Plant Archives Vol. 23, No. 1, 2023 pp. 206-211 e-ISSN:2581-6063 (online), ISSN:0972-5210

Plant Archives

Journal homepage: http://www.plantarchives.org
DOI Url : https://doi.org/10.51470/PLANTARCHIVES.2023.v23.no1.035

GENUS *POLYGONUM* (POLYGONACEAE) : A REVIEW

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(Date of Receiving : 17-11-2022; Date of Acceptance : 02-02-2023)

ABSTRACT

The present paper reviews the distribution, botany, and traditional medicinal property, phytochemistry, pharmacodynamics, and potential applications of bioactive compounds of the genus *Polygonum* L.(s.l.). Substantial works of several workers establish the importance and potentiality of the genus in the pharmaceutical industry. However, there is a scope for further investigations regarding details of molecular characterization, pathways in the production of secondary metabolites, bioactive compounds, and their efficiency and effectiveness, along with GCMS and binding affinity to other ligands which require proper study for their future utilization. Finally, the tendency and perspective for future investigation of the genus *Polygonum* L.(s.l.) are discussed too.
Keywords **:** *Polygonum* L., Traditional use, Phytochemistry, Pharmacological use, structure analysis.

Introduction

Every plant on earth is unique and useful to mankind. Plants had been used as a source of medicine since the prehistoric era. Plants containing these principles are now screened and their derivates are used and studied through GCMS studies, transcriptome analysis, screening, and quantitative analysis for various pharmacological properties. With the recognition of the role of antioxidants in many diseases, there was a worldwide search for natural antioxidants. The genus *Polygonum* belongs to the family Polygonaceae and comprises about 150 species of flowering plants (Graham and Wood, 1965). The herbaceous, annual, and perennial genus grows in marshy areas. Yu *et al.* (2005) reported the genus *Polygonum* L. (s.l.) possesses several medicinal importance with numerous active compounds such as anthraquinones, flavonoids, stilbenes, organic acids, coumarins, catechins, stigmasterol, and lignans. Since the start of the 1950s, a lot of chemical compounds have been isolated from the genus *Polygonum*L. (s.l.) in various countries like China, Japan, Korea, etc. Most investigations on this genus have just focused on the chemical constituents of the roots and shoots which have been used traditionally in herbal medicine from an early age.

Distribution

The genus *Polygonum* L.(s.l.) with a large number of species distributed worldwide in a temperate climate. The genus is mainly concentrated in the Eastern, Central, and Western Himalayas (Hooker, 1905). Maiti and Sikdar, (1985) reported sixteen (16) genera and 110 species of the family Polygonaceae in India. Thirty-one (31) species have been reported from Arunachal Pradesh by (Chowdhury *et al.*, 1988). Barooah and Ahmed, (2014) reported 6 genera and 37 taxa of the family Polygonaceae from Assam. In Assam *Polygonum* L. (s.l.) species is mostly found in North Bank Plain Zone, upper, central, and lower Brahmaputra valley zones (Kanjilal, 1940) where they grow on marshy places as well as in agricultural fields.

Botany

Polygonum L.(s.l.) is a slender twining shrub, frequently climbing up on tall trees or sometimes a herbaceous perennial plant, it has roots with tuberous, hypertrophic, oblong, and dark brown in color. Its stems are approximately 2 to 4 m in length with a twine-like appearance, with many branches, longitudinal ribs, glabrous and micro-rough skin, and exhibit lignification in the lower parts with apparent swollen nodes. The leaves are present seldom oppositely or whorled, they are ovate or broadly elliptic with an acuminate apex and a cordate or subcordate base. Both sides of the leaf are coarse and have entire margins, the petioles are 1.5 to 3 cm in length, and the ochreas are membranous, oblique, glabrous, and 3 to 5 mm in length. The inflorescences are paniculate, terminal, or axillary and approximately 10 to 20 cm in length, the branches are expansive, with longitudinal ridges and small dense protrusions along the ridge. The bracts are triangular and ovate with small protrusions, and the apex is acute. In addition, each inflorescence contains three to four flowers. The pedicels are 2 to 3 mm in length and slender, and the perianths are white or greenish and five-parted. The perianth segments are oblong and of non-standard size. The male flowers have eight stamens, and the lower parts of the filaments are wide and very short, exhibit three styles, and have stigmas with a capitulum. The achenes are ovate with three ribs, black-brown, shiny, and approximately 2.5 to 3 mm in length (Wang *et al.*, 2011). Some *Polygonum* L. species (Fig. 1) found in Assam are,

- *Polygonum hydropiper* (L.) Spach *Polygonum hydropiper* (L.) Spach. ssp. *flaccida* (Meissen.): The inflorescence is a nodding spike with pinkish to whitish color flower, regular, long perianth segments united from base to halfway, and with a white or pinkish

margin and greenish base.

- *Polygonum assamicum* Meissner : The inflorescence is a nodding spike with pink in color flower, flowers solitary or sessile, perianth 4 or 5 partite.
- *Polygonum chinensis* (L.) H. Gross var. *chinensis* : The inflorescence is peduncled heads arranged corymbosely or in panicles, perianth segments 5 white or pink in color.
- *Polygonum chinensis* (L.) H. Gross var *brachiata* (Lamk) : The inflorescence is corymbosely arranged, capitate, perianth whitish in color.
- *Polygonum barbata* (L.) Hara : The inflorescence is a spike with creamy or pink color flowers; flowers are slender and usually glabrous
- *Polygonum posumbu* (Buch-Ham. ex D.Don) H. Gross : The inflorescence is axillary, spicate, bracts are greenish and perianth is pinkish in color, and the pedicel is short.
- *Polygonum capitata* Buch. Ham. ex D.DON H. Gross : The inflorescence is capitate, solitary, or terminal, perianth pinkish, peduncle glandular, and hairy.
- *Polygonum hydropiper* (L.) Spach. : The inflorescence is a spike, where the color of the perianth is creamy to greenish in the lower part.

Traditional Use

With the wide spectrum of biological and pharmacological effects in organisms, the genus *Polygonum* L.(s.l.) has been used as an effective traditional medicine for a long history. The genus is used in traditional food and medicine in different parts of the world (State Administration of Traditional Chinese Medicine, 1999). The genus has been reported to contain a potential source of medicine with high bioactive compounds and is used to treat many diseases like sore throat, cough, infantile cough, edema, and diarrhea (Lv *et al*., 2014). The powder of the root and shoot of *polygonum* L. (s.l.) has been used to cure jaundice, skin burns, scald, and hyperlipemia for normalizing gall bladder (Peng *et al.,*2013). In Japan and China, *Polygonum* L.(s.l.) species are popularly used in traditional medicine where the root iscommonly used for the treatment of inflammation in human body parts (Nonomura *et al*., 1963). In Assam, the genus *Polygonum* L. (s.l.) is used as food, fodder, and herbal medicine by different communities (Hazarika *et al.*, 2006). Ritesh *et al.* (2011) reported that the genus *Polygonum* L. possesses a considerable number of bioactive compounds that show antimicrobial, anti-inflammatory, hepatoprotective, hypertensive and anti-coagulative properties. Some of the species of the genus *Polygonum* L.(s.l.) are also used as a dye (Akimpou*et al.,* 2005).

Phytochemistry

In the early 1950s various workers reported the presence of different phytochemicals and secondary metabolites in the genus *Polygonum* L.(s.l.). The first active compound identified from the *Polygonum* L(s.l.) is quinones and their derivatives. The major phytochemicals found in the genus *Polygonum* L.(s.l.) include stilbenes, quinones, and flavonoids which have been used in clinical practice due to their anti-aging, anti-cancer, and anti-inflammatory effects (Zhang *et al.,* 2012) The first bioactive compound identified from the genus *Polygonum* L.(s.l.) is quinines and their derivatives (Tsukida and Yoneshige, 1954). Xu *et al*. (2009) reported that polydatin is the important bioactive major compound in *Polygonum cuspidatum* Seib et Zucc.which has high medicinal and nutritional value. Qiu *et al.* (2013) reported that the Phenolic constituents such as Stilbenes, anthraquinones, tannins, naphthalenes, and other secondary metabolites were also characterized in the species *Polygonum multiflorum* Thunb. Li *et al.* (2013) reported the presence of stilbene, and glycosides, from the roots of *Polygonum multiflorum*Thunb. Stilbenes are the major components in *Polygonum multiflorum* Thunb. and 2,3,5,40 - Tetrahydroxystilbene-2-O-β-D-glucopyranoside was first characterized by Yang from the genus *Polygonum* L. (1976). Later two more stilbenes 2,3,5,40-tetrahydroxystilbene- 2-O-β-D-(2″-O-monogalloyl esters-glucopyranoside and 2,3,5,40-tetrahydroxystilbene-2-O- β-D-(3″-O-monogalloyl esters-glucopyranoside were isolated by (Nonaka *et al.,*1982) from *Polygonum hydropiper*. Zhou *et al.,* (1994) isolated 2,3,5,40 - Tetrahydroxystilbene-2,3-di-O-β-D-glucopyranoside from the ethyl acetate insoluble fraction of an ethanol extract of the genus *Polygonum*L. (s.l.). Stilbene, 2,3,5,40 - tetradroxystilbene-2-O-β-D-xylose was identified from ethanol extract of *Polygonum multiflorum*Thunb. by (Sun *et al.,* 2013). Chen *et al.* (2001) reported the presence of various phospholipids such as phosphatidyl ethanolamine, copaene, eicosane, hexanoic acid, hexadecanoic acid methyl ester, hexadecanoic acid ethyl ester,octadecanoic acid methyl ester, octadecanoic acid ethyl ester, ethyl oleate, docosanoic acid methyl ester, tetradecanoic acid ethyl ester, squalene etc in *Polygonum multiflorum* Thunb. *Polygonum* L.(s.l.) is also rich in phospholipids which may have effective boosting effects (Xiao *et al*., 2002). Flavonols, Quercetin, Catechin, and Rutin are also detected in the roots and leaves of the genus *Polygonum* L. (s.I.) by several workers (Kuznetsova, 1979; Jayatilake *et al.*, 1993; Xiao *et al.*, 2002). Kimura *et al.* (1983) isolated coumarin 7-hydroxy- 4-methoxy-5-methyl from the acetone extracts of *Polygonum cuspidatum* Sieb et Zucc. The two stilbenes reported in *Polygonum multiflorum* Thunb. exhibits inhibition of lipid peroxidation in rats (Xuan *et al.,* 2003). Jin and Jin (2007) isolated resveratrol from the dried roots of *Polygonum cuspidatum* Sieb et Zucc. reported having inhibitory effects on the humanmelanoma A375 cells. The presence of another two compounds namely gallic acid and ester of torachrysone-8-O-β-D-glucoside and 2,3,5,4'-tetrahydroxystilbene-2-O-β-D-xyloside were reported in *Polygonum multiflorum*Thunb. which plays an important role in hair growth (Du *et al.,* 2009). Chen *et al.,* (2000) reported hepatotoxicity, nephrotoxicity, and embryonic toxicity in the genus *Polygonum* L.

Pharmacodynamics and Potential Applications

Lipids regulating effect

Polydatin isolated from the genus of *Polygonum* L.(s.l.) inhibits the synthesis of lipids in a non-competitive manner on rabbits (Luo *et al.*, 1992). Arichi *et al.* (1982) stated that when 100 mg/kg of polydatin was intragastrically administered to rats and fed with corn oil cholesterol and cholic acid mixture, the triglyceride level was reduced by 40%. The compound polydatin inhibited the platelet release reaction of rabbits in a dose-dependent manner (Liu *et al*., 1998). Another report showed that when Polydatin was employed in a high fat/cholesterol rabbit model such as Syrian golden hamster or Japanese giant ear rabbit for 15 to 21 days, triglyceride concentration, low density of lipoprotein cholesterol (LDLC), total cholesterol (TC) level in the serum, the ratio of total cholesterol/high-density lipoprotein cholesterol (TC/ HDLC) and the liver coefficient (LC) in the

studied samples were reduced to a great extend (Xing *et al.*, 2009).

Estrogenic effect

Hazarika and Sarma, (2007) reported the estrogenic effect of *Polygonum hydropiper* L. root onfemale albino rats. Matsuda *et al.,* (2001) reported the presence of hydroxyanthraquinones such as emodin in the roots of *Polygonum cuspidatum* Sieb at Zucc. Emodin was phytoestrogen with an affinity to bind with human estrogen receptors. They also stated that emodin and emodin-8-O-β-D-glucopyranoside extract of *Polygonum cuspidatum* Sieb at Zucc. could enhance the proliferation of MCF-7 cells, and inhibit with a Ki value of 0.77 and 1.5 μM for ERα and ERβ, respectively. Zhang *et al.* (2006) reported emodin's bioactive components with huge estrogenlevels.

Anti-inflammatory effect

Anti-inflammatory effects of *Polygonum* species have also been reported. Pretreatment with the extraction of the roots of *Polygonum* L.(s.l.) could inhibit iNOS mRNA expression with the induction of Lipopolysaccharides (LPS) and Nitric Oxide (Kim *et al.,* 2007). The inhibitory effect of ethanol extracts of *Polygonum cuspidatum* Sieb et Zucc. (PCE) on-ear inflammation induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) was investigated in mice, and the results showed PCE significantly reduced ear edema in dose-dependent manner ears and along with the treatment when the extraction of *Polygonum cuspidatum* Sieb et Zucc. (Bralley *et al.*, 2008). The aqueous extract of *Polygonum minus* (Huds.) Opiz possesses potent anti-inflammatory activities (George *et al.*, 2014). Ghanim *et al.* (2010) reported the presence of resveratrol in *Polygonum cuspidatum* Sieb et Zucc. which has anti-inflammatory and Reactiveoxygen species suppressive effects.

Antioxidant effects

Pan *et al.* (2007) reported lipid antioxidant activity and hydroxyl radicals scavenging activity in 95% ethanol extract of *Polygonum cuspidatum* Sieb et Zucc. The antioxidant activity was measured by using α, α-diphenyl-β-picryhydrazyl (DPPH), and total antioxidant assays and reported a positive correlation between reducing power and antioxidant activity. Du *et al*. (2013) reported the presence of polydatin in *Polygonum cuspidatum* Sieb et Zucc. which has several favorable therapeutic properties including antioxidant activity and a strong ability to scavenge oxygen free radicals. Meng and Hang, (2000) stated that the 95% ethanol extracts of *Polygonum cuspidatum* Sieb et Zucc. have good scavenging activity against DPPH radicals; arestable under an acidic medium, and are resistant to heat and light. In their study, they reported that 100 μg/mL of the extract possessed the most significant scavenging activity. Ghanim *et al.,* (2010) reported that the extract of *Polygonum cuspidatum* Sieb et Zucc. contains resveratrol which has anti-inflammatory, antiaging, and reactive oxygen species suppressive effects.

Anticancer effect

Resveratrol and emodin isolated from the genus *Polygonum* L.(s.l.) are considered an effectivesubstance in the treatment of cancer, (Tseng *et al.* (2004). Feng *et al.* (2006) stated that these bioactive compounds possess anticancer/ antitumor activity and showed various levels of effects. Application of aqueous extracts of the genus *Polygonum* L.(s.l.) at 20 g/kg/day, for 10 days showed a prolonged life span of tumor-bearing Kunming mice and inhibited Ehrlich's carcinoma's growth Zhou *et al.,*(1989). The ethanol extract of *Polygonum cuspidatum* Sieb etZucc. root at 0.2 mg/ml, 0.4 mg/ml, 0.6 mg/ml, and 0.8 mg/ml exhibited an antiproliferative effect against human lung cancer cells in a dose-dependent manner (Lin *et al.*, 2010). Resveratrol isolated from *Polygonum cuspidatum* Sieb et Zucc. root significantly reduced Lewis lung tumor volume by 42% and tumor weight by 44% , also prevented tumor growth and metastasis in lungs by 56% by inhibiting DNA synthesis of tumor cells, as well as tumor-induced neovascularization in mice bearing highly metastatic Lewis lung tumor (Kimura and Okuda,2001).

Structural Analysis Molecular Docking

Although substantial amount of work has been done on biochemical characterization, very few works have been reported on their molecular interactions related to docking. The volatile components of the genus *Polygonum* L.(s.l.) were identified and studied by Lv *et al.* (2014). The essential oils and bioactive compounds from the leaves of *Polygonum* L.(s.l.) were isolated by steam distillation and solvent extraction and then analyzed by GC/MS, showed 18 peaks (Kim *et al.*, 2007). Among these peaks, the major volatile compounds were 2-hexenal (73.36%), 3-Hexen-1-of (6.97%), n-hexanal (2.81%), 1-penten-3-of (2.55%), 2-penten-1-of (2.21%), and ethyl vinyl ketone (1.13%) which showed the presence of a huge number of oils and bioactive compounds. Muhammad *et al.* (2019) performed molecular interactions between the chemical compounds (ligands) present in the genus, and the desired (proteins), by performing molecular docking with the help of bioinformatics tools. The chemical compounds isolated and used in the study were Phytosterols including beta-sitosterol and stigmasterol. Beta-sitosterol and stigmasterol were isolated from *Polygonum hydropiper* L. Their structures were confirmed via NMR and Mass analysis. Phytosterols were evaluated against HeLa, MCF- 7, and NIH/3T3 cell lines using MTT assays, and the Compounds were docked against Tyrosine kinase an important enzyme in the cell signaling pathways. The compounds Beta- sitosterol and Stigmasterol showed the value with a Docking score of -7.266, binding energy -41.21, Binding affinity-7.76, Ligand O 79 Receptor OD1 ASP776 Interaction H- donor Distance 2.0, and Stigmasterol with Docking score -4.86, binding energy -41.04, Binding affinity-7.68, Ligand O 77 Receptor OG1 THR766 Interaction H- donor Distance 1.8.

Future Perspective and Utilisation

The genus *Polygonum* L.(s.l.) has long been used in traditional and ayurvedic medicine for thetreatment of various diseases. A large number of effective compounds are reported in different species of the genus *Polygonum;* present in different species of the genus *Polygonum* L.(s.l.) which have pharmacological effects. However, adequate information and enough systemic data about the effectiveness of useful secondary metabolites, signaling, and secondary metabolic pathways of the genus *Polygonum* L. (s.l.) are limited. Detailed investigations on the pharmacological effects and molecular mechanisms of an important compound of the genus *Polygonum* L.(s.l.) are essential. Drug target-guided with molecular docking and bioactivity, isolation and purification of the chemical constituents of the genus related to their gene expression pattern, metabolites, and their biosynthetic pathways with subsequent evaluation ofthe

pharmacologic effects will promote the development of new drug and make sure about the functions and efficiency of important chemical constituents or multiple ingredients contributesits pharmacological effects in future.

Conclusion

The present paper reviews the relevant literature to congregate the phytochemicals, secondary metabolites, and pharmacological information on the genus *Polygonum* L.(s.l.) The presence of stilbenes, quinones, sterols, decanal, dodecanal, flavanol, phospholipids, and many other aldehydes make the genus *Polygonum* L.(s.l.) a major source of pharmacologically important plants with good economic value. Phenolic compounds like gallic acid and coumaric acid are responsible for many activities including antioxidant and antiulcer activity. Antioxidant studies revealed the potential of the genus *Polygonum* L.(s.l.) as a food preservative and antioxidant. Compounds isolated from the genus and their cell cultures such as 5-hydroxymethyl furan carboxaldehyde or hydroxymethylfurfural or HMF inhibition of sickle cell blood production properties and responding A has antidiabetic activity. Quinones and stilbenes are considered the major constituents with pharmacologic effects. Although voluminous works have been reported on the genus *Polygonum* L.(s.l.) adequate information on the genus about the pharmacokinetics and toxicity especially target organ toxicity, their gene references, and the signaling pathways related to molecular docking are lacking therefore, more investigations of the genus are required.

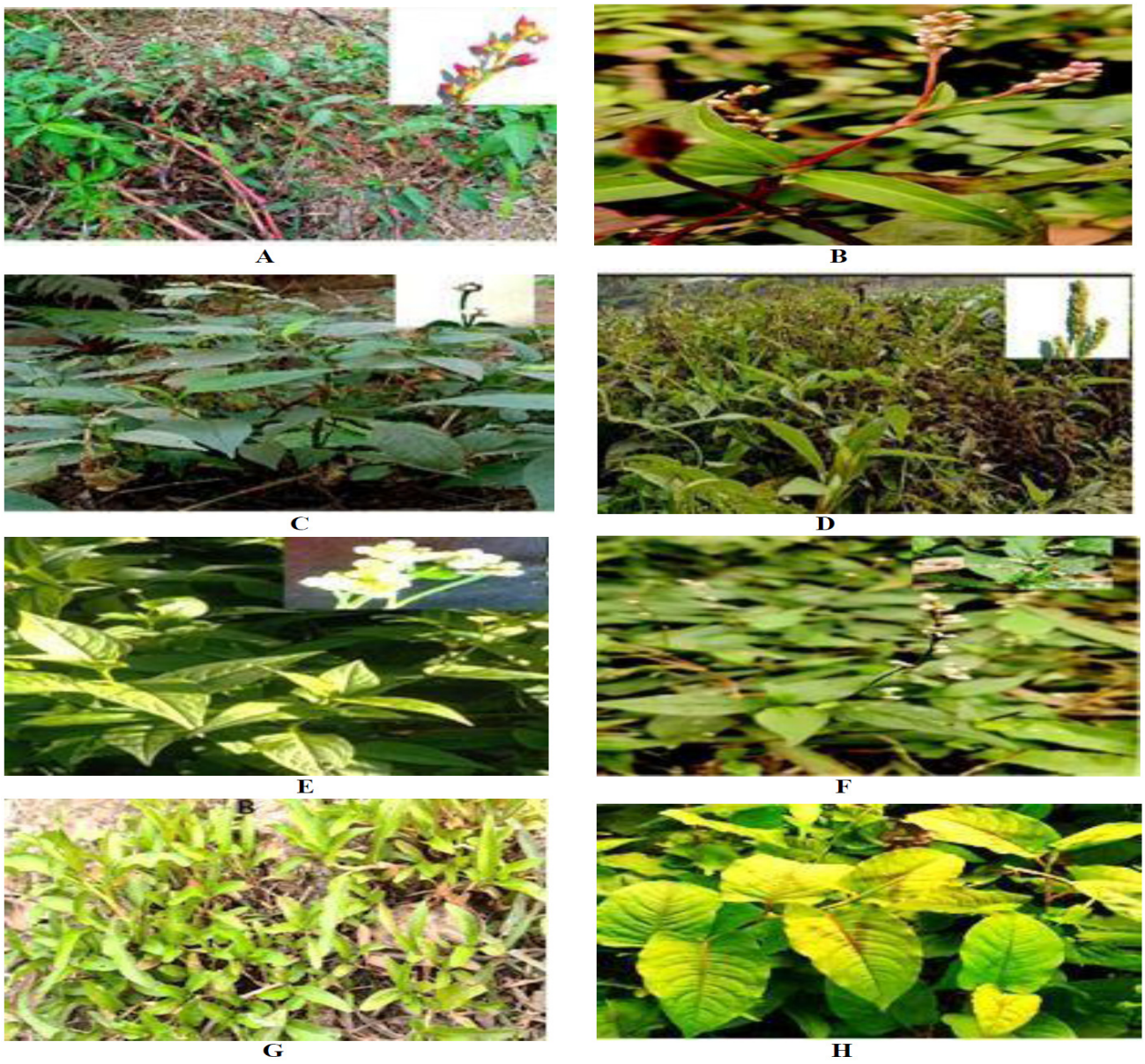

Fig. 1: *Polygonum* L. (s.l.) species found in Assam **A**: *Polygonum hydropiper* (L.) Spach. ssp. *flaccida* (Meissen.). Munshi et Javied , **B:** *Polygonum assamicum* Meissner, **C:** *Polygonum chinensis* (L.) H. Gross var *brachiata* (Lamk) , **D** : *Polygonum barbata* (L.) Hara , **E:** *Polygonum Chinensis* (L.) H. Gross var *Chinensis*, **F:** *Polygonum posumbu* (Buch-Ham.ex D.Don) H. Gross , **G**: *Polygonum hydropiper* (L.) Spach, **H:** *Polygonum capitata* Buch. Ham.ex D. Don H.Gross

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