



## Visiting Bael (*Aegle marmelos*) as a protective agent against COVID-19: A review

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Medicinal plant-based antivirals might reinforce the endogenous antioxidant defences from reactive oxygen species (ROS) and regain an optimum harmony by neutralizing the viral agents. These compounds are readily available, therefore gaining immense value by virtue of the critical role of theirs in COVID disease prevention. In this context, *Aegle marmelos* could rightly be stated as a plant of extensive interest. Therefore, the worth of the use of bael can be pushed to seek out the for the phytochemical which might prevent SARS-CoV-2. Here, we have compiled a piece of information on bael based on the previous studied on bael tree.

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The novel coronavirus 2019 (COVID-19), has created an unanticipated pandemic, that has triggered severe panic among individuals worldwide. In this direction, countries are maximizing their efforts to fight the virus and reduce infection. In such a situation, a vaccine could help reduce mortality and morbidity<sup>1</sup>. However, the possible issue is going to continue to persist until the improvement of an excellent viral vaccine. In order to bring down the transmission of COVID 19, it can be beneficial to make use of personal respiratory protective equipment. Since a selection of routes may transmit infectious microorganisms, respiratory and face protection is necessary for those that are usually given via droplets/aerosols. Transmission of COVID 19 infection mostly occurs through coughing or perhaps sneezing where infectious contaminants (aerosol droplets) of adjustable size, might be inhaled. Although SARS-CoV-2 is predominantly deemed as an inescapable pandemic, scientists are curious about precisely how to defend the general public best before a vaccine may be made available<sup>2</sup>.

Therefore, a good viral inactivation process by exploiting bioactive substances from the healing

plants is much needed. The cultural community of India begets an important part in protecting the biodiversity of various virgin woodlands and also have conserved a lot of plants, if not this particular flora and fauna, would be disappeared from nourishing ecosystems<sup>3-5</sup>. Over 70% of the tribal cities stayed intermingled with the conventional nature and knowledge for several years and would be the custodian of several indigenous plant lives that are used for the formula of several ailments<sup>6,7</sup>.

Among the primary explanations for such a training would be the lack of contemporary health facilities in the remote areas of the cold challenging terrains of the express. There is a prevailing perception that grey medications are healthier and more, harmless or safer when compared with artificial ones. The fruit's therapeutic values are higher at initial stages. Many of the components of the bael grow has antibiotic qualities and also may be used for treating a broad range of health conditions and infections. The ripe fruit as well as unripe fruit, additionally to the roots, are used in regular medicine. In Ayurveda, the mature berry continues to be utilized for persistent diarrhoea and dysentery<sup>8-10</sup>. Due to this particular systematic assessment of various phytoconstituents of the vegetable could be helpful within the elimination

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of damages on account of ageing and might, therefore, boost life expectancy. Below, we've provided detailed info about the various areas of the bael tree which are widely used because of the healing of illnesses more we've mentioned the usage of theirs inside a COVID perspective.

### Leaves

The fresh leaf liquid with honey as a slight laxative in fever, asthma and catarrh. The mixer of black pepper and leaf juice is utilized to overcome dropsy diseases<sup>11,12</sup>. It is also used for respiratory and asthmatic issues. A warm poultice of the foliage is put on on the eyes in ophthalmia, and the syrup is recommended in the bronchitis. New leaves are also eaten as a cure for beriberi disease<sup>13</sup>. Consuming water of overnight soaked leaves is suitable for the patients<sup>14</sup>. The word bilva (bael tree) is frequently employed as bilva patra (leaf of bael). Bael leaves, along with some other areas have been found being helpful in curing diabetes, and medical research has validated this<sup>15-17</sup>. Steam distillation of bael leaves makes an essential oil which has broad-spectrum antifungal exercise much like which of 0.5% Hamycin the liquid out of the bael leaves is beneficial for diabetics when consumed stomach that is empty for just one month<sup>18</sup>. An early practice consists of the usage of the bael leaves, roots and barks for dealing with snakebites. Respiratory illnesses, such as a wheezing, spasm as well as the common cold, perhaps addressed by utilizing medicated oil made out of the foliage of bael plant. An equal amount of bael juice, as well as sesame oil, is warmed up together for the planning of this particular oil<sup>19,20</sup>. A rare alkaloid, shahidine biogenetically, oxazolines might be viewed as the precursor of oxazoles and hydroxyl amides present in plant life. Shahidine showed activity against several gram-positive bacterial strains<sup>21</sup>.

### Fruits, Bark and Root

The ripe fruits possess, cooling, aromatic and as well as a laxative<sup>22,23</sup>. It has all imperatorin, marmelosin that are the same with bsitosterol and imperatorin. It's marmalade, an isomer of imperatorin, that exhibits tyrosinase speeding up and also tryptophan pyrroles inhibiting impact in *Bufo melanosticus*. The existence of psoralin, an important germination inhibitor and also tannic acid is found. The fresh fruits yield 2% of dried, water-soluble gum. Hydrolysis of the gum produces most significantly: galactose 20.4; aralrinose, and also traces of

rhamnose<sup>24</sup>. Aqueous extract of the bael berry pulp offers powerful antioxidant effects and it was discovered that hydroalcoholic content of bael pulp has scavenging tasks in vitro<sup>25,26</sup>. Furthermore, the bael fruit beverage had also been reported to include higher levels of complete phenolic compounds<sup>27-30</sup>. The extract of bael berry (125 along with 250 mg/kg) two times daily to diabetic rats for thirty days decreased the amounts of fasting blood sugar and glycosylated haemoglobin amounts with all the influences being much better than that of glibenclamide. Feeding bael even caused a concentration-dependent reduction in LPx, to improve Sod, CAT, GSH and GPx amounts in both hearts as well as the pancreas of diabetic creatures. Histopathological scientific studies demonstrated that feeding the berry extract improved the practical state of the pancreatic cells<sup>31,32</sup>. Bael happens to be deemed to have a healing advantage for cardiovascular disease. Krushna *et al.*<sup>33</sup> discovered the precise role of the extract of the unripe fresh fruit of bael in rats against the isoproterenol-induced cardiac stress.

The amounts of blood sugar and protein were also within the normal range. Unripe fruit extract (1%) decreases the intraocular pressure created by water loading as well as steroids in cream rabbit<sup>34</sup>. Results propose that bael fruit extract is good at reducing the experimentally induced intraocular strain in experimental animal models and also has got the potential to become of pharmaceutical use. It offers antibacterial consequences on specific enteric bacteria<sup>35,36</sup>. The bark and the root are worn in the type of a decoction as a treatment in melancholia, intermittent fevers as well as palpitation. The root bark continues to be used especially in sporadic fevers and as a fish toxins. Imperatorin, xanthotoxol, marmelide, psoralen, scopoletin, Scoporone, skimmianine, umbeliferone, umbelliferone, marmesin, and marmin had been determined from the bark leaves, root and fruit of the plant<sup>37,38</sup>. It was discovered the root of *A. marmelos* tree features psoralin, scopolotein and xanthotoxin<sup>39</sup>. A decoction of the blossoms and roots of *A. marmelos* is utilized as an antiemetic<sup>40</sup>. Siddique *et al.*<sup>41</sup> proved that leaf extract has improved antioxidant activity than stem bark and root extract. The bark paste of ground origins of *A. marmelos* with cold water is recommended for curing myalgia. It was discovered the paste of ground origins of bael in butter was highly effective in the healing of insomnia.

### Antiviral activity against COVID-19

In connection with the bacteria, some enteroviruses also result in contamination and diarrhoea. Coxsackieviruses, belonging to the category picornaviruses are a frequent root cause of ailments in humans, particularly kids. They mainly result in non-symptomatic or mild illness but might be deadly in immune-compromised folks. Badam *et al.*<sup>42</sup> showed that apart from these bael fruits in its different form and composition is used against diarrhoea, gastroprotective effects, and inflammatory bowel disease<sup>43,44</sup>. Various parts of essentially Consisting of alkaloids, flavones and coumarin compounds, inhibited the replication of coxsackieviruses B (1-6). The experiments demonstrate that naturally occurring battery of compounds (alkaloids, flavoiies, coulnarins, terpenoids, fatty acids etc.) infractions L1, L2; S1, S2, S3 and S4; F1, F2; R1, R2 and marmelide from the fruits, possess antiviral activity. Most significant was marmelide, a coumarin derivative against all the human coxsackieviruses (B1-B6). The ethanolic extract of the fruits has shown antiviral activity against ranikhet disease virus<sup>15</sup>.

Coronaviridae and order Nidovirales. SARS-CoV-2 is considered a novel human-infecting betacoronavirus. It is a well fact that bael fruits are effective in reducing the effect of other respiratory diseases, so it is presumed that consuming bael can help in minimizing COVID disease<sup>45</sup>. Bael also builds immunity body against diseases like diarrhoea and cholera. It is also reported that immunity is a good weapon against corona. Bael, is packed with Vitamins, has numerous health benefits. It's a rich supply of Vitamins A, C and B and also the existence of these multivitamins make bael the top option among fruits within the healing of eye problems, heart ailments, digestive disorders, skin diseases and also by stopping the entire body against infection and improving the overall immunity<sup>46</sup>.

### Potential phytochemicals against COVID-19

Skimmianine ( $C_{14}H_{13}NO_4$ ), an alkaloid, present in the bael and the biosynthesis of skimmianine begins from anthranilic acid, and that is pretty plentiful in bael. It's shown anticancer pastime in human ovarian cancer cell line<sup>47</sup>. Additionally, it inhibits acetylcholinesterase (AChE), cataleptogenic activity, exploratory behaviour and conditioned avoidance reply in animals<sup>48</sup>. Skimmianine, when studied in the pet models, indicates sedative, antipyretic, anticonvulsive, analgesic, hypnotic, antidiuretic and hypothermic effects<sup>49,50</sup>. Additionally, it offers antimalarial activity

by inhibiting Plasmodium falciparum development in vitro ( $IC_{50}=48.2 \mu\text{g/ml}$ )<sup>51</sup>. Aegelin ( $C_{18}H_{18}O_4$ ) is an alkaloid from the foliage of *A. marmelos* that's recognized for cardioactive compound<sup>52</sup>. Even though some evidence from animal research indicates that aegeline could reduce blood sugar, this possible outcome has never been analyzed in humans. Lupeol ( $C_{30}H_{50}O$ ) is a pentacyclic triterpenoid which has healing properties. It's a powerful cardioactive compound that exhibits anti-inflammatory property<sup>53,54</sup>.

Development of oxidative stress<sup>55</sup> and also neutrophil infiltration are typical for inflammatory diseases<sup>56</sup>. A report by Fernández *et al.*<sup>57</sup> showed that topical program of Lupeol reduces myeloperoxidase amounts [neutrophil specific marker], therefore leading to the decrease in cell infiltration into inflamed cells in mice. Cuminaldehyde (4-isopropyl benzaldehyde) is a constituent of the important oils of various trees. It's been discovered to have antibacterial activity<sup>58</sup>. In case it gets accumulated, could lead to chronic diseases as Parkinson's condition, dementia with multiple systems<sup>59</sup>. Among the crucial bioactive compound, remote from bark are marmin and fagarine. Fagarine ( $C_{13}H_{11}NO_3$ ) occurs in the older bark and is a potent abortifacient agent<sup>58</sup>.

Fruits of bael are loaded with marmelosin, psoralen, aurapten, luvangetin, tannin and marmelide. Marmelosin indicates antihelmintic in addition to antibacterial activities. Luvangetin ( $C_{15}H_{14}O_4$ ), an isolate from the seed of bael has proved effective against gastric ulceration in rodents<sup>61,62</sup>. Aurapten (CHO) prevents ( $IC_{50} = 0.6 \mu\text{g/ml}$ ) the chronotropic consequences on the heart muscles and therefore could be helpful within the healing of hypertension<sup>34</sup>. Psoralen ( $C_{11}H_6O_3$ ) demonstrates different tasks for example antispasmodic<sup>63</sup>, and artemicide ( $LD_{50}=5.93 \mu\text{g/mL}$ ). Marmelide ( $C_{16}H_{14}O_4$ ) is extremely potent against viral diseases and it is discovered to affect the first phases of the life cycle of a virus, like penetration and adsorption. Vitamin C contained in bael is able to bring down lung irritation in serious respiratory illnesses due to H1N1 (swine flu) or maybe some other viruses<sup>64</sup>.

### Conclusions

Presently no specific vaccine or therapy authorized for coronavirus an infection. Bael plant produces phytochemical compounds that have the capability to inhibit COVID-19. The are several anti-coronavirus agents present in the bael plant. The hunt for completely new molecules with a preservative

strength of natural origin is based on ethnobotanical scientific studies that will make it feasible to have out inventories of bael. Overall, the comprehensive info provided in this particular evaluation on the phytochemicals, antioxidant, antitoxic and anti-diabetic qualities of the bael extract may offer particular evidence of the usage against COVID-19 disease.

### Conflict of Interest

Authors declare they have no conflict of interest

### Author Contribution Statement

PK and RKJ conceived of and designed the project; supervised the study and corrected the final draft. VKY, GS, PK and RKJ wrote the manuscript. All authors read and approved the final manuscript.

### References

- Murthy S, Gomersall C D, & Fowler R A, Care for critically ill patients with COVID-19, *Jama*, 323(15) (2020) 1499-1500. 10.1001/jama.2020.3633
- Del Rio C & Malani P N, COVID-19—new insights on a rapidly changing epidemic, *Jama*, 323 (14) (2020) 1339-1340.
- Voeks R A, Disturbance pharmacopoeias: medicine and myth from the humid tropics, *Ann Am Assoc Geogr*, 94 (4) (2004) 868-888.
- Saini I, Chauhan J, & Kaushik P, Medicinal Value of Domiciliary Ornamental Plants of the Asteraceae Family, *J Young Pharm*, 12 (1) (2020) 3-10.
- Dutta A, Lal N, Naaz M, Ghosh A, & Verma R, Ethnological and Ethno-medicinal importance of *Aegle marmelos* (L.) Corr (Bael) among indigenous people of India, *A J Ethanol* (5) (2014) 290-312.
- Kaushik P & Kumar S, Transcriptome Analysis of Bael (*Aegle marmelos* (L.) Corr.) a Member of Family Rutaceae, *Forests*, 9 (8) 2018 450.
- Kaushik P & Kumar S, Data of de novo assembly of fruit transcriptome in *Aegle marmelos* L., *Data Brief*, 25 2019 104189.
- Sarkar P K, Bishnoi S K, & Shinde R, 17 Under-Exploited Fruits of the Forests: Eastern Indian Plateau is a Potential Hub. In: Dutta, A. K. and Mondal, B. (Eds.), *Fruits for Livelihood: Production Technology and Management Practices* Published by Agrobios (India), Jodhpur, India. (2017) 261-278.
- Arul V, Miyazaki S, & Dhananjayan R, Studies on the anti-inflammatory, antipyretic and analgesic properties of the leaves of *Aegle marmelos* Corr, *J Ethnopharmacol*, 96 (1-2) (2005) 159-163.
- Singhal V, Salwan A, Kumar P, & Kaur J, Erratum to: Phenology, pollination and breeding system of *Aegle marmelos* (Linn.) Correa (Rutaceae) from India, *New For*, 42 (2011) 85-100.
- Kumar K S, Umadevi M, Bhowmik D, Singh D M, & Dutta A S, Recent trends in medicinal uses and health benefits of Indian traditional herbs *Aegle marmelos*, *Pharma Innovation*, 1 (4) (2012) 1-7.
- De Filipps R A & Krupnick G A, The medicinal plants of Myanmar, *Phyto Keys*, 102 (2018) 1-341.
- Murthy N A, *Ayurvedic cure for common diseases*, (Orient Paperbacks), (1995) 2-7.
- Kaushik P & Kumar S, Data of de novo assembly of the leaf transcriptome in *Aegle marmelos*, *Data Brief*, 19 (2018) 700-703.
- Maity P, Hansda D, Bandyopadhyay U & Mishra D K, Biological activities of crude extracts and chemical constituents of bael, *Aegle marmelos* (L.) Corr. *Indian J Exp Biol*, 47 (2009) 849-861.
- Bhartiya Vidya Bhavan's Swami Prakashanand Ayurveda Research Centre, *Selected medicinal plants of India*, (Chemexil, Bombay), 1992, p. 9-18.
- Shankarananth V, Balakrishnan N, Suresh D, *et al.*, Analgesic activity of methanol extract of *Aegle marmelos* leaves, *Fitoterapia*, 78 (3) 2007 258–259.
- Arumugam S, Kavimani S, Kadalmani B, Ahmed A B A & Akbarsha M A, Antidiabetic activity of leaf and callus extracts of *Aegle marmelos* in rabbit, *Sci Asia*, 34 (2008) 317-321
- Rayburn D, *Let's Get Natural with Herbs*, (Ozark mountain publishing), (2007).
- Upadhyay R K, Bel plant: A source of pharmaceuticals and ethno medicines, *Int J Green Pharm (IJGP)*, 9 (4) (2015) 204-222.
- Pattnaik S, Subramanyam V R, & Kole C, Antibacterial and antifungal activity of ten essential oils in vitro, *Microbios*, 86 (349) (1996) 237–246.
- Baliga M S, Bhat H P, Joseph N, & Fazal F, Phytochemistry and medicinal uses of the bael fruit (*Aegle marmelos* Correa): A concise review, *Food Res Int*, 44 (7) (2011) 1768-1775.
- Rakulini R & Kalaichelvi S, A Review of Anti-Diarrheal Activity of *Aegle marmelos*, *J Altern Complement Med*, 7(2) (2019) 1-10.
- Kozioł E & Skalicka-Woźniak K, Imperatorin—pharmacological meaning and analytical clues: profound investigation, *Phytochem Rev*, 15 (2016) 627-649.
- Das B, & Das R, Medicinal properties and chemical constituents of *Aegle marmelos* correa. *Indian Drugs* 32 (3) (1995), 93
- Jageti G C, & Baliga M S, The evaluation of nitric oxide scavenging activity of certain Indian medicinal plants in vitro: A preliminary study, *J Med Food*, 7, (2004). 343–348.
- Kamalakkannan N, & Prince P S M, Hypoglycaemic effect of water extracts of *Aegle marmelos* correa fruits in streptozotocin diabetic rats, *J Ethnopharm*, 87 (2003) 207-210.
- Abdullakassim P, Songchitsomboon S & Techagumpuch M, Antioxidant capacity, total phenolics and sugar content of selected Thai health beverages, *Int J Food Sci Nutri*, 58(1) (2007) 77-85.
- Venkatesh P, Evaluation of chemopreventive and radioprotective properties of *Aegle marmelos* (bael) in vivo and in vitro. A thesis submitted to Manipal Academy of Higher Education, Manipal, Karnataka, India (2006) 42.
- Singh R, & Rao H S, Hepatoprotective effect of the pulp/seed of *Aegle marmelos* correa ex Roxb against carbon tetrachloride induced liver damage in rats. *Int J Green Pharma*, 2 (2008) 232-234.

- 31 Rajasekaran C, Studies on hepatoprotective activity of methanolic extracts of fruit pulp of *Aegle marmelos* (L.) Corr. *J Pharmacy Res*, 2 (2009) 1419-1423.
- 32 Kamalakkannan N, Prince P S M, The effect of *Aegle marmelos* fruit extract in streptozotocin diabetes: a histopathological study, *J Herb Pharmacother*, 5 (2005) 87-96.
- 33 Krushna G, Kareem M A, & Devi K L, Antidyslipidaemic effect of *Aegle marmelos* Linn. fruit on isoproterenol induced myocardial injury in rats, *Internet J Pharmacol*, 6 (2009) 2.
- 34 Agarwal R, Gupta S K, Srivastava S, Saxena R, Agrawal S S, Intraocular pressure lowering activity of topical application of *Aegle marmelos* fruit extract in experimental animal models. *Ophthalmic Res*, 42 (2009) 112-116
- 35 Rani P & Khullar N, Antimicrobial evaluation of some medicinal plants for their anti-enteric potential against multi-drug resistant *Salmonella typhi*. *Phyto Res*, 18 (2004) 670-673.
- 36 Raja S B, Murali M R, Malathi G K, Anbarasu K & Devaraj S N, Effect of aqueous extract of *Aegle marmelos* fruit on adherence and  $\beta$ -lactam resistance of Enteropathogenic *Escherichia coli* by down regulating outer membrane protein C, *Am J Infect Dis*, 5 (2009) 154-162.
- 37 Farooq S, Medicinal plants: Field and laboratory manual. Dehradun, International Book Distributors, (2005) 40-42.
- 38 Kokate C K, Purohit A P & Gokhale S B, Drugs containing glycoside. In: Pharmacognosy, 21 st edition, Pune, Nirali Prakashan, (2002) 158-239.
- 39 Rangari V D, Traditional drugs of India: Pharmacognosy and Phytochemistry Part-II, edition 1 st. Nasik, Carrier Publications, (2004) 182-184.
- 40 Morton J, Bael Fruit. In: *Fruits of warm climates*, by J F Morton, (Miami FL, USA), (1987) p. 187-190.
- 41 Siddique N A, Mujeeb M, Najmi A K & Akram M, Evaluation of antioxidant activity, quantitative estimation of phenols and flavonoids in different parts of *Aegle marmelos*, *Afr J Plant Sci*, 4 (1) 2010 001-005.
- 42 Badam L, Bedekar SS, Sonawane K B, & Joshi S P, In vitro antiviral activity of bael (*Aegle marmelos* Corr) upon human coxsackieviruses B1-B6, *J Commun Dis*, 34 (2002) 88-99.
- 43 Sigidi M T, Anokwuru C P, Zininga T, *et al.*, Comparative in vitro cytotoxic, anti-inflammatory and anti-microbiological activities of two indigenous Venda medicinal plants, *Trans Med Commun*, 1 (1) (2016) 9.
- 44 Babbar O P, Joshi M N & Madan A R, Evaluation of plants for antiviral activity, *Indian J Med Res*, 76 (1982) 54.
- 45 Bhardwaj R L & Nandal U, Nutritional and therapeutic potential of bael (*Aegle marmelos* Corr.) fruit juice: a review, *Nut Food Sci*, 45 (6) (2015) 895-919.
- 46 Goyal M R, Suleria H A R, Ayeleso A O, *et al.*, The Therapeutic Properties of Medicinal Plants: Health-rejuvenating Bioactive Compounds of Native Flora, (CRC Press), (2019) 324.
- 47 Jagetia G C, Venkatesh P & Baliga M S, *Aegle marmelos* correa inhibits ascites carcinoma in mice. *Biol Pharm Bull*, 28 (2005) 58-64.
- 48 Sinha S, Sandhu K, Bisht N, *et al.*, Ascertaining the Paradigm of Secondary Metabolism Enhancement through Gene Level Modification in Therapeutic Plants, *J Young Pharm*, 11 (4) 2019 337-343.
- 49 Rastogi R P & Mehrotra B N, In: *Compendium of Indian medicinal plants*, Volume 2, edited by Rastogi R P (C.D.R.I., Lucknow & Publications & Information Directorate, New Delhi) (1991) 17.
- 50 Rastogi RP & Mehrotra BN, In: *Compendium of Indian medicinal plants*, by R P Rastogi, (C.D.R.I., Lucknow & Publications & Information Directorate, New Delhi) Volume 3, (1993) 17.
- 51 Khalid S A, Farouk A, Geary T G & Jensen J B, Potential antimalarial candidates from African plants: An *in vitro* approach using *Plasmodium falciparum*, *J Ethnopharmacol*, 15 (1986) 201-209.
- 52 Vimal V & Devaki T, Linear furanocoumarin protects rat myocardium against lipidperoxidation and membrane damage during experimental myocardial injury, *Biomed Pharmacother*, 58 (2004) 393-399.
- 53 Geetha T & Varalakshmi P, Anti-inflammatory activity of lupeol and lupeol linoleate in rats, *J Ethnopharmacol*, 76 (2001) 77.
- 54 Bandyopadhyay U, Das D & Banerjee R K, Reactive oxygen species: Oxidative damage and pathogenesis, *Curr Sci*, 77 (1999) 658.
- 55 Edens H A & Parkos C A, Neutrophil transendothelial migration and alteration in vascular permeability: focus on neutrophil-derived azurocidin, *Curr Opin Hematol*, 10 (2003) 25-42.
- 56 Fernández M A, de las Heras B, García MD, Sáenz MT, Villar A. New insights into the mechanism of action of the anti-inflammatory triterpene lupeol. *J Pharm Pharmacol*, 53 (2001) 1533-1539.
- 57 Duke J A, *Handbook of biologically active phytochemicals and their activities* (CRC press) (1992) 18-27.
- 58 Arima K, Uéda K, Sunohara N, Arakawa K, Hirai S, Nakamura M, Tonozuka-Uehara H, Kawai M, NACP/alpha-synuclein immunoreactivity in fibrillary components of neuronal and oligodendroglial cytoplasmic inclusions in the pontine nuclei in multiple system atrophy", *Acta Neuropathol*, 96 (5) (1998) 439-444.
- 59 Arima K, Uéda K, Sunohara N, *et al.*, Immunoelectron-microscopic demonstration of NACP/alpha-synuclein-epitopes on the filamentous component of Lewy bodies in Parkinson's disease and in dementia with Lewy bodies, *Brain Res*, 808 (1) (1998) 93-100.
- 60 Takase H, Yamamoto K, Hirano H, *et al.*, Pharmacological profile of gastric mucosal protection by marmin and nobiletin from a traditional herbal medicine, *Aurantii fructus immaturus*, *Japan J Pharmacol*, 66 (1994) 139.
- 61 Goel R K & Maiti R N, Antiulcer activity of naturally occurring pyranocoumarin and isocoumarins and their effect on the prostanoid synthesis using human colonic mucosa, *Indian J Exp Biol*, 35 (1997) 1080-1083.
- 62 Ghosh S & Playford R J, Bioactive natural compounds for the treatment of gastrointestinal disorders, *Clin Sci*, 104 (2003) 547.
- 63 Hansel R, Keller K, Rimpler H & Schneider G, *Hager's Handbuch der Pharmazeutischen Praxis* (Springer-Verlag, Berlin) (1994) 1196.
- 64 Kim H, Jang M, Kim Y, *et al.*, Red ginseng and vitamin C increase immune cell activity and decrease lung inflammation induced by influenza A virus/H1N1 infection, *J Pharm Pharmacol*, 68 (3) (2016) 406-420.