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Review Article

Pharmacological Properties of Aegle Marmelos: A Mini Review

Sampat Kumar Kundu[1], Shatabisha Bhattacharjee[1], **Kuntal Pal**[2]*
[1] Gurunanak Institute of Pharmaceutical Science & Technology, Sodepur, West Bengal, India
[2] Faculty of Ayurveda, Institute of Medical Sciences, Rajiv Gandhi South Campus, Banaras Hindu University, Barkachha, Mirzapur
*kuntalpal20@gmail.com

ABSTRACT

Ayurvedic plants have shown their effects on various kind of diseases. Those properties of the plants are sublimed in some molecules in the plants, which can be extracted out by performing various kind of processes (eg. Soxhlation, Percolation). Many plants which are used by the human being in daily life, also have some effects in curing some disease conditions. Likewise in our current review Aegle marmelos (Beal) have Antidiarrhoeal, Antidiabetic activities etc. Many Pharmacological Activities have been revealed & organized in this review article, but there have a wide scope of research to perform on this plant.

Keywords: Aegle Marmelos, Pharmacological Properties, research

INTRODUCTION

The beal fruit has a smooth, woody shell with a green, gray, or yellow peel. It takes about 11 months to ripen on the tree and can reach the size of a large grapefruit or pomelo, and some are even larger. The shell is so hard it must be cracked with a hammer or machete. The fibrous yellow pulp is very aromatic. It has been described as tasting of marmalade and smelling of roses. Boning (2006) indicates that the flavor is "sweet, aromatic and pleasant, although tangy and slightly astringent in some varieties. It resembles a marmalade made, in part, with citrus and, in part, with tamarind." Numerous hairy seeds are encapsulated in a slimy mucilage.

Pharmacological Properties

1. Immunomodulatory activity of *Aegle marmelos* in freshwater fish (*Catla catla*) by non-specific protection.[1]

The present research work investigates immunomodulatory action of *Aegle marmelos* (Linn.) Corr. Serr. (Rutaceae) in *Catla catla* Hamilton (Cyprinidae) for enhancing immune protection of the fish against bacterial infections. Doses of 0, 5, 10, 15, 20, 25 and 30 g aqueous plant leaf extract/kg feed were administered orally to the freshwater fish, Catla catla for a period of 30 days to investigate its efficiency to enhance the non-specific immune responses against the fish pathogen *Pseudomonas aeruginosa* (Schröter) Migula (Pseudomonadaceae). The fish were challenged with pathogens through water medium for 30 days and the immunomodulatory effect of the *Aegle marmelos* was evaluated on the blood samples every 5 days until 15 days after infection. The results obtained from the study shows that the 25 g leaf extract/kg of feed was found to be competent to enhance optimum immune response. The effectiveness of the immunostimulant action was found to be best

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for the first 5 days after challenging with pathogen and subsequently, the immune response was found to decline in all the concentrations of plant extract. The results of the study will be helpful for further investigation in the field to improve the immunocompetence of fish against bacterial pathogens.

2. Effects of aegeline, a main alkaloid of *Aegle marmelos* Correa leaves, on the histamine release from mast cells.[2]

Study shows that Aegeline or N-[2-hydroxy-2(4-methoxyphenyl) ethyl]-3-phenyl-2-propenamide is a main alkaloid isolated from *Aegle marmelos* Correa collected in Yogyakarta Indonesia. In our study, we investigated the effects of aegeline on the histamine release from mast cell. The study was performed by using (1) rat basophilic leukemia (RBL-2H3) cell line, and (2) rat peritoneal mast cells (RPMCs). DNP(24)-BSA, thapsigargin, ionomycin, compound 48/80 and PMA were used as inducers for histamine release from mast cell. In our study, aegeline inhibited the histamine release from RBL-2H3 cells induced by DNP(24)-BSA. Indeed, aegeline showed strong inhibition when RBL-2H3 cells induced by $Ca^{(2+)}$ stimulants such as thapsigargin and ionomycin. Aegeline is suggested to influence the intracellular $Ca^{(2+)}$ pool only since could not inhibit the (45)$Ca^{(2+)}$ influx into RBL-2H3 cells. Aegeline showed weak inhibitory effects on the histamine release from RPMCs, even though still succeed to inhibit when the histamine release induced by thapsigargin. These findings indicate that aegeline altered the signaling pathway related to the intracellular Ca(2+) pool in which thapsigargin acts. Based on the results, the inhibitory effects of aegeline on the histamine release from mast cells depended on the type of mast cell and also involved some mechanisms related to intracellular Ca(2+) signaling events via the same target of the action of thapsigargin or downstream process of intracellular $Ca^{(2+)}$ signaling in mast cells.

3. Effects of marmin, a compound isolated from *Aegle marmelos* Correa, on contraction of the guinea pig-isolated trachea.[3]

The present research work have shown Marmin or 7-(6',7'-dihydroxygeranyl-oxy) coumarin is a compound isolated from *Aegle marmelos* Correa. In the study, we examined the effects of marmin on the contraction of guinea pig-isolated trachea stimulated by several inducers, namely histamine, metacholine, compound 48/80. We also evaluated its action against contraction induced by extracellular or intracellular calcium ion. The possibility of marmin to potentiate the relaxation effect of isoprenaline was also studied. Marmin added in the organ bath at 10 min prior to the agonist inhibited the contraction elicited by histamine and metacholine in a concentration-dependent manner. Moreover, marmin antagonized the histamine-induced contraction in competitive manner. Marmin mildly potentiated the relaxation effect of isoprenaline. In the study, marmin abrogated the contraction of tracheal smooth muscle induced by compound 48/80, an inducer of histamine release. Besides, marmin successfully inhibited $CaCl_{(2)}$-induced contraction in $Ca^{(2+)}$-free Krebs solution. Marmin also inhibited two phases of contraction which were consecutively induced by metacholine and $CaCl_{(2)}$ in $Ca^{(2+)}$-free Krebs solution. Based on the results we concluded that marmin could inhibit contraction of the guinea-pig tracheal smooth muscle, especially by interfering histamine receptor, inhibiting the histamine release from mast, inhibiting intracellular $Ca^{(2+)}$ release from the intracellular store and the $Ca^{(2+)}$ influx through voltage-dependent $Ca^{(2+)}$ channels.

4. Studies on the antidiarrhoeal activity of *Aegle marmelos* unripe fruit: validating its traditional usage.[4]

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Study shows *Aegle marmelos* (L.) Correa has been widely used in indigenous systems of Indian medicine due to its various medicinal properties. However, despite its traditional usage as an anti-diarrhoeal there is limited information regarding its mode of action in infectious forms of diarrhoea. Hence, we evaluated the hot aqueous extract (decoction) of dried unripe fruit pulp of A. marmelos for its antimicrobial activity and effect on various aspects of pathogenicity of infectious diarrhoea. The decoction was assessed for its antibacterial, antigiardial and antirotaviral activities. The effect of the decoction on adherence of enteropathogenic *Escherichia coli* and invasion of enteroinvasive *E. coli* and *Shigella flexneri* to HEp-2 cells were assessed as a measure of its effect on colonization. The effect of the decoction on production of *E. coli* heat labile toxin (LT) and cholera toxin (CT) and their binding to ganglioside monosialic acid receptor (GM1) were assessed by GM1-enzyme linked immuno sorbent assay whereas its effect on production and action of *E. coli* heat stable toxin (ST) was assessed by suckling mouse assay. The decoction showed cidal activity against Giardia and rotavirus whereas viability of none of the six bacterial strains tested was affected. It significantly reduced bacterial adherence to and invasion of HEp-2 cells. The extract also affected production of CT and binding of both LT and CT to GM1. However, it had no effect on ST. The decoction of the unripe fruit pulp of A. marmelos, despite having limited antimicrobial activity, affected the bacterial colonization to gut epithelium and production and action of certain enterotoxins. These observations suggest the varied possible modes of action of *A. marmelos* in infectious forms of diarrhoea thereby validating its mention in the ancient Indian texts and continued use by local communities for the treatment of diarrhoeal diseases.

5. Inhibition of radiation-induced clastogenicity by *Aegle marmelos* (L.) correa in mice bone marrow exposed to different doses of gamma-radiation.[5]

It shows The frequency of micronucleated polychromatic (MPCE), normochromatic erythrocytes (MNCE), and polychromatic / normochromatic erythrocyte ratio (PCE/NCE), was studied in the bone marrow of mice orally administered with 0, 200, 225, 250, 275 and 300 mg/kg body weight of hydroalcoholic leaf extract of *Aegle marmelos* (AME). Treatment of mice with AME, once daily for 5 consecutive days, before exposure to 2 Gy resulted in a significant decline in the frequency of MPCE when compared to the non-drug-treated irradiated control. The greatest reduction in MPCE was observed for 250 mg/kg body weight AME, accompanied by the highest polychromatic erythrocyte to normochromatic erythrocyte ratio, in comparison with the non-drug-treated irradiated control. Therefore, further studies were carried out using this dose of AME, where the animals were administered with 250 mg/kg body weight of AME before exposure to 0, 0.5, 1, 2, 3 and 4 Gy of gamma-radiation and evaluated at 12, 24, 36 and 48 hours post-irradiation. Whole body irradiation of mice to different doses of gamma-radiation resulted in a dose-dependent increase in the frequency of MPCE at all post-irradiation times. Treatment of 250 mg/kg AME orally (p.o.) before irradiation significantly reduced the frequency of MPCE at all post-treatment times. The frequency of MPCE increased with time, reached a peak level at 24 hours, and declined thereafter. The occurrence of MNCE has also shown a pattern similar to MPCE, except that the MNCE frequency reached a peak level by 48 hours. The AME significantly reduced the frequency of MNCE at all post-irradiation times, when compared to the non-drug-treated irradiated group. Treatment of mice with AME before exposure to different doses of gamma-radiation resulted in the inhibition of a

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radiation-induced decline in the PCE/NCE ratio, when compared with the concurrent irradiated controls. To gain insight into the mechanism of action, AME was tested for its antioxidant effects in cell-free chemical systems using H2O2/FeSO4 to generate hydroxyl (*OH) radicals, which were measured by a fluorescent probe, 2V, 7V-dichlorofluorescin diacetate (DCFH/DA). Xanthine/xanthine oxidase was used to generate superoxide (O2*-) anion radical, which was measured by a fluorescent probe dihydroethidium (DHE). AME significantly reduced fluorescence in a concentration dependent manner, indicating its efficacy to scavenge free radicals. Our results demonstrate that one of the mechanism of reduction in the radiation-induced DNA damage in mice bone marrow by AME may be due to scavenging of free radicals and elevation in the antioxidant status, as previously reported.

6. Antidiabetic activity of *Aegle marmelos* and its relationship with its antioxidant properties.[6]

The study shows that Oxidative stress induced by alloxan has been shown to damage pancreatic beta-cell and produce hyperglycemia in rats. Aegle marmelos leaf extract is being used in Ayurveda as a medicine for diabetes. The present study examined the action of *Aegle marmelos* against experimental diabetes as well as the antioxidant potential of the drug. A methanolic extract of Aegle marmelos was found to reduce blood sugar in alloxan diabetic rats. Reduction in blood sugar could be seen from 6th day after continuous administration of the extract and on 12th day sugar levels were found to be reduced by 54%. Oxidative stress produced by alloxan was found to be significantly lowered by the administration of Aegle marmelos extract. This was evident from a significant decrease in lipid peroxidation, conjugated diene and hydroperoxide levels in serum as well as in liver induced by alloxan. Catalase and glutathione peroxidase activity in blood and liver were found to be increased from 9th day onwards after drug administration. Superoxide dismutase and glutathione levels were found to be increased only on 12th day. These results indicate that Aegle marmelos extract effectively reduced the oxidative stress induced by alloxan and produced a reduction in blood sugar.

7. Effect of *Aegle marmelos* and Hibiscus rosa sinensis leaf extract on glucose tolerance in glucose induced hyperglycemic rats (Charles foster).[7]

Study shows In an effort to test the hypoglycemic activity of *Aegle marmelos* and *Hibiscus rosa sinensis* in glucose induced hyperglycemic rats, their alcoholic leaf extracts were studied. Both the groups of animals receiving either. *A. marmelos* or H. rosa sinensis leaf extract for seven consecutive days, at an oral dose equivalent to 250 mg kg-1 showed significant improvements in their ability to utilize the external glucose load. Average blood glucose lowering caused by A. marmelos and *H. rosa sinensis* was 67% and 39% respectively, which shows that former significantly ($p < 0.001$) improves the glucose tolerance curve. The magnitude of this effect showed time related variation with both the plants. Efficacy of *A. marmelos* and *H. rosa sinensis* was 71% and 41% of glybenclamide, respectively. These data throw some light on the possible mechanism of hypoglycemic activity of both the plants. The mechanism of action could be speculated partly to increased utilization of glucose, either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion.

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