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A Review on Medicinal Property of *Hamelia patens* Jacq

Preeti Chauhan[1*], Manju Vyas Singh[2]

[1]M.pharm student, DIPSAR, Delhi, India
[2]Assistance professor, Department of Pharmacognosy department, Dipsar, India

***Corresponding author:** Preeti Chauhan
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Abstract **Review Article**

Ornamental plants are commonly known for their excruciating beauty and meant to decorate the gardens, lawns, streets and roadside areas. Nowadays these ornamental plants are used as herbalism. This review article represents one of such ornamental plant, *Hamelia patens* native to American subtropics and tropics. Its native range extends from Florida in the southern US to Argentina. *Hamelia patens* belong to the coffee Family (Rubiaceae). It is growing worldwide in warm, moist areas and can tolerate the extreme temperature. It is commonly known as firebrush, hummingbird bush and used long before prehistoric time as they are able to prevent, treat or even cure human ailments. *Hamelia patens* is a superb plant which has inflammation, analgesic, antimicrobial, myometrium contraction, hypoglycemic effect, leishmanicidal activity, anti-diarrheal, anthelmintic, antidepressant, hepatoprotective, Anti-urolithiatic, diuretic, wound healing, anti-oxidant and antinociceptive like effect. All these activities are due to the phytoconstituents present in roots, leaves, stems, and bark. Fruit of *H.patens* is edible. In this article, we discussed chemical constituents and medicinal uses of *Hamelia patens*.

Keywords: Hamelia patens, Rubiaceae, Herbalism, American subtropics, Ornamental plant.

INTRODUCTION

Hamelia patens are a neotropical, perennial freely growing and blooming shrub. It consists of 16 shrubs and small trees which are being introduced and cultivated for 250 years. It is well known for its capacity to tolerate heat and changing climates as well as adaptation to a different type of soil. The genus is divided into 2 sections, one of which is strictly tubular red, orange or yellow and another section is Amphituba which has yellow infundibular or sometimes broadly flaring trumpet-shaped flower. *Hamelia patens* with bright orange flower and *Hamelia* sphaerocarpa with a coppery red flower, both were used as a pot plant. *Hamelia patens* is commonly known as fire bush, scarlet brush, bayetilla, trompetilla, coralillo, or hierba coral and, Texas superstar named by horticulture department. *Hamelia patens* Jacq. It is a center of attraction of various insect and Hummingbird due to its beautiful colored flowers. *Hamelia patens* are also divided according to the morphology of Corolla-

1. Hamelia patens section Hamelia - it consists of 8 species, characterized by strictly tubular corolla that does not expand toward the apex.
2. Hamelia patens section Amphituba – it consists of 8 species, has an infundibular corolla that expands gradually or abruptly toward the apex [2].

H. Patens are burdened with flowers and fruits throughout the year. There is a failure of sexual reproduction in H. patens due to gametophytic incompatibility reported by Louis and Radhamany *et al*. [1]. Method of propagation of *Hamelia patens* is through seed and stem cutting. There are different species of the plant exists- *Hamelia axillaris*, *Hamelia barbata*, *Hamelia calycosa*, *Hamelia chrysantha*, *Hamelia cuprea*, *Hamelia longipes*, *Hamelia macrantha*, *Hamelia magnifolia*, *Hamelia ovate*, *Hamelia papillosa*, *Hamelia patens*, *Hamelia rostrata*, *Hamelia rovirosae*, *Hamelia sanguine*, *Hamelia ventricosa*, *Hamelia xerocarp*, and *Hamelia xorullansis*.

PLANT MORPHOLOGY [3]

Hamelia patens is a semi-woody shrub up to 3.7 m to 7 m tall whose leaves are usually decussate, or arranged in whorls of 3, but sometimes up to 7. Young leaves are covered in red, woolly hairs which disappear as the leaves mature. Interpetiolar stipules are triangular, falls at an early stage (caducous). *Hamelia* is burdened with flowers from June to September and best flowering during full sun condition. The orange-red flowers are arranged in cymes, clusters of flowers that occur at the end of forking floral stalks (terminal). Each

flower has small and triangular lobes on a narrow tube (2.5 - 3.8 cm long) with a swollen base and inflorescence type is cyme. Fruits of Hamelia are black, oval to globose, berry-like fruits are fleshy (1.3 cm long). Fruits are yellowish to red at first and mature to dark blue-black.

PLANT DISCRIPTION [10]

Common Names- Firebush and Scarlet Bush, Redhead
Family - Rubiaceae
Kingdom - Plantae
Division - Magnoliophyta
Class - Magnoliopsida
Family - Rubiaceae
Genus - *Hamelia*
Species – *Hamelia patens*
Flower & Plant Sexuality- Bisexual Flowers

ETHNOBOTANICAL USE OF PLANT

Plants are an important part of our life; their constituents and nutritional value have been used to treat, prevent and cure human ailments. The traditional ethnomedical knowledge has been passed on from generation to generation through trial and error method. World health organization has shown great interest in documenting the use of such medicinal plant from tribes in different parts of the world9. They considered being safe, effective, and inexpensive for which there is a global trend for the revival of traditional herbal medicine. Fruits of *Hamelia patens* are edible and its parts have medicinal properties widely used in Peruvian and Mexican folk-medicine like in wound healing and menstrual disorder. Hence, H. patens are used as herbalism against a wide range of ailments. It also possesses anti-bacterial, anti-fungal and anti-inflammatory properties. The decoction of leaves stems and flowers if drunk helps to relieve menstrual cramps [25], or applied externally to treat skin problems like sores, rashes, burns and insects bites. Leaves have a cooling effect and are chewed on a hot day for prevention against heat stroke, and also used to treat dysentery, diarrhea, fever, pain, and headaches1. It is also used for uterine and ovarian affliction [9]. Cytostatic and cytotoxic activity against tumor cell lines proved by Taylor *et al.* [9] and wound healing activity [10]. In Mexico, its fresh leaf sap is used to stop bleeding of a wound while roots are used to treat inflamed uterus [12].

LITERATURE REVIEW

Literature review on Phytochemistry

The maximum number of secondary metabolites is present in the methanolic and ethanolic extract of the plant. Methanolic extract of aerial parts of the plant has Alkaloids, Flavonoids, Saponins, Glycoside, Sterols, Proteins, Phenolic, and acidic compounds. Phenolic compounds including flavonoids have great importance in the plant defense system against invading bacteria and other environmental stress. Flavonoids have anti-inflammatory, anti-allergy, anti-viral, anti-proliferative action [15]. Firebush contains 17.5 percent crude protein and has an in vitro digestibility of 61.6 percent and has a sugar content of approximately 9%, although significant variation exists both within and among trees [24]. Different kinds of chemicals have been successfully isolated from different parts of *Hamelia patens* including kaempferol-3-O-rutinoside and (-) epicatechin from ethyl acetate extract of leaves[40], narirutin, rosmarinic acid and new glycoside 5,7,2', 5'-tertrahydroxyflavanon-7-rutinoside [1], palmirine and rumberine (oxindole alkaloid and heteroyohimbane type) isolated from aerial parts of plant [8]. β-sitosterol and stigmasterol , triterpene, (6E,10E,14E18E)-2,6,10,14,18,23-hexamethyl-2,6,10,14,18,22-tetracosahexane [19], cycloartenols, and triterpenes[34], Isopteropodine [31], stigma-4-ene-3,6-dione [32] are also reported. Micropropagated plantlets allowed the production of monoterpenoid oxindole alkaloid named (-) hameline together with 8 alkaloids like aricine, isopteropodine, pteropodine, uncarine, speciophylline, tetrahydroalstonine, palmirine and rumberine [28]. Ephedrine is reported in leaves and twigs of plant, extracted with n-hexane and methanol, ephedrine (Rf – 0.25) is characterized by 13C NMR, 1H and mass spectroscopy, UV and IR[11]. Nearly 12 phenolic compounds in plant extract- Quinic acid, Hydroxycinnamic acid, Catechin, Caffeoylquinic acid, Procyanidin, (−)-Epicatechin, (+)-Catechin 3-O-glucose, Quercetin 3-O-rutinoside, Kaempferol 3-O-rutinoside, Hydroxyphloretin 2 ′ -O-Glucoside extracted using a different method of extraction[30]. Ruitz-Teran *et al.* [35] shows that the spot of the methanolic extract of a plant on TLC plate developed by Ethyl acetate-methanol (9:1v/v) shows the presence of β-carotene. In TLC and HPLC, a solvent used for separation of phenolic glycon (Dichloromethane: Methanol 9:1v/v) and phenolic aglycon (Ethylacetate: Acetic Acid: Formic Acid: Water with 68:7:7:12v/v) using spraying agent Diphenylborinic acid. In TLC, Rf value of different compounds were found like chlorogenic acid (Rf value=0.624), quercetin (Rf value=0.568), caffeic acid (Rf value=0.260). At least 3 compounds are present in ethanolic extract- chlorogenic acid, caffeic acid, quercetin claimed by Andrade- Cetto. A *et al.* [8]

Literature review on Anti-bacterial activity

Camporese *et al.* [12] first to prove that hexane extract of leaves of *Hamelia patens* shows anti-bacterial activity against *Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa and Staphylococcus aureus* bacteria.

Singh S *et al.* [42] investigated that methanol, ethanol, acetone and water extract of stem and bark of plant also inhibit the growth of *Staphylococcus aureus, Bacillus subtilis, Pseudomonas flurescens, Escherichia coli and Aspergillus niger, Penicillium chrysogenum,*

Alternaria alternate. Here acetone was proved to be a better solvent for extraction of antioxidant and antibacterial substances as compared to other solvents and also provide high extraction yield.This anti-bacterial activity could be attributed to the phenolic components present in the extract. Thus, *Hamelia patens* can be considered as an easily accessible source of natural antimicrobials and antioxidants.

In another study Okoye *et al*. [26] reported that maximum anti-bacterial property is demonstrated in ethanolic extract of leaves and stem of *Hamelia patens* where Minimum Inhibitory Concentration (MIC) ranged from 12.5 mg/ml to 100 mg/ml, while the Minimum Bactericidal Concentration (MBC) ranged from 25 mg/ml to >100 mg/ml among the test organisms *Staphylococcus aureus, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi* and petroleum ether extract shows least anti-bacterial activity.

Paz Wong *et al*. [30] perform the different method of extraction like maceration, Soxhlet and percolation for testing antimicrobial property against gram positive and gram-negative bacteria. Nearly 12 phenolic compounds were reported during the study. The extract obtained by percolation shows the highest anti-bacterial property as compare to other. All 3 extracts obtained from a different method of extraction has 75% efficiency for *Staphylococcus aureus and S.typhi*, 50% against *S.paratyphi* and 100% against *E.coli*. The percentage activity was 100% and the index of susceptibility is 75% with these extracts. The main compound which is antimicrobial and found in all 3 extract is chlorogenic acid other compounds like epicatechin (which is higher in percolation than in maceration and lowest in the soxhlet) is also reported. This show that different method of extraction also affect the extraction of different constituent like Procyanidine is absent in the Soxhlet extraction method but present in maceration and percolation. Hydroxycinnamic acid and catechin are present only in the maceration.

Literature review on anthelmintic and Anti-fungal activity

Sapana Khandelwal *et al*. [41] observed the fungicidal and anthelmintic property in ethanolic extract of leaf, stem, and roots of *H.patens* against fungi-*A.fumigatus, Penicillum spl. and A.flavus* and helminthic like Indian earthworm *Pheritima posthuma* which resembles roundworm in the human intestine. Anthelmintic property is observed in leaf extract in 74 min at 50mg/ml which is very similar to standard Piperazine (10 mg/ml conc.) followed by stem extract in 140 min and least activity is there in root extracts (199 min). Highest anti-fungal activity is observed at 1000 mg/ml in stem followed by leaves and least in the root. At 250 mg/ml no activity is seen against *A.fumigatus and A.flavus* by leaf and root extract but some activity is there in *penicillium spl.* In stem, activity is there only in *Aspergillus fumigatus* but not in rest two.

Okoye *et al.* [26] explained that Candida albicans was more susceptible to ethanolic extract than the Aspergillus Niger among the fungal isolates where Minimum Fungicidal Concentration (MFC) ranged from 25 mg/ml to >100 mg/ml34. Abubaker *et al.* [4] tested the fungicidal activity of water extract of *H.patens* (leaf, flower, and fruit) against. Aspergillus fumigatus, Candida Albicans, Fusarium oxysporum, Rhizoitonia solani. The leaf and flower extract shows 100% growth inhibition against A.Fumigatus as well as for Candida albican. 10% concentration of fruit, leaf and flower extract cause 100% inhibition of Fusarium oxysporum, Rhizoitonia solani. 100% concentration of leaf, fruit and flower extract is comparable with the positive control, Bavistin 0.5% [28].

Literature review on Leishmanicidal activity

Suárez *et al.* [40] reported leishmanicidal activity of methanolic leaves extracts of *H.patens*. Pure indole alkaloids (isopteropodine, palmirine, rumberine and mitrajavine) were tested in-vitro for their ability to inhibit the growth of Leishmania mexicana. Comparison of the leishmanicidal activity showed that palmirine, rumberine have the highest values, with IC_{50} of 56 μM and 61 M respectively. These values are slightly higher than those reported for two alternative drugs used for the treatment of leishmaniasis, the allylamine terbinafine, IC_{50} 8.5 μM, which cause blockage at sterol biosynthesis at the level of squalene epoxidase, and cationic peptide. Dermaseptine, IC_{50} 3 μM, which binds to the surface membrane, inducing alteration in the lipid bilayer [21].

Literature review on biological activity

Kumar A *et al.* [21] noticed that only chloroform extract has significant anti-depressant effect but not methanolic or ethanolic extracts. Forced swimming test, tail suspension test, open field test like models are used which also means immobility test which is similar to anti-antidepressant in human [29]. The anti-depressant like the effect produced by chloroform was not due to the effect of psychostimulant or hypokinesia confirmed by open field test. This activity supports its use as a nervous shock which is used as traditional medicine. Reduction of immobility time elicit by chloroform extract is forced swim test and tail suspension test proved its antidepressant effect. Anti-depressants have no locomotor activity [46].

Pandurangan *et al.* [3] noticed that Ethanolic extract and petroleum ether extract of stems of *Hamelia patens* shows anti-diabetic effect in alloxan induced hyperglycemia in the rat at 400mg/kg. Aerial parts of *H.patens* plant show hypoglycemic effect in STZ-NA-Induced diabetes in the rat. *H.patens* can be used in the treatment of type 2 diabetes. Water extract of *Hamelia* produced the significant anti-diabetic effect in 120 min

while ethanolic extract produces a hypoglycemic effect at 60 min. Also, there is the presence of at least 3 compounds in ethanolic extract- chlorogenic acid, caffeic acid, quercetin and at least 2 active compounds in water extract namely chlorogenic acid and quercetin which may involve in hypoglycemic effect. Chlorogenic acid is the main compound in the ethanolic extract and second major compound in the water extract. Quercetin is present in both extract and has effective α-glucosidase inhibition role. Rutin was not observed but caffeic acid is the major compound in the ethanolic extract reported by Andrade Cetto *et al.* [2]. Then Jimenez-Suarez *et al.* [21] evaluated in-vitro inhibition of α-glycoside in non-insulin dependent patients as it helps in the delay of carbohydrate digestion and absorption, reducing postprandial hyperglycemia [22]. HEX extract shows highest α-glucosidase inhibition followed by MeOH-EtOAc extract. Compounds like triterpene, (6E,10E,14E18E)-2,6,10,14,18,23-hexamethyl-2,6,10,14,18,22-tetracosahexane and β- sitosterol/stigmasterol shows anti-diabetic effect. *H.patens* show antihyperglycemic effect equivalent to metformin at 150mg/kg due to the presence of epicatechin and chlorogenic acid [43].

H.patens also possesses anti-inflammatory activity investigated by Jimenez *et al*. [19]. Leaves are extracted with hexane by maceration result in decreasing the carrageenan-induced inflammation at 200 to 500mg/kg and this anti-inflammatory activity is due terpene unit, its mechanism of action is the inhibition of the nuclear kappa B and the production of pro-inflammatory cytokines (IL-1βand TNF-α). It also downregulates cyclooxygenase and inducible nitric oxide synthase [6, 25]. Sosa *et al.* [39] explained the anti-inflammatory activity using hexane, chloroform, and methanolic extract of *Hamelia patens* and evaluated anti-inflammatory activity against croton oil-induced ear edema in mice. Extract cause dose-dependent oedema reduction. The chloroform extract has an ID value between 108 and 498µg/cm2 as compared to indomethacin (93µg/cm2).

Ahmed. S *et al.* [7] state that *Hamelia* plant also has anti-uroliathic property. He stated 15 families with the number of species have Anti-urolithiatic activity in which Rubiaceae family (*Hamelia patens*) has only 13% anti-urolithiatic activity. The decoction of the root of *Hamelia* show anti-inflammatory, anti-oxidant, and diuretic activity[35]. Perez.GS work on methanol extract of *Hamelia* and studied both in-vitro and in-vivo anti-diarrheal activity on female Wistar rats and female mice. It was found that on the uterus and intestine, the inhibitory response was dose-dependent and the major anti-diarrheal effect was observed at a dose of 100 mg/kg[8].

Anti-oxidant is used for the treatment and prevention of several diseases associated with the oxidative stress [47]. Ruitz-Teran *et al.* [39] shows that antioxidant activity of the methanolic extract was higher than acetone and least in the hexane extract of *Hamelia patens*. The antioxidant property is measured by its ability to reduce couple oxidation of β-carotene and lineolic acid in an emulsified solution which loses its orange color when reacting with radical. *Hamelia patens* have similar anti-oxidant property as BHA (Butylated Hydroxyl Anisole), a commercial antioxidant and but higher than commercial natural anti-oxidant like α-tocopherol. The antioxidant activity in the polar extract may be due to the presence of sesquiterpene, triterpene, and polyphenol in ethanolic and acetone extract [1, 34]. In some of the studies, it is showed that catechin decreases the production of nitric oxide, reactive oxygen species and several pro-inflammatory and ursolic acid as immunomodulator property and strongly reduces the DPPH radical [48]. The MeOH-Aq and MeOH-EtOAc extract shows anti-oxidant and anti-inflammatory property may be due to catechin. MeOH-Et-OAc has great antioxidant property20. Plants rich in phenolic and flavonoids have significant iron reducing power and show DPPH scavenging activity33. Flavonoids present in *Hamelia* seed is 3.91mg/g. Maximum iron reducing power of *Hamelia* is 11.97. In phosphate buffer salt, the extract of *Hamelia* plant shows antioxidant property due to the presence of the phenolics, flavonoids, and proteins [13]. Plant extracted in phosphate buffer salt has a higher content of the phenolic contents [33].

J meseguer *et al*. [20] studied that *Hamelia patens* have great hepatoprotective activity and good oxidant capacity in butanol extract. Activity is evaluated through AST activity on HepG2 cell subjected to death with CCl4. Cytotoxicity was evaluated on Vero cell culture shows significant toxicity. Gomez-Beloz *et al.* [18] did double incision wound healing bioassay with a 5% crude extract of *Hamelia. Hamelia patens* increase the breaking strength of wounds significantly more than the control group [1].

Infusion of *Hamelia* leaves was prepared in 41L water and boil until half the volume if drink constantly on next few days with low fiber diet, administered against flux and dark bleeding after menstruation, or child delivering[31]. Martin *et al.* [25] reported *Hamelia patens* can be used as a remedy for amenorrhea and to reduce excessive bleeding during menstruation [31]. Aqueous extract of *Hamelia patens* helps in decreasing menstrual cramps.

Hamelia could be a good anti-nociceptive agent because of its good activity and low toxicity. In hot plate test, *Hamelia* shows moderate anti-nociceptive effect nearly 25% with 200mg/kg dose but in chemical-induced nociception model, *Hamelia patens* show anti-nociceptive effect similar to naproxen (100mg/kg) at 100-200mg/kg dose. In Acute toxicity test, LD_{50} estimated for H. patens leaves was 2964 mg/kg i.p. and >5000 mg/kg p.o, whereas in subacute test *Hamelia*

patent extract did not affect hematological or biological parameter [33].

Methanolic extract of leaves of *Hamelia patens* contains several oxindole alkaloids – isopteropodine (in abundance nearly 30.5 to 98%), rumberine, palmirine, maruqine (only 0 to 17.5%), alkaloid a (30.5-43%). Methanolic extract of *Hamelia patens* show relaxant effect in KCl –induced contraction in rat myometrium and its effect is concentration dependent. Here it is proved that rumberine and palmirine show a higher muscle relaxant effect but these constituents counteract the effect of isopteropodine (show muscle contraction). Methanolic extract of *Hamelia patens* is used to induce myometrium contraction contractile to aqueous extract which is used to treat amenorrhea and to stop bleeding; this might be because of –

- The chemical constituent could be different in two,
- The difference in species (Human and Rat),

The model used for the evaluation, it would be necessary to evaluate the effect of the extract on the pharmaco-mechanical coupling of the contraction. The overall relaxant effect of methanolic extract of *Hamelia* has poor relaxant effect than verapamil [15].

H.patens assessed for its Analgesic and antipyretic effect in formalin-induced writhing response model by Vijay RB *et al*. At a dose of 50-200mg/kg analgesic activity was observed. Here leaves of *Hamelia patens* are extracted by successive solvents and finally, the analgesic effect is found in ethanolic extract. Analgesic activity is more pronounced than antipyretic. The observed antipyretic effect may be due to the flavonoids and alkaloidal content of leaves. These flavonoids act by blocking prostaglandin E2 (fever mediators) synthesis. The active compounds which can participate in analgesic activity are maruquine, isomariquine, pteropodine, isopteropodine, palmirine, rumberine, speciophylin and stigma 4ene-3, 6-dione [41].

Table-1: Phytochemicals present in *Hamelia patens* with different solvents

Ethanolic extract	Methanolic extract	Water extract	Petroleum ether	Chloroform
Alkaloid	Alkaloid	Alkaloid	Steroids	Alkaloid
Tannins	Tannins	Tannins	Triterpenoids	Glycoside
Glycosides	Glycosides	Glycosides	Fatty Acid	Steroids
Saponins	Saponins	Saponins	Flavonoids	Triterpenoids
Steroids	Steroids	Steroids	Alkaloids	
Flavonoids	Flavonoids	Terpenoids	Glycosides	
Terpenoids	Terpenoids	Phloba tannins		
Phloba tannins	Phloba tannins			
Phenolic and acidic compounds	Phenolic and acidic compounds			

Table-2: Showing different property of *Hamelia patens*, plant part, solvent test organism

S.No.	Functional Property	Plant part	Solvent Show activity	Extraction Method	Test Organism	References
1.	Anti-Bacterial Property	Leaves	Hexane	Soxhlet Extraction	*Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa and Staphylococcus aureus bacteria*	Camprose *et al*. [12]
		Stem, bark, and roots	Water ethanol and acetone	Soxhlet Extraction Percolation	*Staphylococcus aureus, Bacillus subtilis, Pseudomonas flurescens, Escherichia coli and Aspergillus niger, Penicillium chrysogenum, Alternaria alternata.*	Singh *et al*.[42]
		leaves	Ethanol	Soxhlet Extraction	*Staphylococcus aureus, Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi*	Aquino *et al.* [1]
		Leaves	Ethanol	Maceration, soxhlet and percolation	*Staphylococcus aureus, S.typhi, S.paratyphi and E.coli*	Paz Wong *et al.*[30]
2.	Anti-inflammatory	Leaves	Chloroform	Maceration	Croton oil induced oedema in mice	Sosa *et al.* [39]
		Leave	Hexane	Maceration	Carrageenan induced oedema	Jimenez-Suarez *et al*. [19]
3.	Anti-Fungal	Leaf,	Ethanol	Soxhlet	*Aspergillus fluvus,*	Sapana

		stem, and roots		Extraction	*Aspergillus fumigatus, Penicillum sp.*	Khandelwal *et al.* [41]
		Leaf, Flower, seeds, fruits	Aqueous	Maceration	*Aspergillus fumigatus, Candida albican, Fusarium oxysporum, Rhizoitonia solani.*	Abubaker *et al.* [4]
		Stem and leaf	Aqueous, Ethanol	Maceration	*Candida albicans, Aspergillus niger*	Okoye *et al*. [26]
4.	Anthelmintic	Leaf, stem, roots	Ethanol	Soxhlet apparatus	*Pheritima posthuma*	Sapana khandelwal *et al*. [41]
5.	Antidepressant effect	Stems	Chloroform	Soxhlet apparatus	Forced swimming test, tail suspension test, open field test models on wistar mice.	Surana A K *et al.* [21]
6.	Hypoglycemic effect	Aerial parts	Water, ethanol	Boiling	STZ-NA-Induced diabetes in rat	Andrade-Cetto. A *et al.* [2]
		Leaves	Methanol	Fractional extraction and crude extract	Streptozotocin induced hyperglycemia	Rugerio-Escalona C *et al.* [36]
		Stems	Ethanol	Soxhlet Extraction	Alloxan induced diabetic rat	Pandurangan A *et al.* [29]
7.	Hepatoprotective activity	leaves	Butanol		AST activity on HepG2 cell subjected to death with CCl4	Meseguer P *et al.* [20]
8.	Anti-oxidant	Aerial parts	Methanol, acetone, and hexane	Maceration	Oxidation of β-carotene and linoleic acid	Ruitz-Teran *et al.* [35]
9.	Leishmanicidal activity	Leaves	Methanol	Soxhlet apparatus	Leishmania Mexicana	A.I. Suárez *et al.* [40]
10.	Toxicity and nociceptive effect	leaves	Ethanol	Soxhlet apparatus	Thermal-induced nociception	Alonso-Castro *et al.* [5]
11.	Myometrium Contraction	Leaves	Methanol	Maceration	KCl- induced Contraction in rat myometrium	Reyes-Chilpa *et al.* [33]
12.	Analgesic and Antipyretic effect	Leaves	Ethanol	Soxhlet apparatus	Formalin-induced writhing response model.	Vijay R B *et al*. [44]

Table-3: Phytochemicals present in *Hamelia patens* with different solvents

S.No.	Author	Plant part	Chemical constituent isolated
1.	Ripperger H. [31]	Aerial parts of plant	stigma-4-ene-3,6-dione
2.	Ripperger H. [32]	Aerial parts of a plant	Isopteropodine
3.	Borges *et al*. [8]	Aerial parts of plant	Palmirine and rumberine (oxindole alkaloid and heteroyohimbane type) isolated
4.	Aquino *et al.*[1]	Methanolic extract of aerial parts of a plant	Narirutin, rosmarinic acid and new glycoside 5,7,2', 5'-tertrahydroxyflavanon-7-rutoiroside
5.	Chaudhary *et al*.[11]	Leaves and twigs of plant, extracted with n-hexane and methanol,	Ephedrine
6.	Andrade-Cetto. A *et al.* [2]	Ethanolic extract of the whole plant	Chlorogenic acid, caffeic acid, quercetin
7.	Rios and Aguilar *et al.* [34]	Acetone extract of leaves	Cycloartanols, and triterpenes24-methylenecycloartane-3ß-ol, 24-methylcycloart-24-en-3ß-ol, 2 E - 3,7,11,15,19 - pentamethyl-2-eicosane-1-ol, stigmasterol, ß-sitosterol, ursolic acid, aricine, oxindole aricine, rotundic acid and catequine
8.	Suarez *et al.* [40]	Ethyl acetate extract of leaves	Kaempferol-3-O-rutinoside and (-) epicatechin
9.	Ruitz-Teran *et al.* [35]	The hexane extract of aerial parts of the plant	β-carotene
10.	Paniagua-	Micropropagated plantlets	Monoterpenoid oxindole alkaloid named (-) hameline together with 8

	Vega D *et al*. [28]		alkaloids like aricine, isopteropodine, pteropodine, uncarine, speciophylline, tetrahydroalstonine, palmirine and rumberine
11.	Jimenez Suarez *et al*. [19]	Hexane and MeOH-EtOAc extract of leaves	β-sitosterol and stigmasterol , triterpene, (6E,10E,14E18E)-2,6,10,14,18,23-hexamethyl-2,6,10,14,18,22-tetracosahexane
12.	Paz *et al*. [30]	Ethanolic extract of leaves	12 phenolic compounds in plant extract- Quinic acid, Hydroxycinnamic acid, Catechin, Caffeoylquinic acid, Procyanidin, (−)-Epicatechin, (+)-Catechin 3-O-glucose, Quercetin 3-O-rutinoside, Kaempferol 3-O-rutinoside, Hydroxyphloretin 2 ′ -O-Glucoside

CONCLUSION

The different property of *Hamelia patens* studied here which may be due to the presence of many bioactive chemical constituents including alkaloids, carbohydrates, sterols, proteins, glycosides, flavonoids, and acidic compound serve as a potential source of drugs with biological significance. Further research is necessary to discover the dynamic compounds and more ethnomedical to the extravagance of human diseases.

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