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ASYSTASIA GANGETICA: A BIBLIOMETRIC ASSESSMENT OF GLOBAL PUBLICATIONS OUTPUT DURING 1960-2020

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ABSTRACT: There has been an exponential growth in plant-based products during the last few decades for the treatment of various ailments. According to literature, about 25% of prescribed drugs are of plant origin globally. One such important plant is *Asystasia gangetica*, also known as 'Chinese violet' or 'Ganges primrose' is an ornamental, scattering, groundcover herb. The plant is about 0.30 to 0.60 m in height, mainly distributed in sub-Saharan tropical Africa, Arabia, and tropical Asia (including India). Ethnobotanically, the decoction of its leaves is effective in the treatment of rheumatism, stomachache, anthelmintic, heart pains, asthma, astringent, diaphoretic, woman infertility, *etc.* It is mainly reported to contain chalcone, biflavons, glucoside, amino acid, iridoid glycoside, *etc*. Pharmacologically plant is reported to possess anti-asthmatic, anti-hypertensive, anti-diabetic, anti-hyperlipidaemic, anti-microbial, anti-oxidant activity, anti-snake venom, *etc.* The present review is an attempt to describe the important medicinal properties of *A. gangeticain* the traditional and modern scientific research. It is concluded that the plant has numerous therapeutic potential which need to be explored.

INTRODUCTION: There has been an exponential growth in plant-based products during the last three-decade for the treatment of various ailments [1]. According to literature, plants are the important source of secondary metabolite and constituted about 25% of all prescribed drugs globally [2, 3]. The family Acanthaceae comprises medicinal plants and phytoconstituents with an extensive range of biological activities. From this family, the genus Asystasia comprising of nearby 70 species, mainly scattered in sub-Saharan tropical Africa, Arabia, and tropical Asia4where; they were used up as vegetable [5, 6, 7].

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One such species is *Asystasia gangetica*, also known as Chinese violet, coromandel, creeping foxglove, Ganges primrose, etc. In India, it is also known as kaligharani (Gujrati), lavangavalli, lavanavalli (Kannada), Valli-upu-dal (Malayalam), lavanavalli (Marathi), Miti-kirai (Tamil), etc.

Etymology: Asystasia means 'Inconsistency' and is correlated with the more or less regular corolla of the plant. Gangetica means 'The Ganga river' where this species supposed to be grown in India [8, 9].

Taxonomy: *A. gangetica* is a beautiful ornamental herb, which is rapidly growing, perennial, scattering groundcover, and is grown from 0.30-0.60 m in height. Stems (slightly hairy) develop adventitious roots easily at the nodes when it comes in contact with wet soil. Greenish leaves (up to 8 cm long and 4 cm wide) were elliptical or cordate in shape possesses ovate outline occurring in opposite pairs [10].

The flowers (up to 3.5 cm long and 3 cm wide) are white-cream coloured with tessellated purple markings. Fruits are elongated, club-shaped, contain 4 seeds splitting from tip to base, and is of green coloured, which is converted to brown on maturity. Bone coloured flat seeds are 0.5 cm long and 0.1 cm wide. It is semi-hardy and young plant that requires protection in areas of heavy frost. In tropical areas, it can grow wildly [6, 11, 12, 13].

PLANT OF *A. GANGETICA*

Traditional, Unani and Other Ethnobotanical uses: The plant is used traditionally as a decoction for the cure of rheumatism, stomachache, and heart pain. In East African countries, like Kenya, the decoction of leaves is used as a vermifuge to cure intestinal worms. Leaves are prevalently employed in the management of asthma in Nigeria [13, 14, 15]. In India, it is used as astringent, stomachic, and diaphoretic [9, 16]. It is claimed that the decoction of leaves is extremely effective in the treatment of asthma (anti-inflammatory) [9, 13, 15]. In Cameroonian traditional medicine, it is used in the treatment of bone fracture, bone diseases, diarrhoea, and woman infertility [17].

Phytoconstituents Investigated: Preliminary phytochemical analysis: n-hexane, ethyl acetate, and methanol extract of the plant have been investigated for the presence of phytoconstituents which revealed the presence of sugar, steroid, flavonoid, glycoside, anthraquinone in n-hexane extract; saponin, sugar, steroid, flavonoid, glycoside, anthraquinone in ethyl acetate extract; saponin, sugar, flavonoid, glycoside, anthraquinone in methanol extract [18].

The whole plant sample was dried, extracted with different solvents, and then tested for the presence of constituents. The plant is reported to possess steroids (in ethanol, chloroform, petroleum ether, and benzene extract), sugars (in aqueous, ethanol, petroleum ether, benzene extract), phenols (in ethanol, chloroform, petroleum ether, benzene extract), flavonoids (in aqueous, petroleum ether, benzene extract), saponins (in chloroform, benzene extract), tannins (in petroleum ether, benzene extract) and amino acid (in aqueous, chloroform, benzene extract) [19]. Leaves extract (ethanol) is reported to possess alkaloids, saponins, flavonoids, tannins [20].

Phytochemical isolated/Characterised: The ethyl acetate fraction from *A. gangetica* ethanol (80%) extract yielded a glycoside, luteolin-7-o-neohesperidoside (1) which was confirmed byphysical and chemical analysis [21].

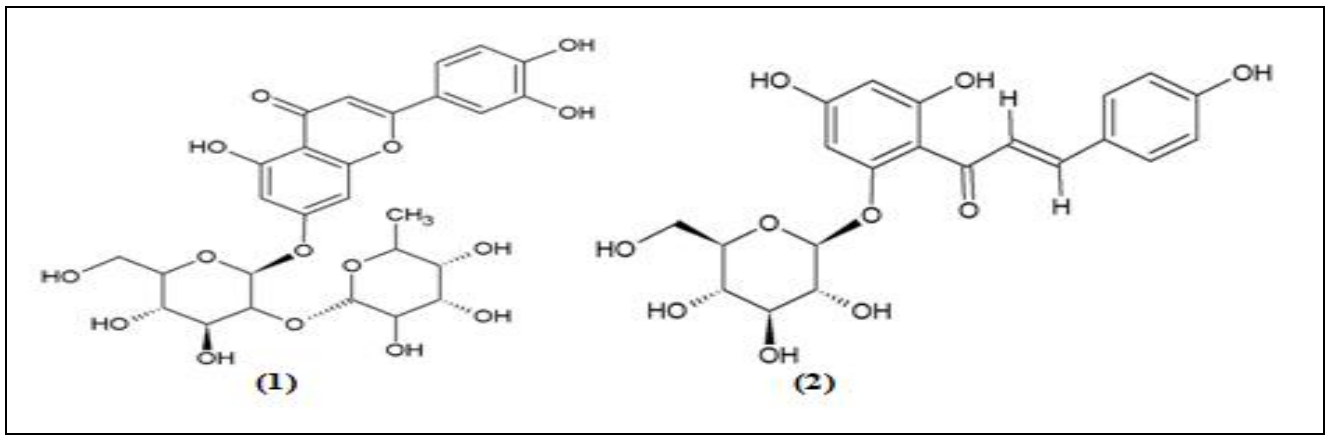
Two chalcones, isosalipurposide(2) and cernuoside (3) has been reported from the yellow coloured flower petals of *A. gangetica* [22]. The plant especially leaves encompass tremendous quantity of amino acids (thiamine), fibers, proteins, sugars, minerals, *etc*., thus it is considered as an important source of food [23, 24]. A methanol extract of the aerial part of *A. gangetica* was defatted with diethyl ether and subjected to silica gel chromatography to obtain 8 compounds, including a new compound; asysgangoside is also known as 5, 11-epoxy-megastigmane glucoside(4). Other constituents are; apigenin 7-O-neohes-peridoside (5); apigenin 7-O-β-D-gluco-pyranoside (6); benzyl β-D-gluco-pyranoside (7); (6S,9R)-roseoside (8); ajugol(9); salidroside (10); and apigenin 7-O-b-Dgluco-pyranosyl (1-6)-β-D-gluco-pyranoside (11) [25].

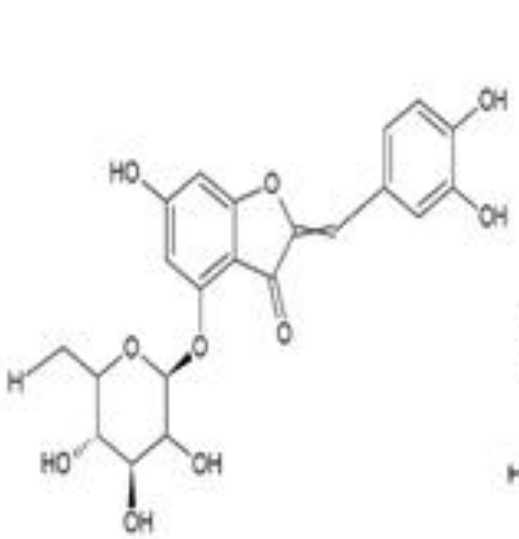
From the methanol extract (ethyl acetate fraction) of yellow portion of the *A. gangetica* flowers, a yellow solid compound has been isolated and was characterized by UV, NMR, MS study as apigenin 7-O-glucosyl(3'-6")luteolin7"-O-glucoside (12) [26]. Aerial, seed and root portion from *A. gangetica* was collected, crushed, and volatile oil was extracted using Clevenger apparatus to give 0.10%, 0.56% & 0.51% yields respectively. These volatile oils were subjected to GC-MS analysis. A total of 54 compounds has been characterised in aerial part [2,2,3,3-tetramethylbutane(13); propylcyclohexane (14); Methylcyclohexane(15); 2,6-dimethyloctane (16); ethylcyclopentane(17); 2-methyl,4-heptanone (18); 1α,2β,4α-trimethylcyclopentane(19); cis-pinane (20); 1α,2α,3β-trimethylcyclopentane(21); methylarsonic acid (22); 2-methylheptane (23); 4-

methylnonane (24); toluene (25); 1-ethyl,2-methylbenzene (26); 1,3-dimethylcyclohexane (27); 1,3,5-trimethylbenzene (28); 1,1-dimethyl-cyclohexane (29); 1-octen-3-ol (30); 1-ethyl,2-methylcyclopentane (31); 1,2,3-trimethylbenzene (32); 2, 4-dimethylheptane (33); n-decane (34); ethylpentanoate (35); 4-methyldecane (36); 1,2-dimethylcyclohexane (37); 1,2,4-trimethylbenzene (38); 1,4-dimethylcyclohexane (39); o-cymene (40); 3,7-dimethylundecane (41); undecane (42); ethylcyclohexane (43); bis-2-ethylhexylphthalate (44); 1,1,3-trimethylcyclohexane (45); bis-7-methyloctylphthalate (46); chlorobenzene (47); bis-butyldecylphthalate (48); 1α, 2α, 4β-trimethylcyclohexane (49); bis-diheptylphthalate (50); isopropylbutyrate (51); bis-hepty-loctylphthalate (52); ethylbenzene (53); bis-decylhexylphthalate (54); 2,5-dimethylheptane (55); bis-isodecylhexylphthalate (56); o-xylene (57); bis-decyloctylphthalate (58); 1-ethyl,4-methylcyclohexane (59); bis-isodecyloctylphthalate (60); p-xylene (61); bis-didecylphthalate (62); nonane (63); bis-diundecylphthalate(64); cis-octahydro-1H-indene (65); 4-methoxy-3-(8-quinolinyloxymethyl) benzaldehyde (66)], 21 compounds in Seed [methylcyclohexane (15); n-heneicosane (67); n-tricosane (68); toluene (25); didodecylphthalate (69); bis-(7-methyloctyl) phthalate (70); 1-octen-2-ol (71); palustrol (72); benzene,1, 2, 3-trimethyl (73); n-tetracosane (74); n-docosane (75); phenyl-3-deoxy-βd-ribo- hexa-pyranoside (76); 11-phenoxy-undecanoic acid (77); heptyloctylphthalate (52); Manoo l(78); octadecanol (79); Methyl 2-methyl hexacosanoate (80); diisooctylphthalate (81); Dinonylphthalate (82);] and 15 compounds in root [methyl-cyclohexane (15); abietal (83); toluene (25); o-xylene (57); tricosane (68); 1-octenol (84); palustrol (72); n-decane (34); abietol (85); decyl-hexylphthalate (54); n-tetracosane (74); neoabietol (86); n-docosane (75); n-pentacosane (87); de-hydroabietal (88)] [27]. Methanolic extract of aerial part of *A. gangetica* contains five iridoid glycoside *viz.* 6β-hydroxyantirrhide (89); angeloside (90); 6-O-α-L-rhamnopyranosyl-catapol(91); 6-O-α-(3”-O-trans-caffeoyl)-L-rhamnopyranosyl-catapol (92); ajugol (9) [28].

GC-MS analysis of benzene extract of plant leads to identification of several no. of phytoconstituents like, benzene ethanol (93); hydrazine (Phenyl-methyl) (94); tetraethyl silicate(95); 1-ethyl-2-methyl-benzene (96); dl-allo-cystathionine (97); benzene, 1, 3, 5-trimethyl (28); anthracene (98); 1, 3-dichloro-2-(2-nitrovinyl)benzene (99); 2-formyl-histamine (100); 1-Octadecanamine (101); dodecane (102); N-ethyl-N’-nitroguanidine(103); 2-Phenazinecarboxylic acid (104); 2,5-cyclo-hexadien-1-one (105); octadecane(106); octa-decanoic acid (107); 1,3-Isoindolinedione (108); isopropyl palmitate(109); N-methyl-1-adaman-taneacetamide (110); propanoic acid(111); cyclo-trisiloxane hexamethyl (112); 2,4,6-cyclo-hepta-trien-1-one (113); 1,2-Benzenediol(114); 5-methyl-2-phenylindolizine (115); dibutyl phthalate (116); 1, 3-bis(trimethylsilyl) benzene (117); 2-Methyl-3-(2- (4-phenyl-1-piperazinyl) ethyl) indole (118) [19].

Methanolic extract of the plant was fractionated using column chromatography and the ethyl acetate: methanol (equal quantity) fraction was characterised using TLC, HPLC, which reported the presence of 4 known flavonoids *viz.* luteolin (119), quercetin (120), kaempferol (121) and isorhamnetin (122) and 2 unknown compounds [29].





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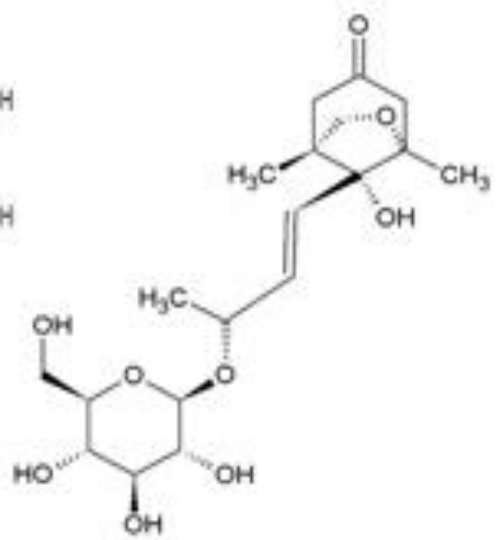

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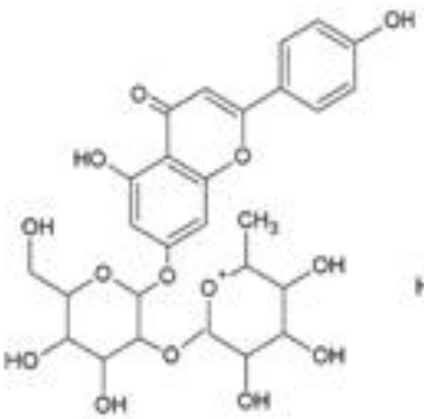

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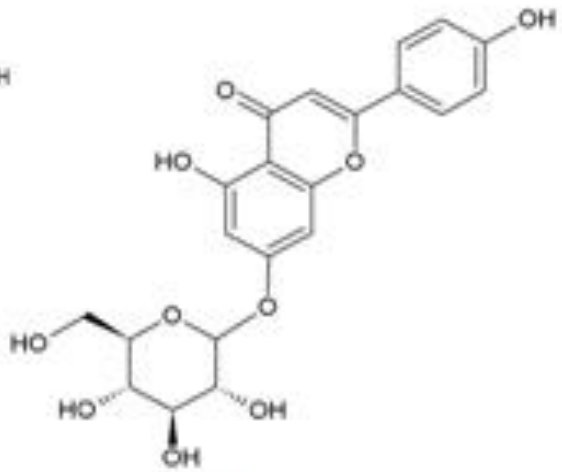

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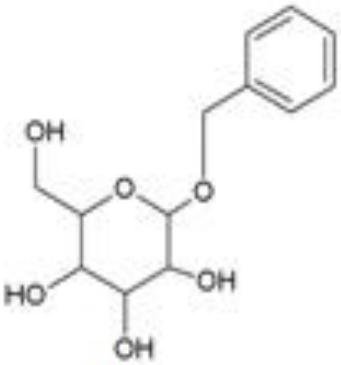

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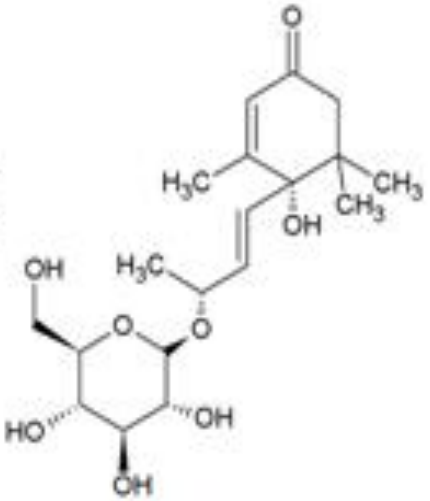

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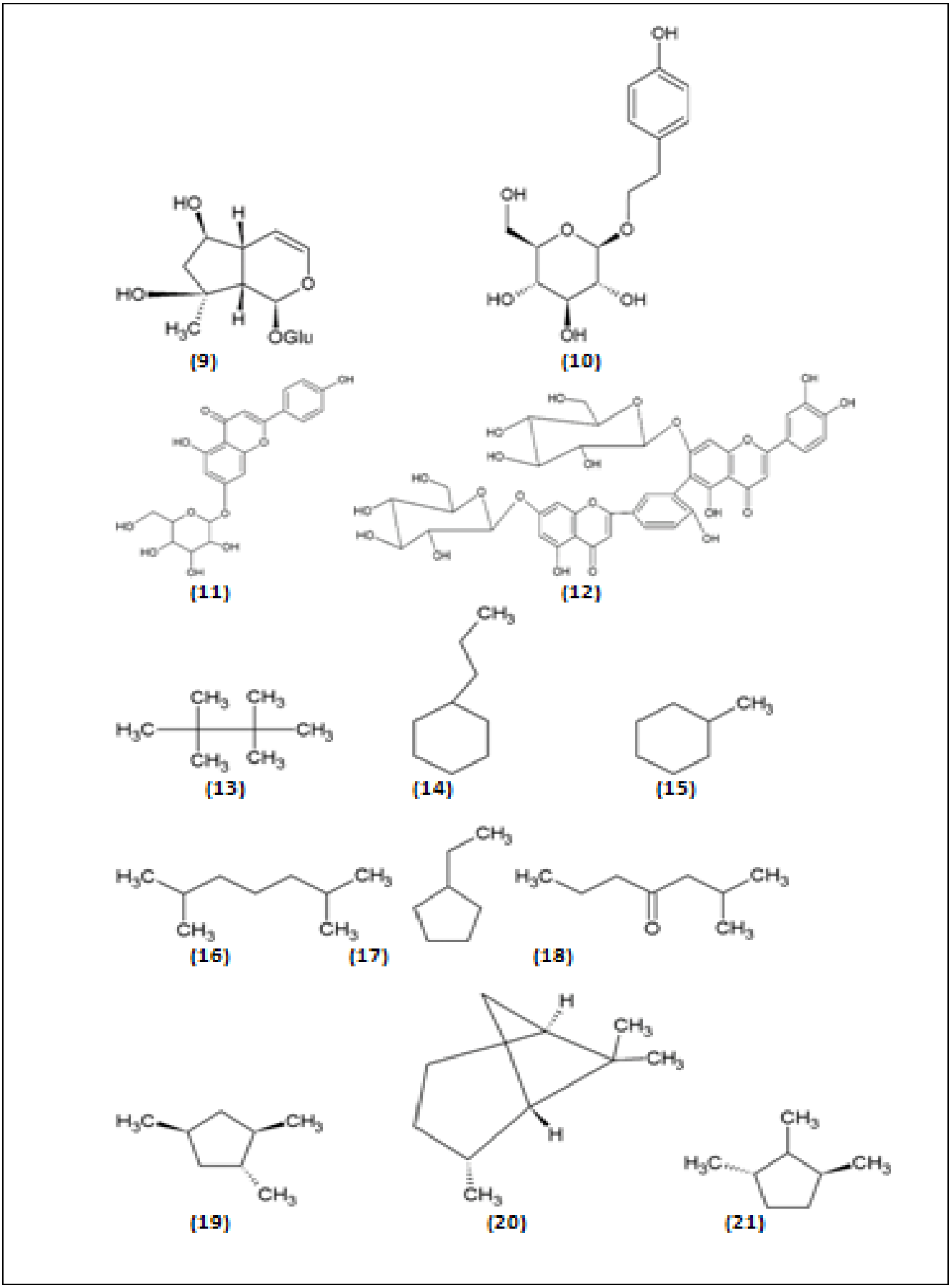
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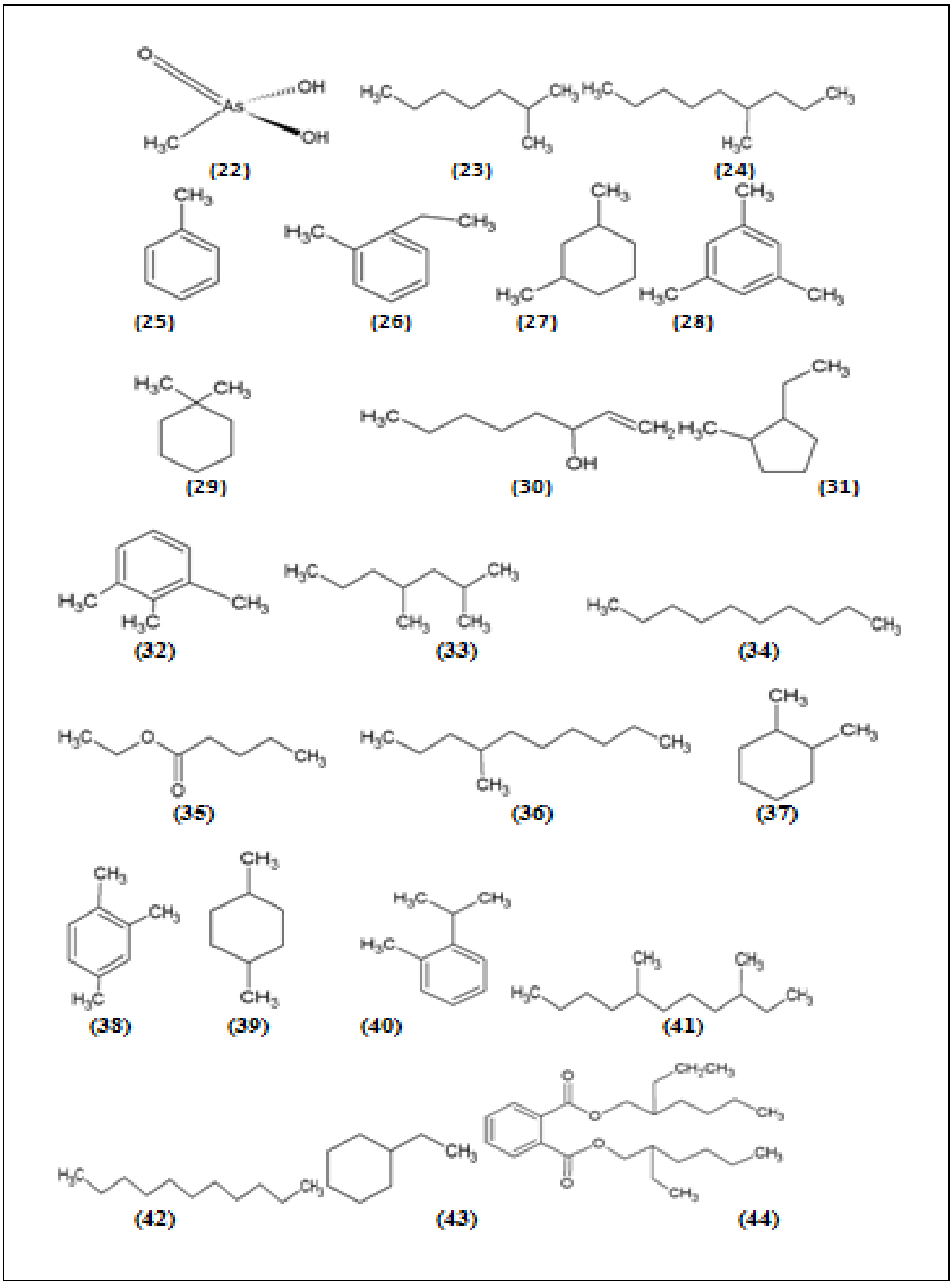
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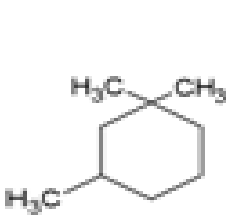

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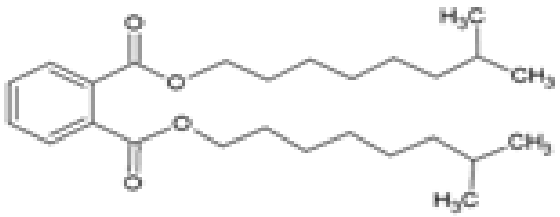

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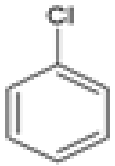

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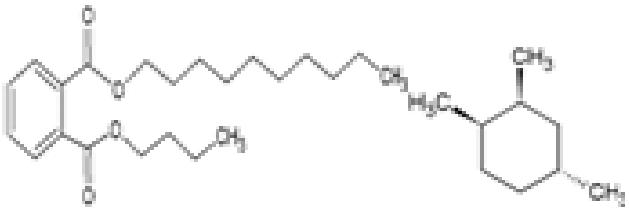

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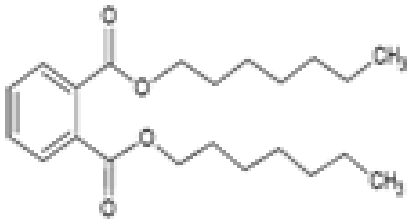

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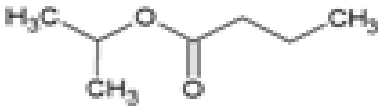

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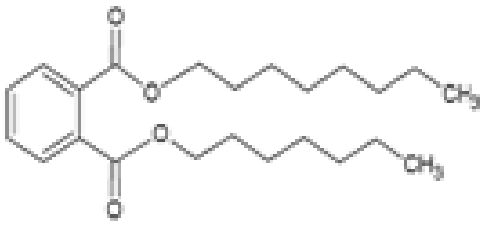

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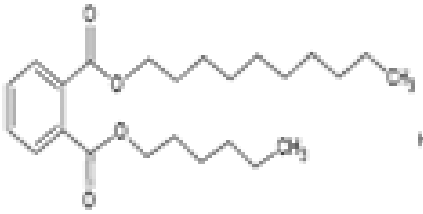

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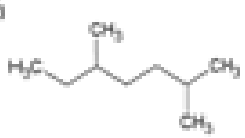

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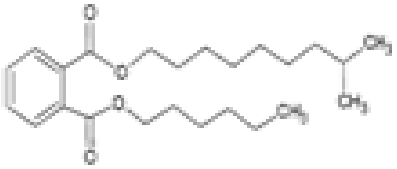

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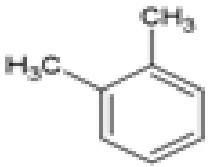

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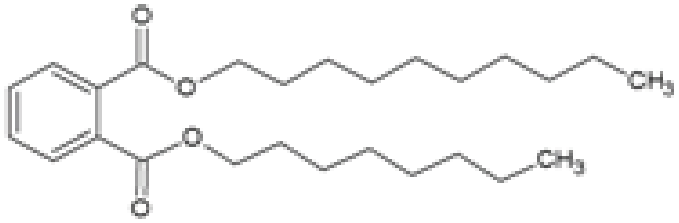

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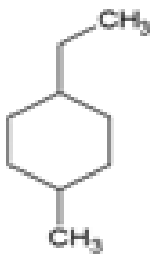

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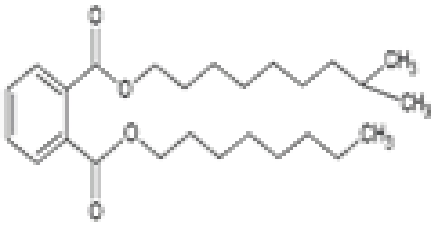

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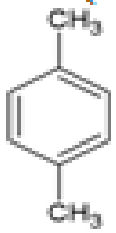

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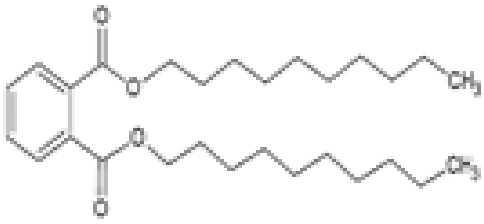

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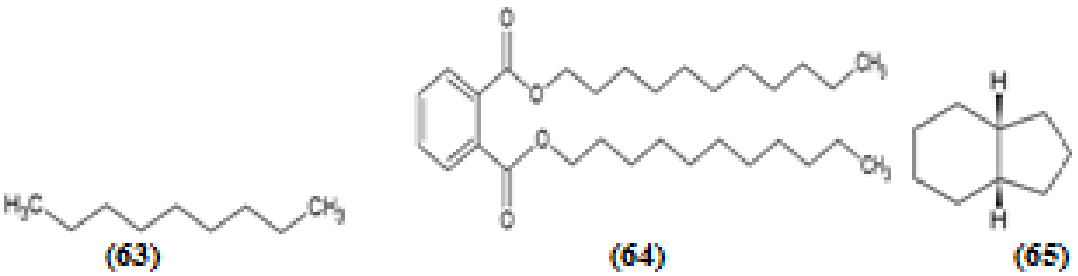

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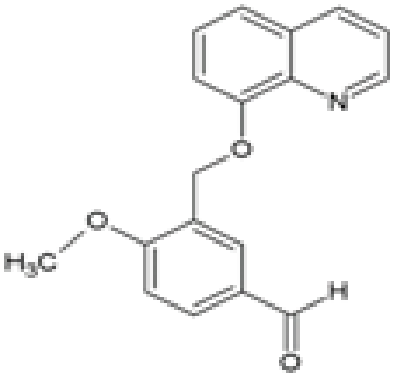

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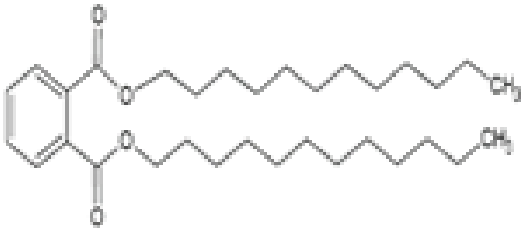

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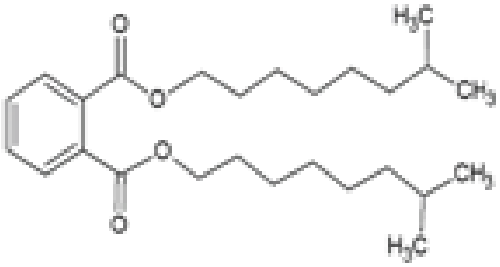

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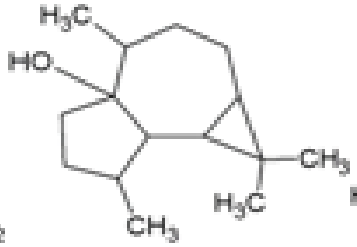

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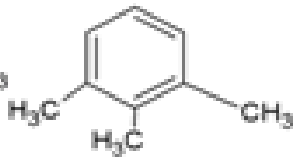

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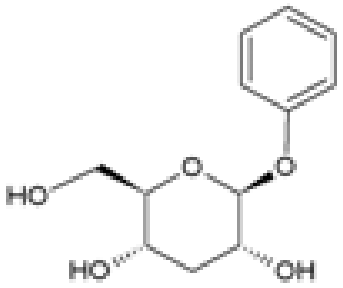

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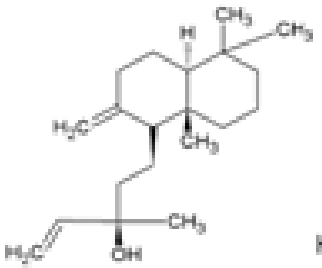

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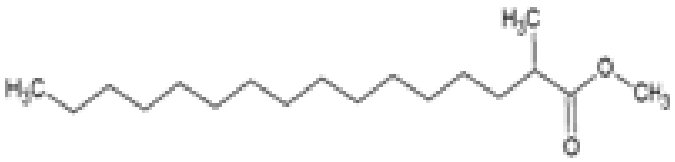

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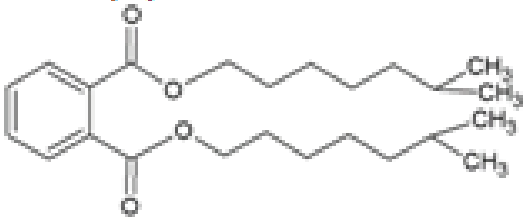

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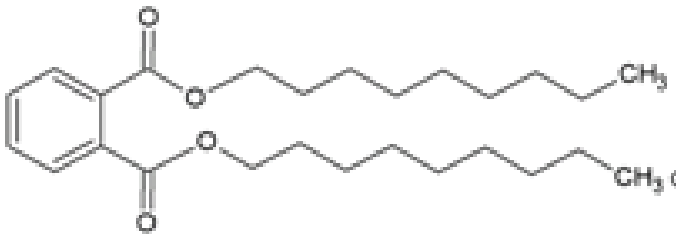

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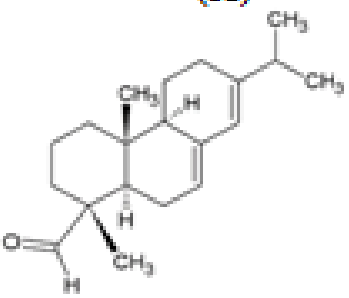

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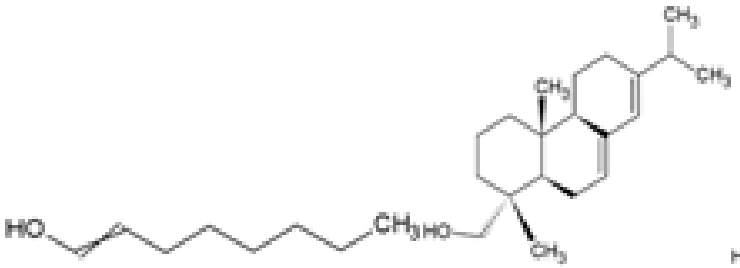

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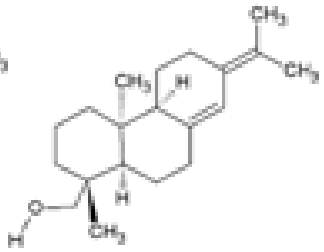

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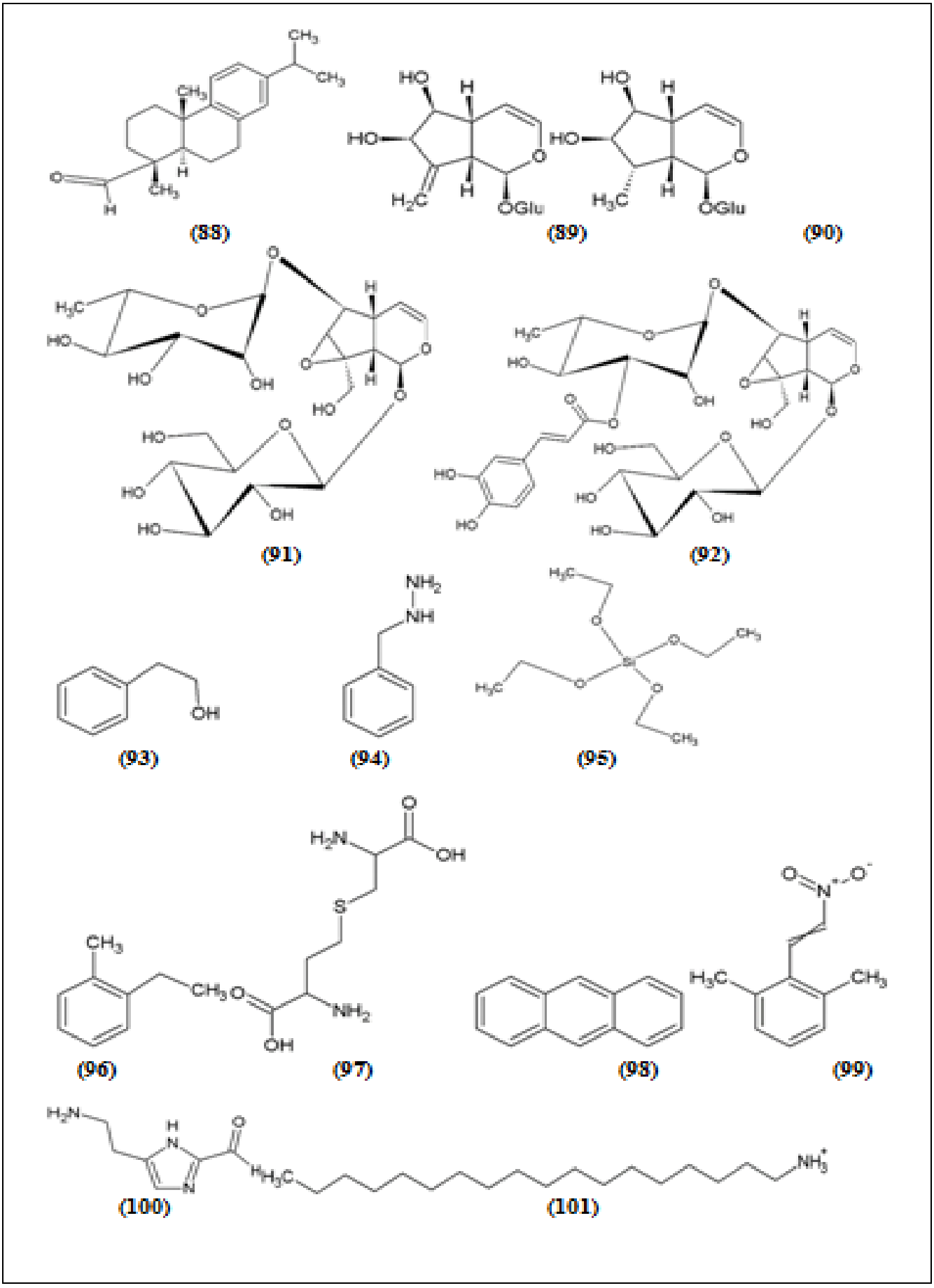
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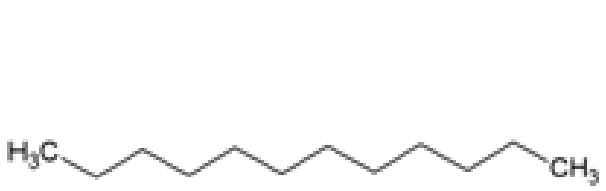

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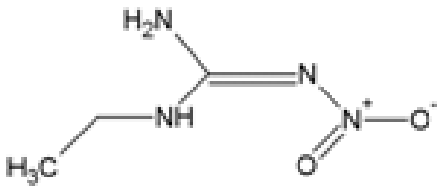

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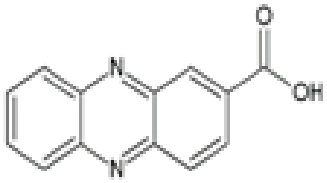

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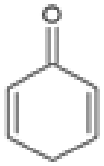

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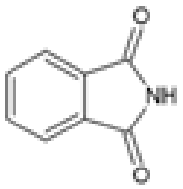

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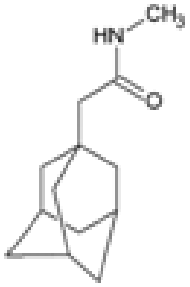

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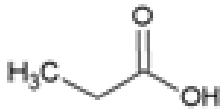

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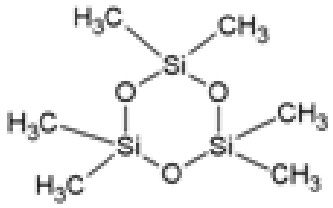

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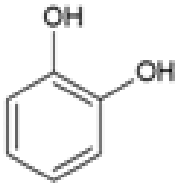

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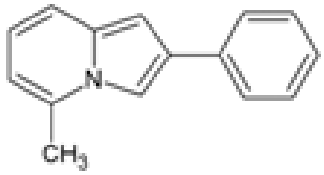

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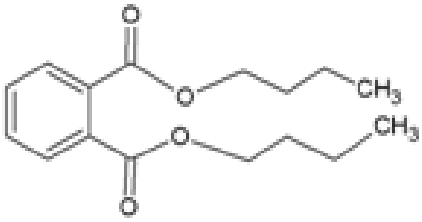

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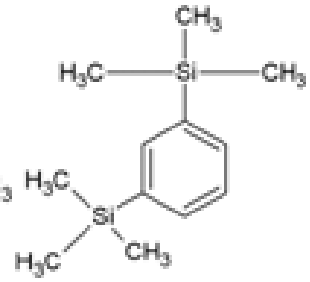

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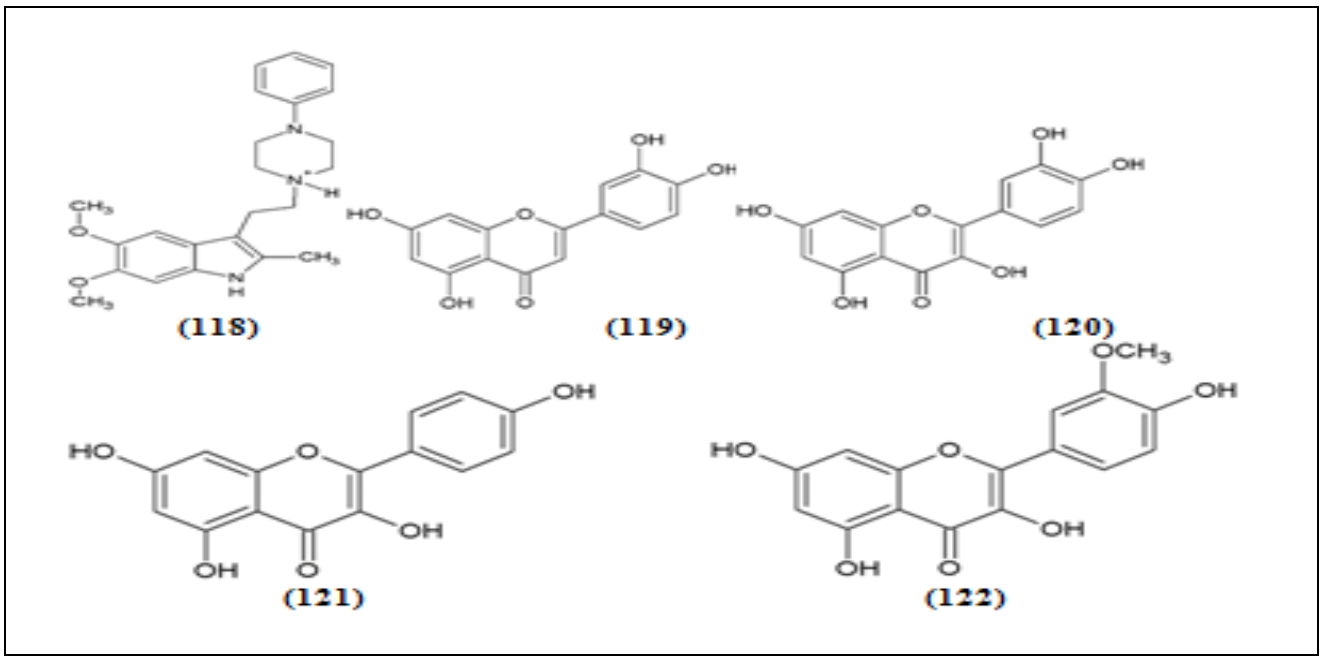

Pharmacologic Inactivity Documented By Researchers:

Anti-inflammatory Activity: *A. gangetica* extract (80% ethanol) and its isolated glycoside, luteolin-7-o-neohesperidoside when subjected to hypotonicity induced haemolysis. It produced dose-dependent %inhibition and exhibited biphasic activity. Anti-inflammatory activity of luteolin-7-o-neohesperidoside was assessed by carrageenan induced rat paw oedema method in albino rats and the effect was found to be significant and comparable to phenyl butazone [21].

Anti-asthmatic Activity: *A. gangetica* leaves possess significant anti-asthmatic property in Guinea pigs by relaxing histamine-pre-contracted tracheal strips. The ethyl acetate extract is found to be more potent than its hexane & methanol extract. These extracts especially methanol, also showed an anti-inflammatory response against egg albumin-induced acute inflammation in Albino rats [13].

Antihypertensive Activity: Methanolic extract of leaves of *A. gangetica* exhibited Angiotensin-1Converting Enzyme (ACE-1) inhibitory activity in vitro with 51% inhibition and thus possessed anti-hypertensive properties [7]. *A. gangetica* decreased the diastolic, systolic, and mean arterial BP significantly ($p<0.01$) and dose-dependently (10-400 mg/kg). It also produces a drop-in heart rate which was significant ($p<0.05$) but not dose-dependent. A mixture of infusion of either angiotensin I or angiotensin II with *A. gangetica* (200 mg/kg) significantly ($p<0.001$ and $p<0.01$ respectively) restrained their hypertensive effect, and this was also accompanying by drops in heart rate9.

Anti-diabetic & Hypolipidemic Action: Administration of ethanolic extract (100 and 200 mg/kg, p.o.) of *A. gangetica* to diabetic rats for 4 weeks, significantly reduced blood glucose, restored lipid levels, thus held significant anti-diabetic action. The effect may be due to the anti-oxidant activity of extract [30]. *A. gangetica* leaves, at three dose level (25%, 50% and 75% juice), suppress the raised blood glucose concentration and improved body weight in the diabetic rat (alloxan-induced). The levels of TC, TG were significantly ($P < 0.05$) reduced in all treated groups [31].

The flowers of *A. gangetica* were extracted with ethanol and acidified using citric acid to obtained anthocyanins extract, which was assayed in vitro against α-amylase and α-glucosidase. Anthocyanins extract possessed significant inhibitory activity (71.46 ± 1.21% and 76.85 ± 0.75%, respectively) and IC_{50} value (260 ml/ml and 244 ml/ml, respectively) at the concentration of 400 mg/ml. Thus, the enzyme inhibition may be the possible mechanism of anti-diabetic activity [32]. Aqueous and alcoholic extract of leaves of *A. gangetica* lowered down the fasting blood glucose level by 48.47 ± 1.01 and 48.46 ± 0.93% respectively, in

type I diabetic wistar rats (alloxan induced) [20]. Leaf extract of *A. gangetica* in the form of herbal formulation with leaf extracts of *Hibiscus rosasinensis*, *Emilia coccinea*, and *Acanthus montanus* significantly improved hyperglycaemia as well as dyslipidaemia in alloxan-induced diabetic male rats [33].

Anti-oxidant Activity: 70% ethanolic extract of *A. gangetica* leaves (100 mg/kg) along and in combination with 90% ethanolic extract of *Morus indica* (400 mg/kg) possessed significant anti-oxidant and antidiabetic action in diabetic albino rats (alloxan induced) [34]. Alcoholic extract of leaves upsurges the levels of glucose-6-phosphate dehydrogenase (G-6-PDH), catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), reduces glutathione (GSH), and declines lipid peroxidation (thiobarbituric acid reactive substances) level; thus, possessed anti-oxidant property [30].

Free radical scavenging activity has been performed on isolated iridoid glycoside *viz.* 6β-hydroxyantirrhide; angeloside; 6-O-α-L-rhamnopyranosyl-catapol; 6-O-α-(3”-O-trans-caffeoyl)-L-rhamnopyranosyl-catapol; ajugol. In DPPH assay, iridoid glycoside, 6-O-α-(3”-O-trans-caffeoyl)-L-rhamnopyranosyl-catapol exhibited the potent scavenging activity with SC50(half maximal scavenging activity) value [20]. 3 mM with respect to the other iridoid glycosides. In the ORAC assay, 6-O-α-(3”-O-trans-caffeoyl) -L-rhamnopyranosyl-catapol was more potent than the positive control [28]. The *A. gangetica* alone or in combination with *Hibiscus rosasinensis*, *Emilia coccinea* and *Acanthus montanus* showed the free radical scavenging activity against 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical, hydrogen peroxide (HP), hydroxyl radical (HR), nitric oxide radical (NOR), and superoxide radicals (SOR) using *in-vitro* models [35]. All these studies suggested the use of plant as anti-oxidant.

Antimicrobial: Hexane, ethyl acetate and methanol extracts of *A. gangetica* at conc. 25 to 200 mg/ml inhibited (dose dependent) the growth of 12 pathogenic microorganisms, including 6 bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonellae typhi*, *Bacillus subtilis* and Klebsiellae pneumonae) and 6 fungi (*Epidermophyton floccosum*, *Rhizopus stolon*, *Aspergillus niger*, *Penicillum notatum*, *Candida albicans* and *Tricophyton rubrum*) to different degrees using agar diffusion pour plate method [18].

Anti-snake Venom: Administration of methanol extract of leaves of *A. gangetica* at 1g/kg i.p., 30 min before administration of Najamelanoleuca’ svenomto mice provided 60% protection which is significant ($p<0.05$) compared to control group. On the other hand, its polyphenolic fraction (flavonoids, tannins, saponin) each at 1 g/kg i.p. provide 60%, 80%, and 60% protection, respectively, against venom, which is significant ($p<0.05$) compared to control group [36].

Anthelmintic Activity: Methanol extract (12.5, 25, 50 mg/ml) of fresh leaves of *A. gangetica* exhibited significant ($P<0.05$) and conc. dependent reduction in death time against Nsukkadrilus be compared to the piperazine [37]. Methanolic extract (10-200 mg/ml) of the plant exhibited dose-dependent decline in time taken for paralysis and subsequently death against *Pheretima posthuma*. 200 mg/ml conc. showed the most potent effect against earthworms comparable to albendazole [29].

Anti-arthritic activity: Dose-dependent (10-1000 µg/ml) inhibition of protein denaturation was reported in the methanolic extract of *A. gangetica* for anti-arthritic activity. The highest % inhibition (78.94%) was noted in 1000 µg/ml conc. compared to diclofenac sodium (84.47%) [29].

Anti-platelet: Methanolic extract of the plant revealed a dose-dependent (100-500 µg/ml) inhibition of aggregation for anti-platelet activity with the highest inhibition was noted down at 500 µg/ml conc. compared with the aspirin [29].

Effect of Blood Viscosity: In blood, methanolic extract and its flavonoid fraction displayed a dose-dependent (100-500 µg/ml) reduction in viscosity in 90 minutes spam. Flavonoid fraction exhibited a higher reduction in viscosity than methanol extract [29].

CONCLUSION: *A. gangetica* is a medicinal plant of enormous significance due to its sundry traditional uses, a range of phytoconstituents including lead molecules and phytopharmaco-logical effect for the treatment of a variety of

ailments. The present review divulges that this plant is a huge source of novel phytoconstituents possessing extensive bioactive responses particularly, anti-diabetic, antioxidant, anthelmintic, anti-asthmatic, anti-bacterial, *etc.* As far as the phytopharmacological importance is concern the plant is still unexplored and finally it can be concluded that, lots of research need to be carried out on the plant so that it can become more useful in therapeutic.

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