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Review Article

IMMUNE-ENHANCING EFFECT OF AN AYURVEDA FORMULATION *VIDHARA-AMALAKI YOG*

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ABSTRACT

Plant extracts and Ayurvedic polyherbal mixtures have been used to treat a variety of diseases since time immemorial. Studies on the therapeutic effects of these extracts in the treatment of various disorders are also extensively established. The synergistic effect of polyherbal medications in repairing and revitalizing the immune system is also highlighted in Ayurvedic classics. *Argyreia speciosa* Linn. (Elephant Creeper, *Vidhara* in Sanskrit; Family: Convolvulaceae) and *Emblica officinalis* Gaertn (Indian gooseberry, *Amalaki* in Sanskrit; Family: Phyllanthaceae) are important drugs explained in Ayurvedic literatures and Nighantus for their *Rasayana* and *Bala-vardhaka* properties (immunomodulatory actions). They also possess the restorative and rejuvenating powers as they act on the immune system and positively affect the response of the body towards disease causing pathogens. In this review a comprehensive account of the pharmacological activities along with the immunomodulatory activities of *Vidhara- Amalaki yog* (compound formulation of *Vidhara* and *Amalaki*) are included in view of the many recent findings of importance on this plant.

INTRODUCTION

The immune system is a way of protecting the body against various infectious diseases by preventing growth of pathogens inside body or by counteracting the effect of toxins produced by them. In Ayurveda, the concept of immunity, *Vyadhikshamatva*[1] or *Bala* plays a key role for prevention and rapid recovery from diseases. This *Bala (Vyadhi kshamatva)* can be achieved by intervention of various *Rasayana.* Different *Rasayana* drugs individually or as compound formulations are described in Ayurveda which possess immunomodulatory activity.

Vidhara-Amalaki Yog[2] has been mentioned in Ashtang Samgraha Uttara tantra, *Rasayana Prakarana* and its properties are mentioned as when the powder is soaked and macerated in the fresh juice of *Dhatri (Amalaki) and* licked for one month with honey and ghee or with milk leads to a life of hundred years without any disease and endowed with intelligence. Moreover, this review is done to evaluate the immunomodulatory and therapeutic effect of *Vidhara Amalaki Yog.*

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Argyreia speciosa Linn. (Elephant Creeper, *Vidhara* in Sanskrit; Family: *Convolvulaceae*) is a popular Indian medicinal plant and is also mentioned as a *Rasayana* drug in Ayurvedic literatures and Nighantus. It is reported to contain flavonoids, sterol glycoside, flavonoids, and essential oil. This plant is pharmacologically studied for nootropic, aphrodisiac, immunomodulatory, hepatoprotective, antioxidant, anti-inflammatory, antihyperglycemic, antidiarrheal, antimicrobial, antiviral, nematocidal, antiulcer, anticonvulsant, analgesic and central nervous depressant activities.[3]

Emblica officinalis Gaertn (Indian gooseberry, *Amalaki* in Sanskrit; Family: *Phyllanthaceae*) is mentioned as a *Rasayana* drug in Ayurveda classical texts.[4] Indeed, *Emblica* is one of the most important plants of Ayurveda. According to the two main classic texts on Ayurveda Charaka Samhita and Sushrut Samhita, *Amalaki* is regarded as "the best among rejuvenative herbs, and "the best among the sour fruits." Fruits of *E. officinalis* have been used for thousands of years in traditional Indian medicine for the treatment of various diseases. So, it is one of the major components in many herbal formulations. Despite many therapeutic effects of *Amalaki*, relatively little data is available on the putative immunomodulatory effects of *Amla* on lymphocyte function, particularly in immuno-suppressive conditions.

MATERIALS AND METHODS

Review of different Ayurveda literatures as a primary source of data along with the literature review as secondary data from reputed journal papers and other e-resources documenting the concept of immunity and immune-modulatory effect of *Vidhara (Argeria speciosa)* and *Amalaki (Emblica officinalis)* were done.

Table 1: Ingredients of *Vidhara- Amalaki Yog* (Ref- Ashtanga Sangraha, Uttar tantra, *Rasayana Prakarana*)

S.No	Drug	Botanical name	Family	Part used	Quantity
1.	*Vidhara*	*Argyeria speciosa*	Convolvulaceae	Root, leaves	1 part
2.	*Amalaki*	*Emblica officinalis* Gaertn	Euphorbiaceae	Fruit	Quantity sufficient for *Bhavana*

Vidhara (*Argyria Speciosa)*

Ayurvedic pharmacological Action

Argyreia speciosa Linn. (Elephant Creeper, *Vidhara* in Sanskrit; Family: Convolvulaceae) is a popular Indian medicinal plant and is also mentioned as a *Rasayana* drug in Ayurvedic literatures and Nighantus. In Bhavprakash Nighantu (*Guduchyadi varga*) properties of *Vidhara* has been explained as: "*Vriddhdaru Kashaya ushna katutikto rasayana. Shukra aayu bala medha agni swar kantikarah."*[5] Meaning proper use of *Vidhara* provides *Rasayan* (rejuvenation), *Vrishya* (aphrodisiac), *Aayu* (longitivity), *Bala* (immunity), *Medha* (intellect), *Agni* (digestive power), *Swar* (voice) and *Kanti* (luster). It has *Katu* (pungent), *Tikta* (bitter)*, Kashaya* (astringent) *Rasa*, *Laghu* and *Snighda* (light and unctuous) *Guna*, *Madhura vipaka, Ushna veerya* (hot) and *Kapha-Vata Shamaka* property. *Vidhara* has been indicated for its immunomodulatory (*Rasayana* and *Balavardhaka*) properties.

Pharmacological Actions

Table 2: Immunomodulatory and Antioxidant Properties

Researcher/Author	Methodology	Outcome
Lubna Azmi et.al [6] 2019	Phenolic content (TPC), reducing power (RP), antioxidant activity (AOA), O·−2 (superoxide anion), DPPḢ (1,1-diphenyl-2-picrylhydrazyl) and ·OH (hydroxyl) radicals scavenging activities, GSH (glutathione), CAT (catalase), SOD (superoxide dismutase) and LPO (lipid peroxidase) are the major parameters which were studied for determining in vitro and in vivo antioxidant property of seed extract & their six fractions obtained from *A. speciosa*. Carbon tetrachloride (CCl_4) induced rat model was used to determine in Total vivo antioxidant assay of extract and its fractions.	*Argyria speciosa* showed strong antioxidant property and protected oxidative DNA damage.
Sunil K. Jaiswal et.al [7] 2011	The butanol fraction of *Argyreia speciosa* leaf (ASE; 50, 100 and 200mg/kg body weight) was administered orally, twice daily for 5 days for prevention from Aspirin (ASP)-, ethanol (EtOH)-, cold-restraint stress (CRS) - and pylorus ligation (PL)-induced ulcers. Estimation of antioxidant enzymes activity was carried out in CRS-induced ulcer model	The gastric wall mucus was significantly ($p<0.001$) enhanced by ASE and is regarded as the first line of defence against EtOH-induced gastric ulcers showing cytoprotective property.
Patel et.al [8] 2011	Hydroalcoholic extract of *A. speciosa* roots (100mg/kg, 200mg/kg) was used in Swiss albino mice and evaluated by using the swimming endurance test, acetic acid–induced writhing test, pentylenetetrazole-induced convulsion test, anoxic tolerance test, cold-restraint, stress-induced gastric ulcers, aspirin-induced ulcers, and biochemical, and histopathological changes in the cold-restraint stress test	The immunostimulant activity of the ASE was indicated by an increase in the antibody titer in mice pre-immunized with sheep red blood cells and subjected to restraint stress
Hubbu et.al [9] 2009	*In Vitro*: Bacteria, fungi and Mycobacterium tuberculosis H_{37} Rv sensitive strain *In vivo:* mice infected with K. pneumoniae	Showed significant inhibition of gram positive and negative bacterial growth

Habbu P et.al [10] 2008	Rats were treated with Ethanolic extract (EtAS) and Ethyl acetate extract (EAAS) of roots of *Argyreia speciosa* at doses of 200 mg and 400 mg / kg body weight p.o. along with CCl4 (0.7ml/kg in olive oil, 1:1 v/v i.p. on every alternate days) for seven days.	Decrease in levels of super oxide dismutase (SOD), catalase and peroxidase activity in liver shows strong anti-oxidant properties
A B Gokhale [11] 2003	Oral administration of the ethanolic extract of *A. speciosa* root (ASEE), at the doses of 50, 100 and 200 mg/kg in mice, dose-dependently potentiated the delayed-type hypersensitivity reaction induced both by sheep red blood cells (SRBC) and oxazolone.	Significantly enhanced the production of circulating antibody titre in mice in response to SRBC. ameliorated the total white blood cell count and also restored the myelo suppressive effects induced by cyclophosphamide.

***Amalaki* (*Emblica Officinalis*)**

Ayurvedic Pharmacological Action

Emblica officinalis Gaertn (Indian gooseberry, *Amalaki* in Sanskrit; Family: Phyllanthaceae) is mentioned as a *Rasayana* (rejuvenating) drug.[12] *Amalaki* is the nutritious drug and termed as "*Amalaki Vayasthaapananama Shreshthama*"[13] meaning best among rejuvinating drugs. It has 5 *Rasas* viz: *Madhura* (sweet), *Amla* (sour), *Katu* (pungent), *Tikta* (bitter) and *Kashaya* (astringent). *Laghu* (light), *Ruksha* (dry) *Guna, Sita Virya, Madhura Vipaka* and *Tridoshahara* as well as *Rasayana.* In Bhavprakash Nighantu it has been mentioned "*Raktapitta Pramehaghnam param vrishyam rasayanam.[14]"*meaning proper use of *Amalaki* cures *Raktapiita* (bleeding disorders), *Prameha* (diabetes), and possess *Rasayana* (rejuvenating) and *Vrishya* (aphrodisiac) properties.

Amalaki is *Rooksha* (dry), *Kashaya* (astringent) and *Swadu* (sweet) in taste. It helps in making balance of *Kapha* and *Pitta*. It is *Jwarghna* (helpful in fever), *Kasaghna* (helpful in cough, cold and breathlessness), *Virechnopaga* (help to induce purgation, *Kusthghna* (helpful in skin disorders) and *Vayasthapana* (anti-ageing).

***Mahakashaya*[15]:** *Kushthaghna* (alleviates skin disorders), *Virechanopaga* (supportive drug for purgation), *Kasahar* (alleviates cough), *Jwarhara* (alleviates fever), *Vayasthapana* (anti-aging).

Gana[16]: Triphala, Mushkakadi, Parushakadi, Mustadi, Amalakyadi

Varga: Haritakyadi varga[18]

Pharmacological Activity and Research Studies

Research studies has proven *Amalaki* has the properties of spasmolytic, mild CNS depressant, hypolipidemic, anti-atherosclerotic, antimutagenic, anti-microbial, anti-oxidant, immunomodulatory, anti-fungal, antitumour, anti-inflammatory, anti-bacterial, anti-ulcer, and adrenergic potentiating. It is reported to contain phenolic constituents like gallic acid and its derivatives, mucic acid and its derivatives, corillagin, chebulagic acid, putrajivain A[17,18]. They possess high amounts of tannins like emblicanin A and B, punigluconin and pedunculagin[19], flavonoids like quercetin[20,21] and alkaloids like phyllantin and phyllantidin[22]. Various groups have reported high amounts of vitamin C[23,24] and considerably high amounts of minerals, proteins and amino acids like proline, alanine, cysteine, glutamic acid, aspartic acid, and lysine. The fruits also contain glucose, fibres, phosphorus, iron and calcium[25]. The fruit is highly beneficial as cytoprotective[26], hepatoprotective[27], radioprotective[28], gastroprotective[29] and antitussive agent[30]. It is used to treat ophthalmic disorders, diarrhea, diabetes, scurvy, tumour, and ulcer[31] and protects against hyperthyroidism[32], cataract[33], ischemic reperfusion induced oxidative stress[34], atherosclerosis and hyperlipidaemia[35]. It is also a potent antibacterial agent against Gram-positive and Gram-negative bacteria[36] as well as an antifungal agent.[37]

Table 3: Immunomodulatory and Antioxidant Properties

Researcher/Author	Methodology	Outcome
Vijay Kumar et.al [38] 2016	Use of *Amla* extract in metal-induced lipid per oxidation in human erythrocytes	A significant reduction in erythrocyte hemolysis induced by hydrogen peroxide was observed using *Amla* extract (P<0.05) shows significant protective potential against lipid peroxidation.
Udupi Vishwanatha	The DNA repair in Human volunteers was analyzed in peripheral blood mononuclear	*Amalaki rasayana* has stably maintained the DSBR in aged

et.al [39] 2016	cells before and after *Amalaki rasayana* administration. UVC-induced DNA strand break repair (DSBR) based on extent of DNA unwinding by fluorometric analysis, nucleotide excision repair (NER) by flow cytometry and constitutive base excision repair (BER) by gap filling method were analyzed.	individuals. There were no adverse side effects. Further, subjects with different BMI showed differential DNA strand break repair capacity.
Manish et.al [40] 2015	Protective efficacy of *Amla* is studied in arsenic induced inflammation and immunotoxicity in mice.	Arsenic induced oxidative stress and apoptosis significantly protected by co-treatment with *Amla* due to its strong antioxidant potential.
Belapurkar P et.al 2014 [41]	The study group of rats was exposed to noise stress of 100dB for 4 h/day for 15 days and their neutrophil function tests and corticosterone levels were assessed.	The study showed that administration of *Triphala* in both groups i.e. noise stress alone and noise stress immunized group greatly prevented the effect of noise stress, which was evident by its immunostimulant effect on neutrophil function and immunosuppressant effect on corticosterone levels of the model animals.
Jignesh Rajni et.al [42] 2012	Two samples of *Amalaki Rasayana* (AR7 and AR21) were studied to evaluate the comparative immunomodulatory activity against the cyclophosphamide immunosuppression in rats.	*Amalaki Rasayana* possesses significant immunostimulant activity and moderate cytoprotective activity. AR21 was found to have better activity profile in terms of both immunostimulant as well as cytoprotective activity.
Mahesh Mysore et.al [43] 2012	Cellular oxidative state using a hepatocyte cell line (HepG2).	Improvement in endogenous antioxidant defenses in HepG2 cells
Xiaoli Liu. et.al [44] 2012	Immunomodulatory properties and anticancer potential of six phenolic compounds from *Emblica* fruit by in vitro proliferation assay.	Results suggested that the antitumour activity of these compounds might be achieved by immunomodulatory properties which could partially be attributed to their antioxidant activity.
Suja RS et.al [45] 2009	Aqueous extract of dried *Emblica officinalis* Gaertn. (*Amla*) fruit pulp powder was evaluated 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 200mg/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.

Sai Ram et.al [46] 2003	The macrophages (J-774) were grown either in 24-well plates or 96-well plates in RPMI 1640 medium for 2 days until a monolayer was formed. The medium was replaced with fresh medium and the fruit extracts of *Amla* and chromium (VI) as sodium dichromate (1µg/mL) were added to the cells and incubated for 24 h.	The cytoprotective and immunomodulating properties of *Emblica officinalis* (*Amla*) against chromium (VI) induced oxidative damage are reported. It possesses anti-apoptotic property and ceases DNA fragmentation, thus countering the immunosuppressive effect of Cr (VI) on lymphocyte proliferation. Restores IL-2 and IFN-γ production
Salil K Bhattacharya [47] 2002	Emblicanin- A (37%) and -B (33%) enriched fraction of fresh juice of *Emblica* fruits (EOT) was investigated for antioxidant activity against ischemia-reperfusion (IRI)-induced oxidative stress in rat heart.	Significant decrease in the activities of cardiac superoxide dismutase, catalase, and glutathione peroxidase. The study confirms the antioxidant effect and cardioprotective action of *E. officinalis.*
M Sai Ram et.al 2002 [48]	In-vitro study was undertaken to determine the relative effects of fruit extracts of *Amla* with regard to cytoprotection and immunomodulation using rat splenocytes as model system.	*Amla* relieved the immuno-suppressive effects of Cr on lymphocyte proliferation and even restored the IL-2 and g-IFN production considerably.
EL-Mekkaw Sahar et.al 1995 [49]	The MeOH extract of the fruit of *P. emblica* (Euphorbiaceae) was chosen for the isolation of its RT inhibitory principles.	The fruit of *Phyllanthus emblica* showed a potent inhibitory activity to HIV-1-RT

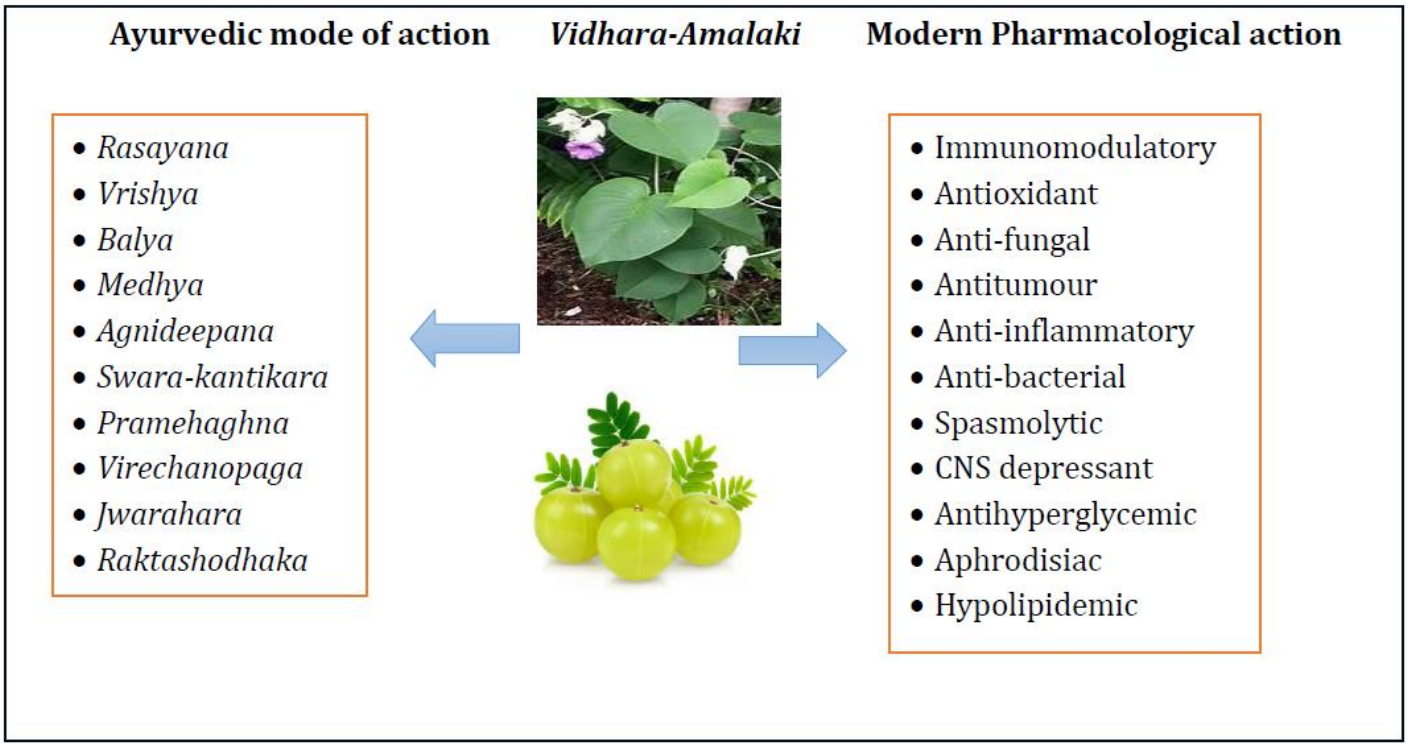

Figure 1: Pharmacological action of *Vidhara-Amalaki yog*

DISCUSSION

Vidhara-Amalaki Yog possess the effective immunomodulatory property as this formulation have different active compounds in *Vidhara* and *Amalaki* such as gallic acid, chebulagic acid, ellagic acid, flavonoids, tannins and phenols. Overall, the *Vidhara-Amalaki Yog* have *Katu, Tikta, Kashaya Rasa, Laghu Guna* and *Madhur Vipaka*. The above formulation also has *Tridoshahara* and *Rasayana,*[5,16][5,16] (rejuvenating) properties. Due to its *Balya* properties, it exhibits an active immunomodulatory activity of this compound formulation and can be understood using the concept of *Rasayana.* This indicates that components of the formulation help promote nutrition at *Rasa, Agni*, and *Srotas* levels, by the virtue of which

immunomodulatory effects become possible. The study by Gokhale et.al revealed that root of *A. speciosa* possess immunomodulatory activity.[50] Lubna Azmi et.al[51] proved A. speciosa has strong antioxidant property and protected oxidative DNA damage. Along with its immunomodulatory action, it has anti-microbial[11], anti-viral[12], Anti filarial[1], anti-fungal, hepatoprotective[50,51,52] actions as well.[52] Similarly, *Amalaki* possess immunomodulatory[39], anti-oxidant[45], hepatoprotective, phagocytotic and anti-inflammatory actions. The clinical studies and pharmacological action of *Vidhara- Amalaki yog*, thus justifies its immunomodulatory effect.

CONCLUSION

Vidhara-Amalaki yog appears to exhibit immunomodulatory and antiviral properties as it contains flavonoids, sterol glycoside, flavonoids, and essential oil. The pharmacological studies reported in the present review confirm the therapeutic value including immunomodulatory action of A. speciosa (Linn. f.) Sweet and *Emblica officinalis.* Many polyherbal formulations containing *Vidhara and Amalaki* plant parts are available in the market. However, less information is available regarding the clinical study, toxicity study, phyto-analytical studies of this plant. More scientific data in the form of high-quality research studies is needed to evaluate the efficacy of immunomodulatory actions of *Amalaki* and *Vidhara.*

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