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Mini Review

A Brief Dig into the Potent Medicinal Plant *Phyllanthus Amarus* Schum. and Thonn.

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Abstract

Phyllanthus amarus Schum. and Thonn., a plant of substantial medicinal significance, is known for its usage in the 'Ayurvedic' system of medicine for over 2000 years. This herb grows throughout the world including India. *P. amarus* along with other species of its genus has been a vital part of several herbal formulations available in the Indian market under the trade name Bhuiamlaki. Several pharmacognostic evaluations over the years established the genus *Phyllanthus* of great commercial value. Ethnopharmacological studies conducted with *P. amarus* to date have shown its diverse therapeutic usage globally. This owes to the vast array of secondary metabolites present in the herb, substantially in the leaf tissue. Different analytical and phytochemistry studies performed across the globe revealed that *P. amarus* is a hub of various classes of secondary metabolites viz. lignans like phyllanthin, hypophyllanthin, flavonoids, alkaloids, triterpenes, sterols, volatile oil, ellagitannins including simple and complex tannins, etc. Different analytical techniques have been employed over the past years for isolating and studying these varied secondary metabolites. Further, bioactivities and pharmacological properties of *P. amarus* that were mainly due to the presence of these wide arrays of secondary metabolites have also been explored extensively across the globe by several research groups. This plant has also been explored at molecular and transcriptome level, although relatively lesser but its extensive molecular and transcriptome analysis have only been performed from our lab. Thus, *P. amarus* has considerable potential to be explored in the future as a significant therapeutic source not only in the traditional medicinal system but also in the modern pharmaceutical industry.

Introduction

The domain of medicinal plants and their applications in alternative medicines continue to rule an important part of the scientific community. One such plant used over decades as an important source of medicinal value is *Phyllanthus amarus* Schum. and Thonn., which is an annual glabrous herb, and belongs to the Phyllanthaceae family. The plant has different nomenclatures in the Unani and Ayurvedic literature like 'Bhuti' and 'Bhoomyaamalakee' respectively. In India, this plant is also known by several common names in different languages all of which define its interpretation of its close resemblance to amla. The Spanish name "chanca piedra" or Brazilian name 'quebra pedra' which translates to stonebreaker owes to one of its important bioactivities of eliminating gall and kidney stones. Multidisciplinary research has been carried out over the past several decades for its substantial medicinal efficacy (Figure 1). Extensive research on *P. amarus* revealed that some of the major bioactivities of the herb included hepatoprotection and anti-Hepatitis B properties [1-4], antioxidant [5-8], antidiabetic/hypoglycaemic [9,10], anti-microbial [11,12], anti-inflammatory and antinociceptive properties [13-17], anti-HIV [18-20], as well as antigenotoxic, antimutagenic and anticancer potentials [21-24]. This therapeutically beneficial

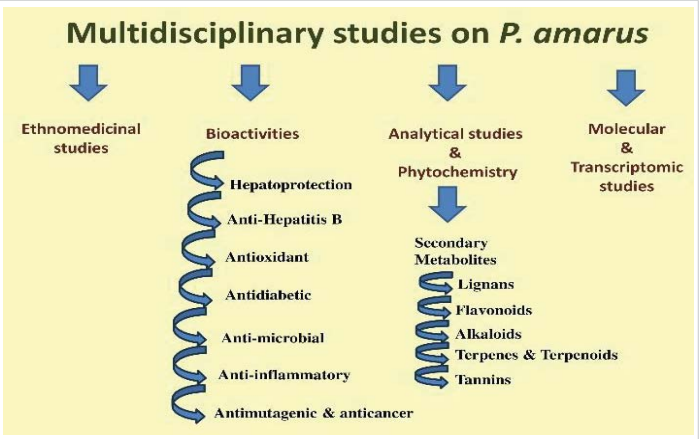

Figure 1: Multidisciplinary research on *P. amarus* for exploring its medicinal efficacy.

plant has also been studied for its role in COVID-19 after the incidence of the massive pandemic [25-27]. Ethnomedicinal studies with *P. amarus* extracts over the years have shown its usage in diverse diseases not only in different parts of India among different tribes [28,29] but across several regions of the world [30-32].

The diverse medicinal activities of this herb are attributed mainly to the wide varieties of secondary metabolites present in *P. amarus* in different plant parts and substantially in the leaf tissues. The main classes of secondary metabolites that have been reported and studied extensively over the past decades have thoroughly imputed the therapeutic potential of this significant herb.

Secondary metabolite categories reported in *P. amarus*

A brief overview of these important phytochemicals that are mainly responsible for the medicinal significance of *P. amarus* is as follows:

Lignans form one important class of secondary metabolites in *P. amarus* and some of the major lignans of this plant include phyllanthin, hypophyllanthin besides niranthin, phyltetralin, nirtetralin, isonirtetralin, hinokinin, lintetralin, etc. [33-35]. This class of compounds is mainly responsible for some significant therapeutic potentials of the plant which include hepatoprotection, antioxidant, antitumor, antimitotic, as well as antiviral properties.

Flavonoids, the second type of secondary metabolites found in *P. amarus*, are polyphenolic compounds and include categories like flavanone, flavones, flavonols, isoflavones, catechins, chalcones, as well as their derivatives. Some of the important flavonoids reported in this herb that owe to the wide arrays of bioactivity of the plant include quercetin, astragalin, kaempferol, and rutin [36,37].

Alkaloids, another category of diversified secondary metabolites reported to have several pharmacological properties, are known to impart some of the varied therapeutic properties of the plant. Securinine, dihydrosecurinine, epibubbialine, isobubbialine, 4 hydrosecurinine, allo-securine, nor-secuinine, etc. are some of the alkaloids that are known to be present in *P. amarus* that are involved in the plant's medicinal potential [38-40].

Terpenes which constitute an important plant secondary metabolite and Terpenoids, frequently referred to as 'modified terpenes', both contribute not only to various plant metabolic functions but also exhibit potentials related to medicinal activities as well. This class of secondary metabolites viz. Lupeol, phyllanthenol, phyllanthenone, phyllantheol, Oleanolic acid, ursolic acid, etc. have been reported in *P. amarus*, contributing to its bioactivities [41].

Ellagitannins and Tannin precursors like gallic acid, ellagic acid, and gallocatechin, are some of the other reported secondary metabolites that are known to play a role in the herb's phytotherapeutic attributes [42,43].

Secondary metabolites isolation studies in *P. amarus*

Several analytical techniques have been employed over the past years by different groups of researchers across the globe to isolate and study the different classes of secondary metabolites present in the herb.

Isolation and study of an alkaloid ent-norsecurinine from *P. amarus* have been performed almost three decades back by X-ray analysis [44]. Simultaneous quantitation of major lignans like phyllanthin, hypophyllanthin along with other secondary metabolites have been performed by High-Performance Liquid Chromatography (HPLC) densitometric method [45]. Further, research continued using coupling of analytical techniques like HPLC, liquid chromatography coupled to mass spectrometry (LC–MS) and gas chromatography coupled to mass spectrometry (GC–MS) for analyzing the different categories of isolated secondary metabolites from *P. amarus* [46,47]. NMR was also another analytical technique that has been employed in different studies for the characterization of the bioactive molecules of this medicinal plant [48,49]. Besides, some other approaches viz. UPLC-QTOF-MSE-based chemometric approach, HPLC-ESI-QTOF-MS/MS, UHPLC–MS/MS have also been used in recent years for extraction, qualitative and quantitative assessment, as well as elucidation of the diverse therapeutic important secondary metabolites found in *P. amarus* [50-52].

Conclusion

P. amarus is thus a hub of myriad significant secondary metabolites that confer the several therapeutic properties of the plant. An in-depth insight into this medicinally significant herb has been recently reported by us [53]. Further, *P. amarus* can be explored at the molecular level. Few works from our laboratory have already been reported [54-57], but further in-depth investigations can lead to the development of a much more robust application of the herb at industrial levels as well, which will ultimately aid in positively exploiting the plant's diverse therapeutic adequacy.

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