International Journal of Food Science and Nutrition
ISSN: 2455-4898
Impact Factor: RJIF 5.14
www.foodsciencejournal.com
Volume 3; Issue 1; January 2018; Page No. 84-87

Phyllanthus emblica: The superfood with anti-ulcer potential

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Abstract
The Indian Gooseberry is one of the commonly used plants in the Indian system of medicine. Amla is a wonder superfood, belonging to the genus *Phyllanthus L.* which is mainly distributed in tropical areas. It represents a phytochemical reservoir of biologically important molecules. The plant contains tannins, alkaloids, amino acids, carbohydrates, vitamins and organic acids. Various parts of the plant have been used to treat a wide array of diseases. The present article highlights the importance of *Phyllanthus emblica* in the prevention and treatment of ulcer. Gastrointestinal ulcer results due to an increase in the offensive factors as compared to defensive ulcer protective elements. The fruit extracts possesses potent anti-oxidant potential which is the key to its therapeutic effect. Additionally it is also capable of inducing neo-angiogenesis thereby helping in repair of gastric lesions. The anti-inflammatory potential of the above further accelerates ulcer healing. Owing to its anti-secretory and cyto-protective capacities, *Phyllanthus emblica* either alone or in combination represents a valuable natural strategy to treat several chronic diseases especially ulcer.

Keywords: Amla, angiogenesis, anti-oxidant, Indian gooseberry, inflammation, ulcer

1. Introduction
Plants have formed the basis of traditional medicine and drug development. The human race started using plants and plant products successfully for treatment of diseases and injuries from the early days of civilization [1]. In present times, the World Health Organization has also been encouraging, promoting and facilitating the effective use of herbal medicine in the developing countries. Owing to its pharmacological importance, *Phyllanthus emblica* commonly known as Indian gooseberry or Amla is one of the abundant medicinal plant utilized in the Indian traditional systems of medicine including Ayurveda [2]. It is an indigenous plant of the Indian subcontinent. India ranks first in the world in area and production of this crop; the others being Sri Lanka, Cuba, Puerto Rico, USA (Hawaii and Florida), Iran, Iraq, Pakistan, China, Malaysia, Bhutan, Thailand, Vietnam, Philippines, Trinidad, Panama and Japan. Due to its hardy nature, suitability to various waste lands, high productivity, nutritive as well as therapeutic value, the commercial importance of Amla is increasing with every passing year.

2. Superfoods
Superfoods comprise a specific set of edible, incredibly nutritious plants that function as both food and medicine. They are a class of the concentrated and nutrient-rich foods having the ability of improving overall health, boosting the immune system, elevating serotonin production, cleansing as well as detoxifying the body. These have the ability of satisfying the nutritional requirements of the human body including proteins, vitamins, minerals, glyconutrients and essential fatty acids. Superfoods are a major focal point of nutrition because not only do they help in nourishment but also correct imbalances and help us towards a more natural and aboriginal diet. Additionally, superfoods also facilitate detoxification. Since superfoods are natural, they provide an abundance of synergistic elements in their natural state that work together in the human body. They can be grown organically and comprise valuable sources of clean, hormone-free, pesticide-free, and chemical-free substances.
Phyllanthus emblica is a wonder superfood, packed with high amounts of nutritional and therapeutic properties. Earlier studies have potentiated its role in balancing female hormonal levels; primarily estrogen and curbing sugar cravings. They have proven to be beneficial to those suffering from improper digestion such as hormone-related Inflammatory Bowel Syndrome and constipation. The fruit has also been shown to suppress cough, fever, pain and stress and provide protection to liver, kidneys and nerves [4]. Amla is a medium sized plant having a crooked trunk and spreading branches. The fruit is spherical, pale yellow with six vertical furrows. The plant has a grey bark, reddish wood and feathery oblong leaves. Amla is well known for its nutritional qualities. It is rich in polyphenols, minerals and is regarded as one of the richest source of vitamin C. Significant quantities of essential minerals like sodium, magnesium, calcium, potassium, iron, phosphorous, chromium, lead, cobalt, nickel, copper and cadmium are also present. Amla is an astringent, anti-diarrheal, anti-dysenteric, anti-scorbutic, carminative and a stomachic possessing no adverse side effects. The genus is the largest in the family Phyllanthaceae, with more than 750 species throughout the world. The botanical classification of the plant is given in table 1.

3. Chemical Composition

Amla is one of the most extensively studied plants. Previous studies have documented it to contain biologically important compounds such as tannins, alkaloids, phenolic compounds and flavonoids [4, 5]. The presence of tannins in the fruit may easily explain some of the proclaimed benefits of Amla, including treatment of respiratory and intestinal disorders, particularly intestinal ulcerations. Furthermore, Amla is also a rich source of various essential amino acids, carbohydrates (pectin), vitamins and citric acid [6]. Amla is well known for its nutritional qualities. It is rich in polyphenols, minerals and is regarded as one of the richest source of vitamin C. The nutritional and chemical constituents of the above together qualify it as a popular superfood [7]. The nutritional and chemical composition of *Phyllanthus emblica* is tabulated in Table 2.

4. Anti-ulcer effects

Ulcer is indicated by the manifestation of a sore in the inner lining of the alimentary canal predominantly in the stomach, oesophagus or small intestine. Under normal circumstances, the mucosal barrier of the gastrointestinal tract along with glycoproteins, cell proliferation, prostaglandins, bicarbonate ions & antioxidant enzymes offer protection against ulcer causing agents such as gastric acids, Reactive Oxygen Species (ROS), drugs and biological agents. These hostile factors are carefully prevented from exerting their action by adequate levels of protective barriers and determinants under conditions of homeostasis. The development of ulcer occurs due an imbalance between the hostile and protective factors under conditions of pathological or environmental stres [8]. Interestingly, *Phyllanthus emblica* has been attributed to ulcer prevention and treatment [9]. The Amla plant especially the fruit has been used to treat an array of ailments such as common cold, fever, gastrointestinal disorders, liver diseases, inflammation and most importantly ulcer. Amla extracts have indeed been documented to increase protective factors including mucus secretion while decreasing gastric Hydrochloric acid and pepsin release [10].

Oxidative insult is one of the major ulcer promoting factors. The Amla fruit possesses potent anti-oxidant action. The most important source of the key natural antioxidant, Vitamin C, is the fruit of *Phyllanthus emblica*. Adequate intake of Vitamin C has been shown to improve prognosis in a number of chronic diseases including cancer. Moreover, previous reports have documented the ability of Vitamin C to prevent asthma attacks, broncho-spasms, wheezing, respiratory infections, nasal congestion and most importantly ulcer by inhibiting the release of histamine. Ulcerative damage mediates release of proteins and carbohydrates including collagen from the luminal barrier. However, intake of Amla extracts has been shown to promote cytoprotection thereby reducing the release of the above [11]. Free radicals including ROS and lipid oxides and peroxides have been shown to contribute to the etiology of ulcer [12]. It has been observed that hydrolysable tannins, Emblicanin A and B possess anti-oxidant efficacy. These tannins have displayed anti-ulcer actions both *in vitro* and *in vivo*. The mechanism behind this antioxidant activity is due to the recycling of sugar reductone moiety and conversion of the polyphenol into medium and high molecular weight tannins. Furthermore, Amla extracts have also been observed to alter the levels of lipid peroxidation and anti-oxidant enzymes [13]. The phenolic fraction of the fruit has been documented to achieve anti-oxidant dependent would healing activity both *in vitro* and *in vivo* [14, 15, 16]. Moreover, butanolic fraction of Amla has been shown to reduce Malondialdehyde (MDA), a product of lipid peroxidation and superoxide radical [15]. Additionally, histopathological studies have shown that oral intake of Indian Gooseberry reduces gastric lesions and mucosal injury *in vivo*. Previous reports have also shown the fruit extract to decrease Myeloperoxidase (MPO) activity which is generally considered as a potent ulcerogenic marker [17]. Pepticare, a herbal formulation containing extracts of *Phyllanthus emblica* has proven its anti-oxidant mediated anti-ulcer effects in mammalian models [18]. Pepticare has been shown to induce an upregulation of Superoxide Dismutase (SOD), Catalase and reduced Glutathione accompanied by an increase in gastric pH [16, 19]. The anti-oxidant actions of the above have also been shown to decrease ulcer promoting factors and increase the protective factors [10]. Another formulation Kalpaamruthaa, consisting of *Semecarpus anacardium* nut milk extract, dried powder of *Phyllanthus emblica* fruit and honey has also demonstrated ulcer protective effects [20]. Moreover, quercetin and flavonoids present in Amla juice have also shown to heal ulcer lesions in rat models [21]. The immunomodulatory potential of the fruit also helps to achieve ulcer protection [22]. Inflammatory pathways plays a major role in development of several diseases including ulcer [23]. *Phyllanthus emblica* has proven its efficacy in increasing the concentration of anti-inflammatory cytokines compared to pro-inflammatory cytokines thereby aiding in ulcer therapy. Additionally, Extracts of the Indian gooseberry possess anti-*Helicobacter pylori* potential [24, 25]. H *pylori* is one of the most important biological agents of gastric ulcer. Hence, anti-*H. pylori* coupled with antioxidant and anti-inflammatory activity of Amla extracts together potentiates ulcer healing effects.

Downregulation of prostaglandin (PG) synthesis along with damage to the mucosal lining is responsible for both acute and chronic ulcers. Physiological and psychological stress factors in addition to pyloric ligation lead to an increased production of gastric acid and pepsin; all of which result in auto digestion of gastric mucus membrane and mucosal necrosis. The alcoholic extracts of Indian gooseberry have been shown to upregulate prostaglandin synthesis and restore the mucosal barrier. An increase in mucosal glycoproteins also strengthens the barrier. This enhancement has been attributed to an increase in mucopolysaccharides which are responsible for the gelatinous mucus. PGs promote angiogenesis which further facilitates ulcer healing. Angiogenesis is mediated by altering the balance of pro and anti-angiogenic factors towards the former.[26] Neo-angiogenesis accompanied by cell proliferation ensures repair of the ulcerated tissue. The PG dependent increase in pro-angiogenic factors along with increased mucus and bicarbonate secretion together contribute to anti-ulcer effects. Regulation of Nitric Oxide Synthase (NOS) activity has also been correlated to ulcer alleviation via angiogenesis. Low levels of Nitric Oxide (NO) are maintained by eNOS.[17] The extract of *Phyllanthus emblica* has been documented to attenuate ulcer lesions by upregulating eNOS and downregulating iNOS mediated expression of NO. Gallic acid

enriched Amla extract has been demonstrated to exhibit ulcer healing effects via cyclooxygenease dependent increase in PG E2, proangiogenesis factors and endothelial NOS.[27] Additionally, gallic acid fractions has also been demonstrated to increase the level of expression of other pro-angiogenic factors including Vascular Endothelial Growth Factor (VEGF) and Hepatocyte Growth Factor (HGF) thereby aiding in ulcer repair. The balance between the synthesis and secretion of pro-inflammatory and anti-inflammatory cytokines plays an important role in ulcer healing. Therefore, regulation of synthesis and secretion of prostaglandins and inflammatory cytokines coupled with anti-oxidant activity and anti-microbial action is jointly responsible for the ulcer protective effects of the Amla fruit.

The Indian Gooseberry therefore employs a number of strategies to bring about anti-ulcer effects. The extracts of the above have been shown to upregulate ulcer protective pathways and factors including an increase in anti-oxidant enzymes, angiogenesis, gastric pH, anti-inflammatory cytokines as well as mucus and glycoprotein dependent cytoprotection. Amla also decreases offensive ulcer factors including pro-inflammatory cytokines, pepsin release, *H pylori* activity and free radicals. The combined effects of *Phyllanthus emblica* towards ulcer protection and healing has been summarized in Figure 1.

5. Conclusion

Amla is a useful medicinal plant used to treat a wide range of diseases. The importance of the plant in prevention and treatment of ulcer is noteworthy. The extracts of *Phyllanthus emblica* have proven its efficacy as an anti-ulcer agent both *in vitro* and *in vivo*. Ulcer manifests itself due to an imbalance between the hostile and protective ulcer causing agents towards the former. The hydrolysable tannins, phenolic compounds and flavonoids present in the above have been correlated with decreasing inflammatory cytokines, free radicals and *H. pylori* activity; all of which are important contributors of gastrointestinal ulcers. Furthermore, the Indian Gooseberry has been shown to upregulate antioxidant enzymes. The fruit extracts have also demonstrated their efficacy in increasing prostaglandin dependent angiogenesis mediated repair of ulcer lesions. Being a natural agent, Amla represents an attractive tool to treat several chronic diseases especially ulcer. The fruit extracts may be used to upgrade commercially available anti-ulcer drugs to provide improved protection and relief.

6. Tables and Figures

Table 1: Botanical classification of the Indian Gooseberry

Kingdom	Plantae
Sub-Kingdom	Viridiplantae
Infra Kingdom	Streptophyta
Super Division	Embryophyta
Division	Tracheophyta
Sub Division	Spermatophytina
Class	Magnoliopsida
Super Order	Rosanae
Order	Malpighiales
Family	Phyllanthaceae
Genus	*Phyllanthus*
Species	*Emblica*

Table 2: Nutritional and chemical composition of *Phyllanthus emblica*

Nutritional constituents		Chemical constituents	
Component	**Percentage**	**Type**	**Chemical constituents**
Carbohydrate	14.1 %	Hydrolysable Tannins	Emblicanin A and B Punigluconin Pedunculagin Ellagitannin) Benzopyran tannin Dehydroellagitannin) Ellagotannin
Protein	0.5 %	Alkaloids	Phyllantine Phyllembein Phyllantidine
Fat	0.1 %	Phenolic compounds	Gallic acid Ellagic acid Trigallayl glucose
Fibre	3.4 %	Amino acids	Glutamic acid Proline Aspartic acid Alanine Cystine Lysine
Calcium	0.05 %	Flavonoids	Quercetin Kaempferol
Phosphorus	0.02 %	Organic acids	Citric acid
Iron	1.2mg/100 gm		
Nicotinic acid	0.2mg/100 gm		
Ascorbic acid	600mg/100 g		
Thiamine	30mg/100 gm		

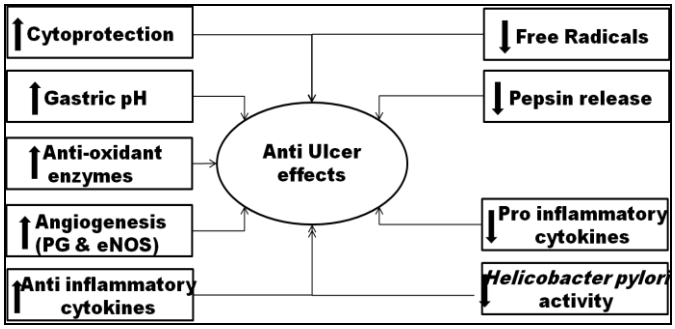

Fig 1: Effects of *Phyllanthus emblica* towards ulcer protection and healing

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