Phytochemical Profile and Pharmacological Aspects of *Achyranthes aspera* Linn- An Overview

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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**ABSTRACT**

**Background:** *Achyranthes aspera* Linn, commonly known as Apamarga in Ayurveda (Prickly Chaff flower in English, Aghara in Hindi, Aghada in Marathi), is an annual, perennial herb that belong to Family Amaranthaceae and Genus *Achyranthes* consisting of several species which are popular as folk remedies. Certain ayurvedic and Unani practitioners use various parts of plant to treat various diseases. The present review aims to provide up-to-date information on different aspects of plant involving its botanical description, phytochemistry and bioactivities of different extracts to assess its therapeutic potential as a valuable source of natural compounds with beneficial effects on human health.

**Methodology:** Systematic search of scientific databases like Google, Google scholar, PubMed, Web of Science, Science Direct, SciFinder, Springer link were used to find potentially significant scientific research and reports of *Achyranthes aspera* Linn using combination of relevant keywords.

**Results:** *Achyranthes aspera* Linn is a popular folk remedy in the traditional medicinal system in all tropical Asian and African countries. So far, 58 important compounds have been isolated and...
identified from various parts of plant. These isolated constituents are mainly flavonoids, tannins, terpenoids, saponins, phytosterols; phenolic compounds etc which possesses activities like anti-inflammatory, antimicrobial, anti-oxidant, hypoglycemic, antihyperlipidemic, spermicidal and other various important medicinal properties.

**Conclusion:** Even though this plant consists of a wide range of phytochemicals and evaluated for biological activities using various *in-vitro* and *in-vivo* models but they are limited. More attention should be paid to identify mechanisms that underlie beneficial therapeutic potential. It is essential to conduct the next level of research, by extending pharmacological to design novel drugs.

**Keywords:** **Achyranthes aspera**; **phytochemistry**; **pharmacological activity**; **antioxidant**; **antimicrobial**.

### 1. INTRODUCTION

Plant resources constitute a significant natural wealth of the Country. Plants have an incredible ability to synthesize aromatic substances that are usually phenols, or their oxygen substituted derivatives. Due to this reason, worldwide plants are used medicinally and as a rich source of many potent and powerful drugs [1,2]. Plant-based natural components can be derived from any part of the plant such as roots, seeds, leaves, bark, flowers, fruits, etc [3]. Over the last two decades, interest in medicinal plants has grown enormously from the utilization of herbal products as natural cosmetics and from self-medication by the general population to evaluate biological effects of plants on human beings by the scientific investigators [4]. Therefore, people are promoting indigenous cultivation and processing of those medicinal plants to be used in several cultures and religions for the treatment of various ailments [5].

The market for plant-based medicines, nutritional goods, nutraceuticals, dietary supplements, cosmetics, etc. is rising in both developing and developed countries, due to the awareness and knowledge that the natural products are non-toxic, have lesser side effects, higher safety of margin than synthetic drugs, and readily available at affordable prices [6]. Secondary metabolites like alkaloids, glycosides, tannins, terpenoid, flavonoid, phenol, volatile oils and many more compounds serve as critical therapeutic agents [7].

*Achyranthes* L. that belongs to Amaranthaceae family is a genus of about 21 species; it is a perennial or annual herb, all of which are distributed in tropical and subtropical regions [8]. Out of those species, *Achyranthes bidentata* and *Achyranthes aspera* are the two mostly used species asa medicinal plant for decades in Asian countries.

*Achyranthes aspera* L. commonly called Prickly Chaff flower in English, Aghara in Hindi, Aghada in Marathi and Apamarga in Ayurveda, which is commonly, found throughout India, tropical Asian countries and other parts of the world. Certain Ayurvedic and Unani practitioners use various parts of the plant to treat Hansen’s disease, bronchial asthma, haemorrhoid, arthritis, wound, snake and insect bites, renal and cardiac dropsy, urinary calculus, diabetes, skin disorders, sexually transmitted diseases, gastroenteritis, lung infections, parasitic infections, gum diseases etc [9]. This plant is a popular folk remedy in the traditional medicinal system in all tropical Asian and African countries. This plant

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**Table 1. Taxonomical classification** [10]

| Kingdom:          | Plantae                        |
|-------------------|-------------------------------|
| Subkingdom:       | Tracheobinota                  |
| Super Division:   | Spermatophyta                 |
| Division:         | Mangoliophyta                 |
| Class:            | Mangoliophsida                |
| Subclass:         | Caryophyllidae                |
| Order:            | Caryophyllales                |
| Family:           | Amaranthaceae                 |
| Genus:            | Achyranthes                   |
| Species:          | Aspera                         |

**Table 2. Vernacular names** [11]

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Latin: Achyranthes aspera
English: Prickly Chaff flower, Rough chaff tree, Red chaff tree
Sanskrit: Aghata
Hindi: Latjira, Chirchira
Gujarati: SafadAgchedo
Tamil: Shiru-kadaladi
Telugu: Uttaraene
Malayalam: Kadalad
Punjabi: Kutri
Unani: Chirchitaa
Ayurvedic: Apamarga, Chirchitaa, Shikhari, Shaikharika

has been reported to be used to treat microbial infections, infertility, low blood sugar level, cardiac stimulant, antihypertensive, immuno suppression, anti-inflammatory, and antioxidant hepatoprotective, analgesic, antipyretic, prothryodic, antisapmodic and diuretic.

Phytochemical research has revealed alkaloids, saponins, sapogenins, sterols, ecdysterone, cardiac glycosides etc. from various parts of the plant. The other species of the genus Achyranthes viz. A. fauriei, A. bidentata, A. japonica, A. ferruginea etc. have also been investigated for their active chemical constituents and medicinal properties. This review includes various aspects of A.aspera quoted in the existing literature that emphasize its phytochemistry and pharmacology.

2. METHODOLOGY

The detailed literature survey was performed using scientific databases like Google, Google scholar, PubMed, Web of Science, Science Direct, SciFinder, Springer link, Flora of China for finding potentially significant scientific research and reports of Achyranthes aspera Linn using combination of relevant keywords like A. aspera, antioxidant, antimicrobial, phytochemistry, pharmacological activities. No any language restrictions were imposed. More than 350 scientific papers were found in the literature review. But emphasis was limited to 144 papers after elimination. ChemDraw Professional 16.0 software was used to draw the chemical structures.

2.1 Inclusion Criteria

Following are different criteria’s which are taken into consideration for selection of article; (1) Research involving crude extracts, identification and isolation of different chemical constituents, or herbal preparations using different parts of A.aspera, (2) In-vitro and in-vivo research for biological activities of crude extracts, isolated compounds, and preparations of A.aspera. (3) Effects of A.aspera extracts combined with other herbal extracts or chemicals.

2.2 Exclusion Criteria

Following are different criteria’s which are taken into consideration for exclusion of article; (1) Research existed clear deformities in the plan or execution, (2) Research papers titles or potentially abstracts just as information duplication didn't accord with the incorporation measures, and (3) Research didn't uncover as expected the flow point.

3. RESULTS AND DISCUSSION

3.1 Botanical Description [12]

It is stiff perennial herb, which can grow up to 2.0 m in height. It has wooden base, angular or ribbed in shape, simple or branched with bulging nodes. It consists of cylindrical root around 1.0 cm thick, yellowish-brown in colour. Stem is yellowish-brown in colour, quadrangular, branched, pubescent. Leaves are simple in type, apex is slightly acuminate, wavy margin, obovate, petiolate or elliptic, opposite, and pubescent on both surfaces. Presence of anomocytic stomata on the lower epidermis. Flowers are arranged in inflorescences of long spikes, bisexual greenish-white, numerous, sessile, bract and bracteoles, actinomorphic, ovary is hypogynous in nature, 5 perianth segments, membranous, stamens are 5 in number; 4 or 2 are very rare, shorter than perianth; filament is shorter, two loculed anthers. Flowers appear during summer. It has dry sac-like fruit which remains closed at maturity. Seeds
are ovoid, truncate at the apex, endospermic, brownish in colour.

4. PHYTOCHEMICAL

*A. aspera* is traditionally recognized as a potent medicinal agent. Chemical constituents have been isolated and identified from different parts of the plant.

4.1 Chemical Constituents Isolated from Root

Few studies isolated a phytoecdysteroid 20-Hydroxyecdysone (ecdysterone or 20E) from the methanolic extract of the root of *A. aspera* [13-15]. A new aliphatic acid n-hexacos-14-enolic acid is obtained from the ethanolic extract of roots. Some other compounds like stigmasta-5, 22-dien-3-E-ol, n-hexacos-11-enic acid, n-hexacos-17-enioic acid, trans-13-docosenoic acid and n-hexacosanyl n-decaniate are also isolated from the ethanolic extract root [16]. Phytosterol strigmasta-5, 22-dien-3-E-ol is isolated from elu of petroleum ether: benzene (75:25) in the form of colourless crystalline mass. Oleanolic acid (0.54%) is found in *A. aspera* root extracts [17-19].

Three terpenoid compounds, have been isolated from petroleum ether extract of roots of *A. aspera*, are ursolic acid, corrosolic acid and achyrantheric acid. FTIR, 1D and 2D NMR [20] confirmed the presence of these compounds (Fig. 1).

4.2 Chemical Constituents Isolated from Stem

Triacantanol a aliphatic alcohol anda newer dihydroxy ketone as 36, 37-dihydroxyhenpentacont-4-one wereisolated from n-hexane extract [21], 17-pentatriacontanol [22], pentatriacontane, Hexatriacontane, 6-pentatriacontanone, Tritriacontane, tetracontanol-2 (C_{40}H_{80}O), 4-methoxyheptatriacont-1-en-10-ol (C_{33}H_{76}O) [23], E-sitosterol and spinasterol [24,25], 10-octacosanone, 10-triacoasone and 4-triacoasone [26], are isolated from the shoots of the plant. From shoots, two long chain compounds have been isolated characterized as 27-cyclohexylheptacosan-7-ol and 16-hydroxy-26-methyleneheptacosan-2-one[24]. (Fig. 2).

![Chemical constituents isolated from root of A.aspera](image-url)
Three bisdesmosidic saponins (I-III) namely 20-
hydroxyecdysone, and quercetin-3-O-β-D-
galactoside were isolated from the methanol
extract of the aerial parts and their
structures were elucidated using NMR
spectroscopic analysis [27]. 3-Acetoxy-6
benzoyloxyapangamide has been isolated from
an ethyl acetate extract of the stem of A. aspera,
and this isolated compound shows mild
antibacterial activity against Bacillus cereus [28].

4.3 Chemical Constituents Isolated from
Leaves

Several volatile oils have been isolated from the
leaves of A. aspera. That Hydroquinone (57.7%)
is the chief constituent; others are p-
benzoquinone, spathulenol, nerol, α-ionone,
asarone and eugenol [29].

Leaves of A. aspera consist of different
phytochemicals like Alkaloids, flavonoids,
saponins, tannins and phenolic compounds [30].
The GC-MS analysis of leaf extract revealed that
there is presence of flavonoid 3,5-
Dihydroxy-6-
Methyl-2,3- Dihydro-4H-Pyran-4-one, terpene
alcohol (2E)-3,7,11,15-Tetramethyl-2-
hexadecen-1-ol, a natural sygar2-Furaldehyde,5-
(Hydroxymethyl), a diterpenenamed as Phytol,
triterpene called as Squalene and Stigmasterol
(phytosterol). (Fig. 3).

4.4 Chemical Constituents Isolated from
Seed

Phytochemical studies of the seeds indicate the
presence of triterpenoid Saponins A and B.
Saponins C and D are reported to be isolated
from unripe fruit [27,31]. Its carbohydrate
components are sugars D-glucose, L-rhamnose,
D-glucuronic acid (Saponin A). Saponin B is
identified as β-D galactopyranosyl ester of D-
Glucuronic acid. The seeds also contain a water-
soluble base, betaine and a water-soluble
alkaloid Achyranthine, 10-tricosanone, 10-
octacosanone and 4-tritracontanone [27].
(Fig. 4).

Three oleonic acid glycosides: α-L-
rhamnopyranosyl-(1→4)-(β-D-
glucopyranosyluronic acid)-(1→3)-oleanolic acid,
α-L-rhamnopyranosyl-(1→4)-(β-D-
glucopyranosyluronic acid)-(1→3)-oleanolic acid-
28-O-β-D-glucopyranoside and α-L-rhamno-
pyranosyl-(1→4)-(β-D-glucopyranosyluronic
acid)-(1→3)-oleanolic acid-28-O-β-D-
glucopyranosyl-(1→4)-β-D-glucopyranoside
isolated from the seeds [32-34].

![Chemical constituents isolated from stem of A. aspera](image-url)
Seasonal variation in chemical composition has been recorded [35]. Carbohydrates, proteins, phenols and enzymes in gall (induced by *Bemisia tabacci*) and normal tissues of the plant had been reported [36]. The fatty acid composition of the seeds showed the presence of palmitic, lauric, arachidic, stearic, myristic, oleic, linoleic acid and behenic acid [37]. *A. aspera* has been recorded as one of the best-adapted plants for the preparation of Leaf Protein Concentrate (LPC) as a food substitute to be used by the rural peoples. Various fractions, such as chloroplast and cytoplasmic proteins were analysed for crude protein contents [38]. Some studies reported a valid HPLC method for the quantitative estimation of oleanolic acid from the roots and different marketed formulations [39]. Densitometric HPTLC method is used by some studies for analysis of oleanolic acid in *A. aspera* [19,40]. Concentrations of various trace elements like Ca, Na, Mg, Cu, Fe, K, Zn, Cr, Ni, Co, Cd, Pb, Mn in the plant was measured [41]. Heavy metals like Pb, Cu, Zn, Cr, Fe and Ni were found to be present in the plant [42]. Several phytochemical tests have been performed for the presence of carbohydrates, alkaloids, flavonoids, tannins, terpenoids and saponins [43].
Fig. 4. Chemical constituents isolated from seed of *A. aspera*

5. PHARMACOLOGICAL ACTIVITY

5.1 Antimicrobial

Several plant activities have been performed to test its antimicrobial [44-50] and antifungal ability [51-52]. This plant has been reported to consist of a powerful antibacterial agent [53-56]. The seeds of the plant [45], ethyl acetate extract of stem [29], leaf extract [57], alcoholic extract of leaf and stem [58-59], an aqueous extract of flower reported possessing antibacterial activity. The essential oil extracted from shoots reported to have antifungal activity against *Aspergillus carneus* [22]. The various extracts of dried leaves using solvents like petroleum ether, chloroform and methanol have reported antibacterial and antifungal activity. The extracts were tested against 3 gram-negative bacteria (*E. coli, P. aeruginosa, K. pneumoniae*) and 2 gram-positive bacteria (*S. aureus and S. epidermidis*) for antibacterial activity and 17 fungal strains for antifungal activity by agar-solid diffusion method [60].

This plant has been found to have antibacterial activity against nosocomial infection [61]. It is also used as an herbal antimicrobial for cotton fabric in healthcare textile industries [62]. Some studies also reported that diethyl ether extract of leaves shows more potent antibacterial activity against *E. coli, P. aeruginosa and E. cloacae* compared to ethyl acetate and acetone extract by agar well diffusion method [63]. This plant's antibacterial and antifungal activity is due to the presence of essential oil, tannins, saponin, flavonoids, and alkaloids.

5.2 Lavicidal

Ecdysterone, an important constituent of the root shows a significant insect molting hormonal activity [14]. An ethanolic crude extract of the plant reported having stronger larvicidal activity on the tick larvae against *Boophilis microplus* [64]. Larvicidal saponins from leaf extracts are tested against yellow-fever mosquito and southern house mosquito [65]. Ethyl acetate extract of the leaf has been found to be active against *Aedes subpictus* mosquito larvae [66]. The plant was mentioned to possess activity in controlling mosquito larvae [67]. Bioactivity of essential oils isolated from leaf and stem extract by steam distillation was active larvicidal against yellow-fever mosquito and southern house mosquito [68]. Leaf extracts of the plant are reported to be active against yellow-fever mosquitoes [69].

5.3 Antifertility

Several activities of the plant have been performed and reported that the plant possesses a stronger antifertility activity [70-75]. Extracts of various parts of the plant showed an abortifacient effect in mice with maximum activity in benzene extract [44]. The aerial parts of the plant were reported to prevent pregnancy in female rats [76]. The extracts of leaves, roots, and seeds of the plant control fertility, placental retention, and postpartum bleeding [77]. Benzene extract of stem bark found to have abortifacient activity in the rat [78]. In-vitro and in-vivo studies of ethanolic extract of the root showed a spermicidal activity [79].
The composite extract of *A. aspera* and *S. harnandifolia* on human semen was studied in-vitro for spermicidal action. The 0.1g/ml concentration of hexane fraction obtained from the hydroethanolic extract of these two plants immobilizes all human sperm samples and all spermatozoa samples of rats [80-82]. The root of *A. aspera* possesses a protein responsible for spermatoxicity in Swiss male albino mice when administered orally [83]. The isolated 58kDa Achyranthes protein (Ap) shows stronger spermicidal activity at a dose of 150 μg compared to nonoxynol-9 at a dose of 250 μg by in-vitro [84]. This protein produces an irreversible spermicidal effect. The ethanolic extract of *A. aspera* root was evaluated for post-coital antifertility activity in female albino rats at an oral dose of 200mg/kg [85]. The chloroform and ethanolic extracts of root were found to possess estrogenic and pregnancy interceptory activity [86]. The alkaloidal fraction of *A. Aspera* in male albino rats showed an antifertility effect in a dose-dependent manner [87].

### Table 3. Antimicrobial activity of *A. aspera* extracts and isolated compounds

| Extract / active compound | Model | Results | Reference |
|---------------------------|-------|---------|-----------|
| Essential oil extracted from leaf | *Aspergillus cameus* | Inhibits mycelial growth of fungus, Antifungal activity | [22] |
| Ethyl acetate extract of stem | *Bacillus cereus* | 3- Acetoxy-6-benzoyloxyapangamide from oil shows mild antibacterial activity. | [29] |
| Methanol and chloroform extract of leaf | Screening for antibacterial activity | Chloroform extract shows stronger antibacterial activity than methanol extract | [46] |
| Sequential extraction of root | Screening for antibacterial and antifungal activity | Strongest antibacterial activity against *Klebsiella sp.*, *B. substilus*, and antifungal activity against *Fusarium sp.*, *Alternaria sp.*, *Heterobardionsp* | [46] |
| Successive extraction | Various bacteria | High antibacterial activity against *S. aureus*, *S. typhi* (methanol and chloroform extract) *B. substilus*, *E. coli* (methanol, n-hexane) | [50] |
| Aqueous extract | *Sclerospora graminicola* | Inhibition of zoosprorangium formation | [51] |
| Aqueous, ethanol and methanol extract of leaf | 11 fungal strains | Antifunagl activity | [52] |
| Aqueous extract of stem and root | *Streptococcus mutans* | Tannins are responsible for antibacterial activity | [53] |
| Various solvent extracts of leaf and stem | *P. aeruginosa*, *P. mirabilis*, and *E. faecalis*. | Ethanol extract of leaf and methanolic extract of stem shows stronger antibacterial activity | [54] |
| Hydrodistillation of seeds | Various gram positive and gram-negative bacterial species, fungal species, dermatophyte | Volatile oil shows stronger antimicrobial activity as compared to standard | [56] |
| Various solvent extracts | 8 bacterial species and 7 fungal strains | Diethyl ether extract shows maximum zone of inhibition as compared to other solvents. | [57] |
| Various solvent extracts of leaf | 3 gram-negative bacteria, 2 gram-positive bacteria and 17 fungal strains | Antibacterial and antifungal activity | [60] |
5.4 Anti-cancer

The plant has been reported to possess chemopreventive activity and antitumor property [88]. Nonalkaloidal fractions of the plant were found to have a valuable antitumour promoter [89]. Leaves extracted in methanol were found to possess inhibitory activity against human carcinoma cells signalling its anti-proliferative and anti-cancer properties. The methanolic extract shows greater sensitivity to pancreatic cancer cell line than cells of prostate, lung and breast origin [90]. This activity’s mechanism is the suppression of transcription of metalloproteases (MMP-1 and 2), inhibition of MMPs and angiogenic factors.

Swiss albino mice induced through intraperitoneal injection of oil were screened for its anticancerous efficacy [91]. Mineral oils consist of free radicles, which can bind with DNA and interact with purine, pyrimidine groups of DNA, which leads to the conversion of normal cells to cancerous cells. The antioxidant property of A. aspera inhibits damage caused by carcinogens to DNA that alters cellular functions. Artemia salina lethality (BSL) bioassay was recorded using the plant extract to pick the secondary metabolites with cytotoxic effect [92]. Extracts of various plant parts were found to inhibit chemically induced hepatocarcinogenesis in rats [93]. The in-vitro study of isolated terpenoid compounds from petroleum ether extract shows potent anticancer activity against HT-29 cancer cell line when studied by MTT assay [20].

5.5 Immunostimulant

Seed and root extract reported a stronger immunostimulatory activity than the stem and leaves of the plant [94-95]. Root extract potentiates antibody production in the fish, Labeo rohita [95]. The aqueous root extract of A. aspera shows anti-proteases activity in Labeo rohita [96]. The plant's seed has been reported to improve the immune response of Cyprinus carpio [97]. The plant was an immunostimulant and antigen clearance enhancer in Catla catla [98-99].

Immunostimulatory compounds in seeds have been reported to boost immunity and sustainability of Labeo rohita infected with Aeromonas hydrophila [100]. The hydroalcoholic extract was reported to stimulating T cell-mediated immunity by increasing phagocytic function [101].

5.6 Hypoglycaemic

Aqueous and methanolic extracts of whole plant material show hypoglycaemic activity by oral administration in normal and alloxan-induced diabetic rabbits. The findings showed that there was a possibility that the plant could act by providing beta-cells with certain necessary elements such as calcium, zinc, magnesium, manganese and copper [102].
Oral administration of ethanolic extract of whole plant material show antidiabetic activity against alloxan-induced diabetic in rats in dose-dependent manner. The extract tries to maintain blood glucose and plasma insulin level near to normal level in diabetic-induced rats. The possible mechanism behind this activity could be promoting insulin secretion by the closing of $K^+$ ATP channel and stimulation of $Ca^{2+}$ ion entry [103].

Aqueous extract of leaves of the plant at higher doses (500mg/kg) significantly reduces blood glucose level, glycosylated haemoglobin and enhances serum insulin, glycogen level in alloxan-induced diabetic rats. It also elevates the activity of glucokinase and glucose-6-phosphate dehydrogenase enzyme in dose-dependent manner as compared to standard drug Metformin [104]. Chloroform fraction of ethanolic extract of leaves, lowers blood glucose level after 48 hrs in streptozotocin-induced diabetic rats. Purification studies reveal that, it contains potent chemicals like ursolic acid, oleonolic acid, sitosterol and triacontane, which can be responsible for antidiabetic activity [105].

Table 5. Anticancer activity of A. aspera extracts and isolated compounds

| Extract / active compound | Model                          | Results                                                                 | Reference |
|---------------------------|--------------------------------|------------------------------------------------------------------------|-----------|
| Terpenoid compound        | In-vitro                       | Potent anticancer activity against HT-29 cancer cell line by MTT assay | [20]      |
| Methanolic extract        | In-vitro (using several cancer cell lines) | Greater sensitivity to pancreatic cancer cell line as compared to others. Suppresses transcription of metalloproteases (MMP-1 and 2), inhibits MMPs and angiogenic factors | [90]      |
| Sequential extraction of powdered plant material | In-vivo model induced by mineral oil | Ether extract inhibits damage caused by free radicles of oils to DNA | [91]      |
| Various solvent extracts  | Artemia salina lethality bioassay | Secondary metabolites shows Cytotoxicity effect | [92]      |
| Ethanolic extract of plant material | N-nitrosodiethylamine and CCl$_4$ induced hepatocarcinogenesis in rats | Suppresses oxidative stress by increasing serum transaminase, alkaline phosphatase and different antioxidant enzymes, recovers liver cell architecture | [93]      |

Table 6. Hypoglycemic activity of A. aspera extracts and isolated compounds

| Extract / active compound | Model                           | Results                                                                 | Reference |
|--------------------------|--------------------------------|------------------------------------------------------------------------|-----------|
| Aqueous and methanolic extract | Alloxan-induced diabetic rabbits | Stimulates beta cells and balances important mineral elements          | [102]     |
| Ethanollic extract       | Alloxan-induced diabetic rat    | Promote insulin secretion, maintains blood glucose and plasma insulin level near to normal level | [103]     |
| Aqueous extract          | Alloxan-induced diabetic rat    | Elevates the activity of glucokinase and glucose-6-phosphate dehydrogenase enzyme in dose-dependent manner | [104]     |
| Chloroform fraction      | STZ induced diabetic rat        | Lowers blood glucose level                                             | [105]     |
5.7 Hypolipidemic Activity

In triton induced hyperlipidemic rats, administration of alcoholic extract of A. aspera lowers serum cholesterol (TC), phospholipid (PL), triglyceride (TG) and total lipids (TL) [106]. The hypolipidemic effect of the whole plant’s aqueous extract was screened in sesame oil feed rats [107]. Administration of extracts of A. aspera significantly reduces lipid peroxidation towards the normal value [108]. Oral administration of ethanolic and aqueous extract of powdered leaves significantly lowers the serum cholesterol and serum triglyceride level in cholesterol-induced hyperlipidemic rats in a dose-dependent manner compared with standard Atorvastatin [109]. The mechanism behind the hypolipidemic activity of A. aspera is to lowering exogenous absorption of cholesterol and rapid excretion of bile acids by endogenous conversion of cholesterol.

5.8 Anti-inflammatory

Alcoholic extract of A. aspera shows maximum inhibition of rat paw oedema in a carrageenan-induced hind paw oedema model. It reduces granuloma weight in the cotton pellet granuloma model [110]. Presence of flavonoids in A. aspera confirms its anti-inflammatory activity by inhibiting phospholipase-A and cyclooxygenase. Quercetin, an active constituent of the stem of A. aspera, suppresses proliferative phase of fibroblasts, leading to a reduction in granuloma weight. Oral administration of alcoholic extract of roots of A. aspera in rats showed promising anti-inflammatory activity against acute and chronic inflammation [111].

5.9 Antioxidant Activity

Several activities of the plant have been performed to test its antioxidant activity. Leaves of A. aspera consist of a high amount of alkaloids and flavonoids responsible for the inhibition of lipid peroxidation, which confirms its antioxidant activity [112]. The in-vitro study of aqueous extract of leaves of A. aspera more significantly prevents the formation of free radicals compared to ethanolic extract when studied by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) scavenging assay and superoxide scavenging activity [113].

Methanolic extract of leaves and roots of A. aspera showed a stronger antioxidant activity when studied by DPPH scavenging assay [114]. The petroleum ether extract of aerial parts of A. aspera var. Porphyristachya shows a stronger antioxidant activity than chloroform extract, ethyl acetate extract when they are screened for antioxidant activity using DPPH assay, ABTS assay and FRAP assay [115]. In-vitro studies on A. aspera var. Rubrofusca were reported to possess a free radical scavenging activity [116]. Some studies reported the antioxidant and DNA protection potential of A. Aspera [117]. Ethanolic leaf extract of leaf powder of A.aspera (IC50= 7.49 µg/ml) shows good antioxidant activity as compared to standard ascorbic acid (IC50= 11.73 µg/ml) by phosphomolydenum assay [118].

Aqueous extract of leaves and its isolated phytochemicals showed a better antioxidant activity as compared to standard ascorbic acid by DPPH radical scavenging assay. The presence of quaternary alkaloids and terpenoids is responsible for antioxidant activity[119]. The sequential extract of roots of A. aspera shows a potent antioxidant activity when studied by DPPH radical scavenging assay and ferric reducing antioxidant power. Reported methods also study total antioxidant capacity. All extract shows a higher antioxidant capacity than standard gallic acid. The ethanolic extract (426.14 mg/g) and chloroform (417.84 mg/g) shows maximum activity [120].

| Extract / active compound | Model | Results | Reference |
|--------------------------|-------|---------|-----------|
| Alcoholic extract        | Triton induced hyperlipidemic rats | Lowers serum cholesterol, phospholipid, triglyceride and total lipids | [106] |
|                          | Sesame oil induced hyperlipidemic rats | Antihyperlipidemic effect | [107] |
| Aqueous extract          | Sesame oil induced hyperlipidemic rats | Secondary metabolites lowers lipid peroxidation | [108] |
| Sequential extraction    | Sesame oil induced lipid peroxidation | | |
| Ethanoic and aqueous extract | Cholesterol induced hyperlipidemic rats | Lowers serum cholesterol and serum triglyceride level | [109] |

Table 7. Hypolipidemic activity of A.aspera extracts and isolated compounds
Table 8. Anti-inflammatory and antioxidant activity of A.aspera extracts and isolated compounds

| Extract / active compound                  | Model      | Results                                                                                       | Reference |
|-------------------------------------------|------------|------------------------------------------------------------------------------------------------|----------|
| Alcoholic extract                         | In-vivo rat| Reduces granuloma weight. Presence of flavonoids and Quercetin confirms its anti-inflammatory activity | [110]    |
| Alcoholic extract of root                 | In-vivo rat| Anti-inflammatory activity against acute and chronic inflammation                              | [111]    |
| Ethanolic and aqueous leaves extract      | In-vitro   | Free radicle scavenging activity, inhibits lipid peroxidation                                 | [113]    |
| Methonolic extract of leaves and roots    | In-vitro   | DPPH scavenging activity and free radical quenching                                           | [114]    |
| Petroleum ether extract of aerial parts   | In-vitro   | Scavenging activity against DPPH ABTS, FRAP radicals                                           | [115]    |
| Ethanol extract of leaf                   | In-vitro   | Phosphomolybdinum assay                                                                      | [118]    |
| Aqueous extract of plant                  | In-vitro   | Isolated terpenoid and quaternary alkaloid shows better antioxidant activity than standard ascorbic acid by DPPH scavenging activity | [119]    |
| Sequential extract of root and inflorescence | In-vitro | Presence of phenolic compounds shows stronger antioxidant activity by DPPH, FRAP assay      | [120]    |

5.10 Anti Asthmatic

Some studies report that the polyherbal formulation consisting of A. aspera, Glycyrrhiza glabra, Albizzia lebbeck, and Tylophora indica shows significant protection against bronchoconstriction and anti-anaphylactic activity. It is due to mast cell stabilization and inhibition of eosinophilia [121]. The ethanolic extract of plant provides protection against occupational asthma in Wistar rats induced by Toluene disocyanate (TDI) [122-123], which confirms its bronchoprotective activity.

5.11 Diuretic

A.aspera reported having its antagonistic action against oxytocin-induced uterine contraction [124]. Diuretic activity of the plant is due to the presence of saponins [125-126]. Achyranthine, a major chemical constituent of A.aspera is present in the marketed polyherbal formulation as Cystone® [127-128]. Cystone® inhibits the action of oxalate synthesising liver enzyme glycolate oxidase in glycolic acid-induced urolithiasis [129].

5.12 Anti-arthritic

Achyranthine from A. aspera reported to have anti-arthritic activity [130]. The ethanolic extract of the whole plant has shown its antiarthritic activity in Freund’s complete adjuvant-induced arthritis [131]. The aqueous extract of A.aspera reported providing protection against formaldehyde-induced arthritis and joint inflammation in rats [132].

5.13 Wound Healing Activity

Topical application of 5.0% (w/w) ointment of methanolic leaf extract showed wound healing activity in burn wound rats. Wound healing activity is assessed by the rate of wound contraction, the elevation of antioxidant enzymes and biochemical assay using Burn wound model, Diabetic wound model and Immunocompromised model. The protein expression by Gelatin zymography confirms its wound healing activity [133-134].

5.14 Cardiac Activity

Some studies reported that the isolated saponin A of A. aspera seed causes an increase in the force of contraction of isolated and intact hypodynamic heart [135]. Leaf decoction was reported for its cardiovascular toxicity [136]. Achyranthine, a water-soluble alkaloid lowers blood pressure, depresses heart and increases in rate and amplitude of respiration in anaesthetized dogs [137]. Effect of isolated saponin on phosphorylase activity of rat heart was noted [138]. The plant has been found to
have activity on cardiovascular system in some parts of Western Africa [139].

5.15 Analgesic and Antipyretic Activity

Methanolic extract of the whole plant [140], hydroalcoholic extraction of leaf and root extract showed stronger analgesic activity using different methods in a dose-dependent manner [141]. The methanolic extract of leaf showed a significant analgesic activity in acetic acid induced writhing syndrome at higher doses. Oral administration at higher doses reduces writhing numbers in rats as compared to control group. In hot plate method and tail flick method, at higher doses, the extract increases reaction time as compared to the control group [142-143].

Ethanolic extract of leaves at 400 mg/kg dose in mice, more significantly reduces paw licking in both neurogenic and inflammatory phases as compared to standard drug Pentazocine and Aspirin in formalin-induced analgesic activity [144].

6. CONCLUSION

A. aspera Linn is a herbal plant which can be used as a natural drug used to regain the alterations made in the normal physiological system by foreign organisms or by any malfunctioning of the body. The whole plant and its parts have been widely studied for its broad-spectrum pharmacological activities such as spermicidal, antiallergic, cardiovascular, nephroprotective, abortifacient, antiparasitic, hypoglycemic, analgesic, antipyretic. Also used in the treatment of many diseases like boils, bronchitis, cold, cough, boils, colic, debility, dropsy, dysentery, ear complications, and headache.

The wide range of phytochemicals shows it as a promising herbal medicine. Further research is essential using chromatographic techniques like HPLC, HPTLC and NMR to identify active principles present in different fractions. To explore its medicinal potency extended the pharmacological experiments are to be carried out and clinical trial to design as novel drugs.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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