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HPLC based Phytochemicals Analysis of *Phyllanthus emblica* (Indian Gooseberry/Amla): A mini Review

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ABSTRACT

High-Pressure Liquid Chromatography (HPLC) is an analytical tool extensively used for the scientific analysis of components in a mixture. Several reports attribute its high analytical potential to bioactive components from different medicinal plants. Hepatic disorders, which have been a major threat to public health for decades, affect cells, tissues, structure, or liver function. The damage caused by this can be triggered by biological causes, autoimmune diseases, excessive alcohol consumption, or the action of different compounds, for instance, few medicines. *Phyllanthus emblica* Linn. is a therapeutic plant that has been used to treat liver disorders in Asia for many decades now. It is mentioned in the Ayurvedic scriptures for its medicinal value. This review focuses on the intricacies of HPLC-based extraction and analysis of medicinally important phytochemicals, notably for hepatic disorders from the *P. emblica* plant. This will be useful for future phytochemical analysts working with medicinal plants.

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1 Introduction

Herbal products have long been used for medicinal purposes in the Asian subcontinent and their growing demand throughout the globe (Siddiqui 1993). The therapeutic benefits of plants are attributable to their less harmful nature, as well as the fact that they are inexpensive and effective (Payyappallimana 2009). Many medicinal or nutritional plants, as well as their compounds, are capable of delaying disease progression at various stages (Surh 2002). *Phyllanthus emblica* (Amla) is a prominent element in several herbal formulations, including patented pharmaceuticals (Gantait et al. 2021). It is a high-value plant in ancient systems of treatment. Fruits of Amla have generally been broadly investigated for their secondary metabolites, natural ingredients, and remedial use, and found to have a wide range of remedies like antidiabetic, antioxidative, hepatoprotective, immuno-modulatory, and other activities (Khan 2009; Kumar et al. 2012; Singh et al. 2015). To determine various physicochemical features of natural products, a number of analytical tools are applied. High Pressure Liquid Chromatography (HPLC) is an analytical technique that is used for the partition, purification, and quantitative analysis of components in a mixture. Several reports attribute its high value to the separation and purification of bioactive components from different parts of the *P. emblica* plant. Therefore, we have done a thorough review of the detection, separation, and purification of different phytochemicals from *P. emblica* having hepatoprotective activities.

2 HPLC based detection of medicinally important phytochemicals from amla plant

The constituents of distinct *Phyllanthus* species may be easily characterized by using HPLC with Mass Spectroscopy (MS), which is a potent analytical method. According to the time of retention (RT) and UV data, the majority of qualitative and quantitative assessments of phenolics in *Phyllanthus* species are reported by High Pressure Liquid Chromatography or High Performance Thin Layer Chromatography (Tripathi et al. 2006; Dhalwal et al. 2006; Dey et al. 2016). For the first time in the *Phyllanthus* species, thorough and original investigations of phenolics revealed the presence of nearly 10 different compounds derived from phenol, including Gallic acid (GA), five Gallic acid derivatives, Ellagic acid (EA), and three Ellagic acid derivatives as shown in Figure 1 (Rose et al. 2018). Using several separating solvents (both non-polar and polar), a recent prospective study

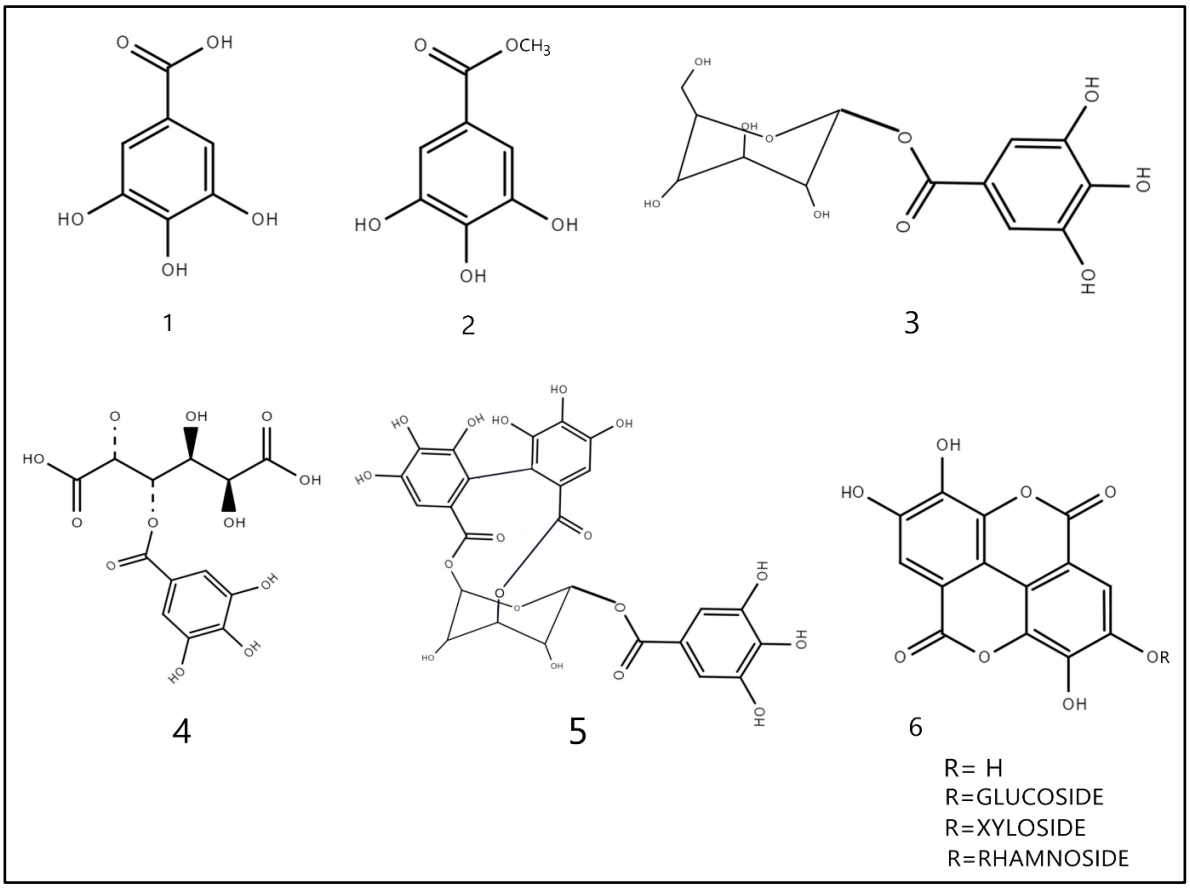

Figure 1 Structures of five GA derivatives (1-5), ellagic acid (6), and three ellagic acid derivatives obtained from Amla (Haddock et al. 1982; Shu et al. 2010; Yang et al. 2012; Rose et al. 2018)

revealed the presence of numerous phenols, flavonoids, and a plethora of other phytochemicals in dried fruits of Amla. The ethanolic extract of *P. emblica* fruits was screened for phytochemicals using conventional techniques. The presence of different primary metabolites like proteins, carbohydrates and many more secondary metabolites were discovered in the ethyl alcoholic extract of *P. emblica* fruits.

The whole phenolic and GA content of amla fruit, seed cover, and seed were measured using HPLC by Mishra and Mahanta (2014). With the comparison according to the standard, GA is found to be the major product among other phenolics in all of the 3 samples investigated; this conclusion accorded with Kumar et al. (2012), who stated that tannic acids and GAs are the crucial phenolics in Amla. Different polyphenols and other beneficial substances are observed in the fruit of *P. emblica* (Habib-ur-Rehman et al. 2007). The tannins emblicanin A, emblicanin B, phyllaemblicin B, pedunculagin, and punigluconin are also found in *P. emblica* fruit extract (Kapoor 2000). According to Liu et al. (2008) phytochemicals isolated from *P. emblica* fruit powder in methanolic extractions have various antioxidant properties.

Recently, β-sitosterol and Quercetin were discovered in alcoholic extracts of *P. emblica* leaves by Gupta et al. (2014). Balasubramanian (2014) found five main phytoconstituents in the methyl alcoholic extract of amla leaves, including Pyrogallol, 5-methyl-2-furylmethyl ketone, benzene carboxylic acid, and GA, Embrirol A, and B, two novel chalconoid analogs with the chemical formula $C_{19}H_{24}O_6$ were recently isolated from the lower parts of Gooseberry tree (Yan et al. 2017). It contains several important flavonoids as well as GA. Ellagi Tannins have a variety of functions and are found in many herbal medications (Krishnaveni and Mirunalini 2010; Variya et al. 2016). Besides, many other investigations have shown its importance in the mammalian body, particularly in liver detoxification and hepatotoxicity (Anilakumar et al. 2007; Reddy et al. 2009a) and lipid metabolism (Balusamy et al. 2020; Akhtar et al. 2011). Yugarani et al. (1993) and Kaleem et al. (2014) used the calorimetric method to extract tannins from freshly made fruit juice in powdered form, and the presence of tannic acid was recognized and validated using the HPLC technique. Starting from mucic acid, GA, and several other compounds in the crude methanolic fruit extracts, according to the author, who also reported 144 peaks identifying other compounds (Pramyothin et al. 2006; Khan 2009; Sharma et al. 2009). Preclinical investigations have demonstrated that amla extract and the phytochemicals ellagic acid, other polyphenols along with kaempferol derivatives are efficient as hepatoprotective agents against chronic liver damage caused by ethanol, mycotoxin, arsenic, and paracetamol (Kinoshita et al. 2007; Girish et al. 2009; Gaire and Subedi 2014; Yang and Liu 2014) (Figure 2).

3 Hepatoprotective behavior of the extracted compounds

Liver diseases remain a threat to humanity even though good advances occurred in the field of assessment and management of patients (Asrani et al. 2019). Compounds isolated from *P. emblica* exhibit hepatoprotective capabilities in several ways, including reducing inflammation, eliminating reactive oxygen species (ROS), inhibiting tumour growth, and so on (Figure 3). *P. emblica* fruits include various ethnomedical extracts rich in vitamin C, which have long been used in Unani and Ayurveda medicines in addition to traditional medicine (Poltanov et al. 2009)

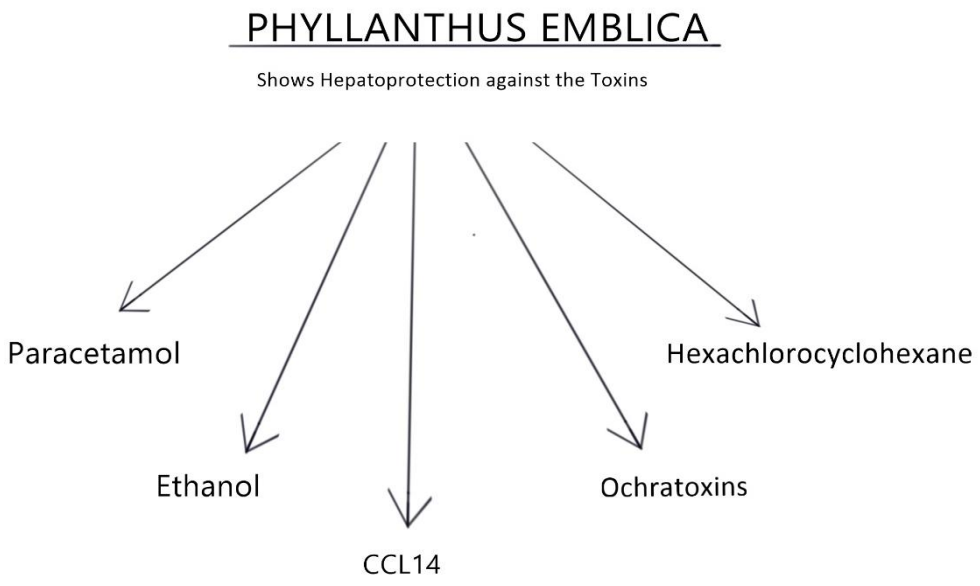

Figure 2 Hepatoprotective nature of Amla

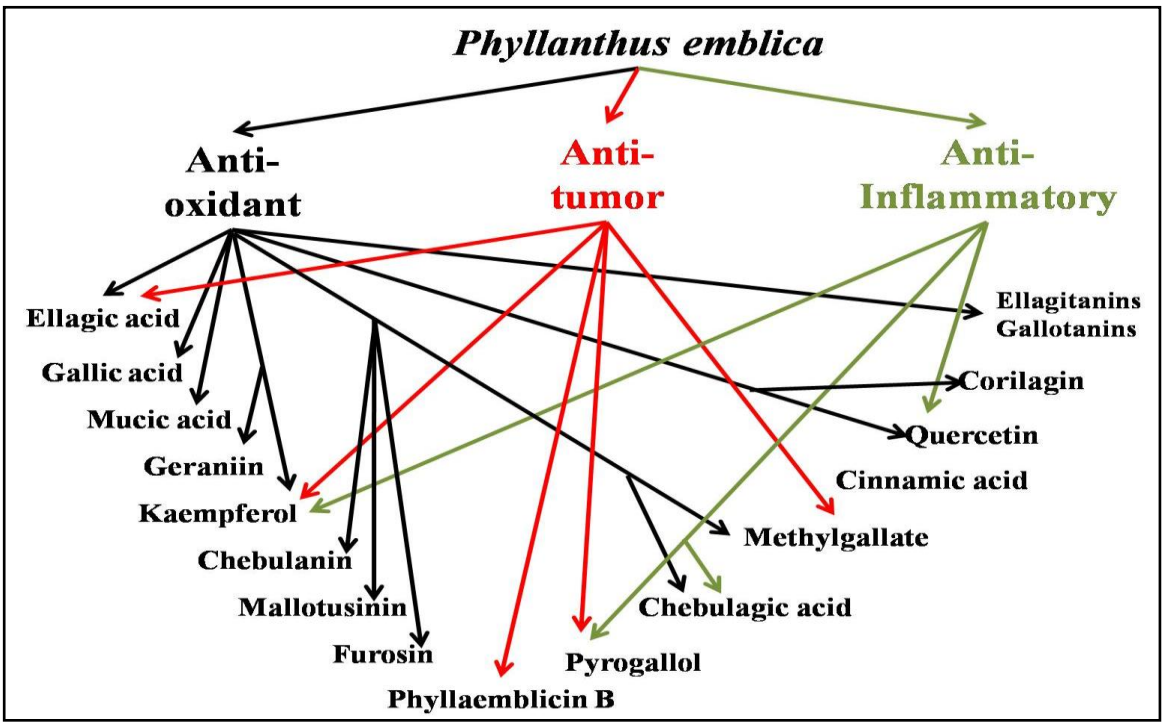

Figure 3 Pharmacological effects of isolated compounds from *P. emblica* showing hepatoprotective activities.

The fruit extracts have a mixture of different phytochemicals and compounds (Muthuraman et al. 2011; Dey et al. 2016). Phenolic extracts from gooseberry fruits are good Antiinflammatory agents when applied in combination with diclofenac (Middha et al. 2015). Butanol extract of *P. emblica's* fruit fraction also exhibits this property in indomethacin-induced gastric cancer (Zhu et al. 2013). The water and polyphenolic extracts of the fruit also showed anti-tumour effects against the ovarian and cervical cancer cells (Kang et al. 2006; Karimi et al. 2020).

Ellagic acid (EA) is a vital constitutes having antioxidant activity along with antiinflammatory responses (Singla et al. 2010). EA suppresses Hepatitis B-e antigen (HBeAg), thus plays a significant role in the reduction of hepatitis virus infection in HBV-infected as well as HBeAg transgenic mice (Fabbrini et al. 2010). EA is also effective against fatty liver disease as it decreases blood triglyceride concentration by increasing serum cholesterol HDL level (Bashar et al. 2021; Sanjay et al. 2021).

The phenolic compound Gallic acid (GA) is a well-established biochemical with therapeutic and pharmacological properties (Esmaeilzadeh et al. 2020). When GA is combined with anti-tuberculosis therapy, a better result is obtained via the reduction of liver function enzymes by maintaining homeostasis through Nrf2 activation and NFκB signalling pathway inhibition with respect to anti-tuberculosis therapy alone (Huang et al. 2021). It also has a very good antioxidant property for which administration of GA results in a significant increase in different enzymes like GSH, CAT, etc., and a remarkable decrease in protein carbonyl, Aspartate transaminase, Alkaline Phosphatase, etc. (Reyes-Farias and Carrasco-Pozo 2019).

Methyl gallate was reported to function as an anti-cell proliferator compound in both hepatocarcinoma cell lines and in the Zebrafish model (Ren et al. 2019). Flavonoid compound Quercetin showed descent pro-apoptotic activity by regulating several pathways like the PI3K / Akt / mTOR, etc. Further, Lin et al. (2011) and Yang et al. (2012) reported the antioxidant and antiinflammatory effects of Quercetin in the db/db mice model. Another flavonoid phytochemical constituent of *P. emblica* extract Kaempferol or kaempferol-3, was studied for the antiinflammatory and radical scavenging effects (Lin et al. 2011). Moreover, it has anti-tumour potential by inducing TNFα mediated tumour necrosis and increasing interleukin-1 (IL-1) by macrophage activation (Reddy et al. 2009b; Yang and Liu 2014).

The extraction of the different parts of the *P. emblica* containing ellagitannins and gallotannins (Reddy et al. 2009b) showed antioxidant effects in mice models (Zhang et al. 2001; Reddy et al. 2010a, b; Koo et al. 2016). Further, Zhang et al. (2001) reported significant radical scavenging activity of mucic acid and its derivatives like mucic acid 2-O-gallate and other lactone compounds, etc. The study by Lee et al. (2007) mentioned that chebulic acid inhibits hepatic fibrosis by regulating the Nrf2 pathway along with oxidative stress mitigation (Kanter 2010).

Conclusion and Future Prospects

The phytochemical Quercetin, which can be found in Amla, has been shown to help prevent liver injury caused by biliary hindrance. Healing with Quercetin before general bile duct constriction reduced changes in liver histology in rats, implying that it protects against liver damage, bile duct increase, and thickening or scarring of the tissue. Amla has been found to protect the liver from a number of toxins, including ethyl alcohol, analgesics, carbon tetra chloride, heavy metals, antitubercular medicines, and many more.

Amla treatment has been proven to reduce hyperlipidemia, metabolic syndrome, liver carcinogenesis, and liver toxicity caused by iron overload. In *P. emblica*, Quercetin, GA, corilagin, and ellagic acid were found to have liver protective effects against known analgesics, microcystins, galactosamine, and lipopolysaccharide toxicity. *P. emblica's* antioxidant, antiinflammatory, and hypolipidemic properties, as well as modulation of detoxifying enzymes, appear to have hepatoprotective properties. In light of these findings, it is reasonable to conclude that Amla needs further research, particularly in the high-risk category. The antioxidant capabilities of *P. emblica* are particularly important because oxidative changes of LDL cholesterol cause the hardening of arteries. More study, particularly on the effects of long-term use patterns, is required. With a growing interest in NSAIDs as a treatment for chronic swelling, research on the use of foodstuff extracts such as *P. emblica* is gaining attraction. In the future, additional scientific evidence depicting the advantages of *P. emblica* in overall health preservation and disease prevention should become available.

Conflict of Interest

There is no conflict of interest.

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