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Review Article

Phyllanthus urinaria: a potential phytopharmacological source of natural medicine

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Abstract: *Phyllanthus urinaria* is an herb species in the family Euphorbiaceae. *P. urinaria*, which grows mainly in tropical regions such as India, Sri Lanka, Indochina, Japan, Malaysia, Indonesia and the United States, has long been used in traditional oriental medicine for the treatment of liver damage, hepatitis, jaundice, renal disorders, enteritis, diarrhea, and dropsy. Experimentally, *P. urinaria* displays antiviral, anti-tumor, hepatoprotective, anti-diabetic, antioxidant, anti-hypertensive, anti-inflammatory, and anti-microbial effects. Phytochemical screening revealed the presence of flavonoids, carboxylic acids, tannins, coumarins, and lignans in *P. urinaria* extracts (PUE). Meanwhile, PUE possess various pharmacological and biological activities. This study summarizes the ethno-medical use, chemical constituents, and pharmacological profile of *P. urinaria*. As a medicinal plant, this herb has emerged as a good source of traditional medicines. However, the composition-activity relationship for this plant deserves further research.

Keywords: *Phyllanthus urinaria*, chemical constituents, antivirus, antitumor, liver protection

Introduction

Phyllanthus urinaria L. (*P. urinaria*), commonly called chamber bitter, is an herb species in the family Euphorbiaceae [1, 2]. Numerous small green-red fruits are found along the underside of its stems. Therefore, the plant is called "YeXiaZhu" in the Pharmacopoeia of the P. R. of China [1]. *P. urinaria* has the features of great number of seeds, high shade tolerance, and extensive root system, and is therefore considered a competitive weed. It is widely found in all tropical regions of the world, including India, Sri Lanka, Indochina, Japan, Malaysia, Indonesia, and the United States.

The whole plant could be used as medicine. As a natural product, *P. urinaria* has long been used in traditional oriental medicine to promote healthy elimination of gallstones and kidney stones, as an immune system inducer, and for liver disease treatment [3, 4]. Evidence indicates that *P. urinaria* extracts possess numerous biological activities (**Figure 1**), including cardioprotective [5], anti-hypertensive [6], antiplasmodial [7], and antioxidant [5, 8] effects. Very recently, the anti-tumor [9], anti-inflammatory [10] and anti-microbial [11] activities of *P. urinaria* were reported. In addition, *P. urinaria* extracts show antiviral activities against hepatitis B virus (HBV) [12-14], herpes simplex viruses (HSV) [15-19], dengue virus [20], enteroviruses [21], hepatitis B virus (HCV) [22], and human immunodeficiency virus (HIV) [23-25]. This herb is also used as traditional medicine for its protective effects against liver disorders [26, 27]. In this review, the beneficial properties of *P. urinaria* and its active components were discussed, so that the potential use of this plant as pharmaceutics or an agricultural resource can be readdressed.

Ethnopharmacology

As a Chinese folk medicine, *P. urinaria* is used for the treatment of liver damage, hepatitis, jaundice, renal disorders, enteritis, diarrhea, and dropsy [28]. *P. urinaria* was shown to have hypoglycemic effects in northern Thailand [29]. In addition, the herb has long been used for liver protection, diabetes, hepatitis, jaundice, and dropsy in India [3]. Furthermore, *P. urinaria*

Figure 1. Schematic effects of *Phyllanthus urinaria* and its active constituents in metabolic syndrome together with some relevant mechanisms.

juice is used for tongue cleaning, appetite stimulation in children, and malaria treatment in Malaysia [30]. The roots and stem of this plant have been used as natural medicine for the treatment of diabetes, hepatitis B virus, and kidney and urinary bladder problems in Korea [31]. Moreover, *P. urinaria* is an important medicinal plant in Indonesia, and traditionally used to treat diseases related to urinary problems, such as kidney stones, and urinary tract infections and malfunction [32]. Meanwhile, *P. urinaria* is used for diabetes and diarrhea treatment in Trinidad and Tobago Trinidad and Tobago [33].

Phytochemistry

Multiple functional compounds with medicinal effects, such as flavonoids, carboxylic acids, tannins, coumarins, and lignans, have been isolated from *P. urinaria* (**Table 1**). In 1993, Yao QQ *et al.* isolated 11 compounds from *P. urinaria* [34]. So far, about 76 compounds have been isolated and identified in this plant.

Polyphenols

Polyphenols are considered the main bioactive compounds in *P. urinaria,* and include 9 flavonoids and 17 tannins. Flavonoids constitute the major chemical components of *P. urinaria*. In 1993, quercetin, rutin and kaempferol were isolated from whole plant extracts of *P. urinaria* [34]. Then, quercetin 3-O-b-D-glucoside, kaempferol 7-methyl ether, rhamnocitrin, and naringin were further isolated from this plant [10, 35, 36]. In addition, two new acetylated flavonoid glycosides, including quercetin 3-O-α-L-(2,4-di-O-acetyl) rhamnopyranoside-7-O-α-L-rhamnopyranoside and quercetin 3-O-α-L-(2,4-di-O-acetyl) rhamnopyranoside-7-O-α-L-rhamnopyranoside, alongside quercetin 3-O-α-L-rhamnopyranoside, were identified [37].

Tannins

Tannins are also very abundant in *P. urinaria*. Zhang LZ *et al.* isolated a novel polyphenolic

Table 1. Chemical constituents of *Phyllanthus urinaria*

Category	Type	Compounds	Reference
Polyphenols	Tannins	Excoecarianin	[40]
		Trimethyl-3,4-dehydrochebulate	[10]
		Phyllanthusiin C	[41]
		Epigallocatechin, epicatechin-3-gallate, epicatechin, epigallocatechin-3-gallate	[42]
		Gallocatechin-3-gallate	[36]
		Repandinin B, Furosin, Repandusinic acid A, Mallotinin, Geraniin, Acetonylgeraniin D, Corilagin	[35]
		phyllanthusin F, phyllanthusiin G	[43]
	Flavonoids	Rhamnocitrin	[10]
		Rutin, quercetin	[10, 36]
		Naringin	[36]
		Quercetin 3-O-α-L-(2,4-di-O-acetyl) rhamnopyranoside-7-O-α-L-rhamnopyranoside, quercetin 3-O-α-L-rhamnopyranoside	[37]
		Quercetin 3-O-b-D-glucoside, Kaempferol 7-methyl ether	[35]
		Kaempferol	[34]
Phenylpropanoid	Coumarin	Ellagic acid, Brevifolincarboxylic acid	[41]
		Methyl brevifolincarboxylate	[10, 34]
		Ethyl brevifolincarboxylate	[34]
	Lignans	Phyllanthin, hypophyllanthin, nirtetralin, niranthin, phyltetralin,	[45]
		(+)-dihydrocubebin, (+)-lyoniresiol, (7R,7'R, 8S, 8'S)-icariol A2, evofolin B, 4-oxopinoresinol, (-)-syringaresinol, (-)-episyringaresinol	[44]
		Virgatusin, lintetralin, 5-demethoxyniranthin, urinatetralin	[45]
	Phenols	Ferulic acid, p-hydroxybenzaldehyde, 3,5-dihydroxy-4-methoxybenzoic acid, dehydrochebulic acid trimethyl ester	[44]
		Gallic acid,methyl gallate	[10, 36]
Terpenoids	Sesquiterpene	Cloven-2β, 9α-diol	[44]
	Monoterpene	(6R)-menthiafolic acid	[44]
	Diterpenoids	Cleistanthol, Spruceanol	[44]
	Triterpenoids	28-norlup-20(29)-ene-3,17β-diol, Betulin, β-betulinic acid, 3-oxo-friedelan-28-oic acid, oleanolic acid, 3R-E-coumaroyltaraxerol, 3R-Z-coumaroyltaraxerol	[46]
		Glochidiol, oleanolic acid	[44]
Volatile oils	Jasmonate derivatives	(+)-cucurbic acid, (+)-methyl cucurbate, methyl[1R,2R,2'Z]-2-(5'-hydroxy-pent-2'-enyl)-3-oxocyclopentaneacetate	[44]
	Aldehyde derivative	5-hydroxymethyl-2-furaldehyde	[44]
Glycosides	Glycosides	β-sitosterol-3-O-β-d-glucopyranoside	[10]
		Gentisic acid 4-O-b-d-glucopyranoside, Syringin	[35]
Steroids	Steroids	β-sitosterol, [3β, 22E]-stigmasta-5,22-diene-3,25-diol	[44]
		daucosterol	[34]

compound phyllanthusin F [38] and an ellagitannin termed phyllanthusiin G was also reported [39]. Further bioassay-guided purification of *P. urinaria* extracts (PUE) led to the isolation of 7 ellagitannins, including repandinin B, furosin, repandusinic acid A, mallotinin, geraniin, acetonylgeraniin D, and corilagin [35]. Meanwhile, Tseng HH reported 4 tannins, including epicatechin, epigallocatechin-3-gallate, epicatechin-3-gallate and gallocatechin-3-gallate. Recently, 4 major compounds, including excoecarianin, phyllanthusiin C, epigallocatechin, and trimethyl-3,4-dehydrochebulate were identified as a plant fingerprint by HPLC/MS [10, 40-42].

Phenylpropanoids

Phenylpropanoids are considered the major bioactive class among *P. urinaria* compounds, and include coumarin, lignans, and phenols. Studies reported 4 coumarin compounds, including ellagic acid, methyl brevifolincarboxylate, ethyl brevifolincarboxylate, and brevifolincarboxylic acid [34, 41, 43]. In addition, 6 phenols (dehydrochebulic acid trimethyl ester, ferulic acid, p-hydroxy-benzaldehyde, 3,5-dihydroxy-4-methoxybenzoic acid, gallic acid, and methyl gallate) were isolated and identified [10, 34, 36, 41, 44].

Lignans constitute the major class of phenylpropanoid compounds. Hu et al. identified 7 lignans, including (+)-dihydrocubebin, (+)-lyoniresiol, (7R,7'R, 8S, 8'S)-icariol A2, evofolin B, 4-oxopinoresinol, (-)-syringaresinol, and (-)-epi-syringaresinol, from this plant [44]. Moreover, Wang CY et al. characterized several lignans from *P urinaria* by HPLC-SPE-NMR, including hypophyllanthin, phyllanthin, phyltetralin, nirtetralin, niranthin, virgatusin, lintetralin, 5-demethoxyniranthin and urinatetralin [45].

Terpenoids

Hu et al. isolated 2 triterpenoids (glochidiol and oleanolic acid), 2 diterpenoids (cleistanthol and spruceanol), 1 sesquiterpene (cloven-2β, 9α-diol), 1 monoterpene [(6R)-menthiafolic acid] from whole plant extracts of *P. urinaria* [44]. Wu Y et al. isolated 7 triterpenoids from *P. urinaria*, including 28-norlup-20(29)-ene-3,17β-diol, betulin, β-betulinic acid, 3-oxofriedelan-28-oic acid, oleanolic acid, 3R-E-coumaroyltaraxerol, and 3R-Z-coumaroyltaraxerol [46].

Other compounds

A number of other compounds have been isolated from *P urinaria*, including glycosides, volatile oils, and steroids. β-sitosterol-3-O-β-D-glucopyranoside, gentisic acid 4-O-b-d-glucopyranoside and syringin are the main glycosides isolated from *P. urinaria* (**Table 1**). In 2007, gentisic acid 4-O-b-d-glucopyranoside and syringin were obtained from whole plant extracts of *P. urinaria* [35]. Then, in 2008, β-sitosterol-3-O-β-d-glucopyranoside was isolated from this plant [10]. Meanwhile, 4 essential oil components, including the 3 jasmonate derivatives (+)-cucurbic acid, (+)-methyl cucurbate, methyl (1R,2R,2'Z)-2-(5'-hydroxy-pent-2'-enyl)-3-oxocyclopentaneacetate, and the aldehyde derivative 5-hydroxymethyl-2-furaldehyde, were isolated from *P. urinaria* [44]. In addition, three Steroids, including β-sitosterol, (3β, 22E)-stigmasta-5,22-diene-3,25-diol and daucosterol were recently isolated from *P urinaria* [34, 44].

Pharmacological properties *P. urinaria*

Antiviral effects

Anti-HBV activity: Despite the availability of effective vaccination programs, HBV infection remains a major world health problem, with about 400 million people affected worldwide [47]. It was demonstrated that *P. urinaria* has good effects on hepatitis B treatment. Indeed, studies reported that PUE markedly inhibit intracellular HBsAg formation [48-50] and repress HBsAg and HBcAg secretion [50, 51]. PUE also significantly reduce HBV DNA levels by inhibiting its synthesis and secretion in HBV infected cells [51, 52]. In *in vivo* experiments, Wu Y et al. demonstrated that PUE markedly repress HBV replication and expression in a HBV transient transfection mouse model [50]. Chen YX et al. showed that PUE significantly reduce serum DHBV DNA in a duck model of HBV infection [53]. In clinical trials, Wang MX et al. demonstrated that *P. urinaria* promotes HBeAg and HBeAb seroconversion from positive to negative in a total of 35 patients with chronic hepatitis B [54]. Tong GD et al. showed that *P. urinaria* effectively decreases HBV-DNA levels, prevents or delays the development of HBV-associated cirrhosis into HCC in 52 patients [55].

P. urinaria compounds exhibit antiviral activities against hepatitis B virus infection [49, 56]. Zhong Y et al. showed that methyl ester dehydrochebulic acid and methyl brevifolin carboxylate possess antiviral activities against HBV [49]. Shin MS et al. identified the flavonoid ellagic acid, which effectively inhibits HBeAg secretion in HepG2 2.2.15 cells (IC50 = 70 μg/ml) [56].

Anti-HSV properties: HSV is one of the most common sexually transmitted diseases worldwide [57, 58]. HSV is a single large double-stranded DNA enveloped virus [58, 59]. In 2005, Yang CM et al. assessed the anti-HSV-1 and HSV-2 activities of different solvent extracts from *P. urinaria in vitro* by plaque reduction assay [16]. The results showed that acetone, ethanolic, and methanolic extracts of *P. urinaria* inhibit HSV-2 but not HSV-1 infection. All 3 extracts likely inhibit HSV-2 infection by altering the early stage of viral infection, diminishing virus infectivity [16].

Further studies demonstrated that Hippomanin A and excoecarianin from the acetone extract of *P. urinaria* effectively repress HSV-2 but not HSV-1 infection *in vitro* [19, 40]. Excoecarianin could inactivate HSV-2 virus particles [40]. Meanwhile, geraniin and 1,3,4,6-tetra-O-galloyl-*b*-D-glucose, isolated from the acetone extract of fresh whole plants, inhibit HSV-1 and HSV-2 infection [18]. Corilagin markedly represses HSV induced brain pathological alterations in an animal model [60]. Corilagin markedly suppresses HSV induced inflammatory cytokines, including TNF-α and IL-1β [60]. Furthermore, findings demonstrated that corilagin protects from HSV-1 encephalitis by inhibiting the TLR2 pathway [61]. Moreover, proteomics showed that *P. urinaria* might affect cytoskeletal protein expression at the early infection and replication stages [62]. Therefore, *P. urinaria* represents a plant that can potentially be used as an alternative anti-herpetic drug.

Other antiviral effects: HCV is associated with several hepatic and extra hepatic disorders, including malignancies [63]. Chung et al. found that the acetone extract of *P. urinaria* alters specific steps of the viral life cycle [22]. They further found its bioactive component loliolide potently inhibits HCV entry [22].

HIV is a lentivirus that causes acquired immunodeficiency syndrome [64]. Zhang et al. demonstrated the polyphenolic extract and gallic acid from *P. urinaria* have anti-HIV-1 activities [65]. In addition, the polyphenolic extract and gallic acid interact with HIV-1 RT, gp120, and P24 [65]. These properties and the anti-HIV-1 activities render the plant interesting for further studies.

Human enterovirus 71 (EV71) and coxsackievirus A16 (CA16) are major causative agents of hand, foot, and mouth disease (HFMD), especially in infants and children under 5 years of age. Yeo et al. showed that corilagin reduces EV71 or CA16 induced cytotoxicity in Vero cells, with significant antiviral activities against EV71 and CA16 [21].

Epstein-Barr virus (EBV) is a gamma herpes virus that modulates the expression of viral genes. Liu KCSC et al. showed that gallotannin, corilagin, ellagic acid, and 7 ellagitannins isolated from *P. urinaria* could inhibit Epstein-Barr virus DNA polymerase [66].

Anti-tumor effects of P. urinaria

In recent years, advances in the anti-tumor effects of *P. urinaria* have been reported. Studies showed that PUE significantly reduce viability in various cancer cell lines [67-70], inducing apoptosis in human cancer cells [71]. The methanolic extract of *P. urinaria* shows higher cytotoxicity in A549 and MCF-7 cells compared with the water PUE [72, 73]. *P. urinaria* extracts, which contain polyphenols such as gallic acid, methyl gallate, epicatechin, epigallocatechin-3-gallate, gallocatechin-3-gallate, rutin, epicatechin-3-gallate, and naringin, markedly inhibit cell invasion and migration [36]. *P. urinaria* also plays a role in angiogenesis *in vivo* [74, 75].

Lung cancer: Lung cancer constitutes one of the malignancies with the greatest incidence and mortality rates, with 1.6 million new cases and 1.4 million deaths recorded yearly [76]. *P. urinaria* exhibits anti-tumor and anti-angiogenic effects in mice with Lewis lung carcinoma. Treatment with PUE significantly inhibits tumor development, with lower occurrence rate and markedly reduced tumor size in mice [69]. Furthermore, tumor neovascularization is repressed by *P. urinaria*-treatment [69]. PUE trig-

ger apoptosis through Bcl-2 downregulation and increased caspase-3 activity in Lewis lung carcinoma cells [67, 68]. Moreover, PUE inhibit A549 metastasis by suppressing ERK1/2 and hypoxia pathways [72, 73]. Tseng HH et al. demonstrated that PUE inhibit metastasis by suppressing MMP-2, MMP-9, and urokinase plasminogen activator, as well as their endogenous inhibitors, i.e. tissue inhibitor of metalloproteinase-2 and plasminogen activator inhibitor-1 [36]. *P. urinaria* also exhibits anti-angiogenic activity by suppressing MMP-2 secretion and inhibiting MMP-2 activity [67]. Therefore, *P. urinaria* could be used as alternative anti-lung tumor drug.

Human osteosarcoma: Human osteosarcoma is one of the toughest malignancies, with few therapeutic modalities [77]. *P. urinaria* inhibits human osteosarcoma cell growth through the extrinsic apoptotic pathway, activating Fas receptor/ligand expression [78]. Meanwhile, PUE repressed Saos-2 cell invasion and migration by inhibiting u-PA via ERK and Akt signaling pathways [79]. Huang ST et al. demonstrated that PUE modulate the mitochondrial dynamics via fusion and fission machineries [70, 80].

Melanoma: Melanoma is the most dangerous type of skin cancer [81]. *P. urinaria* represses melanin formation in melanoma B16 cells [82]. Further studies showed that *P. urinaria* prevents tumor proliferation, metastasis, and angiogenesis by inhibiting MAPKs, Myc/Max, NF-kappaB, and hypoxia pathways in human melanoma cells [83]. Bharali R et al. suggest a possible chemopreventive property of *P. urinaria* in skin papillomagenesis in mice [84].

Hepatocellular carcinoma (HCC): HCC is a highly prevalent health risk, and the third leading cause of cancer related deaths worldwide [85]. Blumberg et al. found that PUE can significantly reduce the liver cancer rate in woodchucks, indicating the overt anti-hepatoma effects of *P. urinaria* [12]. Chudapongse N found that the water-methanolic extract of *P. urinaria* induces cell death in HepG2 cells, in a dose-dependent fashion. This extract profoundly reduces state 3 respirations and the respiratory control ratio [86]. The authors concluded that *P. urinaria* impairs energy metabolism to fight hepatocellular carcinoma [86].

Breast cancer: Breast cancer is the leading type of cancer in women, accounting for 25% of all malignancy cases in females [87]. Lee et al. found that *Phyllanthus* spp. can induce apoptosis, in association with caspase-3 and -7 activation, as well as DNA fragmentation, in A549 and MCF-7 cancer cell lines [73]. Moreover, *P. urinaria* induced apoptosis is mediated by ROS-mediated stimulation of p38 MAPK signaling in the human breast cancer MCF-7 cell line [88].

Prostate Cancer: Prostate cancer is the second most common malignancy and the fifth leading cause of cancer-related death in men [89]. *P. urinaria* induces selective growth inhibition of human cancer PC-3 and MeWo cells through cell cycle modulation and apoptosis induction [90]. Further studies showed that *P. urinaria* suppresses prostate cancer cell proliferation and induces apoptosis through multiple signalling pathways, including MAPK, PI3K/Akt, NF-kappaB, and Hypoxia pathways [90].

Nasopharyngeal carcinoma (NPC): NPC is a common cancer in Taiwan, Hong Kong and southern China [91]. Huang ST et al. (2009) demonstrated that *P. urinaria* reduces NPC-BM1 cell growth *in vitro* through induction of Bax/Bcl-2-mediated apoptosis and reduction in telomerase activity via c-myc signaling [41].

Hepatoprotective effects

Phyllanthus species are well known for their hepatoprotective activities [92, 93]. In an animal model of CCl4-induced acute liver damage, *P urinaria* significantly reduces ALT, inhibits oxidative stress, increases membrane mobility, and decreases liver infiltration and focal necrosis [94, 95]. Further, metabolomics studies identified 17 biomarkers, including L-carnitine, taurocholic acid, and amino acids, in CCl4-induced rats treated with PUE [28]. Moreover, it was shown that *P. urinaria* possesses a dose-dependent hepatoprotective activity in acetaminophen/tert-butyl hydroxide/methionine-and-choline-deficiency induced hepatotoxicity, possibly through inhibition of cytochrome P450, oxidative stress, inflammation, and lipid accumulation [96-98].

The hepatoprotective effects of *P. urinaria* could be attributed to corilagin, phyllanthin, and hypophyllanthin, or the combination of various compounds that constitute this extract. Syamasundar KV et al. showed that phyllanthin and hypophyllanthin protect against carbon tetrachloride- and galactosamine-induced cyto-

toxicity in primary cultured rat hepatocytes [99]. Liu et al. showed that corilagin treatment effectively ameliorates neutrophil accumulation, pro-inflammatory mediator production, and increased enzyme release following hepatic injury. Interestingly, blocking Akt activation abolishes the hepatoprotective effects of corilagin [100]. However, in a clinical trial, *P. urinaria* showed no superiority to placebo in improving histological non-alcoholic fatty liver disease (NAFLD) activity scores in 60 patients (40 and 20 treated with PUE and placebo, respectively [101]. The mechanism underlying the hepatoprotective effects of *P. urinaria* is not fully understood, and requires further studies.

Anti-diabetic effects

Diabetes mellitus (DM) is one of the most common diseases in humans. The ethno-medicinal plant *P. urinaria* has been used as herbal anti-diabetic remedies in Vietnam, and Trinidad and Tobago [33, 102]. PUE may exert hypoglycemic effects by enhancing glucose metabolism and/or suppressing glucose absorption in the gut [103]. In addition, it was found that PUE significantly affect amylase [32], and inhibit glucose diffusion across the plasma membrane into blood vessels [104]. Furthermore, compounds isolated from this herb, including gallic acid, corilagin and macatannin B, significantly inhibitα-glucosidase [32, 102].

Anti-oxidative activities

Studies have shown that *P. urinaria* has potential antioxidant agents [5, 10, 35]. Further studies demonstrated that compounds isolated from *P. urinaria* have strong antioxidant activities, e.g. phenolic compounds [35], trimethyl-3,4-dehydrochebulate [10], methyl-gallate [10], methyl brevifolincarboxylate [10], and geraniin [6]. By dampening oxidative stress, this plant may serve as an alternative source of medicine for steatohepatitis alleviation [98], skin disorder treatment [105], skin aging amelioration [106], protection against DOX cardiotoxicity [5, 107], and modulation of phagocyte associated innate immune response [108].

Other activities

Antihypertensive activity: Geraniin from *P. urinaria* displays anti-hypertensive effects, lowering systolic and diastolic blood pressures [6].

Thrombolytic effects: Shen ZQ et al. showed that corilagin has a dose-dependent thrombolytic effect in rats. Meanwhile, corilagin significantly inhibits PAI-1 activity in rat plasma, while increasing plasma tPA activity [4].

Bladder contraction: Dias MA et al. showed that contraction induced by water-ethanolic PUE in the guinea pig urinary bladder involves direct effects on smooth muscle and relies on the mobilization of extracellular calcium influx [109].

Antimicrobial activities: Helicobacter pylori is associated with the majority of peptic ulcers and some types of gastric cancer, and shows antibiotic resistance worldwide. Lai CH et al. demonstrated that treatment with PUE markedly inhibits bacterial adhesion and invasion to AGS cells *in vitro*, in a model of *H. pylori* infection. Furthermore, PUE remarkably inhibits *H. pylori*-induced NF-κB activation and IL-8 release [11].

Materials and methods

Relevant literature was retrieved by searching major scientific databases, including PubMed, Google scholar, and CNKI, for phytochemical, phytopharmacological, and medicinal significance of *P. urinaria*. Additional articles were obtained by tracking citations from the selected publications or directly accessing the journals' websites. Articles were considered based on geographical regions of origin. The literature search included all available reports covering the period from 1988 to 2017.

In summary, through comprehensive assessments in recent studies, the effects of *P. urinaria* (e.g. antiviral, anti-tumor, and liver protective activities) have been demonstrated. Consequently, tablets, granules, capsules, and other formulations based on *P. urinaria* have surfaced, with good curative effects in liver diseases such as hepatitis B. Therefore, exploitation and further evaluation of *P. urinaria* is urgent thanks to its clinical significance and great potential for application. It is believed that broad application of *P. urinaria* with improved treatment effects can be achieved in the future.

Disclosure of conflict of interest

None.

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