Medicinal values of the genus *Phyllanthus* - A review

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Abstract

Phyllanthus species are known for their many medicinal values used in folklore medicine in many parts of the world. They have array of phytochemicals in the leaf, flower, seed, stem and root, that confer medicinal advantage on them. Extracts have shown a broad range of pharmacological activities like hepatoprotective, antioxidant, antiviral, antimicrobial, antidiabetic, anti-inflammatory, anticancer, antimalarial, nephroprotective, diuretic, and several other properties. This review highlighted different research results from other scientists in the past and present, all tailored towards exploring the inherent pharmacological properties of this herb for ethno-medicine, alternative medicine and pharmaceutical purposes.

Keywords: Folklore medicine, Herb, Pharmacological activity, *Phyllanthus* species, Therapeutic use
Running title: Medicinal values of *Phyllanthus*

Introduction

Phyllanthus is a native genus largely used as antipyretic, antiviral, antidiarrheal, antispasmodic, antinociceptive, anti-inflammatory, antioxidant, antitumoral, antigenotoxic, antimutagenic, hepatoprotection, hypoglycemic, hypotensive, diuretic, antidiabetic and bactericidal agent (Maria *et al*., 2019). It was also efficient for fighting jaundice, hepadnaviral DNA polymerase, AIDS and kidney disorders (Mao *et al*., 2016; Devi *et al*., 2017; Meena *et al*., 2018). *Phyllanthus amarus* Schum and Thorn and *Phyllanthus niruri* L. have been frequent targets of ethnopharmacological work all over the world, mainly in Brazil, U.S.A, Malaysia, Cuba, Peru, Caribbean, China, Nigeria, Africa and India (Devi *et al*., 2017; Meena *et al*., 2018).

Phyllanthus sp. contains bioactive compounds, including flavonoids, terpenes, lignins, phenols, saponins, terpenoids, alkaloids, and tannins (Bahar *et al*., 2011; Hidanah *et al*., 2022). This plant has a natural antioxidant, antimicrobial, and immunomodulator, which will increase the immune system's components and improve the immune system's function (Hidanah *et al*., 2018). Bioactive compounds have antimicrobial (Adeolu and Sunday, 2013; Unigwe *et al*., 2021), anti-inflammatory (Dada *et al*., 2014; Unigwe *et al*., 2020), anti-diabetic (Evi and Degbeku, 2011), antioxidant (Lim and Murtijaya, 2007), anticonvulsant activity (Manikkoth *et al*., 2011), anti-diarrhoeal

(Unigwe *et al*., 2021), anti-carcinogenic and anticancer (Rajeshkumar *et al*., 2002) as well as antiviral (Salazar *et al*., 2011; Prasad *et al.,* 2013).

The most dominant bioactive compounds in *Phyllanthus* sp. are hypophyllanthin, catechin, epicatechin, rutin, and quercetin, and chlorogenic, ellagic, caffeic acid, malic, and gallic acids (Mediani *et al.,* 2017). These compounds have been reported to have antibacterial properties (Mujeeb *et al.,* 2014). *Phyllanthus niruri* L. extract inhibited the growth of *Escherichia coli,* which was indicated by a clear zone at 19.3 mm (Lestariningsih *et al.,* 2015a). *P. niruri* L. powder at a level of 1.2% can minimize *E. coli* in the broiler intestine (Lestariningsih *et al.,* 2015b). It was also reported that 65% *P. niruri* L. extract at a dose of 1 mL/kg body weight, administered orally for 7 days reduced white blood cells in chickens infected with *Mycoplasma gallisepticum* (Hidanah *et al.,* 2018). The administration of 10 g/kg *Phyllanthus amarus* powder to chickens not infected with bacteria decreased the number of leucocytes but increased the red blood cell count (Unigwe *et al.,* 2020). When 100 mg/mL concentrations of the water, 50% ethanol and petroleum ether extracts of *P. amarus* was screened for preliminary mycobactericidal activity, the water and 50% ethanol extracts showed activity against *Mycobacterium smegmatis* with a zone of inhibition of 1.5 ± 0.2 and 2 cm ± 0.5 respectively. *P. amarus* had a minimum inhibitory concentration (MIC) of 50 mg/mL and 100 mg/mL for the 50% ethanol and aqueous extracts respectively, while rifampin had an MIC of 0.1 µg/mL (Bekoe *et al*., 2020). Therefore, this review was aimed at underscoring the medicinal values hidden in *Phyllanthus* species of herb, which is easily seen around our surrounding as weed.

History of *Phyllanthus amarus*

Phyllanthus niruri also known as *Phyllanthus amarus* Schum and Thonn is a member of *Euphobiaceae* family. The origin of *Phyllanthus amarus* is tropical America; from there it spread as a weed to other tropic and sub-tropics. It is a tropical annual herb shrub which grows as weed in moist humid waste land (Adeneye and Senebo, 2008). *P. niruri* is among more than 500 *Phyllanthus* species that are widely spread in temperate and tropical climates region (Iizuka *et al*., 2007). It grows 30 - 40 cm in height, has small leaves and yellow flowers; the stem has green capsule, and blooms with flowers with 5 white sepals and apical acute anther. The fruit has green capsules, and smooth and fruiting pedicels while seeds are longitudinally rugose (Obianime and Uche, 2009). It is found throughout the tropics and sub- tropics such as West Africa (including Nigeria and Ghana), Europe, Asia (including China, Pakistan, India and Malaysia indian ocean), central and south America as medicinal plant for the treatment of various diseases (Etta, 2008; Jain *et al*., 2008). The plant has been used for a long period of time (thousands of years) in Ayurvedic traditional medicine for various illnesses (Adedapo *et al*., 2005). In India, *Phyllanthus niruri* is one of the most important traditional medicines used for the treatment of jaundice, asthma, hepatitis and urolithic disease (Ishimaru *et al*., 1992).

Phyllanthus is the largest genus of Phyllanthaceae family. It is further subdivided into 11 subgenera including Gompidium, Bortryanthus, Conani, Cicea, Emblica, Ericocus, Isocladus, Kirganelia, Phyllanthodendron, Xyllophylla, and Phyllanthus. There are 1,270 species of *Phyllanthus* distributed throughout most of the subtropical and tropical regions including tropical Africa, tropical America, Oceania, and Asia (Hoffmann *et al*., 2006). About 200 *Phyllanthus* species are widely distributed in tropical America, mainly in the Caribbean and Brazil (Unander *et al*., 1995). There are 20 species of *Phyllanthus* commonly found throughout Malaysia which include *P. amarus*, *P. albidiscus*, *P. chamaepeuce*, *P. columnaris*, *P. debilis*, *P. elegans*, *P. emblica*, *P. filicifolius*, *P. gomphocarpus*, *P. gracilipes*, *P. oxyphyllus*, *P. pachyphyllus*, *P. pulcher*, *P. reticulates*, *P. ridleyanus*, *P. roseus*, *P. sikkimensis*, *P. urinaria*, *P. virgatus*, *and P. watsonii* (Burkill, 1966). Of all these, *Phyllanthus* species, *P. amarus*, *P. emblica*, *P. urinaria*, *P. niruri*, *Phyllanthus acidus L.*, *P. fraternus*, *P. reticulatus*, and *P. simplex* are widely used in traditional medicine to heal immune-related diseases and their reported immune-modulating properties in cell, animal, or human studies.

Figure 1: *Phyllanthus* species (Phyllanthaceae) pictorials; **(A)** *P. amarus*, **(B)** *P. urinaria*, **(C)** *P. emblica*, **(D)** *P. niruri*, **(E)** *P. acidus*, **(F)** *P. fraternus*, **(G)** *P. reticulatus*, and **(H)** *P. simplex*.

P. amarus Schum and Thonn (synonym: *P. niruri* Auct) is found in tropical and subtropical regions. It is an erect annual herb, usually found in fields, grasslands, and forests and is erect annual herbs, 10–60 cm tall. Leaves distichous, flowers small in leaf axils, 1–2 together. Perianth segments 5 or 6, green with broad scarious margins, enlarged in fruiting. Stamens 3; filaments entirely connete. Styles bifid at the apex. Fruits globose, trigonous, depressed at the apex. Seeds 3-gonous, with 5–7 sub-parallel longitudinal ribs (Mitra and Jain, 1985).

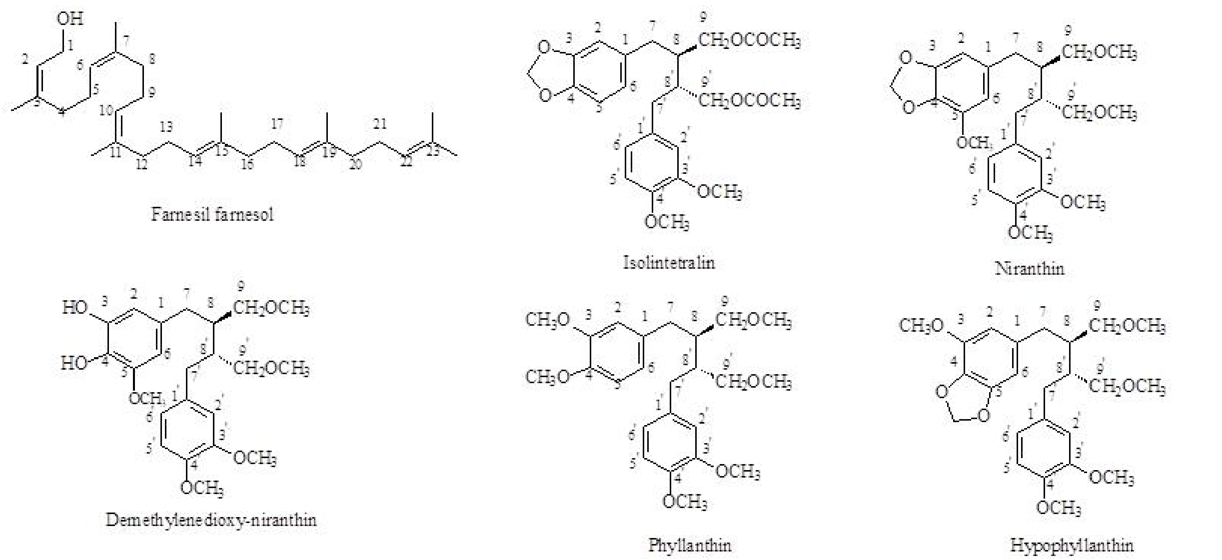

Figure 2: Chemical structures of some *Phyllanthus amarus* bioactive constituents.

Source: Maria *et al*. (2019)

Table 1: Phytochemicals in *Phyllanthus amarus*

Compound	Constituent
Alkaloids	Isobubbialine and Epibubbialine (Houghton *et al*., 1996)
Tannins	Geraniin, corilagin, 1,6-digalloylglucopyranoside rutin , quercetin-3-*O*-glucopyranoside , Amarulone, Phyllanthusiin D and Amariin **(**Foo and Wong, 1992; Foo, 1993).
Lignans	Niranthin, Nirtetralin, Phyltetralin, Hypophyllanthin, Phyllanthin, demethylenedioxy-niranthin, 5-demethoxy-niranthin, Isolintetralin **(**Kassuya *et al*., 2006; Leite *et al*., 2006; Maciel *et al*., 2007 ; Srivastava *et al*., 2008).
Ellagitannins	Amariin, 1-galloyl-2,3-dehydrohexahydroxydiphenyl (DHHDP)-glucose, Repandusinic acid, Geraniin, Corilagin, Phyllanthusiin D, and flavonoids namely rutin, and quercetin 3-O-glucoside, 1 Ogalloyl- 2,4-dehydrohexahydroxydiphenoyl-glucopyranose elaeocarpusin, repandusinic acid A and geraniinic acid **(**Foo, 1995 ; Londhe *et al*., 2009)
Volatile oil	Linalool and Phytol **(**Moronkola *et al*., 2009).
Tritepene	(2Z, 6Z, 10Z, 14E 18E, 22E-farnesil farnesol) **(**Maciel *et al*., 2007).

P. niruri Linn. (synonyms: *Diasperus chlorophaeus* (Baill). Kuntze. *Nymphanthus niruri (L)*. Lour., *P. carolinianus* Blanco, *P. chlorophaeus* Baill., *P. parvifolius* Steud., *P. purpurascens* Kunth., *P. rosellus* (Müll.Arg). Müll.Arg., *P. williamsii* Standl). It is a small erect annual herb growing up to 30–40 cm in height and is indigenous to the Amazon rainforest and other tropical areas, including South East Asia, Southern India, and China. Its leaves are 7–12 cm long, and they are alternate, sessile oblong. It has small off-white-greenish flowers, which are solitary, auxiliary, pedicellate, apetalous, and monoecious (Mitra and Jain, 1985). *P. niruri* is closely related to *P. amarus* in appearance and phytochemical contents, but a recent cladistic analysis indicated that the *Phyllanthus* genus is paraphyletic, and therefore, these two problematic and confusing species, *P. niruri* and *P. amarus*, are two individual species (Lee *et al*., 2006).

P. urinaria L. (synonym: *P. leprocarpus* Wight) is widely distributed in pantropic areas. It is a monoecious and short-lived perennial herb and may grow up to 60 cm tall. Erect, annual, glabrous herbs, leaf-bearing branchlets short, flattened, or slightly winged. Leaves are distichous, closely placed. Flowers are minute, axillary, solitary, subsessile. Stamens are 3; filaments connect into a column. Fruits depressed globose, echinulate and scarcely lobed. Seeds are trigonous, rounded on back, transversly rugose (Kuttan and Harikumar, 2011).

P. emblica L. (synonym: *Emblica officinalis* Gaertner). Distributed throughout tropical and subtropical India, wild or planted. It is a deciduous tree. The tree is small to medium in size, reaching 1–8 m in height. Young branch lets reddish brown, hairy, leaves apiculture obtuse, rounded, or chordate at base, glabrous beneath, about 18 × 1.2 cm. Flowers are greenish yellow, usually monoecious. Fruit fleshy more than 1.5 cm in diameter is nearly spherical, light greenish-yellow, quite smooth, and hard on appearance, with six vertical stripes or furrows. The branchlets are not glabrous or finely pubescent, 10–20 cm long, usually deciduous; the leaves are simple, subsessile and closely set along branchlets, light green, resembling pinnate leaves (Kuttan and Harikumar, 2011).

P. acidus L. (synonyms: *P. distichous L.*, *Cicca acida* L., *Cicca disticha* L). is native to Malaya Islands and Madagascar and is found throughout Asia and also in the Caribbean region, Central and South America. It is a deciduous trees reaching 2 to 9 m high. Leaves are distichous, light green above, glaucous beneath. Flowers are densely clustered and elongated, simple or branched racemes from old, defoliated branches, male flowers numerous, female 1–2, stamens 4, much longer than perianth. Ovary is 3–4 locular. Fruits fleshy, depressed globose, 6–8 lobed, pale yellow. Fruits borne in loose clusters are pale yellow or white, waxy, crisp, juicy, and very sour with edible small yellow (Kuttan and Harikumar, 2011).

P. fraternus G.L. Webster (synonyms: *P. fraternus* subsp. *togoensis* Jean F. Brunel & J.P. Roux *P. lonphali* Wall.) distributed in Tropical Asia especially in Indian subcontinent and Pakistan. It is an erect, annual plant growing up to 45 cm, occasionally to 60 cm (Balakrishnan and Chakrabarty, 2007).

P. reticulatus Poir (synonym: *Kirganelia reticulata* Poir). An Asian species of *Phyllanthus* distributed throughout tropical India. It is a large, glabrous or pubescent, straggling shrub which grows up to 5 m high. Flowers are auxiliary; the male flowers in fascicles of 2–6, the females are solitary. Perianth segments 5–6, oblong, alternatively with disk glands. Stamens are 5, the inner 3 with their filaments connete into column, the outer 2 free, shorter. Ovary is 5–10 locular, styles 3, minute. Fruits fleshy, depressed globose, dark purple or black, shining. Seeds 8–10, trigonous granulate (Kawakita and Kato, 2009).

P. simplex Retz. (synonyms: *P. virgatus* G. Forst). Distributed in South Asia; India, Sri Lanka to SE. Asia, S. China, Indo-China, and

Malesia to Pacific Islands. It is fairly common along roadsides, in open fields and dry deciduous forests. Erect or diffuse perennial herb, up to 20 cm high. Leaves are distichous, subsessile. Flowers are usually solitary, on slender axillary pedicels. Perianth segments oblong, obtuse, slightly enlarged in fruit. Stamens are 3, distinct; anthers didymous. Style short, bifid. Fruits are globose, 3-lobed. Seeds trigonous, rounded on back, covered with minute tubercles in irregular lines, dark brown (Kuttan and Harikumar, 2011).

Ethnomedicinal values

Several *Phyllanthus* species have been utilized for a long time by traditional healers of India, China, Brazil, and countries in the Southeast Asian regions as potent ethnomedicines to treat numerous diseases including those related to the human immune system. *P. amarus*, *P. emblica*, *P. niruri*, *P. reticulatus*, *Phyllanthus corcovadensis*, and *P. fraternus* are among others that are widely used as ethnomedicines in many parts of the world. In Brazil and in many South American countries, the infusion of roots, stems, and leaves of most *Phyllanthus* species have been used to cure a broad spectrum of diseases including intestinal infections, hepatitis B, diabetes, kidney, and urinary bladder disturbances (Calixto *et al*., 1998). In Asia, several *Phyllanthus* species are used as febrifuge, diuretic, deobstruent, stomachic, and antiseptic. Ayurveda uses the most number of *Phyllanthus* species where 15 species have been used in the management of genitourinary, hypertension, cancer, skin, digestive, hepatic, and respiratory disorders (Nain *et al*., 2012; Sarin *et al*., 2014). Among these, *P. niruri* is the mostly used as a remedy for inflammation, fever, malaria, lithiasis, gonorrhea, and hepatitis. *P. amarus* is used widely in Ayurvedic medicine for the treatment of stomach, liver, kidney, genitourinary system and spleen problems, menorrhagia, gonorrhea, and other genital infections. It is also beneficial in intermittent fevers, diarrhea, ulcers and wounds, gastropathy, dysentery, ophthalmopathy, and scabies (Bagalkotkar *et al*., 2006; Ifeoma *et al*., 2013). In Thailand, six *Phyllanthus* species are used extensively as ethnomedicines. *P. urinaria, P. amarus*, and *P. virgatus* are used for the treatment of gonorrhea, diabetic, jaundice, and hepatic disorders while the other species, *P. niruri*, *P. acidus*, and *P. reticulatus* are used to treat hypertensive, malarial fever, constipation, and skin and urination disorders. In China, five species are widely used in Tibetan and Traditional Chinese Medicine to treat anuria, dropsy, hypertension, sore throat, and hepatitis B as well as blood and bile disorders. Particularly, *P. niruri*, *P. simplex*, and *P. reticulatus* are used for the treatment of inflammation, urinary infection, rheumatism, and ophthalmic diseases (Nain *et al*., 2012). In Africa, six *Phyllanthus* species are used to treat tetanus, malarial fever, and wound (Omulokoli *et al*., 1997; Ifeoma *et al*., 2013). Specially, in Cameroon, Ghana, Ivory Coast, Kenya, Nigeria, and Zambia, the stem, root, and leaves of various species of *Phyllanthus* are used for the remedy of tetanus, wound, fever, and sexually transmitted diseases.

Phytochemistry

Many phytochemical, biological, and pharmacological studies of *Phyllanthus* species have been performed due to tremendous ethnomedicinal and therapeutic potentials of the plants. More than 510 compounds have been isolated and identified from several *Phyllanthus* species. Most of the species were reported to comprise of diverse combinations of secondary and bioactive metabolites including lignans, triterpenes, sterols, alkaloids, flavonoids, ellagitannins, and other polyphenols. These compounds provide important medicinal properties to the plants. There are already a few reviews on the phytochemistry and pharmacological properties of *Phyllanthus* species (Calixto *et al*., 1998; Nahar *et al*., 2011; Patel *et al*., 2011; Sarin *et al*., 2014). Specially, the lignans and tannins isolated from genus *Phyllanthus* have been evaluated for their wide variety of biological activities. Corilagin (**1**), geraniin (**2**), and gallic acid (**3**) are the three most predominant metabolites found in this genus. Mostly, corilagin (**1**), geraniin (**2**), gallic acid (**3**), phyllanthin (**4**), hypophyllanthin (**5**), ellagic acid (**6**), phyltetralin (**7**), niranthin (**8**), catechin (**9**), quercetin (**10**), astragalin (**11**), and chebulagic acid (**12**) are the bioactive metabolites that have been intensively investigated and reported to exhibit diverse biological and pharmacological effects including immunomodulatory activities (Jantan *et al*., 2014).

Chemical components of *Phyllanthus*

An initial phytochemical exploration of *Phyllanthus* species reported the occurance of terpenoids, alkaloids, glycosides, flavonoids, tannins, and saponins (Mao *et al*., 2016; Lee *et al*., 2016). Phenolic compounds, especially tannins, are the major constituents of *Phyllanthus* plants. More than 100 phenolic constituents with diverse biological activities were comprehensively identified in the fruits of *P. emblica* L. using HPLC-MS (Yang *et al*., 2012). It is also emphasized that different parts of *Phyllanthus* plants have different isomers of the same compounds. *Phyllanthus* species are rich in phytochemical diversity, with compounds such as tannins, phenylpropanoids, terpenoids, phenolic compounds, flavonoids, alkaloids, saponins and many of their glycosides. Almost 81 compounds have been isolated from *Phyllanthus* spp. During 2016–2018, the majority of which were phenylpropanoids, triterpenoids, diterpenoids, and flavonoids.

The components isolated from each *Phyllanthus* species

a) Phenylpropanoids

Phenylpropanoids constitute the most prevalent class of compounds in the genus Phyllanthus. Thirty seven compounds were identified from *P. glaucus* (Nguyen *et al*., 2016), *P. amarus* (Muthusamy *et al*., 2016; Pereira *et al*., 2016 ; Pereira *et al*., 2017), *P. urinaria* (Muthusamy *et al*., 2016) and *P. brasiliensis* (Borges *et al*., 2018). Among these compounds lignans such as neolignan, norlignan and sesquineolignan were the most prominent. Interestingly, most of the compounds were present in the form of enantiomers in *P. glaucus*, including nine pairs of enantiomeric lignans **1**–**18**.

b) Terpenoids

Terpenoids are another major class of chemicals in the genus Phyllanthus. About 19 compounds including 11 triterpenoids **38**–**48**), seven diterpenoids **49**–**55**, and one monoterpene **56**) were identified in *P. hainanensis* (Fan *et al*., 2017) and *P. urinaria* (Chung *et al*., 2016; Wu *et al*., 2017). It is noteworthy that compound **38** is a new skeleton compound, which incorporates an unprecedented 6/9/6 heterotricyclic system in the lower-left and a highly oxygenated 5,5-spirocyclic ketal lactone motif in the upper-right. Compounds **42**–**48** are lupine type pentacyclic triterpenoids.

c) Phenolic Compounds

Seven phenolic compounds, including one new mucic acid 1-ethyl 6-methyl ester 2-O-gallate (**57**), together with six known phenolic compounds such as gallic acid (**58**), methyl gallate (**59**), ellagic acid (**60**), 1,6-di-O-galloylglucose (**61**), mucic acid 1,4-lactone methyl ester 5-O-gallate (**62**), and mucic acid dimethyl ester 2-O-gallate (**63**) were isolated from the fruits of *P. emblica* L. (Zhang *et al*., 2017, Yan *et al*., 2017).

The gallotannins corilagin (**64**) and geraniin (**65**) were also isolated from *P. niruri* and *P. muellerianus* respectively (Boakye-Gyasi *et al*., 2016).

d) Flavonoids

Compounds **66–69** are kaempferols, which contain one kaempferol (**66**) and three kaempferol glycosides (**67–69**), and were identified from *P. acidus* (Tram *et al*., 2016). Quercetin (**70**) and its glycoside rutin (**71**) were found in extracts of both *P. niruri* L. (Kaur *et al*., 2016) and *P. amarus* (Putakala *et al*., 2017). Two new chalconoid analogues with anti-tobacco mosaic virus (TMV) activity, namely emblirol A (**72**) and B (**73**), and flavanol catechin (**74**) were isolated from the roots of *P. emblica* L. (Yan *et al*., 2017).

e) Alkaloids

Five securinega alkaloids including (+)-allonorsecurinine (**75**), ent-norsecurinine (**76**), nirurine (**77**), bubbialine (**78**), and epibubbialine (**79**) were isolated from *P. fraternus* G.L. Webster (Komlaga *et al*., 2017).

Biological activities of *Phyllanthus*

i) Parasitology

The study of parasites and their relationships with the host, called parasitology, has been a quite vast area of research in the last few decades. A lot of studies have focused on plants to find active ingredients that can fight various pathogens and stop their activity in the host. *P. fraternus* G.L.Webster (Phyllanthaceae) is enriched with various alkaloids such as the securinega alkaloid (+)-allonorsecurinine and many other previously known alkaloids. These compounds showed highly antiplasmodial activity against chloroquine-resistant (W2) and -sensitive (3D7) strains of *Plasmodium falciparum* (Komlaga *et al*., 2017). Higher oxidative stress features prominently in the pathogenesis of malaria, especially anaemia and patho-physiological modifications in certain body organs. Seed extracts of *P. amarus*, chloroquine (CLQ) and artesunate (ATS) may effectively reduce this oxidative stress alone or in combination with various vitamins (A, B, C and E) in *Plasmodium berghei*-infected mice. The highest antioxidant activity was shown by *Phyllanthus* seed extracts alone or in combination with vitamins (A, B, E) in *P. berghei* (NK 65 strain) infected mice. The combined activity of artesunate/vitamins also showed an enhanced antimalarial activity due to their antioxidant activity, while combination with vitamin C was counterproductive (Ojezele *et al*., 2017). Human schistosomiasis is an important but neglected disease in tropics caused by blood flukes (*Schistosoma* spp.), which affects around 0.3 million people annually. The only known reported treatment is the use of paraziquantel (PZQ). De Oliviera *et al*. (2017) tried crude hexane (HE) and ethanolic (EE) extracts of *P. amarus* in mice infected with *Schistosoma mansoni* (BH strain).

The in vivo schistosomicidal activity evaluation of mice fed with extracts of *P. amarus* once, for two different infection periods at 30 and 45 days post-infection showed that histopathologically, granuloma decreased in both number and size for groups treated with 250 mg/kg of HE (45 dpi) or EE (30 or 45 dpi). Both HE and EE of *P. amarus* have antischistosomal activities, however, they act differentially according to the parasites' age. The schistosomicidal activity results in groups treated 30 days post-infection is extremely important since praziquantel does not show any activity against the juvenile forms of *Schistosoma* spp. (De Oliviera *et al*., 2017). *P. amarus* HE and EE extracts showed promising results against *S. mansoni* in vivo (De Oliviera *et al*., 2017). The dried fruits of *Emblica officinalis* (syn. *Phyllanthus emblica*) showed antitrypanosomal activity and cytotoxic effects in vitro. Vero cell line cells were incubated with *Trypanosoma evansi* over 12 h and treated with various concentrations (250~1000 g/mL) of *E. officinalis* for an in-vitro cytotoxicity assay. A sharp decrease in trypanosome number was observed at 250 g/mL concentration, and trypanosomes were completely killed after 5 h of treatment. This is statistically equivalent to the 4th hour of diminazine aceturate (Berenil) treatment, the standard reference drug used. *E. officinalis* dried fruits demonstrated a potential pathway for the development of new trypanocides if in-depth investigations were to be put in place (Peter *et al*., 2016).

ii) Cardiovascular protection

A large number of people across the globe suffer from heart/stroke attacks, mainly due to poor life styles and increased sugar/carbohydrate intakes. In a recent study, the cardioprotective action of aqueous extracts of *P. amarus* was studied against high-sugar (fructose) diet-mediated cardiac damage in Wistar rats. Following 60-days of sugar diet, heart and aorta tissue samples were collected for further histopathological and biochemical analyses. Co-administration of *P. amarus* aqueous extracts plus glucose-diet for a specified time period (60 days) inhibited cardiac and aortic lipids levels (total lipids, triglycerides, total cholesterol and free fatty acids) and reduced phospholipid formation (Putakala *et al*., 2017). Histopathological evaluations of the heart and aorta tissues highlighted that the plant aqueous extracts treatment lessened the deposition of fats and necrosis. This study showed the obvious cardioprotective potential of *P. amarus* aqueous extract for treatment of high sugar-diet mediated oxidative stress in rats is mainly due to its ameliorative antioxidant potential along with its antihyperglycemia and antihyperlipidemic properties (Putakala *et al*., 2017). Moreover, the phytochemical profiling of the aqueous extracts of *P. amarus* indicated it may contain the flavonoids quercetin and rutin, the lignans phyllanthin and hypophyllanthin, saponins and the phenolic compound gallic acid, all of which are potent drivers of cardioprotective action (Putakala *et al*., 2017). In another study, a combined ethanolic extract of *P. emblica* fruits with an ethanolic extract of *Alpinia galanga* rhizomes (7:3) showed a strong synergistic antioxidant response against various reactive oxygen species in endothelial cells (ECV304) in a dose-dependent fashion, and caused an increase in cell viability. It was found that the potent and active ingredient is quercetin, which at 10 g/mL concentration reduced the H_2O_2-mediated lipid peroxidation. When combined with ellagic acid and hydroxycinnamic derivatives, quercetin may aid antioxidant-mediated cytoprotection (Chansriniyom *et al*., 2018).

iii) Antioxidant Activity

Antioxidants are active compounds that have the potential to mitigate the oxidation and degradation of various cellular proteins and ingredients by reactive oxygen species (ROS). Antioxidants play a crucial role in good health as in at-rest conditions ROS and antioxidants maintain a steady balanced level in the body (Devi *et al*., 2016). Medicinally important flora have played a role in resolving health issues throughout the world for centuries, and have currently gained international focus in recent decades. The presence of antioxidant molecules in plants is well documented and there is an ever increasing demand for natural antioxidants over synthetic additives (Akporowhe *et al*., 2016). Normal metabolism of oxygen and exogenous factors continuously generates free radicals i.e. ROS which may initiate a cascade of chemical reactions that could be damaging to the human body (Rusmana *et al*., 2017).

Once these chemical cascades are initiated *in vitro* they may produce damage that leads to a decrease in number of viable cells (Singh *et al*., 2016). The fruit and leaf extracts of *P. acidus* have been reported to possess a variety of antioxidants, which are well known to quench ROS generated by the cellular metabolism, and check oxidative stress-mediated ailments such as cardiovascular diseases and inflammation (Angamuthu *et al*., 2016). Moreover, leaf water extracts of *P. amarus* are desirable due to their maximum yield of the biologically potent antioxidant compounds for in vitro antioxidant activity, ROS scavenging and inhibition of lipid peroxidation (Nguyen *et al*., 2017). Singh and colleagues studied ethanolic and aqueous extracts of *P. niruri* to find antioxidant activity by using DPPH (2,2-diphenyl-1-picrylhydrazyl) radical and H_2O_2 scavenging assays (Singh *et al*., 2016). A standard antioxidant (ascorbic acid) was used as control to compare the aqueous extract antioxidant efficacy and confirmed the strong antioxidant activity, however, ethanolic extracts of *P. amarus* and *P. niruri* showed higher ROS scavenging response compared to aqueous extracts (Singh *et al*., 2016; Ramandeep *et al*., 2017).

Many studies have confirmed the presence in *P. niruri* extracts of quercetin, which is considered as potential natural antioxidant which is even more powerful antioxidant than vitamin E (Dai *et al*., 2016; Rusmana *et al*., 2017). *P. acidus* fruit ethanol and water extracts were also studied to find antioxidant and cytotoxic levels, which showed that water extracts are more potent antioxidant and cytotoxic compared to fruit ethanolic extracts (Andrianto *et al*., 2017). Different solvents viz. acetonitrile, alcohols like ethanol and methanol, water, ethyl acetate, and dichloromethane were used through multiple extraction methods such as conventional, ultrasound-assisted, microwave-assisted, etc. to determine the extraction efficiency and antioxidant capacity of *P. amarus* (Nguyen *et al*., 2016). Moreover, water and microwave-assisted extraction has been demonstrated as the most efficient solvent and technique for the maximum isolation of biologically active compounds from *P. amarus* for wide application in industry (Nguyen *et al*., 2016). The aqueous extracts of three endemic Cuban *Phyllanthus* species, viz. *P. chamaecristoides* Urb., *P. microdictyus* Urb., and *P. williamioides* Gr. Were examined to determine their antioxidant, photoprotective and antimutagenic activities (Menéndez-Perdomo *et al*., 2017). This study claimed that DNA damage was reduced by *Phyllanthus* aqueous extracts and is not linked with desmutagenic effect in vitro, and genoprotective activity is due to the induction of expression of DNA repair proteins, reduction of ROS and related mechanisms (Menéndez-Perdomo *et al*., 2017). Among the various *Phyllanthus* species, *P. chamaecristoides* extracts have higher antioxidant activity than those of *P. microdictyus* and *P. williamioides*. It is generally believed that the higher antioxidant potential of any compound ultimately lowers the UVR mediated oxidative damage (Menéndez-Perdomo *et al*., 2017). Zhang *et al*. (2014) reported two new compounds (bisabolane-type sesquiterpenoid diphenyl ether derivatives) along with previously 23 known compounds from the fruit extracts of *P. emblica*. These two new isolates were tested for antioxidant capability through DPPH assays and for cytoprotective effects and showed activity against H_2O_2-mediated injury to PC12 cells (Zhang *et al*., 2014).

Long term exposure to pesticides may cause severe effects to most body organs, which have been attributed to an elevation of ROS and genomic DNA damage. *P. emblica* was also reported to be beneficial for in vivo protection against the effects of fungicidal pesticides such as captan, which causes genotoxicity and help generate ROS (Noorudheen and Chandrasekharan, 2016). The extracts could mitigate captan-mediated oxidative stress and genotoxicity which is presumed to be due to the potential antioxidant activity of the *P. emblica* extracts. *P. indofischeri* leaves and bark extracts were prepared in water and ethanol, and found to possess significant amylase inhibitory and antioxidant activity (Kalpana *et al*., 2016). The methanol leaf extracts had better activity than bark extracts, hence providing a clue that *P. indofischeri* can be a useful addition to use as a potent antioxidant and hypoglycemic candidate to combat ROS-mediated ailments. The methanolic leaf extracts of *P. emblica* were examined, and it was said that the polyphenolics present in it may provide strong protection against lipid peroxidation damages, and increased levels of SOD, glutathione peroxidise and catalyse enzymes are primarily due to the presence of gallic acid, rutin, caffeic acid, and kaempferol (Tahir *et al*., 2016; Sabir *et al*., 2017).

P. muellerianus (Kuntze) Exell., is used as a wound healing agent in different African countries.

Geraniin, a powerful antioxidant, was identified as a major constituent in the aqueous extracts of *P. muellerianus* that help reduce oxidative stress and boost the healing process in chronic wounds (Boakye *et al*., 2016). The effects of geraniin in treating chronic wounds are mainly due to elevation of SOD, CAT and APx levels, and decreased malondialdehyde (MDA) levels at the wound site. Moreover, geraniin significantly and efficiently reduced ferric ion *in vitro*, which helped block the iron-mediated amplification of ROS (Boakye *et al*., 2016). The ethanolic leaf extracts of *P. amarus* were studied to find the cause of modification in serum antioxidant levels along with ROS-mediated MDA in mice,and it was reported that the antioxidant defense capacity and revitalization of the blood in treated mice was increased, which might due to the presence of previously reported compounds (Akporowhe and Onyesom, 2016). *P. urinaria* has a well known history in traditional medicine systems to treat cancers, particularly osteosarcoma, which is one of the most aggresive cancers of bones. Osteosarcomas originally arise from the primitive transformed cells of mesenchymal origin that form malignant osteoids (Huang *et al*., 2016). The aqueous preparations of *P. urinaria* affect human osteosarcoma in vivo and significantly reduced tumorigenesis, but have no effect on the rest of the body organs. The reduction in tumor development was suggested to mainly be due to mitochondrial dysfunction linked with dynamic changes brought up by apoptosis and anti-angiogenesis induced by *P. urinaria* (Huang *et al*., 2016). The in vitro anti-oxidant and anti-proliferation potential of the water extracts made from the aerial parts and roots of *P. debilis* be studied with special focus on the role of polyphenolics and its broad utilization. The roots of *P. debilis* have more flavonoid contents than the aerial parts (Perera *et al*., 2016).

iv) Organ protective effects

Among many other ailments, renal disease is considered as the 9th major cause of mortality across the world, and is considered the sole clinical sign of this disease. The disease is characterized by reduced excretory function by the kidney, and hence reduced glomerular filtration rate (GFR), with abnormal homeostasis in blood chemistry. Renal failure disease is mainly caused by environmental pollution, particularly by heavy metals which pose a threat to the biosphere and and particular to people exposed to industrial wastes or effluents, or farm workers, primarily attacking the kidneys. For instance, cadmium (Cd) enters the kidneys where it deposits in the proximal tubules (Olubunmi *et al*., 2017). Cadmium causes a decline in kidney activity by elevating blood urea and creatinine levels, which leads to further kidney damage by exposure to leaf extracts of *P. amarus*. It was suggested by Olubunmi *et al*. (2017) that *P. amarus* extracts have no prophylactic or ameliorative effects on Cd-mediated kidney damage, and rather that continuous exposure to these extracts are deleterious to the kidney, but the Ayurvedic system of medication reports that *P. emblica* fruits are potent herbs, and hydroalcoholic extracts provide protection against hepatic disorders. Ethanolic extracts of fruits of *P. emblica* provide hepatoprotection mainly because of the high ROS scavenging and antioxidant activity of their main constituents like gallic acid and ellagic acid (Abbas *et al*., 2017; Chaphalkar *et al*., 2017). In different human diseases like diabetes, obesity and cardiovascular issues, insulin resistance is increased which is primarily due to higher intake of sugars. The ethanolic extracts of *P. amarus* are quiet beneficial and ameliorate insulin resistance by reducing metabolic syndrome and hepatic ROS levels in rats (Putakala *et al*., 2017). Ethanolic extracts of *P. emblica* L. dried fruits, have been reported to show positive gastroprotective effects in patients by reducing pain, vomiting, insomnia and sleeping disturbances or associated problems (Iqbal *et al*., 2017). Water extract of *P. emblica* potentially reduced lipid peroxidation, mRNA expressions of CYP2E1, TNF and IL-1_, while increasing antioxidant activity and reducing non-alcoholic steatohepatitis in vivo (Tung *et al*., 2018). However, although *P. niruri* extracts are enriched with anti-oxidant and anti-inflammatory activities, no significant clinical benefits were observed in non-alcoholic steatohepatitis treatment (Hassan *et al*., 2017). The fruit extracts of *P. emblica* have ellagic acid as the major component, which helps reduce the ROS generation and fat accumulation, while modulating the expression of lipogenesis- linked genes and up-regulating AMPK signaling in $HepG_2$ cells. Extracts showed an inhibition in cellular steatosis and liver fibrosis in vitro (Lu *et al*., 2016).

v) Analgesic and anti-inflammatory activity

Inflammations are the immune responses to any disturbance in cells or tissues under stress. Prolonged exposure to these various stresses such as pathogens, chemicals, UVR, and pollutants, etc. may lead to serious inflammation that leads to chronic diseases. Inflammation and pain are quiet frequent causes of medical discussion which generally occurs when a tissue is injured (Wagle *et al*., 2016). Recently much focus has been devoted to screening and isolating novel drugs with analgesic potential from various plant sources in order to minimize pain or inflammation with less side effects compared toWestern medicines (Wagle *et al*., 2016). The members of the genus *Phyllanthus* are well studied for their analgesic and anti-inflammatory effects. In a recent study where Swiss albino mice were evaluated for the anti-inflammatory and analgesic properties of leaf ethanolic extracts of *P. acidus*, and it was observed that these extracts displayed remarkable action against inflammation and pains when applied at a final concentration of about 200 mg/kg of total body weight (Hossain *et al*., 2016). A comparative study to find anti-inflammatory, anti-arthritic and analgesic activity of various herbal extracts of *Bacopa monnieriis*, *Cassia fistula* and *P. polyphyllus* was conducted by Yoon and Lee (2017), which claimed that the extracts in various combination (w/w/w = 1/2/1) had significant anti-inflammatory and analgesic actions. The aqueous extracts of the aerial parts of *P. muellerianus* along with its prominent secondary metabolites, e.g., geraniin, were found to have potential both peripheral and central anti-nociceptive effects in murine models of chemical nociception with the anti-nociceptive action of geraniin involving possibly the opioidergic pathways (Boakye-Gyasi *et al*., 2016). The green synthesis of silver nanoparticles (AgNPs) using aqueous fruit extracts of *P. acidus* represents an environmentally friendly and cheaper source of materials with potential therapeutic roles in cytoprotection and antiinflammation through scavenging nitric oxide and superoxide anions (Manikandan *et al*., 2017). Furthermore, short-term exposure to *P. acidus*-mediated green-synthesized AgNPs did not affect the viability of peritoneal macrophages, and could be a potential therapeutic to treat inflammatory diseases by reducing the expression of IL-1 (Manikandan *et al*., 2017).

The central nervous system (CNS) depressant activity was measured along with antidiarrheal and antipyretic activities of ethanolic leaf extract of *P. acidus* L., which reduced CNS depression significantly in animal models in a dose dependent way (Hossain *et al*., 2016). Moreover, *P. acidus* showed significant antidiarrheal and antipyretic actions, and therefore it could be an excellent source for natural CNS depressant, antidiarrhoeal and antipyretic agents for medical applications (Hossain *et al*., 2016). The comparative therapeutic efficacy of *P. emblica* fruits extract and procaine penicillin in the treatment of subclinical mastitis was studied in 30 subclinical mastitis positive buffaloes. It is concluded that *P. emblica* fruit extract is an inexpensive source to treat subclinical mastitis in dairy buffaloes and can be used as an alternative to antibiotic therapy like procaine penicillin (Khan *et al*., 2018). In inflammatory ulceration *P. niruri* is commonly applied in traditional medication systems to treat ulcers and inflammation. The methanolic extract of *P. niruri* leaves was used for its anti-inflammatiory and anti-ulcer activities, which suggests that leaf extracts are strong enough to reduce inflammation and provide protection against ulceration, as ascertained by regeneration of mucosal layer and substantially prevented hemorrhage and edema (Mostofa *et al*., 2017).

Another study recently evaluated the anti-nociceptive and anti-inflammatory potential of phytosterols isolated from the chloroform extracts of *P. maderaspatensis* (CEPM) through the carrageenan-induced hind paw oedema and hot plate method in male Wistar rats. CEPM extract and pentazocin had significant effects on the increase of the basal reaction time compared to control. This demonstrated the potential anti-inflammatory and analgesic effect of the CEPM which supports the claims by traditional medicine practitioners (Wagle *et al*., 2016). Significant hypoglycemic, anti-diarrheal, analgesic, and anesthetic activities were shown by *P. acidus* pulp extracts (Afrin *et al*., 2016).

vi) Immunomodulatory effects

The human immune system is an organized system comprised of many different immune cells such as macrophages, neutrophils, T-lymphocytes, natural killer cells and various other specialized immune molecules that have evolved to mediate resistance against infections. Wide ranging ethnomedicinal or traditional uses of *Phyllanthus* plants are mainly linked to its active ingredients and broad pharmacological actions, e.g., immunomodulation, anti-viral and antibacterial, diuretic, anti-hyperglycemia and hepatoprotector properties (Tjandrawinata *et al*., 2017). Phytochemicals used as immune-stimulants, are superior to conventional chemotherapeutics and antibiotics. Tuberculosis (TB) is a severe disease, and its progression mainly depends on the strength of the host immune system. *P. niruri* has been reported to boost the immune system in traditional medicine, and it is said that it has a great potential to induce immune cell activity in TB patients in vitro, The *P. niruri* extracts mainly help the release of nitric oxide and hence elevate the phagocytic activity of macrophages in a dose dependent fashion, ultimately modulating the immune responses (Putri *et al*., 2018). Moreover, *P. niruri* leaf extracts have immunostimulating effects on neutrophil activation and the antibody response of *Oreochromis mossambicus*. It is further demonstrated that *P. niruri* plant extracts and their components can be used either as a routine feed supplement to activate the immune system of farmed fishes or as an adjuvant to enhance the efficacy of vaccines (Muthulakshmi *et al*., 2016). *P. amarus* strongly inhibits the phagocytic activity of human neutrophils and reduces cellular immune responses in rats. Moreover, the plant extracts have strong inhibitory effects on cellular and humoral immune responses (ceruloplasmin and lysozyme) suggesting the potential of the plant to be developed as an effective immunosuppressive agent which mainly acts through the inhibition of myeloperoxidase activity and nitric oxide release leading to the release of serum level immunoglobulins (Ilangkovan *et al*., 2016a). Phyllanthin, one of the main and active ingredient in many *Phyllanthus* species (*P. amarus*), has recently been reported to have hepatoprotective and immunosuppressive effects on various in Balb/C mice in a dose-dependent way through the inhibition of CD11b/CD18 adhesion, nitric oxide and myeloperoxidase activity release (Ilangkovan *et al*., 2016a). Based on the level of doses of phyllanthin, a significant inhibition in the proliferation of B and T lymphocytes and down-regulation of Th1 (IL-2 and IFN-) and Th2 (IL-4) cytokines, CD4+ and CD8+ was noted (Ilangkovan *et al*., 2016a).

vii) Antibacterial activities

The ability of a diverse class of microbes to resist known anti-microbial drugs is always been a universal problem leading to exploration of novel anti-microbial drugs from diverse natural sources such as medicinal plants, especially the medicinal flora which has not been examined for their pharmacological potential as anti-bacterial potentials. *Phyllanthus niruri* L. is one of the plants that can be used as a preventive and alternative treatment as a substitute for antibiotics for the treatment of Chronic Respiratory Disease (CRD) in broiler chickens caused by *Mycoplasma galisepticum*. The chemicals contained in meniran (*P. niruri* L.) include antibacterial tannins, saponins, and alkaloids. A 30% plant extract caused up to 65% growth inhibition in *Mycoplasma galisepticum* (Sabdoningrum *et al*., 2017). In continuation of a similar study, Ramandeep and colleagues found that *P. niruri* extracts could potentially inhibit the growth of *Escherichia coli*, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Moreover, *P. niruri* is rich in phytochemicals that have antioxidant and antimicrobial activity, suggesting the need for further in-depth investigations for its systematic use in traditional medicine (Lee *et al*., 2016).

The extracts from *P. amarus* leaves were examined for complete chemical analyses along with their anti-microbial potential. Various stable extracts, i.e., hexane (59%), acetone (57%), and water extracts (48%) were prepared, which contain many alkaloids, saponins, anthraquinones, tannins and phenolics in acidic medium. In general, combining leaf extracts with either bacitracin or erythromycin alone has synergistic effects, thus depicting the crucial advantage of such combinations of these universal antibiotics with extracts of *P. amarus* to treat various infections (Senjobi *et al*., 2017). Various other studies examined the anti-microbial activities for aqueous extracts of above ground parts of *P. muellerianus*, and it was stated that geraniin is the major component in these extracts. In certain an agar-well diffusion assay, micro-dilution method, and time-kill kinetic studies were applied to find the anti-microbial potential of areal plant parts extracts, where geraniin have strong inhibitory effects on *E. coli, P. aeruginosa, S. aureus, B. subtilis*, and two clinical isolates viz. *S. pyogenes* and *C. albicans*, and significantly inhibited the zones of growth. Moreover, the minimal inhibitory concentrations of these aerial plant parts extracts and geraniin were in a variable ranges i.e., 0.31 to 5 and 0.08 to 1.25 mg/mL, respectively. In another experiment where minimum cidal concentration were recorded for the plant extracts (5.0 to 50.0) and geraniin (2.5 to 10 mg/mL), respectively, thus proven that both the extracts and geraniin have strong anti-microbial potential. All these initial studies regarding in-depth exploration of various chemical constituents in *P. muellerianus* extracts further confirmed the occurrence of various terpenes, flavones, saponins, tannins, alkaloids and glycosides. It is further said that, these extracts have geraniin as primer constituent which pose strong anti-microbial potential against the above mentioned bacterial strains (Boakye *et al*., 2016).

In continuation of similar finding, a study examined the antimicrobial potential of volatile oils extracted from leaves of *P. muellerianus*, where they found good inhibitory effects partly on the isolated pure extracellular protease of pathogenic *Klebsiella granulomatis*. These volatile oils showed strong antimicrobial potential as depicted by their inhibitory capability against these proteases. Further the authors proposed that in-depth studies and clinical trials using these oils could define their effectiveness to combat various skin conditions such as third degree burns, cuts, injuries and post-operative wounds infections caused by *K. granulomatis* as well as many related strains (Adesegun *et al*., 2016). Pathmavathi and Thamizhiniyan (2016) prepared various leaf extracts (methanolic, hexane, chloroform, and ethyl acetate) of *P. amarus* and *Plectranthus ambionicus* to study their antifungal and anti-microbial potential. Four Gram positive and three Gram negative bacterial strains along with three species of fungi were tested to screen the best isolate among the various organic plant extracts. The anti-microbial activity of various extracts of both these plant species showed mixed levels of anti-microbial potential towards the selected fungal and bacterial strains, but the ethyl acetate extracts of *Plectranthus ambionicus* and *P. amarus* showed superior antimicrobial potential compared to other extracts. Recently zinc sulphide nanoparticles were synthesized from *P. emblica* leaves and fruit extract to analyze the activity of these significant phytochemicals. These zinc sulphide nanoparticles possess potential antimicrobial activity against many pathogenic organisms (Sathishkumar *et al*., 2017). The anti-*Helicobacter pylori* and urease inhibitory activity of hydroalcoholic extracts of *P. niruri* L. was studied, and it was found that quercetin is one of the major constituents which is thought to be the cause of noncompetitive urease inhibition (Kaur e*t al*., 2016). The leaf extracts of *P. amarus* showed inhibitory effects on *Streptococcus pyrogenes, Streptococcus pneumonae, S. aureus, P. aeruginosa* and *Candida albicans* in a study by Oluboyo *et al*. (2016). Many of the phytochemicals (flavones, terpenoides, various alkaloids, benzenoids, steroids, saponins and complex lipid molecules) were compared with ampicillin, gentamicin and pefloxacin, and observed to possess significant inhibition activity against the growth of selected studied microorganisms in a dose dependent fashion. Moreover, well known antibiotics had no significant inhibitory effect on the tested microorganisms compared to the leaf extracts of *P. amarus* (Oluboyo *et al*., 2016). Gunawan *et al*. (2016) have reported that *P. niruri* extracts mainly contain alkaloids, triterpenoids and flavones, which are highly efficcient to treat dysentery, rheumatism, inflammation and gut worms in children in traditional medication systems. Furthermore, active triterpenoids in the chloroform extracts from the bark of *P. niruri* possess strong antibacterial activity and control the proliferation of *S. aureus* at an optimum concentration (1000 ppm) evidenced by a great 12 mm inhibition zone (Gunawan *et al*., 2016). In another study, remarkable anti-bacterial potential against various fungal and bacterial strains was seen by using silver nanoparticles (AgNPs) obtained from a supercritical CO2 extract of *P. niruri* (Haris *et al*., 2017). The phytochemical analyses of *P. amarus* leaf extracts were studied and presence of alkaloids, saponins, tannins, flavonoids, cyanogenic glycosides and steroids for antimicrobial activity.

The phytochemical examination of the leaf extract of *P. amarus* shows the presence of a variety of bioactive components: alkaloids, saponins, tannins flavonoids, cyanogenic glycosides and steroids in ethanol and ethyl acetate. The extracts of both these solvents were applied to find their potential as anti-microbial agents against *Staphilococcus aureus, Escherichia coli* and *Clostridium albicans*, and were found pretty suitable for the production of advanced anti-microbial drugs (Uzor *et al*., 2016). The leaf methanolic extracts of *P. niruri* showed a well defined antimicrobial activity against Coney lunata and Salmonella typhi, and it was suggested by the authors that this plant is of great clinical importance and may potentially be used in the pharmaceutical industry (Ahamath *et al*., 2017). Chewing gums were prepared having constituents of fruit extract of *P. emblica* and studied in detail for their potential in alleviating and soothing oral health problems (Gao *et al*., 2018). Fruit extracts of *P. emblica* have great pharmacological potential against bacterial growth, inflammation, cellular oxidative stress induced by ROS, and various types of cancers as well as different oral diseases. The focus of the study was changes in the oral microflora in a gum-base-controlled crossover manner caused by the effect of *P. emblica* leaf extracts. Moreover, chewing gums prepared with the extracts of *Phyllanthus* fruits help to stimulate saliva production, producing a significant reduction in the recurrence of clinical oral microflora for a short time period, and are thus proven as a safer way of improving oral health (Gao *et al*., 2018).

Conclusion

The medicinal potentials of these herbs have been documented over some decades. There is therefore, the need to explore its integration in standardized form into alternative medicine and pharmaceutical industries to cure an array of diseases in man and animals. It could also be harnessed as a replacement for the hitherto antibiotic growth promoters in production of animals since the conventional synthetic antibiotics have been banned in most countries of the world due to antibiotic resistance they confer on recipient animals and the end users; humans. Therefore, this compilation will aid further research into the veracity of claims that these plants contain phytochemicals that aid cure/prevention of some diseases.

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