oil is smeared over the body before bathing. This oil is said to be useful in removing the peculiar burning sensation in the soles.

The roots and the bark of the tree are used in the treatment of fever by making a decoction of them. The leaves are made into a poultice and used in the treatment of ophthalmia<sup>12-15</sup>.

### 4 Pharmacological activities of *Aegle marmelos*

**Wagh *et al.*, (2017)** study of Anthelmintic Activity of *Aegle Marmelos* fruit extract on Indian earthworm Model. Earthworms were washed with distilled water and placed in various concentration of the aqueous extract of ripe shed dried fruits of *Aegle marmelos* (1, 2, 10, 20 mg/ml). Distilled water control was used to compare the results. The selected doses of aqueous extract of ripe shed dried fruits of *Aegle marmelos* at the concentration of 1mg/ml dose showed significant difference in paralysis and death time when compared with the vehicle control group<sup>16</sup>.

**Kumar *et al.*, (2016)** studied antioxidant activity of leaf extract of *A. marmelos* (AME). High levels of total phenolic content and total flavonoid content were found in AME which showed antioxidant activity comparable to vitamin C. Significant correlation between TPC, TFC and antioxidant activity of AME was found when Pearson's correlation is applied. This study proved that the leaves of *A. marmelos* have high antioxidant component<sup>17</sup>.

**George *et al.*, (2016)** evaluated Antidepressant and Antianxiety activity of Ethanolic leaf extract of *Aegle marmelos*. The result suggests that the ethanolic extract of *Aegle marmelos* contains some active principles which may be responsible for these activities<sup>18</sup>.

**George *et al.*, (2016)** evaluated anti-inflammatory activity and to determine phytochemical constituent of ethanolic leaf extract of *Aegle marmelos* (L.) Corr. Serr. Ethanolic extract was screened for different phytochemical constituents. Ethanolic extracts were screened for anti-inflammatory activity (induced by Carrageenan) in Wistar Albino rats<sup>19</sup>.

**Karumaran *et al.*, (2016)** investigated antimicrobial and antioxidant activity of leaf extract of *Aegle marmelos*. Acetone and hexane extracts were found to be highly active against bacterial species like *Bacillus subtilis* and *Pseudomonas aurogenosa* and fungal species like *Aspergillus niger*. Ethanol fraction of leaves exhibited highest radicals scavenging activity, that is,  $63.84 \pm 0.05$ . The ethanolic extract of leaves of *Aegle marmelos* shows the highest scavenging activity followed by the acetone<sup>20</sup>.

**Saha *et al.*, (2016)** investigated pharmacological activities of *Aegle marmelos* fruit. Two extracts were used. One was methanolic extract and another was lectin extract. VLC fraction of methanolic extract of the *Aegle marmelos* fruit contains flavonoids and other biologically active compounds. The extract showed antibacterial activities against several bacteria. The lectin extract also showed antibacterial and anti-diabetic activity<sup>21</sup>.

**Wali *et al.*, (2015)** investigated antioxidant potential and phenolic content of methanolic extract and ethyl acetate fraction

of *Aegle marmelos* leaves. The highest free radical scavenging activity was observed in leaf ethyl acetate fraction. The results revealed that the metal ion chelating activity of leaves methanolic extract ( $IC_{50}$  value:  $165.7 \pm 2.3 \mu\text{g/mL}$ ) and of leaves ethyl acetate fraction ( $IC_{50}$  value:  $410 \pm 13.9 \mu\text{g/mL}$ ). RP-HPLC

analysis of the leaf methanolic extract and ethyl acetate fraction of *Aegle marmelos* revealed the presence of different phenolic acids viz. gallic acid, p-coumaric acid, vanillic acid, p-hydroxy benzoic acid, syringic acid, ferulic acid and chlorogenic acid<sup>22</sup>.

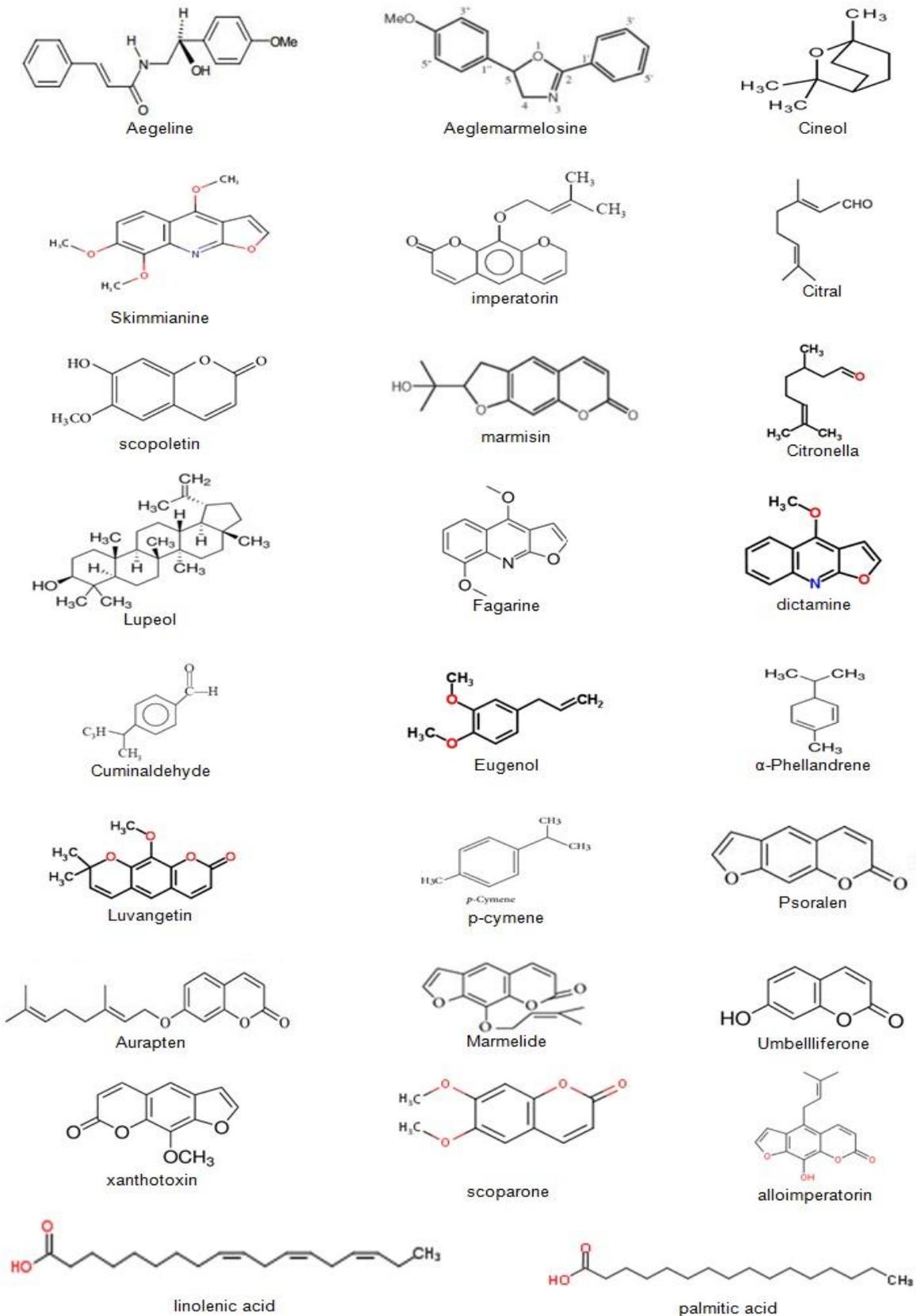


Fig 1: Phytoconstituents present in *Aegle marmelos*

**Dahiya et al, (2015)** evaluated the antimicrobial properties of *Aegle marmelos*. In this study, antimicrobial activities of different extract of *Aegle marmelos* fruit were evaluated against different microbial strains like *Escherichia coli* (MTCC-443), *Bacillus subtilis* (MTCC-441), *Pseudomonas aeruginosa* (MTCC-4673), *Staphylococcus aureus* (MTCC-3160), *Aspergillus brasiliensis* (MTCC-1344) and *Candida albicans* (MTCC-227) by agar well diffusion method & MIC determination by broth dilution method<sup>23</sup>.

**Chinchansure et al, (2015)** investigated phytochemical of nbutanol fraction of acetone extract of *Aegle marmelos* fruit has afforded four compounds coumarins marmelosin, marmin and xanthotoxol and flavonoid kaempferol 3O-rhamnoside, afzelin. All the isolated compounds were evaluated for their antimycobacterium activity against *Mycobacterium tuberculosis* H37Ra and *Mycobacterium bovis*<sup>24</sup>.

**Gangai et al, (2014)** determined the antibacterial activity of three extracts of leaves of *Aegle marmelos* which was screened for its potential against five bacterial strains: *Lactobacillus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli* and three fungal strains *Pestotlotia foedans*, *Paecilomyces variotii*, *Fusarium oxysporum*. Chloroform extract showed good antibacterial and antifungal against *E. coli* and *Fusarium oxysporum*<sup>25</sup>.

**Chatterjee et al, (2014)** evaluated the nephroprotective activity of an aqueous extract of Leaves of *Aegle marmelos* in Wistar rats. Gentamicin nephrotoxicity was recorded by increased serum creatinine and blood urea nitrogen level. Gentamicin increased MDA level whereas decreased catalase, reduced glutathione level, while AEAM significantly reduced the elevated MDA levels and increased GSH and catalase concentration. Gentamicin increased serum creatinine, urea and blood urea nitrogen level, while AEAM reduced serum creatinine, urea and blood urea nitrogen level in gentamicin toxicity indicating a nephroprotective effect<sup>26</sup>.

**Singh et al, (2013)** conducted the hepatoprotective activity of hydroalcoholic extract of *Aegle marmelos* against paracetamol induced liver damage in rats. The methanolic extract of (500mg/kg) was administered orally to the animals with hepatotoxicity induced by Paracetamol (3gm/kg). The plant extract was effective in protecting the liver against the injury induced by Paracetamol in rats. This was evident from significant reduction in serum enzymes alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and bilirubin. It was concluded from the result that the methanolic extract of possesses hepatoprotective activity against paracetamol induced hepatotoxicity in rats<sup>27</sup>.

**Rani et al, (2013)** worked on methanolic extract of fruit pulp of *Aegle marmelos* having antimicrobial effect against multi drug resistant clinical pathogens isolated from stool samples, by the

bio-autography technique. Hence the method has potential in determining the efficacy of medicinal plants against other clinical pathogens as well<sup>28</sup>.

**Rao et al, (2012)** investigated the antidiarrhoeal activity of the aqueous extract from the leaves of *Aegle marmelos*. Preliminary phytochemical screening, acute toxicity study and antidiarrhoeal activity were studied on castor induced diarrhea, Magnesium sulphate induced diarrhea, and gastric transit time at 50, 100 and 200mg/kg body weight. The preliminary phytochemical screening of the extract results with the presence of anthraquinone glycosides, catechins, fixed oils and saponins etc<sup>29</sup>.

**Modi et al, (2012)** investigated hepatoprotective activity of various extracts of *Aegle Marmelos* in Wistar Female rats with liver damage induced by ethanol. Body weight exhibited hepatoprotective effect by lowering the Serum Glutamate Pyruvate Transaminase, Serum Glutamate Oxaloacetate Transaminase, alkaline phosphate and total bilirubin to a significant extent. Results of biochemical studies of blood samples of ethanol treated rats showed significant increase in the levels of serum enzyme activities, reflecting the liver injury caused by ethanol and blood samples from the animals showed significant decrease in the levels of serum markers, indicating the protection of hepatic cells against ethanol induced hepatocellular injury<sup>30</sup>.

**Subramanian et al, (2012)** investigated antimicrobial activity of ethanolic leaf extracts of *Aegle marmelos*. Phytochemicals present in the ethanolic leaves extracts of *A. marmelos* exhibit considerable antibacterial activity. Further, at concentration of 300µl and above, ethanolic leaf extracts of *A. marmelos* exhibited significant activity towards all the selected bacterial strains. However, *B. subtilis* and *E. coli* were more sensitive towards the treatment when compared to *S. aureus*, *P. aeruginosa* and *K. pneumonia*<sup>31</sup>.

**Kuncha et al, (2011)** evaluated hepatoprotective activity of *Aegle marmelos* leaves against carbon tetrachloride induced hepatic damage in albino rats. After the *Aegle marmelos* leaf powder administration for 14 days to the rats with hepatic damage induced by CCl<sub>4</sub>, it was found that the concentrations of the hepatic enzymes in the rats were comparable to that of healthy control rats. Strikingly, it has also been noticed that concentrations of the hepatic markers of rats treated with standard drug (Liv.52) and that of rats treated with the crude leaf powder are similar, within statistical errors, to each other indicating that *Aegle marmelos* leaves powder may contain lead phytochemicals that may presumably pave the way of designing highly potent hepatoprotective compounds/drugs<sup>32</sup>.

**Sharma et al, (2011)** evaluated anti-inflammatory effect of aqueous and methanol extracts of *Aegle marmelos* seeds was using carrageenan induced paw edema and cotton pellets

induced granuloma in rats. To prove the dependency of pharmacological activity on certain phytoconstituents, total flavonoid contents were estimated, using a spectrophotometric technique<sup>33</sup>.

**Trivedi *et al.*, (2011)** reported antiarthritis activity of *Aegle marmelos* against collagen induced arthritis in Wistar rats. Methanol extract treatment of rats showed the reduction of paw swelling and arthritic index. Radiological and histopathological changes were also significantly reduced in methanol extract treated rats<sup>34</sup>.

**Sathiyaraj *et al.*, (2010)** reported antifertility effect of the aqueous extracts of leaves of *Aegle marmelos* in male Albino rats. The rats were administered with aqueous extracts (250 mg/kg body weight) of leaves of *Aegle marmelos* for 45 days. Treatment resulted in reduction in the weights of testis, epididymes and seminal vesicle. The extract also resulted in reduction of testicular sperm count, epididymal sperm count and motility and abnormal sperm count<sup>35</sup>.

**Kaur *et al.*, (2009)** revealed antigenotoxic activity exhibited by the extracts of *A. marmelos* may be attributed in part to the polyphenolic constituents, which possess the potential to protect DNA from reactive oxygen species and S9 dependent mutagens. Further studies are required to isolate these constituents and decipher their mode of action for their eventual application in cancer chemoprevention<sup>36</sup>.

**Mohammad *et al.*, (2009)** worked on Clinical evaluation of antidiabetic activity of Trigonella Seeds and *Aegle marmelos* leaves. The study was performed in four different groups for a period of 16 weeks. Each group was having 20 NIDDM patients, whereas five patients were kept as control subjects. Inclusion and exclusion criteria were formed for the study. Written consent was taken from the patients. Initial postprandial blood glucose level was estimated at the time of enrolment in the study and then after each week during the entire period of the study. At the end of the study, the initial and final readings were compared<sup>37</sup>.

**Joshi *et al.*, (2009)** reported *in vitro* antidiarrheal activity of dried fruit pulps of *A. marmelos*. Antidiarrheal activity was performed by MIC method against the causative organisms of diarrhea. The ethanolic extract showed good activity against *Shigella boydii*, *S. sonnei* and *S. flexneri*, moderate against *S. dysenteriae*<sup>38</sup>.

**Vinodhini *et al.*, (2009)** reported cytoprotective effect of the leaves of *Aegle marmelos* in *Cyprinus carpio* (freshwater fish) exposed to heavy metals. *C. carpio* was exposed to heavy metals followed by the treatment with the dried powder of *Aegle marmelos* leaves. Treatment resulted in cytoprotective effect by stabilization of plasma membrane and modulation of antioxidant enzyme system<sup>39</sup>.

**Ghangale *et al.*, (2007)** evaluated the methanol extract of leaves of *Aegle marmelos* (L.) at a dose level of 200 and 300 mg/kg and observed significant analgesic activity on acetic acid induced writhing and tail flick test in mice<sup>40</sup>.

**Lampronti *et al.*, (2003)** reported antiproliferative effects of the different solvent fractions of ethanolic extract of the stem barks of *A. marmelos* against human tumor cell lines. The results showed the inhibition of *in vitro* proliferation of human tumor cell lines, including the leukemic K562, T lymphoid Jurkat, Blymphoid Raji, erythroleukemic HEL, melanoma Colo38, and breast cancer MCF7 and MDAMB-231 cell lines<sup>41</sup>.

## 5 Conclusion

This review presents a comprehensive summary of the traditional uses, phytochemistry and pharmacology activity of *Aegle marmelos*. *Aegle marmelos* is incomparable source of a varied range of chemical compounds having diverse medicinal properties. Pharmacology studies are mainly focused on the antimicrobial, hypoglycemic, anti-inflammatory, analgesic, nephroprotective, neuroprotective, hepatoprotective activity. Hence, more mechanistic studies are required before *Aegle marmelos* can be considered for further clinical use. The present information concerning *Aegle marmelos* may serve as the baseline data to impose to do extensive studies for the discovery of new potent compounds and further investigations for their biological activities.

## 6 Competing interest

None

## 7 Author's contributions

YC and AS carried out literature review and draft the manuscript. YK, SK and VP participated in collection of data. All authors read and approved the final manuscript.

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