

A Comprehensive Review of Therapeutic and Ethnobotanical Aspects, Phytoconstituent and Pharmacological Activity of *Aesculus indica*

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ABSTRACT

Aesculus indica Wall. Ex Camb. Hook, a member of the Hippocastanaceae family, exhibits robust growth in colder climates worldwide, showcasing its remarkable adaptability. Within its various components lie a diverse array of constituents, each harboring a treasury of advantageous compounds that have found utility across a spectrum of applications. These applications encompass the amelioration of gastrointestinal disturbances, facilitation of hemostasis, management of diabetes, and mitigation of various dermatological afflictions. Through a comprehensive synthesis of information gleaned from an array of authoritative sources including meticulous literature surveys, our study provides a thorough dissection. It traverses the multifaceted tapestry of this plant's applications, develops into its intricate chemical composition, and elucidates its nuanced effects on human health and well-being. This compendium stands as an invaluable reservoir, poised to aid and embolden scientists and researchers engaged in the exploration of natural products. Its content, meticulously aggregated and meticulously crafted, promises a resourceful springboard for their scholarly inquiries while assuring originality and authenticity in their pursuits.

Keywords: *Aesculus indica*, Pharmacognosy, Phytochemistry, Pharmacology activity, Anti-diabetic activity, Antioxidant, Antimicrobial Activity.

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INTRODUCTION

Traditional medicine encompasses holistic remedies like, Chinese, Unani Ayurvedic, and Siddha traditions.^[1] More than half of the globe's medications are derived from natural sources.^[2] In less industrialized nations, a substantial 80% of the population depends on herbal therapies, a fact emphasized in a World Health Organization report.^[3] Globally, approximately 21,000 plant species are recognized for their medicinal properties, with a significant number thriving in developing regions.^[4] In India alone, there exists an approximate count of 3,000 plant species.^[4] The Eastern Himalayan region within India harbors a rich reserve of invaluable medicinal plants. In contrast, natural compounds derived from plants tend to offer enhanced safety and efficacy compared to synthetic pharmaceuticals. However, obstacles like solubility and bioavailability have impeded the

advancement of plant-based drug development. Innovative formulation technologies hold the potential to surmount these challenges, potentially unlocking the health benefits inherent in plant compounds. The recognition of the advantages associated with medicinal plants and their derivatives in promoting health and combating diseases has been steadily increasing.^[5] The realm of natural products has played a significant role in modern medicine, yielding discoveries such as antibiotics, anti-cancer agents, anti-inflammatory compounds, and analgesics, gleaned from centuries of exploring natural resources.^[6] Across the globe, derivatives from medicinal plants are highly coveted as the primary option for healthcare. India has earned the title of the 'Medicinal Garden of the World' due to its abundant diversity of medicinal plant species.^[7] Noteworthy therapeutic advancements have emerged from potent drugs like tiotropium and ipratropium for lung ailments, morphine-6-glucuronide for potent pain alleviation, and exotica for cancer treatment.^[8] Numerous compounds of therapeutic significance, including caffeine and theophylline, were originally sourced from plants and are now produced commercially.^[9] *Aesculus indica* (*A. indica*), encompassing 20 species.



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Aesculus indica is distributed across colder regions worldwide and falls within the Hippocastanaceae family. It holds a significant position in traditional medicine due to its curative properties. Its seeds, bark, and roots find application in the treatment of rheumatism, while its fruits are utilized for their anti-diabetic attributes and in addressing colic disorders. Notably, the leaves exhibit anti-cancer properties.^[10] This plant demonstrates remarkable effectiveness against conditions such as hemorrhoids, varicose veins, and ulcers due to its anticoagulant properties. It also offers benefits in managing ailments like migraines, blood effusions, and frostbite.^[11] This comprehensive review casts illumination on the geographical, historical, botanical, and pharmacological dimensions of *Aesculus indica*.

The morphology of *Aesculus indica*, commonly known as the Indian horse chestnut, is characterized by distinct features in its various plant parts.

The morphology of *Aesculus indica*

Roots

The plant possesses a well-developed taproot system that anchors it in the soil and aids in absorbing water and nutrients. Lateral roots also spread out from the taproot, further enhancing its stability and resource uptake.

Stem

Aesculus indica typically features a sturdy, woody stem with a relatively smooth bark that may display some fissures as the plant matures. The stem often exhibits branching, producing multiple shoots that contribute to the plant's bushy appearance.

Leaves

The leaves of *Aesculus indica* are palmately compound, meaning they are composed of multiple leaflets that radiate from a central point. Each leaf usually comprises 5 to 7 leaflets with serrated edges. The leaflets are broadly ovate in shape, providing an attractive appearance.

Inflorescence

The plant produces showy, erect inflorescences in the form of large panicles or racemes. These inflorescences bear a collection of individual flowers that are typically white or pale pink in color, characterized by a combination of both male and female reproductive structures.

Flowers

Aesculus indica flowers are relatively large and have a distinctive structure. They typically consist of five sepals and five petals, which form a tubular to bell-shaped corolla. The flowers also feature several stamens and a pistil, housing the reproductive organs.

Fruits

Following successful pollination, the plant develops fruits in the form of spiky capsules, colloquially referred to as conkers or horse chestnuts. These capsules encase shiny, inedible seeds with a light-brown hue. When mature, the capsules split open, releasing the seeds for dispersal.

Habitat and Growth

Aesculus indica is well-adapted to cooler climates and is often found in temperate regions. It tends to thrive in well-draining soils and can tolerate a range of environmental conditions. The plant's height can vary, with mature specimens reaching up to 15-20 m, depending on growing conditions.

In summary, the morphology of *Aesculus indica* is marked by its distinctive palmately compound leaves, striking inflorescences, and characteristic capsules. These features contribute to the plant's visual appeal and its ecological role in colder climates.

METHODOLOGY

We performed an exhaustive internet investigation utilizing prominent databases such as PubMed, Scopus, Science Direct, Web of Science, and Google Scholar. Our research centered on exploring the pharmacological characteristics of *Aesculus indica*, encompassing data accessible up until January 2022. The search terms employed in our study comprised "*Aesculus indica*" and "Horse chestnuts."

Description of the geographic area

Aesculus indica is a strikingly large tree, attaining heights of 20-30 m. Characterized by its straight trunk and branches arranged in whorls, this tree is notably abundant in the Northern Western Himalayas.^[12] It thrives within the Himalayan Forest, flourishing at altitudes spanning 900 to 3000 m.^[13,14] Its habitat includes mountain slopes and damp, shaded valleys within the northwestern Himalayan forests. This species is indigenous to regions extending from Nepal to Kashmir in northern India, stretching across the Indus River into and northeastern Afghanistan, as well as various parts of Asia and southeastern Europe. Ordinarily, *Aesculus indica* yields white blossoms from May to June, bearing both male and female reproductive components.^[15]

Historical perspective

The term "*Aesculus*" is derived from the Latin word "Esca," which translates to "Food." Turkish communities historically utilized horse chestnuts to nourish fatigued horses, enhancing their stamina and addressing respiratory ailments. It was also harnessed for treating issues like broken wind, coughs, and fevers in horses. Over time, horse chestnuts gained popularity as ornamental plants, experiencing extensive cultivation in Europe and America during the late 1740s. The fruits of these trees were

also employed as remedies by local inhabitants. Crushed leaves, nuts, and bark possess the potential to offer pain relief, soothe inflamed hemorrhoids, and mitigate discomfort.^[16]

Aesculus indica Colebr., belonging to the family Hippocastanaceae, is commonly recognized as Indian horse chestnut in the English language. It is also known by synonymous names like *Pavia indica*, *Pawia indica* Kuntz, and *P. indica* Royle. This plant assumes diverse regional identities across India, being called Bankhor, Fangar, Gugu, and Kanor in Hindi, Hanudun and Hane in Kashmiri, Kanor and Kanur in Kannada, Pangar and Kishing in Kumaon, Khanor and Tatwokhar in Himachal Pradesh, Kanur, Gun, and Khanor in Punjabi, and Karu, Phangro, and Ghode in Nepali.^[17] This wide array of names reflects its extensive regional presence.

Taxonomically, *Aesculus indica* Colebr. falls within the Hippocastanaceae family.

The *Aesculus* genus comprises a total of 13 distinct species that are spread across five subgenera, namely *Aesculus*, *Parryana*, *Pavia*, *Calothyrsus*, and *Macrothyrsus*. These species have a global distribution, primarily inhabiting temperate regions within the northern hemisphere.^[18] A specific member of this genus, known as *Aesculus indica* Wall. ex Camb. Hook. or Indian horse chestnut, is a notable tree characterized by its substantial size and rounded form. It is categorized under the *Calothyrsus* subgenus, and its precise taxonomic classification can be found in Table 1.^[19,20]

Regarding its macroscopic features, *Aesculus indica* is an aesthetically pleasing tree that typically reaches a height of approximately 15 m. The trunk's diameter measures around 97 cm, and as the tree matures, it develops an exquisite rounded canopy that adds to its visual appeal.

As depicted in Figure 1, the leaves of this plant are arranged oppositely, digitate, and exstipulate, featuring 5 to 10 leaflets that exhibit variable sizes. These leaflets are oblong to lanceolate, characterized by sharp serrations, glabrous surfaces, and a tapered base. Typically, this plant bears white flowers with hermaphroditic attributes, primarily pollinated by bees. The seeds measure around 3.5 cm in diameter and mature in October.

During the winter season, the tree undergoes leaf shedding, initiating new leaf growth in late March. By April, fresh buds emerge, eventually leading to the tree being adorned with white blossoms measuring approximately 3.5 mm in length, and with a fully open diameter of 2-2.5 cm, which typically occurs in May-June. These blooms take on an upright panicle arrangement, spanning a length of 35-40 cm. Concurrently, spiny green fruits emerge, housing numerous brown seeds, and these fruits disintegrate between October and November. The wood's natural color is pale white or creamy white upon initial cutting; upon exposure to light, it transitions to a pale brown hue with a light brown shade.^[17,21]

Toxicological Studies

Throughout history, herbal remedies have been employed to address a variety of ailments. However, the exact dosages have yet to be scientifically established, potentially giving rise to concerns over toxicity. Ensuring the safety of plant extracts necessitates studies focusing on toxicity prevention.^[22] Toxicity involves the intricate interaction between chemical substances and biological systems. In the case of this particular plant, newly sprouted leaves and flowers are recognized as toxic, while the seeds contain detrimental saponins. Various components of *Aesculus indica*. Different elements of *Aesculus indica* have shown advantageous impacts in both animals and humans. The lethal dose (LD₅₀) for chicks was established at 10.6 mg/g of body weight when given a sole dose of horse-chestnut seed extract, and 10.7 mg/g of body weight for hamsters. When *Aesculus indica* was administered on two consecutive days, the LD₅₀ was observed to be 6.5 mg/g of body weight.

Toxic manifestations associated with *Aesculus indica* encompassed fatigue, paralysis, coma, and fatality.^[23] Additional symptoms of ingesting a substantial amount of *Aesculus indica* seeds comprised dilation of pupils, diarrhea, alterations in awareness, increased thirst, and reddening of the face. The utilization of processed seeds was limited to medicinal objectives. In 1986, the decoction of *Aesculus indica* seeds resulted in liver harm, along with an anaphylactic shock, upon intravenous injection.^[24]

Traditional Applications

Fodder Use

In the elevated terrains of the Kashmir valley, horse chestnut leaves and seeds play a pivotal role as essential livestock fodder.



Figure 1: *Aesculus indica*.

Table 1: Taxonomical classification.

Phylum	Angiosperms
Class	Eudicots
Order	Sapindales
Family	Hippocastanaceae
Sub-family	Sapindaceae
Genus	<i>Aesculus</i>
Species	<i>indica</i>

Due to their high starch content, crushed seeds are fed to cattle, leading to improvements in both milk quality and quantity.^[17]

Culinary Use

The seeds of this plant are not only edible but have also served as sustenance for diverse tribes in North and North-Eastern India during times of famine. *Aesculus indica* seeds are crushed to produce a flour known as Tattwakhar. These crushed seeds possess a bitter taste, which can be alleviated by soaking them in water for approximately 12 hr.^[25] Alternatively, the seeds can be prepared as gruel (Daliya).^[26,27]

Medicinal Properties

In the realm of Ayurvedic practices, the *Aesculus* genus holds a prominent place in various remedies, showcasing distinctive attributes such as antioxidant, antiviral, immune-modulatory, anti-inflammatory, and spasmolytic properties.^[28,29] These seeds find application in addressing a wide array of conditions, including fevers, piles, wound healing, skin ailments, leukorrhea, cardiovascular disorders, and diarrhea when combined with salt.^[13] Additionally, these seeds are administered to horses to manage colic disorders. Notably, the stem bark also exhibits fungicidal activity.^[30] Moreover, extracts from the flowers and leaves have demonstrated effectiveness in significantly controlling pests that affect rice and sugarcane crops.^[31] This tree holds a significant position in the treatment of rheumatic pain.^[32]

Phytochemical Properties

The roots, seeds, bark, leaves, and twigs of *Aesculus indica* (commonly known as horse chestnut) showcase a diverse array of phytochemicals. These compounds encompass alkaloids, saponins, tannins, glycosides, flavonoids, and phenolic compounds. In the different plant parts, specific compounds such as aescin, quercetin, and β -sitosterol are notably abundant in the leaves. Meanwhile, the stem contains rutin, astragaloside, and esculin, while the seeds contain aescin, aesculoside A and B, along with aliphatic esters. Additionally, the fruits of the plant harbor quercetin, mandelic acid, and kaempferol. The fundamental chemical constituents are visually summarized in Figure 2. An extensive overview of the diverse pharmacological activities associated with *Aesculus indica* and their potential underlying mechanisms is provided in Table 2. In the following sections, we delve into the key phytoconstituents of *A. indica*.

One of the primary compounds derived from *Aesculus indica* is aescin, also known as Escin. This natural mixture of saponins includes triterpenes and exists in two forms: α and β .^[33] The production of α -aescin involves structural rearrangements, leading to the introduction of hydroxyl groups at C21, C22, and C28 through the heating of β -aescin in an aqueous solution at 100°C. β -Aescin, the predominant isolated component, holds significant importance in various pharmaceutical products. It

contributes to a range of pharmacological properties, including anti-edematous, anti-inflammatory, and vagotonic effects.^[34]

Quercetin displays a diverse array of pharmacological activities, spanning anti-inflammatory, neurological, antiviral, inhibition of platelet aggregation, antimicrobial, hepatoprotective, and regulation of capillary permeability.^[35,36] Studies conducted on living organisms have indicated that quercetin extract sourced from

Heterotheca inuloides can counteract oxidative damage triggered by the compound CCl_4 . Moreover, it has exhibited potential *in vitro* for inhibiting angiogenesis in breast cells, underscoring its potential as an effective anticancer agent.^[37,38]

Astragaloside, a natural flavonoid present in various plant components, has been investigated through *Eucommia ulmoides* leaf extract to explore its impact on the Central Nervous System (CNS). Notably, it effectively delays convulsions by suppressing seizure rates. Prior investigations involving *E. ulmoides* have highlighted its significant hypnotic CNS effects. Astragaloside demonstrates efficacy in an array of biological activities, including anticancer, anti-inflammatory, neuroprotective, antidiabetic, cardioprotective, antifibrotic, and antioxidant effects. Its anti-inflammatory response is achieved by inhibiting the activation of Nuclear Factor (NF- κ B) induced by Lipopolysaccharides (LPS), thereby impeding the degradation of I κ B α and curtailing nuclear translocation.^[39]

Pharmacological activities

Literature review has shown that *Aesculus indica* has many traditional uses, but the following are novel practices that have shown significant results.

Anti-nociceptive activity

A research endeavor led by Sundas Firdous and coauthors focused on evaluating the anti-nociceptive potential of *Aesculus indica* leaves' aqueous-ethanol extract against acetic acid through tail immersion and hot plate assays. The outcomes indicated that the plant extract exhibited heightened effectiveness in showcasing peripheral analgesic activity.^[40]

Anti-proliferative activity

Anti-proliferative exertion Yamin Bibi and herco-researchers excavated into the eventuality in vibrant-tumor goods essential in the excerpt of *Aesculus indica* leaves. Their study encompassed assays exercising varying attention (10-500 $\mu\text{g}/\text{mL}$) and employed an MTT-grounded cytotoxicity assay to gauge the reduction in viability of the MCF-7 bone cancer cell line. The findings unveiled a cure-dependent inhibition of cell viability by the crude excerpt, ranging from 34.2 at 10 $\mu\text{g}/\text{mL}$ to 94 at 500 $\mu\text{g}/\text{mL}$. specially, the waterless bit displayed more substantial inhibition when varied with the hexane bit.^[40] In a separate study, the HepG2 hepatocellular melanoma cell line, characterized by its high

Table 2: Chief constituents of *A. indica* with their biological activities.

Sl. No.	Phytoconstituent	Plant species	Model	Mechanism	Biological activity
1	Saponin (Aescin)	<i>A. indica</i>	Serous peritonitis induced by injection of formalin in rats/Carrageenan in mice.	Sensitization to Ca ²⁺ ions and reduction of activation of human endothelial cells.	Anti-edematous
		<i>A. indica</i>	<i>In vitro</i> human saphenous veins	Increase secretion of prostaglandin F2 α .	CVI
		<i>A. hippocastanum</i>	Carrageenan-induced edema in rats	Activation of 5-HT ₂ receptors and decrease TNF- α IL-1 β , PGE ₂ and COX-2.	Anti-inflammatory
		<i>A. hippocastanum</i>	<i>In vitro</i> anti-obesity in mice	Reduced leptin, FT level and enhanced HDL-C concentration.	Anti-obesity
		<i>A. hippocastanum</i>	Sulforhodamine B (SRB) assay	β -aescin sodium enhances TSP-1 expression and reduces PKC- α , phosphor-P38 [mitogen-activated protein kinase) and phosphor- ERK expression.	Proliferation, migration and apoptosis
		<i>A. hippocastanum</i>	<i>In vivo</i> and <i>In vitro</i>	<i>In vivo</i> studies suggest that β -aescin inhibits colon cancer in rats, or <i>in vitro</i> suggests that β -aescin inhibits HT29 colon cancer cell proliferation and reduces Cdk2.	Anti-cancer
2	Glucoside (Esculin)	<i>A. indica</i>	Neutrophil adhesion test and delayed type hypersensitivity.	Increased lymphokines secretion and stimulate cell-mediated immunity.	Immunomodulator
3	Flavonoid [Rutin)	<i>A. indica</i>	<i>In vivo</i> tail immersion and hot plate method.	Inhibit prostaglandin synthesis Reduction of acetic acid-induced writhings.	Anti-nociceptive effect
4	Quercetin	<i>A. indica</i>	<i>In vitro</i> DPPH and ABTS assay.	Scavenging reactive oxygen species	Antioxidant
5	Mandelic acid	<i>A. indica</i>	<i>In vitro</i> DPPH and ABTS assay.	Inhibit lipid oxidation	Antioxidant

growth eventuality and unbridled proliferation in cancer cells, was employed as a model. Shahbaz and his collaborators delved the eventuality of *Aesculus indica* as an anticancer agent, with a focus on its capability to stymie the proliferation of HepG2 cells. Their findings indicated that the methanol excerpt, chloroform bit, and ethyl acetate bit held murderous cure 50 (LD₅₀) values of 225 μ g, 150 μ g, and 170 μ g, independently.^[41]

Anti-diabetic activity

The seeds of *Aesculus indica* are dried and processed to create flour known as 'Talwalkar'. *In vivo* investigations have demonstrated that the inclusion of aescin in this flour is adept at reducing blood

glucose levels, showcasing effectiveness in managing diabetes mellitus.^[42]

Antioxidant activity

Muhammad Zahoor and his collaborators conducted an inquiry into the antioxidant activity of *Aesculus indica* fruit extract across various fractions. Their study delved into the potential contributions of phenolic and flavonoid compounds, which are frequently linked to antioxidant attributes in diverse plant species. Phenolic compounds such as quercetin and mantellic acid were isolated in their pure forms from the crude extract. The assessment of antioxidant activity was carried out using the DPPH and ABTS methods. The outcomes highlighted that

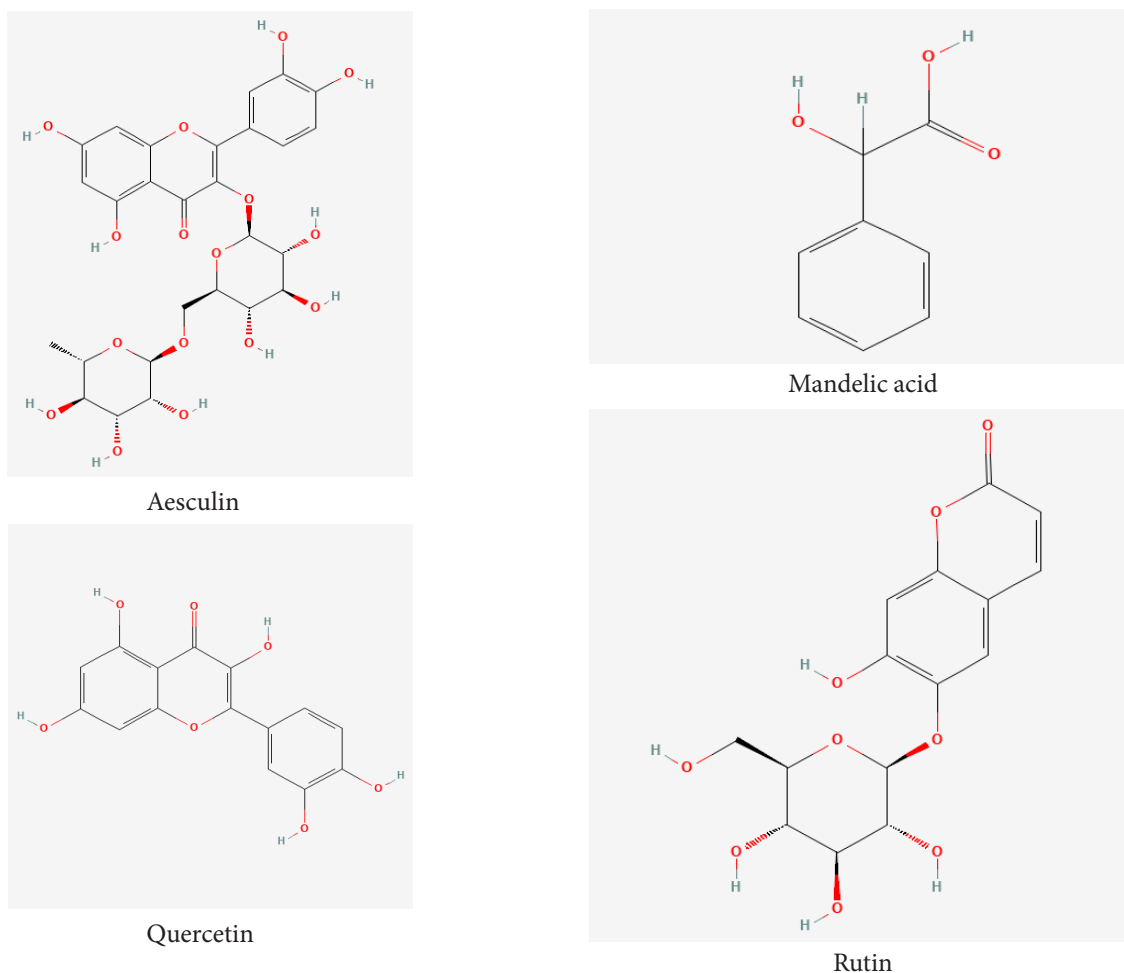


Figure 2: The main bioactive phytoconstituents that have been extracted from *Aesculus indica*.

the fruit of *Aesculus indica* possesses the capability to mitigate oxidative stress initiated by reactive oxygen species. Notably, this plant exhibited its most significant scavenging activity against 'active-oxygen'

Immunomodulatory activity

These substances encompass both natural and artificially created agents that either enhance or inhibit the immune response. The *in vivo* immunomodulatory impact of *Aesculus indica* leaf extract was assessed through oral administration at doses of 50-100 mg/kg. This study demonstrated the extract's ability to modulate the immune response in both humoral and cellular models. Notably, the administration of the extract resulted in a notable rise in neutrophil adhesion, indicating its influence on cell-mediated immunity.^[28]

Anti-inflammatory parcels

The anti-inflammatory characteristics of *Aesculus indica* are apparent in its seed oil painting and dinghy juice. exploration indicates that the effectiveness of these factors in reducing

inflammation caused by carrageenin in rats is attributed to the essential acyl group present in aescin, a emulsion deduced from both the seed and dinghy excerpts of the factory. colorful forms of aesc in attained from steed groaner have been considerably studied for their different pharmacological goods. This emulsion has demonstrated the capability to offset the vascular permeability convinced by acetic acid in mice, as well as the vascular permeability touched off by histamine in rats passing acute inflammation. More recent findings punctuate the defensive and regenerative parcels of *Aesculus indica* in mortal Adipose-Deduced Mesenchymal Stem Cells (hADMSCs) subordinated to stress convinced by monosodium iodoacetate. This positive impact seems to stem from the reduction of oxidative stress and the anti-inflammatory goods, which are apparent in the dropped protein expression of pro-inflammatory cytokines and NF- κ B.

Antimicrobial Activity

Some studies suggest that *Aesculus indica* extracts might have antimicrobial properties, which could make them useful in managing certain infections.

Wound Healing

There is some limited evidence to suggest that *Aesculus indica* extracts might promote wound healing due to its potential anti-inflammatory and antioxidant effects.

Analgesic Activity

Traditionally, extracts from *Aesculus indica* have been used to relieve pain, potentially due to its anti-inflammatory properties.

Future perspective

Medicinal flora is distributed globally, holding unexplored potential for addressing a multitude of health concerns. The wide array of ecological niches, particularly in regions such as the eastern Himalayas, renders them a valuable reservoir of these therapeutic plants. Within this context, *Aesculus indica* emerges as a beacon of hope for the innovation of novel pharmaceuticals, considering our limited comprehension of how new therapeutic agents intricately target intricate physiological and cellular responses. Its historical applications in addressing ailments like rheumatism, diabetes, and abdominal colic underscore its significance. Notably, the methanolic extract of *Aesculus indica* has exhibited cytotoxic effects *in vitro*; however,

further inquiries utilizing diverse methodologies remain crucial to assess its impact on normal cells and potential variances. Delving deeper into the exploration of this plant holds the promise of cultivating fresh herbal remedies aimed at fulfilling human health requirements.

CONCLUSION

Based on the information collected in this review, it can be concluded that the plant *Aesculus indica* possesses abundant medicinal properties and is commonly used in traditional folk remedies, as supported by various literature sources. In contemporary times, there is a growing interest in plant-based medicines due to their reduced toxicity and cost-effectiveness. *Aesculus indica* has demonstrated effectiveness in various therapeutic areas, including anti-diabetic, anti-cancer, anti-inflammatory, immunomodulatory, and antioxidant activities. The diverse range of medicinal attributes makes *Aesculus indica* a valuable resource for developing herbal medicines. Further exploration of its chemical constituents is warranted to provide a more detailed understanding. The compounds found in *Aesculus indica*, including saponins, flavonoids, and others, suggest its potential for providing various health benefits. However, to establish its true pharmacological activities and to determine its safety and efficacy for different health conditions, further research, including well-designed clinical trials, is necessary. Consulting a qualified healthcare professional is highly recommended before considering the use of *Aesculus indica* or any other herbal remedy for medicinal purposes. This cautious approach ensures both the responsible

use of natural remedies and the avoidance of potential interactions with existing medications or underlying health conditions.

AUTHOR CONTRIBUTION

Shubham Anand and Arijit Chaudhuri; conceptualization, review writing and editing. Neha Chopra, Udichi kataria, Devendra dhanorya, Manoj kumar bajhaiya, Gujjala sai sri harsha Conceptualization literature search, data collection editing.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CNS: Central nervous system; **LPS:** Lipopolysaccharides; **NF- κ B:** Nuclear Factor Kappa B; **Cox-2:** Cyclooxygenase-2; **5-HT₂:** 5-Hydroxytryptamine 2; **TNF-alpha:** Tumor Necrosis Factor Alpha; **PEG₂:** Prostaglandin E₂; **IL-1 β :** Interleukin-1 Beta; **F₂-alpha:** F₂-Alpha Prostaglandin; **CDK₂:** Cyclin-Dependent Kinase 2; **CVI:** Chloroform Vapor Inhalation; **CCl₄:** Carbon Tetrachloride; **sRB assay:** Sulforhodamine B Assay; **ABTS assay:** 2,2'-Azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) Assay; **MCF-7:** Michigann Cancer Foundation-7; **MTT-based cytotoxicity:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium Bromide-based Cytotoxicity; **HepG₂:** Hepatocellular Carcinoma Cell Line; **LD₅₀:** Lethal Dose 50%; **DPPH:** 2,2-Diphenyl-1-picrylhydrazyl; **ABTH:** 2,2-Azobis(2-amidinopropane) Dihydrochloride; **sADMSCs:** Synovium-Derived Adipose-Derived Mesenchymal Stem Cells.

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