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Aesculus indica: An ethnomedicinal, phytochemical, and pharmacological review

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Aesculus indica, commonly known as Indian horse chestnut, is an indigenous tree of the family Sapindaceae, distributed in Nepal, India, Pakistan, and Afghanistan. As an ethnomedicine, its seeds are used to cure jaundice, chest diseases, stomach and joint pain, roots for leucorrhea, and bark for fever and anaemia. The phytochemicals of class phenolic, triterpenoid, glycoside, saponin, and fatty acid have been identified from their different parts and various biological activities such as antioxidant, anti-diabetic, hypocholesterolemic, hypoglycaemic, anti-nociceptive, anti-inflammatory, neuro-depressive, spasmolytic, immunomodulatory, anticancer, enzyme inhibitory, antimicrobial and insecticidal have been reported, which reflected its medicinal importance. However, most biological activities are on the extracts or fractions and need more in-depth study. Therefore, further research is required on the isolation, identification, and characterization of active phytochemicals from the extracts with their mechanism of pharmacological action and detailed toxicological evaluation. In this review, we aim to provide all information regarding traditional uses, morphology, phytochemistry, pharmacology, and toxicity of *A. indica* and address the research gaps; therefore, will provide a source of information to the researchers for further studies.

Keywords: *Aesculus indica*, Ethnomedicinal, Pharmacology, Phytochemicals, Sapindaceae

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Introduction

Aesculus indica is an indigenous tree of woodland habitat usually known as Indian horse chestnut or Himalayan chestnut[1]. In different regions, it is called by various names, such as *hanudon* in Kashmir, *goon* in Himachal Pradesh, *khajushing* in Bhutan, *pangro* in Nepal, and *jawaz* in Pakistan[2-4]. This plant belongs to the genus *Aesculus* which contains 12 species distributed in America, Europe, and Asia[5]. *A.indica* has many folk medicinal uses such as indigestion, stomach pain, joint pain, venereal, chest diseases, skin ulcer, haemorrhoids, and jaundice[6-9]. The seed extract of *A. indica* was effective against human nasopharynx epidermoid carcinoma, P-388 lymphocytic leukaemia, and has antimicrobial and haemagglutination properties[10-12]. The seed oil has anti-inflammatory properties[13]. The seed shell adsorbs cadmium (II) ions from an aqueous solution[14] and leaves have antioxidant properties[15]. The preliminary phytochemical screening of *A. indica* showed the presence of phenol, flavonoid, alkaloid[16], coumarin, protein, amino acid, steroid, carbohydrate, saponin, tannin, terpenoids in the leaf extracts[17]; glycoside, saponin, flavonoid, tannin[18] carbohydrate and phenol in the seed extracts[19]. The current study aims to review folk uses, phytochemistry, and pharmacology of *A. indica*.

Methodology

Literature was searched using plant names and synonyms in Pubmed, Google Scholar, and publisher databases such as Bentham, Springer, and ScienceDirect. Books, conference papers, patents, and a few websites such as Kew botanical garden, Centre for Agriculture and Bioscience International, India Biodiversity Portal, Tropicos, Pubchem and ChemSpider were also utilized.

Plant description

Geographical distribution

A. indica is distributed in Asian countries along the northwest Himalayas from west Nepal, north India, and northwest Pakistan to northeast Afghanistan at an altitude of 3000 m[20]. It is distributed in India's moist and shady valleys of Kashmir, Uttrakhand, and Himachal Pradesh. In Himachal Pradesh, it is found in the forests of districts Sirmour, Mandi, Shimla, Chamba, Solan, Kangra, and Kullu[21].

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Taxonomy

Kingdom: Plantae, phylum: tracheophyta, class: magnoliopsida, order: sapindales, family: sapindaceae, genus: *Aesculus,* species: *Aesculus indica*[22]. Synonyms: *Aesculus indica* var. *concolor* Browicz, *Pavia indica* Wall. ex Cambess[23].

Morphology

A. indica (Fig. 1a-g) is a medium to large-sized tree with a straight, cylindrical trunk and a round to broadly spreading canopy. It has a 25 - 30 m average height and a 2.5 m diameter trunk. The bark is smooth grey and peels off from upwards in narrow bands when it ages. The petiole is about 8 - 19 cm long, having 5 - 9 leaflets; leaves are 15 - 25 cm long and up to 8 cm wide, opposite, digitate, exstipulate, glabrous, serrated, oblong to lanceolate and narrowed at the base. The calyx is gamosepalous, tubular, 5 - lobed, 4 - 8 mm long, with short and rounded lobes. Flowers are white-yellowish streaked coloured, having 3.5 mm length and 2 - 2.5 cm diameter, pedicellate, perigynous, bisexual, and present in about 32 cm long compound raceme inflorescence average of 385 flowers. The flower has four unequal petals: the upper petals are (oblanceolate) 15 - 24 mm long, and the lateral petals (oblong to obovate) 15 - 20 mm long. Ovary with a single style, androecium is polyandrous (5 - 9 stamens, 3.5 cm long), perigynous, glabrous and up to 30 mm long. The gynoecium is tomentose, fruit capsule is ovoid, about 2 cm long and 4.1 cm in diameter, with rusty brown spots on the epicarp. The capsule contains 1 - 2 shiny dark brown coloured with white scars seeds and two lemon white cotyledons. Flowering occurs in April-May, and seeds mature in october[24-29].

Traditional uses

A. indica is used for several purposes, its seeds are eaten by wild animals and humans[30] but are considered harmful for humans if consumed without any previous treatment[31]. Pre-treatments include water soaking, blanching, and cooking, which removes anti-nutritional factors like saponins[32]. In Himachal Pradesh, seeds are crushed and treated with water to remove bitter contents (saponins), dried, and prepared into flour/powder called *tatwakhar,* and various food items like porridge, *chappatis* are prepared from it and sold in the markets[33]. Seeds contain saponins, so they are used as an alternative soap[34]. The leaves are fed to livestock and collected for the winter when there is a scarcity of green fodder[35]. *A. indica* is also used as a fish toxicant[36]. Its flowers are used in apiculture as bee forage[37,] and wood is used in the fences[38], as fuel[39,] and in the preparation of various household articles and agricultural tools like hoe and yoke[40]. Despite the above uses *A. indica* is also

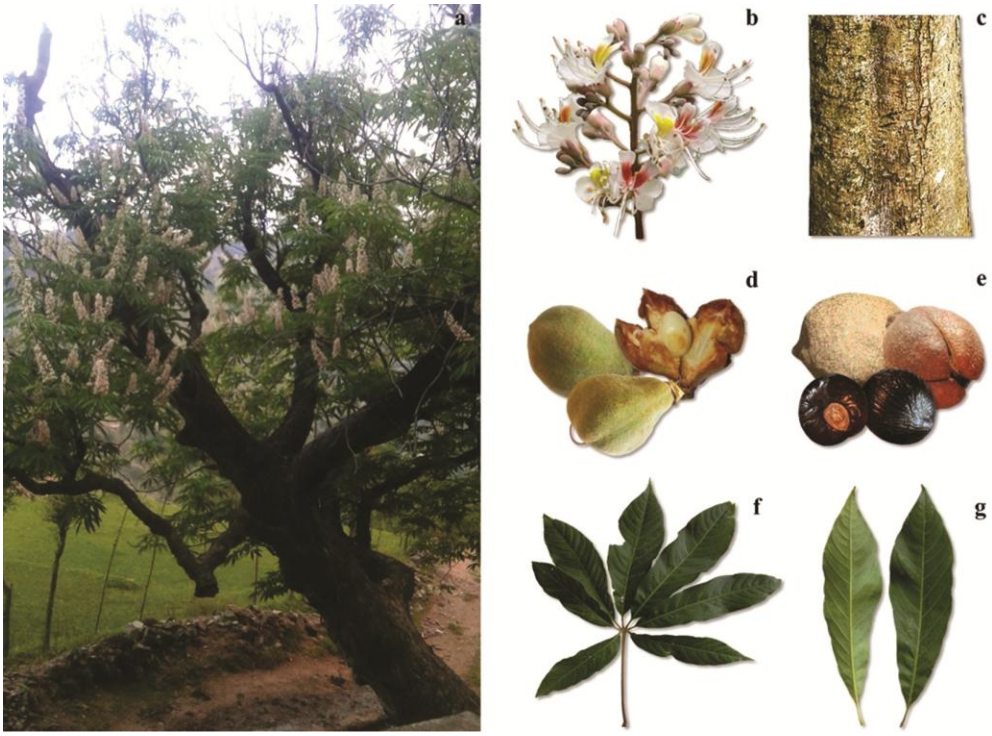

Fig. 1 — *Aesculus indica*, a) Whole plant; b) Inflorescence; c) Stem bark; d) Unripe fruit; e) Ripe fruit; f) Leaflets; and g) leaf.

utilized to cure different types of health problems as leaves extract are used to cure whooping and cough[41], fruits are used to kill stomach worms[42], prevent hair fall[43], paste applied to cure mumps[44], and its powder is overcome general weakness[45], sometimes powder is mixed with husk and fed to animals to get relief from abdominal pain[46]. The seed powder roasted in butter is used to prevent excess bleeding and pain in menses, also given to women during the pre- and post-period of pregnancy[47]. The seed paste relieves rheumatic pain[48] and seed oil is applied to relieve headaches and skin infections[49]. The bark is used to treat hepatitis[50], anaemia, chest pain[51], dislocated joints[52], and curing fever[53]. The roots are used for the treatment of leucorrhea[54].

Physicochemical composition

A. indica has several traditional uses, as discussed in the previous section. One of those is that the seeds are washed with water to remove saponins before using as food. So the researcher studied and reported various methods (Soxhlet, percolation, boiling, roasting, microwave, and pressure cooking) to optimize toxic/bitter contents and nutritional mineral composition[55-57]. Also, some quality evaluation studies have been carried out on the products of seed flour[58,59] and results are found to be almost similar to standard recipes[60]. *A. indica* contains various nutrients and minerals[61,62] (Table 1) such as phosphorus, potassium[56], calcium, manganese, zinc, iron, copper[56,57], protein, carbohydrates and fat[63,64].

Phytochemistry

Many studies carried out on different parts of *A. indica* have confirmed the presence of compounds that belongs to the category of phenol, flavonoid, flavonol glycoside, terpenoid, terpenoid glycoside, fatty acid and phytosterol.

Phenolic compounds

The presence of chlorogenic acid, phloroglucinol, hydroxybenzoic acid was detected in various (fruit) fractions and isolated a phenolic, mandelic acid; a flavonol, quercetin from the ethyl acetate fraction[65] (Fig. 2a-d) and flavonol glycosides, astragalin[66], rutin[67] and quercitrin from the chloroform leaf extract[68] (Fig. 2g-i). A phytosterol, β-sitosterol (Fig. 2j) was also isolated from the hexane leaves extract[68]. Two other phenols, catechol and epicatechin are also reported[52,69] (Fig. 2e,f).

Triterpenoids

The triterpenoids, barringtogenol-C, proto-aescigenin, aescigenin (Fig. 3a-c) and acyl-triterpenoids, 21-angeloylbarringtogenol-C, 21, 22 diangeleylbarrintogenol-C and 22-angeloyl-R1-barrigenol are characterized from the hydrolysate mixture of the seeds of *A. indica*[5,70] (Fig. 3d,e). The triterpenoid glycosides, aesculusides A[71], aesculusides B[72] were isolated from the methanol seed extract and 3-O-[{Beta-3-D-glucopyranosyl(1-2)}{Beta-D-glucopyranosyl (1-4)}-Beta-D-gluconopyranosyl] 21, 22-diangeloyl-barringtogenol C was isolated from the 90% methanol seed-coats extract[73] (Fig. 3f-h). A triterpene saponin aescin was isolated from the chloroform leaves extract[68], aqueous ethanol seed extract[74], and an isomer β-aescin from hydroalcoholic seed extract[75]. The chemical structures are depicted in Fig. 3[5,73,76].

Fatty acid

The presence of saturated long-chain fatty acids, palmitic acid, myristic acid, stearic acid, arachidic acid, lauric acid, and oleic acid (Fig. 4a-f) was detected in the gas chromatography of the saponified hexane extracts of the seeds, leaves, and husks[77]. In another study, palmitoleic acid, 10-heptadecenoic acid, and unsaturated fatty acids such as gondoic acid,

Table 1 — Physicochemical composition of *Aesculus indica*[63,64]

Seed elements	Value	Parameters	Seed (%)	Seeds flour
Calcium	0.08%	Moisture	51.5±1.25	10.71±1.23
Nitrogen	1.15%	Ash	1.93±0.15	3.16±0.05
Phosphorus	0.18%	Crude fibre	1.73±0.19	6.34±0.22
Potassium	0.79%	Crude fat	1.30±0.43	3.27±0.39
Sulphur	0.07%	Protein	1.39±0.5	6.78±1.19
Copper	41.2 ppm	Starch	38.18	59.59
Iron	159 ppm	Carbohydrate	42.15	69.74
Manganese	6.95 ppm	Sugar	3.97	10.15
Zinc	25.6 ppm	Energy (cal/100 g)	185.86	327.51
Oil	2.02%			

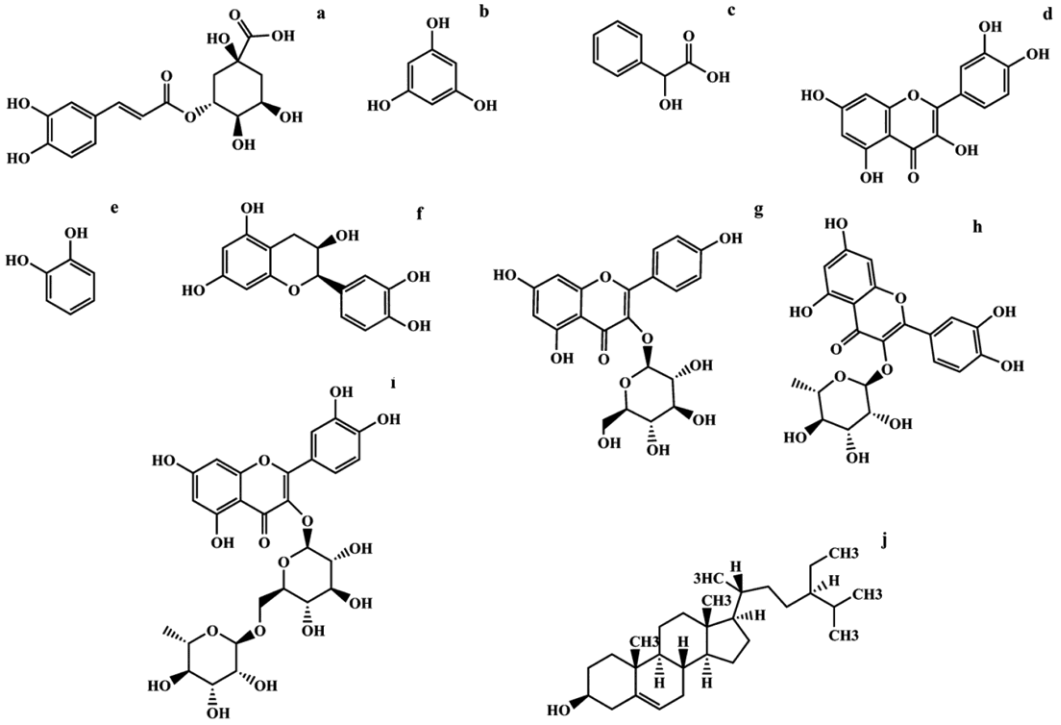

Fig. 2 — Phenol, flavonoids, and a phytosterol of *Aesculus indica*. a) Chlorogenic acid; b) Phloroglucinol; c) Mandelic acid; d) Quercetin; e) Catechol; f) Epicatechin; g) Astragalin; h) Quercitrin; i) Rutin; and j) Beta sitosterol.

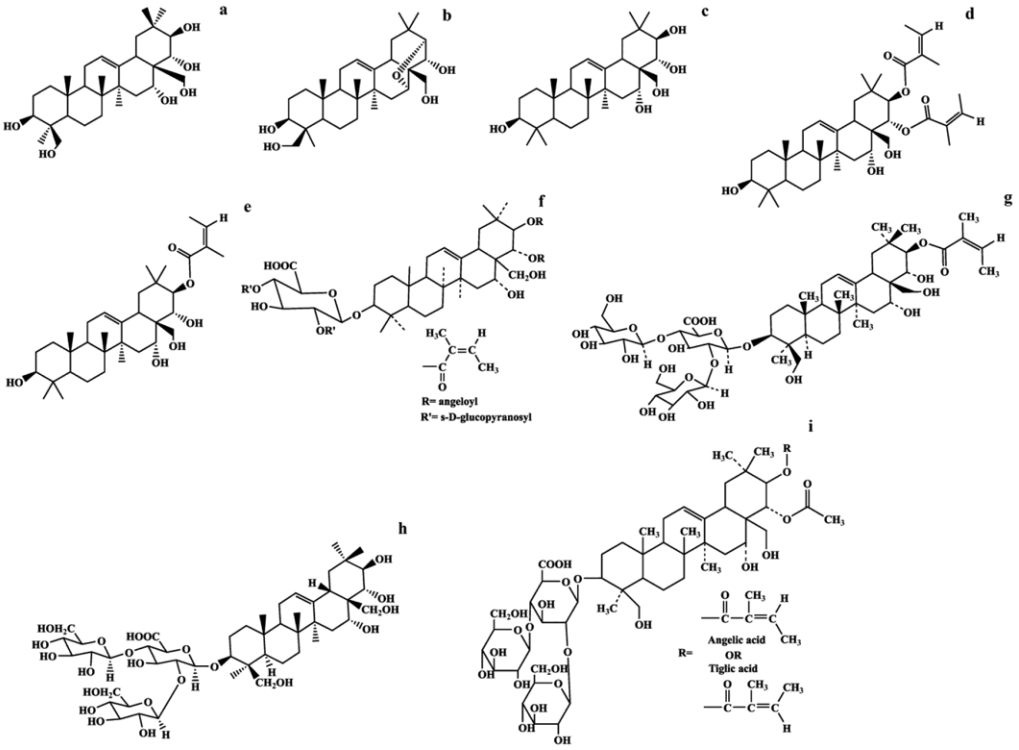

Fig. 3 — Triterpenoids and triterpene saponins of *Aesculus indica*, a) Protoaescigenin; b) Aescigenin; c) Barringtogenol-C; d) 21, 22 diangeleylbarrintogenol-C; e) 21-angeloylbarringtogenol-C; f) 3-O-[{Beta-3-D-glucopyranosyl(1-2)} { Beta-D-glucopyranosyl (1 -4)}-Beta-D-gluconopyranosyl] 21, 22-diangeloyl-barringtogenol C; g) Aesculusides-A; h) Aesculusides-B; and i) Aescin.

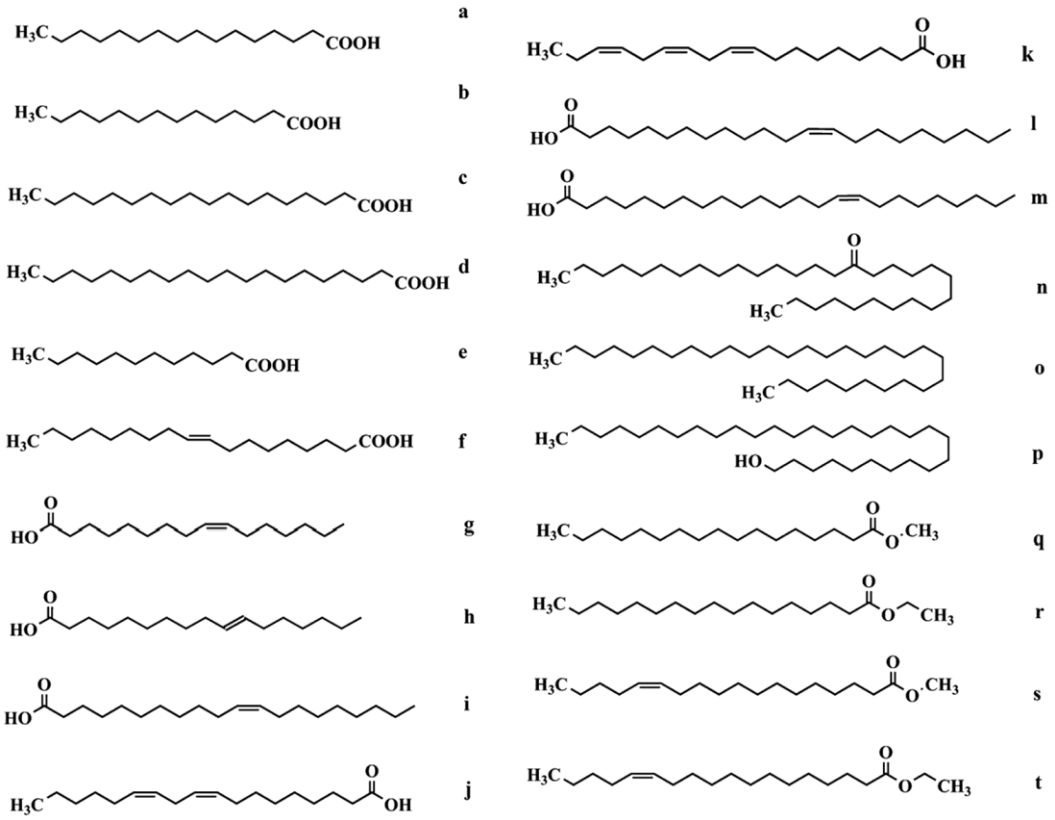

Fig. 4 — Fatty compounds of *Aesculus indica*, a) Palmitic acid; b) Myristic acid; c) Stearic acid; d) Arachidic acid; e) Lauric acid; f) Oleic acid; g) Palmitolic acid; h) 10-heptadenoic acid; i) Gondoic acid; j) Linoleic acid; k) Linolenic acid; l) Erucic acid; m) Nervonic acid; n) Palmitone; o) N-hentriacontane; p) N-hentriacontanol; q) Methyl heptadecanoate; r) Ethyl heptadecanoate; s) Methyl octadec-(13Z)-enoate; and t) Ethyl octadec-(13Z)-enoate.

linoleic acid, linolenic acid, erucic acid, nervonic acid (Fig. 4g-m) were identified, as well as their composition was determined from the petroleum seed extract[34]. Bhattacharya *et al.*[78], found palmitone, n-hentriacontanol, n-hentriacontane (Fig. 4n-p) in the leaves, and Singh *et al.*[79], isolated aliphatic esters, methyl heptadecanoate, ethyl heptadecanoate, methyl octadec-(13Z)-enoate, and ethyl octadec-(13Z)-enoate (Fig. 4q-t) from the chloroform seeds extract.

Pharmacological properties

A. indica has exhibited various activities.

Anti-diabetic effect

Mishra *et al*.[31], orally administrated 25, 50, and 75% processed seed flour of *A. indica* to Wistar rats and didn't find any toxic effect. However, the 75% processed seed flour diet was more effective than the 25 and 50% diet for alloxan-induced diabetic rats. There were mild swelling and necrosis in the liver, mild tubular swelling, and congestion in the kidney. The eosinophilic muscle fibres increased with the heart inflammation, and a fully developed islet of Langerhans was observed in the pancreas. It was inferred that the activity might be due to aescin in the flour.

Enzyme inhibitory activity

The methanolic fruit extract and fractions (chloroform, ethyl acetate, aqueous, and n-hexane) of *A. indica* significantly (P <0.001) inhibited the activity of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) as compared to the standard drug galanthamine. The extract showed inhibition of IC_{50} = 145 µg/mL and IC_{50} = 200 µg/mL and galanthamine IC_{50} = 48 µg/mL and IC_{50} = 66 µg/mL, respectively, against AChE and BChE. However, among the fractions, the chloroform fraction displayed the highest inhibition (IC_{50} = 85 µg/mL and IC_{50} = 160 µg/mL), followed by ethyl acetate (IC_{50} = 190 µg/mL and IC_{50} = 210 µg/mL) and aqueous fraction (IC_{50} = 350 µg/mL and IC_{50} = 400 µg/mL). In comparison, n-hexane exhibited the least (IC_{50} = 760 µg/mL and IC_{50} = 870 µg/mL) inhibition, respectively, against AChE and BChE[65].

Antioxidant activity

Pal *et al.*[18], reported the effect of seed (petroleum ether, chloroform, ethyl acetate, ethanol, and aqueous) extracts on (non-enzymatic haemoglobin glycosylation) antioxidant activity. The ethanol and chloroform extract exhibited the highest (76.9±0.92 and 70.3±0.45 respective) antioxidant activity at 1 mg/mL concentration. However, the petroleum ether, ethyl acetate, and aqueous extract showed low (45.5±0.53, 62.5±0.35, and 57.1±0.40, respectively) activity. The flavonoid and tannins detected in the extract might be responsible for antioxidant activity. In another activity, the chloroform leaf extract showed 27.62±1.67% and 48.65±1.71% inhibition against nitric oxide and superoxide radicals at the highest (250 µg/mL) concentration. The activity increased significantly (P <0.01) with the increase in (20-250 µg/mL) concentration. The IC_{50} value of 513.84 µg/mL and 235.4 µg/mL were respectively found in the extract as compared to standard rutin (IC_{50} = 67.8 µg/mL) and quercetin (IC_{50} = 62.5 µg/mL)[80].

Hypocholesterolemic and hypoglycaemic activity

The level of total blood cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL), and blood LDL/HDL cholesterol ratio was 386.2±7.68, 121.64±2.95, 327.16±6.89, 24.33±0.59, 9.44±0.46 mg/dL respectively found in the serum of 1% cholesterol-fed control group rats. Which was significantly (P ≤0.05) decreased to 247.73±6.00, 54.54±4.22, 197.41±6.24, 10.91±0.85, 5.02±0.32 mg/dL in 75% processed *A. indica* seed flour fed group respectively. However, the level of high-density lipoproteins was 34.72±1.88 mg/dL in the 1% fed cholesterol control, which was significantly (P ≤0.05) increased to 39.41±1.60 mg/dL in the 75% processed seed flour-fed group. The level of blood glucose significantly (P ≤0.05) decreased from 228 mg/dL to 95 mg/dL in alloxan-induced diabetic rats fed with 75% processed flour. It was inferred that aescin might be responsible for these activities[81].

Immunomodulatory activity

The oral administration (50 and 100 mg/kg/day) of methanolic leaves extract of *A. indica* to Wistar rats significantly (P, 0.001) increased the neutrophil adhesion at the highest dose compared to the control group. Although, the haemagglutinating antibody titre did not show any significant increase. However, the delayed-type hypersensitivity response to sheep red blood cells exhibited a dose-dependent and significant (P, 0.001) increase in the paw volume. Thus, *A. indica* stimulated cell-mediated immunity without affecting humoral immunity[82].

Anti-nociceptive activity

The 70% ethanolic leaves extract of *A. indica* dose-dependent (10, 30, 60 mg/Kg, i.p.) significantly (P ≤0.001) decreased the acetic acid-induced writhing in balb/c mice as compared to the saline control group. The extract dose (100, 300, 600 mg/kg, i.p.) increased latency time in the hot plate test and reaction time in the tail immersion test, measured at 30, 60, 90, and 120 min intervals. The analgesic effect of the extract and standard drug tramadol was significant (P ≤0.001) and almost similar when compared with saline control. The presence of flavonoids and tannins in the extract might be responsible for the anti-nociceptive effect possibly through the inhibition of peripheral and central nociception mechanisms[83].

In another study, ethanol seeds extract (100, 200, 300 mg/kg) showed significant (P <0.001) anti-nociceptive activity compared to normal control in the hot plate test, tail withdrawal in the tail immersion test, and reduced number of writhing in acetic acid-induced writhing test in albino mice. The presence of saponins, flavonoids, tannins, and other phytochemicals in seeds, might be responsible for activity[84].

Anti-spasmogenic activity

The alcoholic leaves extract (400 and 800 µg/mL) of *A. indica* exhibited an anti-spasmogenic effect in the isolated guinea pig ileum. Extract acts as an antagonist of the spasmolytic effect produced due to acetylcholine[85]. In another study, the crude extract dose-dependently reduced spontaneous contraction in isolated tissue of rabbit's jejunum, and the K^+ (80 mM) induced contraction showed EC_{50} values of 0.1083 mg/mL (0.04793-0.2447, 95% CI). They concluded that activity was due to the blocking of calcium channels[86].

Anti-inflammatory activity

A. indica extract (100 mg/kg) significantly (P, 0.03) reduced 1% carrageenan-induced paw oedema as compared to standard aspirin (12 mg/kg) drug. There was no significant difference found between 300 mg/kg *A. indica* extract and aspirin effect. Both imparted almost equal anti-inflammatory effects[87].

In another study, the methanol seed extract significantly (P, 0.001) increased proliferation, viability, and superoxide dismutase enzyme activity in

the human adipose-derived stem cells and decreased lactate dehydrogenase enzyme, reactive oxygen species release in the cells with the downregulation of nuclear factor kappa-light-chain-enhancer of activated B cells pathway (NF-κB) markers tumour necrosis factor-alpha, interleukin-1,6 compared to the monosodium iodoacetate induced stress cells[88].

Antiviral activity

The composition of *A. indica* seeds containing β-aescin exhibited 90-94% inhibition against cucumber mosaic virus with an effective concentration of 1000-2000 ppm. The composition was 40, 50, 60, and 100% more effective than standard drugs zidovudine, amantadine, acyclovir, and 2-thiouracil respectively[89].

Antimicrobial activity

A. indica leaves extract was reported to possess a significant (P <0.05) antibacterial effect. The methanolic leaves extract showed the highest 14±0.5 and 14.5±1 mm zone of inhibition against *Micrococcus luteus* and *Staphylococcus aureus* respectively. The chloroform fraction demonstrated the highest 14.5±0.1 mm inhibition against *Pseudomonas pickettii* and aqueous fractions 16±1, 14±0.5, and 15±0.5 mm against *Bacillus subtilis, Micrococcus luteus*, and *Salmonella Setubal* respectively. Although standard drug cefotaxime showed 33±0, 32±0.01, 31±0.5, 30±0.4 and 30±0.05 mm zone of inhibition against *Staphylococcus aureus, Pseudomonas pickettii, Bacillus subtilis, Micrococcus luteus*, and *Salmonella Setubal* respectively. The lower activity of other (ethyl acetate and methanol) fractions might be due to the low presence of phytochemicals[90].

Toxic activities

A. indica seeds are eaten by wild animals and humans. Though large consumption could cause vomiting, depression, diarrhoea, dilated pupils, poor coordination, paralysis, and stupor[32]. In a toxicity study, a single dose of seed extract showed LD_{50} of 10.6 and 10.7 mg/g body weight, respectively, against chicks and hamsters. The administration for 2 consecutive days showed 6.5 mg/g LD_{50} for chicks. The symptoms of fatigue, poor coordination of muscles, paralysis, coma, and death were reported[91]. At the same time, the study carried out by Mishra *et al*.[31], reported that the oral administration of 25 to 75% processed seed flour was found nontoxic to Wistar rats, and a similar study on ethanol seed extract 2000 mg/kg was also found safe to albino mice[84].

Cytotoxic/anticancer activity

The methanolic leaves extract of *A. indica* dose-dependently (10 µg/mL to 500 µg/mL) inhibited (34.2% to 94%) the growth of breast adenocarcinoma (MCF-7) cells in the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide) assay. Among the fractions of methanol crude extract, they showed significant ($P \leq 0.05$) inhibition. The aqueous fraction showed the highest (59%) growth inhibition, followed by the methanol fraction (53%), ethyl acetate fraction (45%), and chloroform fraction (30.6%), while the hexane fraction showed the lowest (29.8%) inhibition. It was concluded that the high activity of the aqueous fraction might be due to the presence of saponins or flavonoids that might act on MCF-7 cells either alone or synergistically[92]. In another study, methanol seeds extract and its chloroform and ethyl acetate fractions induced cytotoxicity in the human hepatocyte carcinoma cell line (HepG2), inhibited the cell migration and colony formation, and significantly (P <0.001) reduced the spheroid formation of HepG2 cells compared to the control group[93].

Neurodepressive activity

Piscicides are chemical substances poisonous to fish and are primarily used to eliminate the desired or unwanted fish from the pond. Bhatt[94], demonstrated that a 2.6 mg/L concentration of a piscicidal, triterpenoid glycoside of *A. indica* degraded neurons, tactile, and sensory impulses in the medulla oblongata of fish. The absence of schooling, bottom sinking, difficulty breathing, air bubbles swallowing, and slight pinkness of the gills were observed due to the damaged respiratory centre of the treated fish[94].

Insecticidal activity

Anwar *et al*.[95], reported the insect-killing effect of acidified alcoholic (ethanol + 2% acetic acid) leaf and flower extract of *A. indica*; they found that one-time topical application of 5 µL extracts over yellow rice stem borer (*Schirpophaga incertulas*) larvae exhibited significant (P 0.05) mortality 70% and 60% respectively after 48 h. Although, in the case of sugarcane mealybug (*Saccharicoccus sacchari*), where they were fed with sugarcane leaves (previously treated with extracts), the mortality of 41.67% was observed in the leaves extract after 24 h, and in the case of flower extract 75% after 12 h which

last for 24 h. The activity of flower extract was higher than the leaves extract in both insects. The presence of constituents such as aescin and saponins in the *Aesculus* species might be responsible for their surfactant property.

Discussion and future perspective

The present review highlights the information on traditional uses, nutrients, minerals, phytochemicals, and biological activities of *A. indica*. The compiled data from the literature revealed that *A. indica* has versatile uses. Especially the seed products consumed as food by folks contain various nutrients and minerals. However, seeds are also reported toxic for human consumption, so multiple methods have been used to remove toxins/bitter contents from the seeds, including traditional water wash and many other scientific methods to optimize toxicity and nutritional composition. The composition varied from method to method, so further research should be done. Similarly, other parts of *A. indica* might contain nutrients and minerals; hence, research is needed in this direction. *A. indica* exhibited anti-nociceptive, anti-inflammatory, insecticidal, antioxidant, cytotoxic, enzyme inhibitory, hypocholesterolemic, hypoglycaemic, immunomodulatory, antimicrobial, and antiviral activity, which revealed its medicinal importance. There are several research gaps found in the literature study. The mode of pharmacological action is absent in most studies, which requires further research. A comparative study with the normal cells is lacking in the cytotoxic activity of cancer cells. The enzyme inhibitory and antioxidant activities have been performed *in vitro*; therefore, further *in vivo* study is needed to prove the efficacy of extracts in the living system. In the acute oral toxicity study, 75% processed seed flour and 2000 mg/kg ethanol seed extract of *A. indica* was reported nontoxic for rodents. At the same time, biological activities such as anticancer/cytotoxic, neuro-depressive, and insecticidal showed the toxic effect of *A. indica*; thus, a detailed toxicological study is recommended. Furthermore, most of the research has been carried out on extracts or fractions, and the effect has been considered due to aescin. Undoubtedly aescin has several pharmacological properties, but there are several other phytochemicals reported in *A. indica*, so the effect might be synergic or alone or by an unknown phytochemical that cannot be neglected. Therefore, further research is required on the isolation, purification, and characterization of compounds and their individual pharmacological and toxicological evaluation.

Conclusion

This review focuses on the traditional uses, botany, phytochemical constituents, and pharmacological attributes of *A. indica*. Literature studies have revealed that *A. indica* contains various nutrients and minerals and has exhibited significant biological activities such as enzyme inhibitory, antioxidant, immunomodulatory, hypocholesterolemic and hypoglycaemic, anti-nociceptive, anti-spasmogenic, anti-inflammatory, antimicrobial, which reflects its ethnomedicinal importance. However, it has also shown neuro depressive, cytotoxic, and insecticidal toxic activities. Nevertheless, some of the traditional uses still require validation by pharmacological studies. The literature study identifies many research gaps that need further investigation.

Conflict of interest

The authors declare no conflicts of interest.

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