

## Review Article

# An Overview of Important Ethnomedicinal Herbs of *Phyllanthus* Species: Present Status and Future Prospects

Bharti Sarin,<sup>1</sup> Nidhi Verma,<sup>2</sup> Juan Pedro Martín,<sup>3</sup> and Aparajita Mohanty<sup>1</sup>

<sup>1</sup> Department of Botany, Gargi College, University of Delhi, Siri Fort Road, New Delhi 110049, India

<sup>2</sup> National Bureau of Plant Genetic Resources, IARI Campus, New Delhi 110012, India

<sup>3</sup> Departamento de Biología Vegetal, Escuela Técnica Superior de Ingenieros Agrónomos, Universidad Politécnica de Madrid, Ciudad Universitaria s/n, 28040 Madrid, Spain

Correspondence should be addressed to Aparajita Mohanty; [aparajita.gargi@gmail.com](mailto:aparajita.gargi@gmail.com)

Received 29 August 2013; Accepted 30 October 2013; Published 3 February 2014

Academic Editors: R. Aroca, W. L. Morris, and S. Sakr

Copyright © 2014 Bharti Sarin et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The genus *Phyllanthus* consists of more than 1000 species, of which many are used as traditional medicines. The plant extracts have been used since ancient times, for treating hypertension, diabetes, hepatic, urinary, and sexual disorders, and other common ailments. Modern day scientific investigations have now confirmed pharmacognostic properties of *Phyllanthus* herbs. The phytochemicals attributing these medicinal properties have been identified in many of the *Phyllanthus* herbs. The morphologically similar herbs of *Phyllanthus* grow together and admixture of species during collection for manufacture of herbal medicines is quite common. Hence, along with pharmacognostic and phytochemical studies, appropriate protocols for correct identification of species are also important. As the use of these herbs as green medicines is becoming more popular, it is imperative to assess its genetic diversity and phylogenetic relatedness for future conservation strategies. This review is an attempt to present an overview of the existing studies on pharmacognostics, phytochemistry, species identification, and genetic diversity of *Phyllanthus* herbs and consequently (i) highlight areas where further research is needed and (ii) draw attention towards extending similar studies in underutilized but potentially important herbs such as *P. maderaspatensis*, *P. kozhikodanus*, *P. rheedii*, *P. scabrifolius*, and *P. rotundifolius*.

## 1. Introduction

The genus *Phyllanthus* (Phyllanthaceae) consists of approximately 1000 species, spread over the American, African, Australian, and Asian continents [1, 2]. All three major habits, that is, trees, shrubs, and herbs, are seen amongst the *Phyllanthus* species. Most of the herbs belonging to genus *Phyllanthus* have been shown to contain different combinations of secondary metabolites which render them with medicinal properties. The major class of bioactive compounds like alkaloids, flavonoids, lignans, phenols, tannins, and terpenes has been isolated from these herbs [3, 4].

Of a number of *Phyllanthus* herbs that are used all over the world as traditional herbal remedies, 12 important herbaceous species are discussed here. The species included are *P. ajmerianus* Rao and Choudhary, *P. amarus* Schum and

Thonn, *P. debilis* Klein ex Wild, *P. fraternus* Webster, *P. kozhikodanus* Sivadasan and Manilal, *P. maderaspatensis* L., *P. rheedii* Wight, *P. rotundifolius* Klein ex Wild, *P. scabrifolius* Hook.f., *P. tenellus* Roxb, *P. urinaria* L., and *P. virgatus* G Forst. Of these 12 species, *P. ajmerianus* is reported only from India [5]. All of these herbs, except *P. ajmerianus*, *P. rotundifolius*, and *P. scabrifolius*, have been scientifically investigated and proven to be of pharmacological value. The ethnic tribes of India and other Asian countries have used the herbs of *Phyllanthus* species since ancient times, as traditional home remedies. The decoctions of various parts of the herbs are used for treating hepatic, urinary, and sexually transmitted diseases, diabetes, hypertension, cancer, and wounds. Taking cue from the ethnic medications and potential of herbal treatments, the modern society is now eager to resort to green medicines which are without adverse side effects. Many of the *Phyllanthus* herbs form an integral

part of Ayurveda, an Indian system of medicine. Considering the importance and potential of these herbs, it is natural that most of the studies are directed towards the phytochemical analysis and pharmacognosics (references detailed in Tables 1 and 2). However, for appropriate utilization of the herbs for ethnopharmacological investigations and preparation of herbal medicines, the correct identification of *Phyllanthus* species is very important. Also, with the growing utilization of these herbs in pharmaceutical industries, the risk of loss of genetic diversity exists. There are comparatively a lesser number of reports focusing on molecular taxonomy for identification of species and interspecific/intraspecific genetic diversity studies.

Keeping this present scenario in view, 12 important *Phyllanthus* herbs (*P. ajmerianus*, *P. amarus*, *P. debilis*, *P. fraternus*, *P. kozhikodanus*, *P. maderaspatensis*, *P. rheedii*, *P. rotundifolius*, *P. scabrifolius*, *P. tenellus*, *P. urinaria*, and *P. virgatus*) are reviewed with the following objectives: (i) to assess and hence direct efforts towards further studies on phytochemistry and pharmacognosics of the important herbs, (ii) to focus on the need to initiate studies of underresearched but potentially important medicinal herbs, and (iii) to assess the existing studies on identification of species, genetic diversity, and phylogeny, which will have an impact on formulating conservation strategies in future. The detailed assessment of clinical studies pertaining to the *Phyllanthus* herbs has not been elaborated in the present review.

## 2. Pharmacognosy of *Phyllanthus* Herbs

Of the 12 *Phyllanthus* herb species, nine species (*P. amarus*, *P. debilis*, *P. fraternus*, *P. kozhikodanus*, *P. maderaspatensis*, *P. rheedii*, *P. tenellus*, *P. urinaria*, and *P. virgatus*) have been scientifically analyzed whereas the remaining three species (*P. ajmerianus*, *P. rotundifolius*, and *P. scabrifolius*) have not been investigated for their medicinal properties. The pharmacognosics of each of the nine herbs is discussed here.

**2.1. *P. amarus*.** This herb finds its use worldwide for treating problems of stomach, genitourinary system, liver, kidney, and spleen. It plays an important role in Ayurveda, an Indian system of medicine, and is used to treat jaundice, gastropathy, diarrhoea, dysentery, fevers, menorrhagia, scabies, genital infections, ulcers, and wounds [62]. Decoctions of whole plants are used for treating migraine, jaundice [63–65], gonorrhoea and syphilis, skin disease, and malaria [66, 67]. Paste of leaves or its decoction [68–72] and juice of roots [73] are used for treating jaundice. Chronic dysentery, menstrual problems, anorexia, urinary tract infection, and diabetes are also treated by leaf extract taken orally [65, 69, 72, 74]. Extracts of the plant can prevent mutation of cells in the presence of chemical agents [75].

**2.2. *P. debilis*.** This herb shows antihepatotoxic [25] and anti-inflammatory [76] properties. Leaf juice is taken orally by the Kamar, Gond, and Halba tribes of Chattisgarh in India, for relief of problems related to sickle-cell anemia [77]. The aqueous extract of the plant shows antihyperglycemic

property [78]. *P. debilis* has been shown to possess maximum antioxidant activity compared to *P. amarus*, *P. maderaspatensis*, *P. urinaria*, and *P. virgatus* [79].

**2.3. *P. fraternus*.** Traditionally, in India, the herb was used as a mild laxative, to expel worms and intestinal gas. The plant extracts are used for treating many types of biliary and urinary conditions like gall bladder, kidney stones, and bacterial infections such as cystitis, prostatitis, viral infections, hepatitis, flu, tuberculosis, liver diseases, anemia, venereal diseases, and urinary tract infections [80]. The antimicrobial property of *P. fraternus* has been reported by Chanda et al. [81]. The aqueous extract of the plant shows antioxidant property [82] and has protective effect against bromobenzene induced mitochondrial dysfunction [83]. Also the extract can reduce toxicity of drugs such as cisplatin and cyclophosphamide and therefore can be used to raise the therapeutic potential of anticancer drugs [84]. Ethanolic extract of the herb has antioxidant and anticoagulant property in experimental models [85]. According to Hukeri et al. [86], the flavonoids present in the herb show hypoglycemic effect in rats.

**2.4. *P. kozhikodanus*.** This herb provides protection to liver against chemical induced liver damage [87]. The herb was screened for hepatoprotective activity against liver damage induced by paracetamol in rats. Histological examination of liver confirmed hepatoprotective and antihepatotoxic properties [88].

**2.5. *P. maderaspatensis*.** Ethanolic extract of this herb demonstrated chemoprotective effect in modulating cisplatin-induced nephrotoxicity and genotoxicity, thus proving its antioxidative property [89]. This extract is also taken as a popular dietary supplement in the southern part of India. It has been experimented as an ameliorative for adriamycin-induced toxicity and oxidative stress in mice [90]. Whole plant extracts have shown antihepatotoxic, hepatoprotective, and choleric activities [88, 91].

**2.6. *P. rheedii*.** The Muthuvan tribe of Kerala use all parts of this herb as a cure for liver diseases. The plant also shows hepatoprotective, antihyperglycemic, antihyperlipidemic, and antioxidant effects [92, 93].

**2.7. *P. tenellus*.** Extracts of fresh and dried plants have antiviral and antimicrobial activity [94, 95]. The callus extracts of this herb have potential analgesic properties against neurogenic and inflammatory pain [96]. Although this herb is beneficial for diabetes and treatment of hepatitis, urolithiasis, and bowel diseases, it induces depression, spasms, increased respiratory rate, and dyspepsia, as shown from experiments on mice [97].

**2.8. *P. urinaria*.** This herb has multiple uses with many pharmacognostic properties. Aqueous/methanolic extract of whole plant is used for treating cancer [98–100]. The ethanolic extract of this herb has anti-inflammatory and antioxidant activity [31]. The acetone extract of the plant has been found

to inhibit herpes simplex virus infection [55, 101]. The plant parts have been successfully used in treating hypertension, jaundice, and diabetes [102]. Chloroform and methanolic extract have shown antibacterial activity against *Helicobacter pylori*, which causes peptic ulcers and gastric cancers [103]. Since *H. pylori* shows resistance to most antibiotics, this herb may be seriously studied for preparation of medicines against infections caused by this bacteria.

**2.9. *P. virgatus*.** In China, the extract of this herb is fed to children suffering from malnutrition due to worm infestation. This herb is used as an antiseptic and anti-inflammatory agent by the Gond tribe of India [104]. The plant extract shows high antioxidant property [105]. The lignin virgatusin is found in the plant parts and it inhibits growth of Gram-positive bacteria [61].

*Phyllanthus* herbs with potential ethnomedicinal properties that have not been scientifically analyzed are as follows.

**2.10. *P. ajmerianus*.** This herb is found in Ajmer in India, and its identity has been confirmed by Vishwanatha et al. [5]. This plant has not been assessed for medicinal properties.

**2.11. *P. rotundifolius*.** This species has been analysed along with other *Phyllanthus* herbs for hepatoprotective property and it was found that *P. urinaria* and *P. amarus* have comparatively higher potential than *P. rotundifolius* [106]. There are no other reports on its pharmacognostic properties.

**2.12. *P. scabrifolius*.** The occurrence of this herb was reported in Karnataka, India [107]. This is an endemic species and scientific evaluation for its economic uses is yet to be done. However, local people use plant's decoction for treating chronic gonorrhoea and dysentery and as a diuretic. The paste of seeds is used on wounds. Leaf paste is used on scabies and elephantitis and roots find its use in treating jaundice.

### 3. Phytochemistry of *Phyllanthus* Herbs

The major phytochemicals which have/may have a role in rendering the herbs with medicinal properties are listed in Table 1. Out of the 12 herbs reviewed, seven species (*P. amarus*, *P. debilis*, *P. fraternus*, *P. maderaspatensis*, *P. tenellus*, *P. urinaria*, and *P. virgatus*) have been reported to contain one or more classes of compounds such as lignans, flavonoids, tannins, and alkaloids.

Nahar et al. [4] have listed the various classes of phytochemicals found in *Phyllanthus* species. Of all the *Phyllanthus* herbs, the phytochemistry of *P. amarus* is well studied [62]. It has the maximum reports of pharmaceutically important compounds isolated from aqueous or organic solvent extracts. The lignans phyllanthin, hypophyllanthin, niranthin, nirtetralin, virgatusin, and heliobupthalmin lactone are common to *P. amarus*, *P. maderaspatensis*, *P. urinaria*, and *P. virgatus* [8]. However, according to Khatoon et al. [108], phyllanthin is absent in *P. maderaspatensis*. Also, Sharma et al. [106] have reported the absence of phyllanthin and hypophyllanthin from *P. maderaspatensis* and *P. urinaria*. In

*P. fraternus*, phyllanthin is absent, according to the studies of Khatoon et al. [108], whereas Tripathi et al. [26] have reported that both phyllanthin and hypophyllanthin are present in *P. amarus* and *P. fraternus* but the concentration of these two lignans varies substantially in the two species. Presence of the lignan, phyltetralin, is common to *P. amarus*, *P. fraternus*, *P. maderaspatensis*, *P. virgatus*, and *P. urinaria* (Table 1). The lignan hinokinin has been isolated from *P. amarus*, *P. tenellus*, and *P. virgatus* [10]. Flavonoids such as rutin, quercitrin, quercetin, kaempferol, and astragalins are present in both *P. amarus* and *P. urinaria* [14, 39]. Presence of several ellagitannins such as geraniin, corilagin, and phyllanthusiins is also common to *P. amarus* as well as *P. urinaria* (Table 1).

To the best of our knowledge, there are no reports of isolation of any phytoconstituents from *P. ajmerianus*, *P. kozhikodanus*, *P. rheedii*, *P. rotundifolius*, and *P. scabrifolius*. These five herbs can be experimented for isolation and identification of pharmaceutically important phytochemicals.

**3.1. Major Phytochemicals and Associated Pharmacological Activities.** The phytochemicals with associated pharmacological activities of six *Phyllanthus* herbs (*P. amarus*, *P. debilis*, *P. fraternus*, *P. tenellus*, *P. urinaria*, and *P. virgatus*) are listed in Table 2.

The lignan phyllanthin renders hepatoprotective property to *P. amarus* [43]. However, *P. fraternus*, *P. maderaspatensis*, and *P. urinaria* do not contain phyllanthin [106, 108] but are hepatoprotective [106]. Therefore phyllanthin being the sole compound contributing to hepatoprotective property needs to be further investigated. Srirama et al. [109] also pointed out that phyllanthin and hypophyllanthin may not be the only compounds responsible for this property. According to Londhe et al. [52], hepatoprotective property of *P. amarus* is attributed to amariin and geraniin (which are ellagitannins), whereas phyllanthin and hypophyllanthin have been suggested to be anti-inflammatory and antiapoptotic [48].

Decalactone isolated from *P. debilis* is shown to possess antihepatotoxic ability [25]. The presence of this compound may be checked in other herb species which probably can throw light on potential of other *Phyllanthus* herbs as anti-hepatotoxic. Anticancer and/or antitumor properties have been related to the presence of phyllanthin, hypophyllanthin, niranthin, and polyphenols in *P. amarus* (Table 2). Of these three phytochemicals, niranthin is present in *P. fraternus*, *P. maderaspatensis*, *P. urinaria*, *P. virgatus* [8], and *P. tenellus* [10]. However, niranthin has not been investigated for anticancer potential in these herbs.

Antibacterial activity has been shown by phyllanthin and virgatusin in *P. amarus*. The lignin virgatusin from *P. virgatus* also shows antibacterial activity (Table 2). Virgatusin is present in *P. maderaspatensis* and *P. urinaria* as well (Table 1) and therefore the potential of this compound from these herbs can also be assessed for antibacterial activity. Antioxidant activity is shown by rutin, quercetin-3-O-glucoside (flavonoids), phyllanthin (lignan), amariin, repandusinic acid A, corilagin, phyllanthusiin A, B, C, geraniin (ellagitannins), methyl brevifolin (coumarin), methyl gallate, and trimethyl 1-3,4-dehydrochebulate (triterpenes) (see Table 2). Most of

TABLE 1: Major phytochemicals isolated from *Phyllanthus amarus*, *P. debilis*, *P. fraternus*, *P. maderaspatensis*, *P. tenellus*, *P. urinaria*, and *P. virgatus*.

Species	Class	Phytochemical	References
<i>P. amarus</i>	Lignans	Phyllanthin, hypophyllanthin	[6, 7]
		Niranthin, nirtetralin	[8, 9]
		Phyltetralin	[9]
		Heliobupthalmin lactone, virgatusin	[8]
		Isonirtetralin, lintetralin	[7]
		Isolintetralin, demethylenedioxy-niranthin, 5-demethoxy-niranthin	[10]
		Hinokinin	[11]
		3-(3,4-Dimethoxy-benzyl)-4-(7-methoxy benzo[1, 3]dioxol-5-yl-methyl)-dihydrofuran-2-one, 4-(3,4-dimethoxy-phenyl)-1-(7-methoxybenzol[1, 3]dioxol-5-yl)-2,3-bis-methoxymethyl-butan-1-ol	[12]
		Rutin	[13]
		Kaempferol, quercetin, quercitrin	[14]
		Astragalin, quercetin-3-O-glucopyranoside	[12]
	Flavonoids	Quercetin-3-O-glucoside	[15, 16]
		Galic acid, galocatechin	[17]
	Tannins precursors	Ellagic acid	[14]
		Corilagin	[10]
	Tannins	Geraniin	[16]
		Amariin, furosin	[18]
		Repandusinic acid A	[18]
		Phyllanthusiin A, B, C, and D	[15, 16]
		Geraniinic acid B, amariinic acid, amarulone, isocorilagin, elaeocarpusin	[19, 20]
		Securinine	[20]
	Alkaloids	Dihydrosecurinine, tetrahydrosecurinine,	[20]
		Securinol, phyllanthin, allo-securine	[21]
		Norsecurinine	[22]
Epibubbialine, isobubbialine		[15]	
Phenazine and phenazine derivatives		[23]	
Triterpenes	Ursolic acid, oleanolic acid	[7]	
	2Z,6Z,10Z,14E,18E,22E-Farnesyl farnesol	[14]	
	Lupeol, phyllanthenol, phyllanthenone	[24]	
Volatile oil	Linalool, phytol	[25]	
<i>P. debilis</i>	Oxirano-furanocoumarin	Decalactone	[26, 27]
<i>P. fraternus</i>	Lignans	Phyllanthin, hypophyllanthin	[28]
	Alkamides	Niranthin, nirtetralin, phyltetralin	[28]
<i>P. maderaspatensis</i>	Lignans	E,E-2,4-Octadienamide, E,Z,4-decadienamide	[8]
	Lipids	Phyllanthin, hypophyllanthin, niranthin, phyltetralin, nirtetralin, Heliobupthalmin lactone, virgatusin	[29]
<i>P. tenellus</i>	Lipids	Linoleic acid, linolenic acid, myristic acid, oleic acid, palmitic acid, stearic acid	[10]
	Lignans	Niranthin, nirtetralin, hinokinin	[30]
<i>P. tenellus</i>	Tannins	Pinocembrin-7-O-[4'',6''-(S)-hexahydroxydiphenoyl]-β-D-glucose, pinocembrin-7-O-[3''-O-galloyl-4'',6''-(S)-hexahydroxydiphenoyl]-β-D-glucose	[30]

TABLE I: Continued.

Species	Class	Phytochemical	References	
<i>P. urinaria</i>	Lignans	Phyllanthin, hypophyllanthin, niranthin, nirtetralin, virgatusin, heliobupthalmin lactone	[8]	
		Phyltetralin	[31]	
		5-Demethoxyniranthin	[32]	
		Lintetralin, urinatetralin, urinaligran, dextrobursehernin	[33]	
	Ellagitannin	Geraniin	[34]	
		Ellagic acid	[35–37]	
		Corilagin	[36, 38]	
	Flavonoid	Phyllanthusiin U	[36]	
		Gallic acid	[35]	
		Quercitrin, rutin, astragaln, quercetin, isoquercitrin, kaempferol	[39]	
		Rhamnocitrin	[31]	
		Acid	Hexacosanoic acid	[40]
		Alkanol	Triacontanol	[40]
		Phytallate	Phyllester	[40]
	Triterpenes	$\beta$ -Sitosterol, daucosterol	[35]	
$\beta$ -Amyrin, lupeol acetate		[31, 40]		
Coumarin	Methyl brevifolin carboxylate	[31]		
<i>P. virgatus</i>	Lignans	Phyllanthin, hypophyllanthin, niranthin, nirtetralin, heliobupthalmin lactone, virgatusin	[8]	
		Hinokinin, isolintetralin, phyltetralin, (+)-8-3,4-methylenedioxybenzyl-8'-(3',4'-dimethoxybenzyl)-butyrolactone	[41]	
	Tannins	Virgatyne, virganin, norlignan	[42]	
	Ellagitannins	Geraniin	[10]	
	Flavonoid sulfonates	Galanin-8-sulfonate, galanin-3-O-beta-D-glucoside-8-sulfonate, Kaempferol-8-sulfonate	[42]	
	Acid	Indole-3-carboxylic acid	[41]	

the compounds have been investigated in *P. amarus* for antioxidant property. Rutin and quercetin are found in *P. urinaria* but have been shown to exhibit antiviral property [31]. It may be worthwhile to investigate the role of rutin and quercetin for antioxidant property in *P. urinaria* and for antiviral property in *P. amarus*.

In separate studies, the antiviral property of *P. amarus* has been attributed to the compounds niranthin, nirtetralin, hinokinin, geraniin, and corilagin [10, 51]. The antiviral activity in *P. tenellus* and *P. virgatus* is also attributed to niranthin, nirtetralin, and hinokinin [10]. Geraniin is the common compound found in *P. amarus*, *P. urinaria*, and *P. virgatus*, which shows antiviral property in the three herbs [10, 55]. Anti-inflammatory activity in *P. urinaria* is attributed to the phytochemicals, phyltetralin, phyllanthin, quercetin, rutin, rhamnocitrin, and  $\beta$ -sitosterol [31, 59]. These compounds are found in other *Phyllanthus* herbs also (Table 1) and therefore the herbs can be assessed for anti-inflammatory property. Some of the flavonoids (rutin and quercetin-3-O-glucoside) and ellagitannins (geraniin, amariin, repandusinic acid, corilagin, and phyllanthusiin) in *P. amarus* have a role

in radioprotective property (Table 2). Since most of these compounds are also present in *P. urinaria* (Table 1), the role of these phytochemicals in contributing radioprotective property in this herb can be investigated.

The alkaloid norsecurinine is associated with antifungal property of *P. amarus* and the compounds,  $\beta$ -sitosterol and  $\beta$ -amyrin, are associated with analgesic property of *P. urinaria* (Table 2). Two alkamides (E,E-2,4-octadienamide and E,Z-2,4-decadienamide) have been isolated from *P. fraternus* which contributes to the antiplasmodial property of the herb (Table 2). This is another pharmaceutically very relevant property that can be investigated for potential antimalaria drugs.

In the six herbs (i.e., *P. ajmerianus*, *P. kozhikodianus*, *P. maderaspatensis*, *P. rheedii*, *P. rotundifolius*, and *P. scabrifolius*), to the best of our knowledge, there are no studies correlating a phytochemical with its pharmaceutical property. The plant extracts of *P. kozhikodianus* and *P. rheedii* have been analysed for pharmacognostic properties and *P. kozhikodianus* is shown to be hepatoprotective [87, 88] and *P. rheedii* to have antihyperglycemic, antihyperlipidemic, and antioxidant

TABLE 2: Pharmacological effect of major phytochemicals in *Phyllanthus amarus*, *P. debilis*, *P. fraternus*, *P. tenellus*, *P. urinaria*, and *P. virgatus*.

Species	Class	Phytoconstituent	Pharmacological effect	Reference			
<i>P. amarus</i>	Lignan	Phyllanthin	Hepatoprotective	[43]			
			Anticancer, antitumour	[44]			
			Antileukemia	[45]			
			Antibacterial	[46]			
			Antiamnestic	[47]			
			Antiaging				
			Antioxidant	[6]			
			Anti-inflammatory, antiapoptotic	[48]			
			Hypophyllanthin	Antitumor, anticancer	[44]		
			Niranthin	Antitumor	[20]		
				Antiviral	[10]		
				Anti-inflammatory	[9]		
			Flavonoid		Phyltetralin	Anti-inflammatory	[9]
	Nirtetralin	Anti-inflammatory			[9]		
		Antiviral			[10]		
		Reverses multidrug resistance			[49, 50]		
	Hinokinin	Antiviral			[10]		
	Rutin	Radioprotective			[12]		
		Antioxidant			[18]		
	Tannin	Quercetin-3-O-glucoside				Antioxidant	[18]
					Geraniin	Antiviral	[10, 51]
						Radioprotective	[12]
				Hepatoprotective	[52]		
Amariin			Antioxidant	[18]			
			Radioprotective	[12]			
			Hepatoprotective	[52]			
Repandusinic acid A			Antioxidant	[18]			
			Radioprotective	[12]			
Corilagin			Antioxidant	[18]			
	Radioprotective	[12]					
	Antiviral	[51]					
	Phyllanthusiin A, B, C, D	Antioxidant	[18]				
		radioprotective	[12]				
Alkaloid		Norsecurinine	Antifungal	[21]			
		Volatile oil	Linalool, phytol	Antimicrobial	[24, 53]		
				Polyphenol	Anticancer	[54]	
<i>P. fraternus</i>	Alkamide	E,E-2,4-Octadienamide	Antiplasmodial	[28]			
		E,Z-2,4-Decadienamide	Antiplasmodial	[28]			
<i>P. debilis</i>	Oxirano-furanocoumarin	Debelalactone	Antihepatotoxic	[25]			
<i>P. tenellus</i>	Lignan	Niranthin	Antiviral	[10]			
		Nirtetralin	Antiviral	[10]			
		Hinokinin	Antiviral	[10]			

TABLE 2: Continued.

Species	Class	Phytoconstituent	Pharmacological effect	Reference	
<i>P. urinaria</i>	Lignan	Phyltetralin	Anti-inflammatory	[31]	
		Phyllanthin	Anti-inflammatory	[31]	
	Flavonoid	Quercetin	Anti-inflammatory	[31]	
		Rutin	Anti-inflammatory	[31]	
		Rhamnocitrin	Anti-inflammatory	[31]	
	Coumarin	Methylbrevifolin carboxylate	Antioxidant	[31]	
	Ellagitannin	Geraniin		Antiviral	[55]
				Antioxidant	[56]
			Ellagic acid	Antiangiogenic	[57]
				Antiviral	[37]
	Sterol	$\beta$ -Sitosterol		Analgesic	[58]
				Anti-inflammatory	[59]
	Triterpene		$\beta$ -Amyrin	Analgesic	[60]
Methyl gallate			Antioxidant	[31]	
Trimethyl 1-3,4 dehydrochebulate			Antioxidant	[31]	
<i>P. virgatus</i>	Lignan	Niranthin	Antiviral	[10]	
		Nirtetralin	Antiviral	[10]	
		Hinokinin	Antiviral	[10]	
		Virgatusin	Antibacterial	[61]	
	Ellagitannin	Geraniin		Antiviral	[10]

effects [92, 93]. However, the compounds responsible for these pharmaceutical properties have not been identified. *P. ajmerianus*, *P. rotundifolius*, and *P. scabrifolius* have not been researched at all for either phytochemicals or pharmacological properties.

### 3.2. Phytochemicals with Multiple Pharmaceutical Properties.

The lignan phyllanthin has been shown to possess maximum number of medicinal properties such as hepatoprotective, anticancer, anti-amnesic, antiaging, antioxidant, and anti-inflammatory (Table 2). All these properties (except anti-inflammatory which is shown in *P. urinaria*) have been assessed in *P. amarus*. Another lignan, niranthin, is shown to have both antitumor and antiviral property. The flavonoids (rutin and quercetin-3-O-glucoside) and ellagitannins (geraniin, amariin, repandusinic acid, corilagin, and phyllanthusiin) have antioxidant as well as radioprotective property (Table 2).

## 4. Studies on Genetic Diversity, Species Identification, and Phylogeny

Genetic diversity studies, phylogenetics, identification of species, and characterization of germplasm are very important for appropriate utilization and conservation of plant genetic resources. The total number of genetic diversity studies on herbs of *Phyllanthus* is few, compared to pharmacognostic/pharmacological studies. The extent of genetic diversity

has been investigated in *P. amarus*, *P. debilis*, and *P. virgatus* using RAPD (random amplified polymorphic DNA) and ISSR (Intersimple sequence repeats) markers, and an average polymorphism of 68.2% and 69.7%, respectively, was observed [110]. Genetic diversity analysis using RAPD markers, within *P. amarus* collected from different geographical locations in India, showed that the accessions from the southern part of India have high intrapopulation variation [111]. This variation may be attributed to the cross-pollination mechanisms in populations and also because they grow as weeds without much anthropogenic intervention [112].

Isozymes also have been used to assess the genetic variability in south Indian populations of *P. amarus* to identify superior genotypes for improving drug quality and for formulating strategies for *in situ* conservation and sustainable utilization [113]. Ravikant et al. [114] have also described southern India to be the genetic hot spot of *Phyllanthus* sp.

The ethnomedicinal uses and pharmacological activities among *P. amarus*, *P. fraternus*, *P. debilis*, and *P. urinaria* are varied but these plant species commonly grow together in the same open habitats and wastelands. In Bangladesh, China, India, Pakistan, and Thailand, *P. amarus*, *P. fraternus*, *P. debilis*, and *P. urinaria* grow together and lead to confusion in identification of these herbaceous species. Systematic studies on herbaceous *Phyllanthus* species, using morphological and anatomical parameters, could identify these *Phyllanthus* herbs [115]. Earlier, *P. amarus*, *P. fraternus*, and *P. debilis* were grouped under the single species named *P. niruri* and were later mentioned as species of "niruri complex." Now, it is

clarified that *P. niruri* is an American species and not at all found in India. Hence, the species identified as *P. niruri* is actually *P. amarus*, *P. fraternus*, and/or *P. debilis* [112, 116].

The use of molecular markers for identification of *Phyllanthus* species has proved to be a reliable tool. Species-specific SCAR (sequence characterized amplified regions) markers were developed for identification of *Phyllanthus* species (*P. amarus*, *P. fraternus*, *P. debilis*, and *P. urinaria*) used in dry leaf bulk trade [117, 118]. Bandyopadhyay and Raychaudhuri [119] compared RAPD, SCAR, and AFLP (amplified fragment length polymorphism) markers for identification of five *Phyllanthus* spp. and concluded that AFLP is a better polymorphic marker. Senapati et al. [120] identified species-specific diagnostic markers for ten *Phyllanthus* species, using intersimple sequence repeat-polymerase chain reaction (ISSR-PCR). Srirama et al. [121] assessed species admixtures in raw drug trade of *Phyllanthus* using DNA barcoding tools. They analyzed sequence variations of *psbA-trnH* region of the chloroplast to identify the *Phyllanthus* species present in the admixtures. AFLP profile along with morphological study could confirm the identification of *P. ajmerianus* Chaudhary and Rao in Ajmer, India [5]. The study also pointed to the distinct characteristic of the taxon and close relatedness to *P. kozhikodianus* and *P. rheedii*. PCR-RFLP approach of ITS (internal transcribed spacers) region has been successful in discriminating *P. amarus*, *P. debilis*, and *P. urinaria* [122].

Bandyopadhyay and Raychaudhuri [123] sequenced ITS regions of five species of *Phyllanthus*. The ITS sequences generated phylograms which aided in deducing affinities among *P. emblica*, *P. reticulatus*, *P. amarus*, *P. fraternus*, and *P. urinaria*. Phylogenetic relationships of 23 *Phyllanthus* species of Thailand have been analysed by sequencing ITS regions [122]. RAPD and ISSR markers have also been used to analyse phylogenetic relationship between twelve species of *Phyllanthus* [124].

## 5. Conclusions and Future Prospects

There are practically no studies on pharmacognosics and identification and/or isolation of pharmaceutically important compounds in *P. ajmerianus*, *P. rotundifolius*, and *P. scabrifolius*. Considering the medicinal properties of the *Phyllanthus* herbs, these species should be assessed for pharmacognosics and pharmacological properties. In case of *P. maderaspatensis*, *P. kozhikodianus*, and *P. rheedii*, although pharmacognostic properties are known, the compounds responsible for such properties have not been identified. Therefore these herbs can be experimented for isolation and identification of phytochemicals, based on existing knowledge of compounds observed in other *Phyllanthus* herbs and subsequently can be used for preparation of herbal medicines. Studies on pharmacognosy and pharmaceutical activity of phytochemicals published under the identity of *P. niruri* may be reevaluated especially the studies from India, as now it is confirmed that *P. niruri* is not found in India [112]. The studies, mentioning *P. niruri*, actually may be of *P. amarus*, *P. fraternus*, or *P. debilis*. Also, to our knowledge, there are

either few or no studies on genetic diversity of most *Phyllanthus* herb species, some of which are endemic species with a few populations, for example, *P. scabrifolius* in India. Considering the growing popularity of ethnopharmacological value of *Phyllanthus* species and its use in herbal medicines, it is imperative to assess the genetic diversity of these species, which will have implications for formulating conservation strategies in future.

## Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

## Acknowledgment

The funding provided by Department of Science and Technology (DST), Ministry of Science and Technology, India, is gratefully acknowledged.

## References

- [1] D. W. Unander, G. L. Webster, and B. S. Blumberg, "Usage and bioassays in *Phyllanthus* (Euphorbiaceae)—IV: clustering of antiviral uses and other effects," *Journal of Ethnopharmacology*, vol. 45, no. 1, pp. 1–18, 1995.
- [2] G. L. Webster, "Synopsis of the genus and suprageneric taxa of Euphorbiaceae," *Annals of the Missouri Botanical Garden*, vol. 81, pp. 33–144, 1994.
- [3] J. B. Calixto, A. R. S. Santos, V. C. Filho et al., "A review of the plants of the Genus *Phyllanthus*: their chemistry, pharmacology and therapeutic potential," *Medicinal Research Reviews*, vol. 18, no. 4, pp. 225–258, 1998.
- [4] L. Nahar, S. D. Sarker, and A. Delazar, "Phytochemistry of the genus *Phyllanthus*," in *Phyllanthus Species: Scientific Evaluation and Medicinal Applications*, R. Kuttan and K. B. Harikumar, Eds., pp. 119–138, Taylor and Francis Group, CRC Press, London, UK, 2011.
- [5] V. Vishwanatha, T. N. Parameswaran, R. R. Rao et al., "Reconfirmation of the identity and occurrence of *Phyllanthus ajmerianus* Chaudhary & Rao in Ajmer, Rajasthan, India," *Current Science*, vol. 91, no. 1, pp. 24–26, 2006.
- [6] R. Krithika, R. Mohankumar, R. J. Verma et al., "Isolation, characterization and antioxidative effect of phyllanthin against CCl<sub>4</sub>-induced toxicity in HepG2 cell line," *Chemico-Biological Interactions*, vol. 181, no. 3, pp. 351–358, 2009.
- [7] M. A. M. Maciel, A. F. Cunha, N. T. C. Dantas et al., "NMR characterization of bioactive lignans from *Phyllanthus amarus* Schum and Thonn," *Journal of Magnetic Resonance Imaging*, vol. 6, no. 3, pp. 76–82, 2007.
- [8] K. Shanker, M. Singh, V. Srivastava, R. Verma, A. Gupta, and M. Gupta, "Simultaneous analysis of six bioactive lignans in *Phyllanthus* species by reversed phase hyphenated high performance liquid chromatographic technique," *Acta Chromatographica*, vol. 23, no. 2, pp. 321–337, 2011.
- [9] C. A. L. Kassuya, D. F. P. Leite, L. V. De Melo, V. L. C. Rehder, and J. B. Calixto, "Anti-inflammatory properties of extracts, fractions and lignans isolated from *Phyllanthus amarus*," *Planta Medica*, vol. 71, no. 8, pp. 721–726, 2005.

- [10] R.-L. Huang, Y.-L. Huang, J.-C. Ou, C.-C. Chen, F.-L. Hsu, and C. Chang, "Screening of 25 compounds isolated from *Phyllanthus* species for anti-human hepatitis B virus in vitro," *Phytotherapy Research*, vol. 17, no. 5, pp. 449–453, 2003.
- [11] M. Singh, N. Tiwari, K. Shanker, R. K. Verma, A. K. Gupta, and M. M. Gupta, "Two new lignans from *Phyllanthus amarus*," *Journal of Asian Natural Products Research*, vol. 11, no. 6, pp. 562–568, 2009.
- [12] J. S. Londhe, T. P. A. Devasagayam, L. Y. Foo, and S. S. Ghaskadbi, "Radioprotective properties of polyphenols from *Phyllanthus amarus* Linn," *Journal of Radiation Research*, vol. 50, no. 4, pp. 303–309, 2009.
- [13] S. P. Thyagarajan and S. Jayaram, "Natural History of *Phyllanthus amarus* in treatment of hepatitis B," *Indian Journal of Medical Microbiology*, vol. 10, no. 2, pp. 64–80, 1992.
- [14] L. Yeap Foo and H. Wong, "Phyllanthusiin D, an unusual hydrolysable tannin from *Phyllanthus amarus*," *Phytochemistry*, vol. 31, no. 2, pp. 711–713, 1992.
- [15] L. Y. Foo, "Amarulone, a novel cyclic hydrolysable tannin from *Phyllanthus amarus*," *Natural Product Letters*, vol. 3, no. 1, pp. 45–52, 1993.
- [16] L. Y. Foo, "Amarinic acid and related ellagitannins from *Phyllanthus amarus*," *Phytochemistry*, vol. 39, no. 1, pp. 217–224, 1995.
- [17] K. Dhalwal, Y. S. Biradar, and M. Rajani, "High-performance thin-layer chromatography densitometric method for simultaneous quantitation of phyllanthin, hypophyllanthin, gallic acid, and ellagic acid in *Phyllanthus amarus*," *Journal of AOAC International*, vol. 89, no. 3, pp. 619–623, 2006.
- [18] J. S. Londhe, T. P. A. Devasagayam, L. Y. Foo, and S. S. Ghaskadbi, "Antioxidant activity of some polyphenol constituents of the medicinal plant *Phyllanthus amarus* Linn," *Redox Report*, vol. 13, no. 5, pp. 199–207, 2008.
- [19] A. K. Singh, M. B. Pandey, S. Singh et al., "Antifungal activity of securinine against some plant pathogenic fungi," *Mycobiology*, vol. 36, no. 2, pp. 99–101, 2008.
- [20] C. A. L. Kassuya, A. Silvestre, O. Menezes-de-Lima Jr., D. M. Marotta, V. L. G. Rehder, and J. B. Calixto, "Antiinflammatory and antiallodynic actions of the lignan niranthin isolated from *Phyllanthus amarus*. Evidence for interaction with platelet activating factor receptor," *European Journal of Pharmacology*, vol. 546, no. 1–3, pp. 182–188, 2006.
- [21] S. Sahni, S. Maurya, and U. P. Singh, "Antifungal activity of nor-securinine against some phytopathogenic fungi," *Mycobiology*, vol. 33, no. 2, pp. 97–103, 2005.
- [22] P. J. Houghton, T. Z. Woldemariam, S. O'Shea, and S. P. Thyagarajan, "Two securiniga-type alkaloids from *Phyllanthus amarus*," *Phytochemistry*, vol. 43, no. 3, pp. 715–717, 1996.
- [23] H. Ali, P. J. Houghton, and A. Soumyanath, " $\alpha$ -Amylase inhibitory activity of some Malaysian plants used to treat diabetes; with particular reference to *Phyllanthus amarus*," *Journal of Ethnopharmacology*, vol. 107, no. 3, pp. 449–455, 2006.
- [24] D. O. Moronkola, I. A. Ogunwande, I. O. Oyewole, K. Husnu Can Başer, T. Ozek, and G. Ozek, "Studies on the volatile oils of *Momordica charantia* L. (Cucurbitaceae) and *Phyllanthus amarus* Seh. et Thonn (Euphorbiaceae)," *Journal of Essential Oil Research*, vol. 21, no. 5, pp. 393–399, 2009.
- [25] B. Ahmed, S. Khan, and A. Verma, "Antihepatotoxic activity of debelalactone, a new oxirano-furanocoumarin from *Phyllanthus debilis*," *Journal of Asian Natural Products Research*, vol. 11, no. 8, pp. 687–692, 2009.
- [26] A. K. Tripathi, R. K. Verma, A. K. Gupta, M. M. Gupta, and S. P. S. Khanuja, "Quantitative determination of phyllanthin and hypophyllanthin in *Phyllanthus* species by high-performance thin layer chromatography," *Phytochemical Analysis*, vol. 17, no. 6, pp. 394–397, 2006.
- [27] T. Sebastian and O. H. Setty, "Protective effect of *P. fraternus* Against ethanol-induced mitochondrial dysfunction," *Alcohol*, vol. 17, no. 1, pp. 29–34, 1999.
- [28] A. A. Sittie, E. Lemmich, and C. E. Olsen, "Alkamides from *Phyllanthus fraternus*," *Planta Medica*, vol. 64, no. 2, pp. 192–193, 1998.
- [29] D. S. Bhakuni, "Chemical examination of the seed of *Phyllanthus maderaspatensis* Linn," *Journal of Scientific and Industrial Research B*, vol. 18, pp. 446–447, 1959.
- [30] Y.-L. Huang, C.-C. Chen, F.-L. Hsu, and C.-F. Chen, "Two tannins from *Phyllanthus tenellus*," *Journal of Natural Products*, vol. 61, no. 4, pp. 523–524, 1998.
- [31] S.-H. Fang, Y. K. Rao, and Y.-M. Tzeng, "Anti-oxidant and inflammatory mediator's growth inhibitory effects of compounds isolated from *Phyllanthus urinaria*," *Journal of Ethnopharmacology*, vol. 116, no. 2, pp. 333–340, 2008.
- [32] C.-C. Chang, Y.-C. Lien, K. C. S. C. Liu, and S.-S. Lee, "Lignans from *Phyllanthus urinaria*," *Phytochemistry*, vol. 63, no. 7, pp. 825–833, 2003.
- [33] C.-Y. Wang and S.-S. Lee, "Analysis and identification of lignans in *Phyllanthus urinaria* by HPLC-SPE-NMR," *Phytochemical Analysis*, vol. 16, no. 2, pp. 120–126, 2005.
- [34] T. Okuda, K. Mori, and T. Hatano, "The distribution of geraniin and mallotusinic acid in the order geraniales," *Phytochemistry*, vol. 19, no. 4, pp. 547–551, 1980.
- [35] Q. Q. Yao and C. X. Zuo, "Chemical studies on the constituents of *Phyllanthus urinaria* L.," *Acta Pharmaceutica Sinica*, vol. 28, no. 11, pp. 829–835, 1993.
- [36] H. Luo, L. Chen, Z. Li, Z. Ding, and X. Xu, "Frontal immunofluorescence chromatography with mass spectrometric detection: a method for finding active compounds from traditional Chinese herbs," *Analytical Chemistry*, vol. 75, no. 16, pp. 3994–3998, 2003.
- [37] M. S. Shin, E. H. Kang, and Y. I. Lee, "A flavonoid from medicinal plants blocks hepatitis B virus-e antigen secretion in HBV-infected hepatocytes," *Antiviral Research*, vol. 67, no. 3, pp. 163–168, 2005.
- [38] L. Jikai, H. Yue, T. Henkel, and K. Weber, "One step purification of corilagin and ellagic acid from *Phyllanthus urinaria* using high-speed countercurrent chromatography," *Phytochemical Analysis*, vol. 13, no. 1, pp. 1–3, 2002.
- [39] T. K. Nara, J. Glyeye, E. L. Cervel et al., "Flavonoids of *Phyllanthus niruri*, *Phyllanthus urinaria*, *Phyllanthus orbiculatus*," *Plantes Médicinales et Phytothérapie*, vol. 11, pp. 82–86, 1977.
- [40] K. S. Satyan, A. Prakash, R. P. Singh, and R. S. Srivastava, "Phthalic acid bis-ester and other phytoconstituents of *Phyllanthus urinaria*," *Planta Medica*, vol. 61, no. 3, pp. 293–294, 1995.
- [41] Y.-L. Huang, C.-C. Chen, F.-L. Hsu, and C.-F. Chen, "A new lignan from *Phyllanthus virgatus*," *Journal of Natural Products*, vol. 59, no. 5, pp. 520–521, 1996.
- [42] Y.-L. Huang, C.-C. Chen, F.-L. Hsu, and C.-F. Chen, "Tannins, flavonol sulfonates, and a norlignan from *Phyllanthus virgatus*," *Journal of Natural Products*, vol. 61, no. 10, pp. 1194–1197, 1998.
- [43] H. Chirdchupunsere and P. Pramyothin, "Protective activity of phyllanthin in ethanol-treated primary culture of rat hepatocytes," *Journal of Ethnopharmacology*, vol. 128, no. 1, pp. 172–176, 2010.

- [44] A. Islam, T. Selvan, U. K. Mazumder, M. Gupta, and S. Ghosal, "Antitumour effect of *Phyllanthin* and Hypophyllanthin from *Phyllanthus amarus* against Ehrlich Ascites Carcinoma in mice," *Pharmacologyonline*, vol. 2, pp. 796–807, 2008.
- [45] K. B. Harikumar, G. Kuttan, and R. Kuttan, "Inhibition of viral carcinogenesis by *Phyllanthus amarus*," *Integrative Cancer Therapies*, vol. 8, no. 3, pp. 254–260, 2009.
- [46] A. Mazumder, A. Mahato, and R. Mazumder, "Antimicrobial potentiality of *Phyllanthus amarus* against drug resistant pathogens," *Natural Product Research*, vol. 20, no. 4, pp. 323–326, 2006.
- [47] H. Joshi and M. Parle, "Evaluation of antiemetic potentials of [6]-gingerol and phyllanthin in mice," *Natural Products*, vol. 2, pp. 109–117, 2006.
- [48] A. D. Kandhare, P. Ghosh, A. E. Ghule et al., "Protective effect of *Phyllanthus amarus* by modulation of endogenous biomarkers and DNA damage in acetic acid induced ulcerative colitis: role of phyllanthin and hypophyllanthin," *Apollo Medicine*, vol. 10, no. 1, pp. 87–97, 2013.
- [49] D. F. P. Leite, C. A. L. Kassuya, T. L. Mazzuco et al., "The cytotoxic effect and the multidrug resistance reversing action of lignans from *Phyllanthus amarus*," *Planta Medica*, vol. 72, no. 15, pp. 1353–1358, 2006.
- [50] H. Dhir, A. Kumar Roy, A. Sharma, and G. Talukder, "Protection afforded by aqueous extracts of *Phyllanthus* species against cytotoxicity induced by lead and aluminium salts," *Phytotherapy Research*, vol. 4, no. 5, pp. 172–176, 1990.
- [51] F. Notka, G. Meier, and R. Wagner, "Concerted inhibitory activities of *Phyllanthus amarus* on HIV replication in vitro and ex vivo," *Antiviral Research*, vol. 64, no. 2, pp. 93–102, 2004.
- [52] J. S. Londhe, T. P. A. Devasagayam, L. Y. Foo et al., "Geraniin and amariin, ellagitannins from *Phyllanthus amarus*, protect liver cells against ethanol induced cytotoxicity," *Fitoterapia*, vol. 83, no. 8, pp. 1562–1568, 2012.
- [53] M. Ogunlesi, W. Okiei, E. A. S. Osibote, and C. Muotoh, "Antimicrobial activity of the essential oil and the fractional samples obtained from the leaves and seeds of *Phyllanthus atnarus* (Euphorbiaceae)," *Research Journal of Phytochemistry*, vol. 3, no. 4, pp. 77–84, 2009.
- [54] S. H. Lee, I. B. Jaganath, S. M. Wang, and S. D. Sekaran, "Antimetastatic effects of *Phyllanthus* on human lung (A549) and breast (MCF-7) cancer cell lines," *PLoS ONE*, vol. 6, no. 6, article e20994, 2011.
- [55] C.-M. Yang, H.-Y. Cheng, T.-C. Lin, L.-C. Chiang, and C.-C. Lin, "The in vitro activity of geraniin and 1,3,4,6-tetra-O-galloyl- $\beta$ -D-glucose isolated from *Phyllanthus urinaria* against herpes simplex virus type 1 and type 2 infection," *Journal of Ethnopharmacology*, vol. 110, no. 3, pp. 555–558, 2007.
- [56] S.-Y. Lin, C.-C. Wang, Y.-L. Lu, W.-C. Wu, and W.-C. Hou, "Antioxidant, anti-semicarbazide-sensitive amine oxidase, and anti-hypertensive activities of geraniin isolated from *Phyllanthus urinaria*," *Food and Chemical Toxicology*, vol. 46, no. 7, pp. 2485–2492, 2008.
- [57] S.-T. Huang, C.-Y. Wang, R.-C. Yang et al., "Ellagic acid, the active compound of *Phyllanthus urinaria*, exerts in vivo anti-angiogenic effect and inhibits MMP-2 activity," *Evidence-Based Complementary and Alternative Medicine*, vol. 2011, Article ID 215035, 10 pages, 2011.
- [58] S. S. Handa, A. S. Chawla, and A. K. Sharma, "Plants with antiinflammatory activity," *Fitoterapia*, vol. 63, no. 1, pp. 3–31, 1992.
- [59] A. R. S. Santos, V. C. Filho, R. A. Yunes, and J. B. Calixto, "Analysis of the mechanisms underlying the antinociceptive effect of the extracts of plants from the genus *Phyllanthus*," *General Pharmacology*, vol. 26, no. 7, pp. 1499–1506, 1995.
- [60] M. C. Recio, R. M. Giner, S. Manez, and J. L. Rios, "Structural requirements for the anti-inflammatory activity of natural triterpenoids," *Planta Medica*, vol. 61, no. 2, pp. 182–185, 1995.
- [61] M. Maruyama, S. Yamauchi, K. Akiyama, T. Sugahara, T. Kishida, and Y. Koba, "Antibacterial activity of a virgatusin-related compound," *Bioscience, Biotechnology and Biochemistry*, vol. 71, no. 3, pp. 677–680, 2007.
- [62] J. R. Patel, P. Tripathi, V. Sharma, N. S. Chauhan, and V. K. Dixit, "*Phyllanthus amarus*: ethnomedicinal uses, phytochemistry and pharmacology: a review," *Journal of Ethnopharmacology*, vol. 138, no. 2, pp. 286–313, 2011.
- [63] C. P. Kala, P. P. Dhyan, and B. S. Sajwan, "Developing the medicinal plants sector in northern India: challenges and opportunities," *Journal of Ethnobiology and Ethnomedicine*, vol. 2, article 32, 2006.
- [64] P. S. Udayan, K. V. Tushar, S. George et al., "Ethnomedicinal information from Kattunayakas tribes of Mudumalai Wildlife Sanctuary, Nilgiris district, Tamil Nadu," *Indian Journal of Traditional Knowledge*, vol. 6, pp. 574–578, 2007.
- [65] R. P. Samy, P. N. Pushparaj, and P. A. Gopikrishnakone, "Compilation of bioactive compounds from Ayurveda," *Bioinformation*, vol. 3, no. 3, pp. 100–110, 2008.
- [66] K. Chenniappan and M. Kadarkarai, "In vitro antimalarial activity of traditionally used Western Ghats plants from India and their interactions with chloroquine against chloroquine-resistant *Plasmodium falciparum*," *Parasitology Research*, vol. 107, no. 6, pp. 1351–1364, 2010.
- [67] B. Upadhyay, P. Parveen, A. K. Dhaker, and A. Kumar, "Ethnomedicinal and ethnopharmaco-statistical studies of Eastern Rajasthan, India," *Journal of Ethnopharmacology*, vol. 129, no. 1, pp. 64–86, 2010.
- [68] A. Jain, S. S. Katewa, P. K. Galav, and P. Sharma, "Medicinal plant diversity of Sitamata wildlife sanctuary, Rajasthan, India," *Journal of Ethnopharmacology*, vol. 102, no. 2, pp. 143–157, 2005.
- [69] P. Mahishi, B. H. Srinivasa, and M. B. Shivanna, "Medicinal plant wealth of local communities in some villages in Shimoga District of Karnataka, India," *Journal of Ethnopharmacology*, vol. 98, no. 3, pp. 307–312, 2005.
- [70] C. Muthu, M. Ayyanar, N. Raja, and S. Ignacimuthu, "Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India," *Journal of Ethnobiology and Ethnomedicine*, vol. 2, article 43, 2006.
- [71] S. Ignacimuthu, M. Ayyanar, and K. Sankarasivaraman, "Ethnobotanical study of medicinal plants used by Paliyar tribals in Theni district of Tamil Nadu, India," *Fitoterapia*, vol. 79, no. 7-8, pp. 562–568, 2008.
- [72] S. Shanmugam, K. Manikandan, and K. Rajendran, "Ethnomedicinal survey of medicinal plants used for the treatment of diabetes and jaundice among the villagers of Sivagangai District, Tamil Nadu," *Ethnobotanical Leaflets*, vol. 13, no. 1, pp. 189–194, 2009.
- [73] N. Rajakumar and M. B. Shivanna, "Ethno-medicinal application of plants in the eastern region of Shimoga district, Karnataka, India," *Journal of Ethnopharmacology*, vol. 126, no. 1, pp. 64–73, 2009.
- [74] J. K. Samuel and B. Andrews, "Traditional medicinal plant wealth of Pachalur and Periyur hamlets Dindigul district, Tamil

- Nadu," *Indian Journal of Traditional Knowledge*, vol. 9, no. 2, pp. 264–270, 2010.
- [75] K. B. Hari Kumar and R. Kuttan, "Inhibition of drug metabolizing enzymes (cytochrome P450) in vitro as well as in vivo by *Phyllanthus amarus* Schum & Thonn," *Biological and Pharmaceutical Bulletin*, vol. 29, no. 7, pp. 1310–1313, 2006.
- [76] K. S. Chandrashekar, A. B. Joshi, D. Satyanarayana, and P. Pai, "Analgesic and anti-inflammatory activities of *Phyllanthus debilis* whole plant," *Pharmaceutical Biology*, vol. 43, no. 7, pp. 586–588, 2005.
- [77] V. Acharya, V. Sharma, P. K. Patra et al., "Plants used by Kamar, Gond and Halba tribe of Dhamtari district of Chhattisgarh for relief of sickle cell disease," *Recent Research in Science and Technology*, vol. 4, no. 3, pp. 1–3, 2012.
- [78] K. K. Wanniarachchi, L. D. C. Peiris, and W. D. Ratnasooriya, "Antihyperglycemic and hypoglycemic activities of *Phyllanthus debilis* aqueous plant extract in mice," *Pharmaceutical Biology*, vol. 47, no. 3, pp. 260–265, 2009.
- [79] A. Kumaran and R. Joel Karunakaran, "In vitro antioxidant activities of methanol extracts of five *Phyllanthus* species from India," *LWT—Food Science and Technology*, vol. 40, no. 2, pp. 344–352, 2007.
- [80] J. L. Nishiura, A. H. Campos, M. A. Boim, I. P. Heilberg, and N. Schor, "*Phyllanthus niruri* normalizes elevated urinary calcium levels in calcium stone forming (CSF) patients," *Urological Research*, vol. 32, no. 5, pp. 362–366, 2004.
- [81] S. Chanda, M. Kaneria, and Y. K. Vaghasiya, "Evaluation of antimicrobial potential of some Indian medicinal plants against some pathogenic microbes," *Indian Journal of Natural Products and Resources*, vol. 2, no. 2, pp. 225–228, 2011.
- [82] R. Sailaja and O. H. Setty, "Protective effect of *Phyllanthus fraternus* against allyl alcohol-induced oxidative stress in liver mitochondria," *Journal of Ethnopharmacology*, vol. 105, no. 1–2, pp. 201–209, 2006.
- [83] S. Gopi and O. H. Setty, "Protective effect of *Phyllanthus fraternus* against bromobenzene induced mitochondrial dysfunction in rat liver mitochondria," *Food and Chemical Toxicology*, vol. 48, no. 8–9, pp. 2170–2175, 2010.
- [84] K. K. Kumari and O. H. Setty, "Protective effect of *Phyllanthus fraternus* against mitochondrial dysfunction induced by co-administration of cisplatin and cyclophosphamide," *Journal of Bioenergetics and Biomembranes*, vol. 44, no. 1, pp. 179–188, 2012.
- [85] G. A. Koffuor and P. Amoateng, "Antioxidant and anticoagulant properties of *Phyllanthus fraternus* GL Webster (Family: Euphorbiaceae)," *Journal of Pharmacology and Toxicology*, vol. 6, no. 7, pp. 624–636, 2011.
- [86] V. I. Hukeri, G. A. Kalyani, and H. K. Kakrani, "Hypoglycemic activity of flavonoids of *Phyllanthus fraternus* in rats," *Fitoterapia*, vol. 59, no. 1, pp. 68–70, 1988.
- [87] S. P. Thyagarajan, S. Jayaram, V. Gopalakrishnan, R. Hari, P. Jeyakumar, and M. S. Sripathi, "Herbal medicines for liver diseases in India," *Journal of Gastroenterology and Hepatology*, vol. 17, no. 3, pp. S370–S376, 2002.
- [88] V. V. Asha and P. Pushpangadan, "Preliminary evaluation of the antihepatotoxic activity of *Phyllanthus kozhikodanus*, *P. maderaspatensis* and *Solanum indicum*," *Fitoterapia*, vol. 69, no. 3, pp. 255–259, 1998.
- [89] M. J. N. Chandrasekar, P. Bommu, M. J. Nanjan, and B. Suresh, "Chemoprotective effect of *Phyllanthus maderaspatensis* in modulating cisplatin-induced nephrotoxicity and genotoxicity," *Pharmaceutical Biology*, vol. 44, no. 2, pp. 100–106, 2006.
- [90] P. Bommu, C. M. J. Nanjan, N. M. Joghee, S. M. Nataraj, and S. Bhojraj, "*Phyllanthus maderaspatensis*, a dietary supplement for the amelioration of adriamycin-induced toxicity and oxidative stress in mice," *Journal of Natural Medicines*, vol. 62, no. 2, pp. 149–154, 2008.
- [91] V. V. Asha, S. Akhila, P. J. Wills, and A. Subramoniam, "Further studies on the antihepatotoxic activity of *Phyllanthus maderaspatensis* Linn," *Journal of Ethnopharmacology*, vol. 92, no. 1, pp. 67–70, 2004.
- [92] V. Sivajothi, A. Dey, B. Jayakar, and B. Raj Kapoor, "Anti-hyperglycemic, antihyperlipidemic and antioxidant effect of *Phyllanthus rheedii* on streptozotocin induced diabetic rats," *Iranian Journal of Pharmaceutical Research*, vol. 7, no. 1, pp. 53–59, 2008.
- [93] V. Suresh and V. V. Asha, "Preventive effect of ethanol extract of *Phyllanthus rheedii* Wight. on d-galactosamine induced hepatic damage in Wistar rats," *Journal of Ethnopharmacology*, vol. 116, no. 3, pp. 447–453, 2008.
- [94] S. R. N. Ignácio, J. L. P. Ferreira, M. B. Almeida, and C. F. Kubelka, "Nitric oxide production by murine peritoneal macrophages in vitro and in vivo treated with *Phyllanthus tenellus* extracts," *Journal of Ethnopharmacology*, vol. 74, no. 2, pp. 181–187, 2001.
- [95] D. F. Oliveira, A. C. Pereira, H. C. P. Figueiredo et al., "Antibacterial activity of plant extracts from Brazilian southeast region," *Fitoterapia*, vol. 78, no. 2, pp. 142–145, 2007.
- [96] A. R. S. Santos, V. C. Filho, R. Niero et al., "Analgesic effects of callus culture extracts from selected species of *Phyllanthus* in mice," *Journal of Pharmacy and Pharmacology*, vol. 46, no. 9, pp. 755–759, 1994.
- [97] T. C. D. L. Silva, F. J. Veras, I. A. Souza et al., "Acute toxicity study of stone-breaker (*Phyllanthus tenellus* Roxb.)," *Revista de Ciências Farmacêuticas Básica e Aplicada*, vol. 33, no. 2, pp. 205–210, 2012.
- [98] S.-T. Huang, R.-C. Yang, and J.-H. S. Pang, "Aqueous extract of *Phyllanthus urinaria* induces apoptosis in human cancer cells," *American Journal of Chinese Medicine*, vol. 32, no. 2, pp. 175–183, 2004.
- [99] S.-T. Huang, J.-H. S. Pang, and R.-C. Yang, "Anti-cancer effects of *Phyllanthus urinaria* and relevant mechanisms," *Chang Gung Medical Journal*, vol. 33, no. 5, pp. 477–487, 2010.
- [100] Y.-Q. Tang, I. B. Jaganath, and S. D. Sekaran, "*Phyllanthus* spp. induces selective growth inhibition of PC-3 and MeWo human cancer cells through modulation of cell cycle and induction of apoptosis," *PloS ONE*, vol. 5, no. 9, article e12644, 2010.
- [101] M. Zhong, Y. Xiang, X. Qiu et al., "Natural products as a source of anti-herpes simplex virus agents," *RSC Advances*, vol. 3, no. 2, pp. 313–328, 2013.
- [102] C. A. Lans, "Ethnomedicines used in Trinidad and Tobago for urinary problems and diabetes mellitus," *Journal of Ethnobiology and Ethnomedicine*, vol. 2, article 45, 2006.
- [103] C.-H. Lai, S.-H. Fang, Y. K. Rao et al., "Inhibition of *Helicobacter pylori*-induced inflammation in human gastric epithelial AGS cells by *Phyllanthus urinaria* extracts," *Journal of Ethnopharmacology*, vol. 118, no. 3, pp. 522–526, 2008.
- [104] V. J. Tiwari and M. D. Padhye, "Ethnobotanical study of Gond tribe of Chandrapur and Gadchiroli districts of Maharashtra State, India," *Fitoterapia*, vol. 64, no. 1, pp. 58–61, 1993.
- [105] K. Poompachee and N. Chudapongse, "Comparison of the antioxidant and cytotoxic activities of *Phyllanthus virgatus* and *Phyllanthus amarus* extracts," *Medical Principles and Practice*, vol. 21, no. 1, pp. 24–29, 2012.

- [106] S. K. Sharma, S. M. Arogya, D. H. Bhaskarmurthy, A. Agarwal, and C. C. Velusami, "Hepatoprotective activity of the *Phyllanthus* species on *tert*-butyl hydroperoxide (*t*-BH)-induced cytotoxicity in HepG2 cells," *Pharmacognosy Magazine*, vol. 7, no. 27, pp. 229–233, 2011.
- [107] R. Murugan, R. R. Rao, and V. Vishwanatha, "Occurrence of *Phyllanthus scabrifolius* Hook. f. in Amingad, Bagalkot district, Karnataka—a new distributional record," *Current Science*, vol. 91, no. 7, pp. 870–871, 2006.
- [108] S. Khatoon, V. Rai, A. K. S. Rawat, and S. Mehrotra, "Comparative pharmacognostic studies of three *Phyllanthus* species," *Journal of Ethnopharmacology*, vol. 104, no. 1-2, pp. 79–86, 2006.
- [109] R. Srirama, H. B. Deepak, U. Senthilkumar et al., "Hepatoprotective activity of Indian *Phyllanthus*," *Pharmaceutical Biology*, vol. 50, no. 8, pp. 948–953, 2012.
- [110] M. Palaniappan and M. Marappa, "RAPD and ISSR analyses reveal low levels of genetic diversity in *Phyllanthus amarus*," in *Proceedings of the 27th International Horticultural Congress-IHC, International Symposium on Plants as Food and Medicine: The Utilization and Development of Horticultural Plants for Human Health*, ISHS Acta Horticulture 765, 2006.
- [111] N. Jain, A. K. Shasany, V. Sundaresan et al., "Molecular diversity in *Phyllanthus amarus* assessed through RAPD analysis," *Current Science*, vol. 85, no. 10, pp. 1454–1458, 2003.
- [112] R. L. Mitra and S. K. Jain, "Concept of *Phyllanthus niruri* (Euphorbiaceae) in Indian floras," *Bulletin of the Botanical Survey of India*, vol. 27, no. 1–4, pp. 161–176, 1985.
- [113] B. S. Geetha, K. K. Sabu, and S. Seenii, "Genetic variation in South India populations of *Phyllanthus amarus* Schum & Thonn. (Euphorbiaceae) assessed using isozymes," in *Proceedings of the 15th Kerala Science Congress*, pp. 196–201, 2003.
- [114] G. Ravikant, R. Srirama, U. Senthilkumar et al., "Genetic resources of *Phyllanthus* in Southern India: identification of geographic and genetic hot spots and its implication for conservation," in *Phyllanthus Species: Scientific Evaluation and Medicinal Applications*, R. Kuttan and K. B. Harikumar, Eds., pp. 97–118, Taylor and Francis Group, CRC Press, London, UK, 2011.
- [115] D. Kandavel, S. K. Rani, M. G. Vinithra et al., "Systematic studies in herbaceous *Phyllanthus* spp. (region: Tiruchirappalli district in India) and a simple key to authenticate 'Bhumyamalaki' complex members," *Journal of Phytology*, vol. 3, no. 2, pp. 37–48, 2011.
- [116] G. L. Webster, "A monographic study of the West Indian species of *Phyllanthus*," *Journal of the Arnold Arboretum*, vol. 38, pp. 295–373, 1957.
- [117] N. Jain, A. K. Shasany, S. Singh, S. P. S. Khanuja, and S. Kumar, "SCAR markers for correct identification of *Phyllanthus amarus*, *P. fraternus*, *P. debilis* and *P. urinaria* used in scientific investigations and dry leaf bulk herb trade," *Planta Medica*, vol. 74, no. 3, pp. 296–301, 2008.
- [118] P. Theerakulpisut, N. Kanawapee, D. Maensiri, S. Bunnag, and P. Chantaranothai, "Development of species-specific SCAR markers for identification of three medicinal species of *Phyllanthus*," *Journal of Systematics and Evolution*, vol. 46, no. 4, pp. 614–621, 2008.
- [119] S. Bandyopadhyay and S. S. Raychaudhuri, "Development and comparison of RAPD, SCAR and AFLP markers for distinguishing some medicinally important species of the genus *Phyllanthus*," *Plant Biosystems*, vol. 147, no. 1, pp. 12–20, 2013.
- [120] S. K. Senapati, S. Aparajita, and G. R. Rout, "Identification of species-diagnostic inter simple sequence repeat markers for ten *Phyllanthus* species," *Zeitschrift fur Naturforschung C*, vol. 66, no. 3-4, pp. 167–172, 2011.
- [121] R. Srirama, U. Senthilkumar, N. Sreejayan et al., "Assessing species admixtures in raw drug trade of *Phyllanthus*, a hepatoprotective plant using molecular tools," *Journal of Ethnopharmacology*, vol. 130, no. 2, pp. 208–215, 2010.
- [122] J. Manissorn, S. Sukrong, N. Ruangrunsi, and H. Mizukami, "Molecular phylogenetic analysis of *Phyllanthus* species in Thailand and the application of polymerase chain reaction-restriction fragment length polymorphism for *Phyllanthus amarus* identification," *Biological and Pharmaceutical Bulletin*, vol. 33, no. 10, pp. 1723–1727, 2010.
- [123] S. Bandyopadhyay and S. S. Raychaudhuri, "Development of ITS based SCAR markers for some medicinally important species of *Phyllanthus*," *Asian Journal of Plant Sciences*, vol. 9, no. 5, pp. 264–270, 2010.
- [124] G. R. Rout, S. K. Senapati, and S. Aparajita, "Study of relationships among twelve *Phyllanthus* species with the use of molecular markers," *Czech Journal of Genetics and Plant Breeding*, vol. 46, no. 3, pp. 135–141, 2010.