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A review on immunomodulatory activity of amla and *Aloe vera*

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Abstract
To encourage a disease free healthy life Mother Nature has gifted mankind medicinal plants. Numerous medicinal plants are present in a collection of herbal preparations of the Indian traditional health care system (Ayurveda) named *Rasayana*, recommended for their interesting antioxidant activities.
Emblica officinalis Gaertn. or *Phyllanthus emblica* Linn, commonly known as Indian gooseberry or *Amla*, is perhaps the most important medicinal plant in the Indian traditional system of medicine, the Ayurveda. Several parts of the plant are used to treat a variety of diseases, but the most important is the fruit. Many ailments are treated by the fruit which is used either alone or in combination with other plants. These include common cold and fever; as a diuretic, laxative, liver tonic, refrigerant, stomachic, restorative, anti-inflammatory, hair tonic; to prevent peptic ulcer and dyspepsia, and as a digestive. *E. officinalis* possesses antipyretic, analgesic, antitussive, antiatherogenic, adaptogenic, cardioprotective, gastroprotective, antianemic, antihypercholesterolemic, wound healing, antidiarrheal, antiatherosclerotic, hepatoprotective, nephroprotective, and neuroprotective properties as demonstrated in numerous preclinical studies.
It is well known that many drugs including antimicrobials are known to either stimulate or depress the immune system and produce antimicrobial Resistant thereby alter the course of the diseases. Immunomodulatory properties of fruit extracts of Amla in immuno-compromised states. Amla is widely accepted as an immune 'booster among the people, the supportive scientific proof available is limited, hence the present study will be undertaken for further Research activities.

Keywords: Medicinal plants, phytochemical, immunomodulation, amla, *Aloe-vera*

Introduction
To encourage a disease free healthy life Mother Nature has gifted mankind medicinal plants. Numerous medicinal plants are present in a collection of herbal preparations of the Indian traditional health care system (Ayurveda) named *Rasayana*, recommended for their interesting immunomodulatory and antioxidant activities etc.
Emblica officinalis Gaertn. or *Phyllanthus emblica* Linn, commonly known as Indian gooseberry or *Amla*, is perhaps the most important medicinal plant in the Indian traditional system of medicine, the Ayurveda. Several parts of the plant are used to treat a variety of diseases, but the most important is the fruit. Many ailments are treated by the fruit which is used either alone or in combination with other plants. These include common cold and fever; as a diuretic, laxative, liver tonic, refrigerant, stomachic, restorative, anti-inflammatory, hair tonic; to prevent peptic ulcer and dyspepsia, and as a digestive. *E. officinalis* possesses antipyretic, analgesic, antitussive, antiatherogenic, adaptogenic, cardioprotective, gastroprotective, antianemic, antihypercholesterolemic, wound healing, antidiarrheal, antiatherosclerotic, hepatoprotective, nephroprotective, and neuroprotective properties as demonstrated in numerous preclinical studies.
A. vera is a rich source of bioactive compounds. It has been widely used in alternative medicine as health and nutritional supplements in addition to its cosmetic applications. Polyphenol-rich A. vera extracts possess various pharmacological activities. The plant has about 99–99.5% water and only 0.5–1.0% solid matter which contains more than 75 diverse compounds (Radha and Luxmipriya, 2015). On dry matter basis, aloe gel consists of polysaccharides (55%), sugars (17%), minerals (16%), proteins (7%), lipids (4%), and phenolic compounds (1%). Polysaccharides present in the inner leaf parenchymatous tissue of leaf extracts have been credited with curative potential. A. vera gel contains polymannans which consist of linear chains having higher amount of mannose with lower amount of glucose molecules (Ni *et al*., 2004) [2]. Among polymannans, acemannan is the major polysaccharide which is made up of one or more polymers of different chain lengths of glucose and mannose in a 1:3 ratio (Chow *et al*., 2005; Femenia *et al*., 1999) [3].

A. vera is also known to contain a variety of useful secondary metabolites, including anthraquinones with tricyclic aromatic quinine structure (Reynolds and Dweck 1999) [4]. Aloe-emodin and chrysophanol are key naturally-occurring anthraquinone compounds (Tan *et al*., 2011) [5]. Two types of exudates are secreted by aloe leaves. One is a bitter reddish-yellow juice due to the presence of aloin, aloe-emodin and related compounds. The other exudate is transparent and resembles colorless gelatin. In ancient times, this mucilage was applied to inflamed skin, and during the 20th century it was used for treatment of radiation burns. *Aloe vera* possess wound healing, Anti-inflammatory, Anti-cancer, anti diabetic, Anti- ulcer, Antihyperlipidemic activity, Antioxidant effects and Immunomodulatory activity.

It is well known that many drugs including antimicrobials are known to either stimulate or depress the immune system and produce antimicrobial Resistant thereby alter the course of the diseases. Immunomodulatory properties of extracts of Amla and its interaction with *Aloe vera* in immuno-compromised states. Amla is widely accepted as an immune 'booster among the people, and *Aloe vera* also used as most potent skin healer or scar inhibitor.

Immunomodulatory activity evaluation of medicinal plants

Manish *et al.* (2013) [7] studied on Immunomodulatory role of Emblica officinalis in arsenic induced oxidative damage and apoptosis in thymocytes of mice. Arsenic exposure to mice caused a significant increase in the lipid peroxidation, ROS production and decreased cell viability, levels of reduced glutathione, the activity of superoxide dismutase, catalase, cytochrome c oxidase and mitochondrial membrane potential in the thymus as compared to controls. Increased activity of caspase-3 linked with apoptosis assessed by the cell cycle analysis and annexin V/PI binding was also observed in mice exposed to arsenic as compared to controls. Co-treatment with arsenic and amla decreased the levels of lipid peroxidation, ROS production, activity of caspase-3, apoptosis and increased cell viability, levels of antioxidant enzymes, cytochrome c oxidase and mitochondrial membrane potential as compared to mice treated with arsenic alone. The results of the present study exhibits that arsenic induced oxidative stress and apoptosis significantly protected by co-treatment with amla that could be due to its strong antioxidant potential.

Wei WANG *et al.* (2010) [10] worked on to investigate the immunomodulatory effects of andrographolide on both innate and adaptive immune responses. Andrographolide (10 μg/mL *in vitro* or 1 mg/kg *in vivo*) was used to modulate LPS-induced classical activated (M1) or IL-4- induced alternative activated (M2) macrophages *in vitro* and humor immune response to HBsAg *in vivo*. Cytokine gene expression profile (M1 *vs* M2) was measured by real-time PCR, IL-12/IL-10 level was detected by ELISA, and surface antigen expression was evaluated by flow cytometry, whereas phosphorylation level of ERK 1/2 and AKT was determined by Western blot. The level of anti-HBs antibodies in HBsAg immunized mice was detected by ELISA, and the number of HBsAg specific IL-4-producing splenocyte was enumerated by ELISPOT. Andrographolide treatment *in vitro* attenuated either LPS or IL-4 induced macrophage activation, inhibited both M1 and M2 cytokines expression and decreased IL-12/IL-10 ratio (the ratio of M1/M2 polarization). Andrographolide down-regulated the expression of mannose receptor (CD206) in IL-4 induced macrophages and major histocompability complex/costimulatory molecules (MHC I, CD40, CD80, CD86) in LPS-induced macrophages. Correspondingly, anti-HBs antibody production and the number of IL-4-producing splenocytes were reduced by *in vivo* administration of andrographolide. Reduced phosphorylation levels of ERK1/2 and AKT were observed in macrophages treated with andrographolide. study conclude that andrographolide can modulate the innate and adaptive immune responses by regulating macrophage phenotypic polarization and Ag-specific antibody production. MAPK and PI3K signaling pathways may participate in the mechanisms of andrographolide regulating macrophage activation and polarization.

Jyotsana Madanatal; (2008) also worked on Immunomodulatory properties of *Aloe vera* gel (AVG) in mice and evaluate the effect on Antibody Production AVG extract in the dose of 300 mg/kg, i.p was found to enhance the production of circulating antibody titre The highest antibody titre of 266 was observed on the 18th day for the dose of 300 mg/kg, i.p, whereas control animals showed a maximum antibody titre of 34 on the same day. The animals treated with the dose of 150 mg/kg, i.p did not show any enhancement in antibody production. The present experiments revealed that AVG extract (300 mg/kg, i.p) has immuno-stimulatory action. However negligible or no eff ects were observed at a dose of 150 mg/kg. The higher dose stimulates the proliferation of stem cells, as seen from an increase in total white blood cells. Further increase in PFC and circulating antibody titre, suggests that AVG extract may stimulate the humoral immunity. More over the extract was found to stimulate phagocytic activity. Hence it can be concluded that the AVG extract may be a potential candidate in several immuno-suppressed clinical conditions.

M. Sai Ram *et al.* (2002) [8] studied to determine the anti-oxidant and immunomodulatory properties of Amla using chromium (VI) as an immunosuppressive agent. Chromium (Cr) treatment results in enhanced cytotoxicity, free radical production, lipid peroxidation and decreased glutathione peroxidase (GPx) activity and diminished glutathione (GSH) levels. There was a significant inhibition of both lipopolysaccharide and concanavalin-A-stimulated lymphocyte proliferation. Chromium also inhibited Con A stimulated interleukin-2 and g-interferon production significantly. Further, there was enhanced apoptosis and DNA fragmentation in the presence of Cr. Amla significantly inhibited Cr-induced free radical production and restored the anti-oxidant status back to control level. Amla also inhibited apoptosis and DNA fragmentation induced by Cr. Interestingly, Amla relieved the immunosuppressive effects of Cr on lymphocyte proliferation and even restored the IL-2 and g-IFN production considerably.

R. S. Suja *et al.* (2009**)** [11] was evaluated of Aqueous extract of dried Emblica *officinalis* For immunomodulatory effect on male Swiss Albino mice. The mice were divided into three groups. The first group received vehicle alone to serve as control. The second and third groups received the extract orally at 100 and 200 mg! kg body weight dose levels respectively per day for a period of 19 days. There was significant dose dependent increase in haemagglutination antibody titre, sheep red blood cells induced delayed type of hypersensitivity reaction, macrophage migration index, respiratory burst activity of the peritoneal macrophages, total leukocyte count, percentage lymphocyte distribution, serum globulin and relative lymphoid organ weight in Emblica treated mice indicating its ability to stimulate humoral as well as cell mediated immunity along with macrophage phagocyte.

Reddy *et al.* (2012**)** [9] an experiment was conducted with three types of herbal preparations (amla, turmeric and tulsi) either alone or in combination in nine dietary treatments to study the bio-chemical parameters and immune responses in broilers. The treatment groups consisted of control (T1), 0.25% amla (T2), 0.5% amla (T3), 0.25% turmeric (T4), 0.5% turmeric (T5), 0.25% tulsi (T6), 0.5% tulsi (T7), 0.25% amla+turmeric+tulsi (T8) and 0.5% amla+turmeric+tulsi (T9) were included in broiler diet. The different types of herbals either alone or in combination at 0.25 and 0.5% levels in broiler diets did not influence the SGOT, SGPT and serum cholesterol levels. The immune response (HI titre) to ND vaccination slightly increased which were insignificant in broilers fed with different herbals either alone or in combination compared to control. The weight of bursa and spleen increased slightly with supplementation of herbals which were insignificant. The results suggested that herbals like amla, turmeric and tulsi can be supplemented in broiler feeds as they have direct effect on improving immunity against Newcastle Disease.

Zohreh Farahnejad *et al.* (2011) [13] worked on Immunomodulatory effects of *Aloe vera* and its fractions on response of macrophages against *Candida albicans* and the study, investigated the effect of *A. vera* extract and its fractions on infected macrophages with *C. albicans*. Viability of intraperitoneal macrophages was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) test. Cell viability of infected macrophages was increased by the extract and dose of some isolated fractions dependently. The extract as well as R100, R50, R30, and R10 fractions of *A. vera* significantly increased cell viability of macrophages in most doses. R5 and F5 fractions showed no significant difference in comparison with control group. Further studies in animal models and human are necessary to clarify the modulatory effects of *A. vera* on macrophage function. Isolation and purification of *A. vera* components are also needed to find out the effective molecules.

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