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Review Article

THERAPEUTIC EXPLOIT AND RELEVANCE OF *MARTYNIA ANNUA* LINN: AN INTRICATE ASSESSMENT

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ABSTRACT

Martynia annua Linn. or *Martynia diandra* Gloxin is a herbaceous plant belonging to the family Martyniaceae. It is usually recognized as "Devil's claw" or "Cat's claw". It is abundantly found in the Tropical and Subtropical regions of America. It was first found in Mexico and since then has been naturalized in many countries. The herb is cultivated to be used as an ornamental and a medicinal plant. The entire plant contains a substantial amount of biologically active constituents that have been reported to show potentially significant pharmacological activities including anti-inflammatory, antibacterial and anticonvulsant. Therefore, the herb is widely used in traditional systems of medicines. The most common constituents found all over the plant are alkaloids, tannins, glycosides, flavonoids, terpenoids, proteins, amino acids, phenols, steroids, anthocyanins, and carbohydrates. Researchers have demonstrated that the presence of flavonoids and phenolic compounds are associated with bioactivities like antioxidant activity which is greatly beneficial for maintaining good health. Another important constituent identified with the plant is luteolin, which is responsible for wound healing activity. However, the studies of these pharmacological activities are inadequate and further research will be required for the determination of the benefits as well as the toxic effects of the plant. This article provides an assessment of the various phytochemical and pharmacological activities of *Martynia annua* Linn.

Keywords: *Martynia annua* Linn, Herbal medicine, Health, Traditional medicine.

1. INTRODUCTION

Herbs are plants or parts of those plants that are recognized for the benefits of their scent and flavor in culinary roles and their remedial properties. Herbal medicines are natural products and consumed significantly as traditional medicines throughout the world in the form of herbal extracts, energetic decoctions, juices, etc. They constitute the basis for numerous of the world's traditional systems of medicines. Many laboratory investigations and herbalism have indicated that some herbal medicines and herbal products are greatly beneficial against ailments and diseases [1]. Modern medicine has developed and evolved from the traditional systems of medicine with the help of detailed screening of the chemical constituents and the pharmaceuticals. Even with such modernization, plants remain a vital source of medicinal compounds. This happens because most modern drugs are made of synthetic compounds which can cause mild to severe side effects while herbal drugs ensure safety, efficacy, and rarely any side effects. This makes people inclined to their choices towards using products obtained from plants and other natural sources [2, 3].

All the medicinal plants require a different growing environment like harvesting season, soil fertility, climate, etc. This results in substantial differences in the quality and quantity of the chemical constituents of the plants. This in turn causes differences in their therapeutic activity [4, 5].

Herbs contain nutritional components, and their pharmaceutical elements have polyvalent interactions with each other. This is how herbal medicines are used in other ways than conventional drugs are used. In this manner, the clinical effects of herbs have favorable effects with limited adverse reactions than that of drug therapies. The patient medications are not only based on the pharmacology but also the indications for the herbs [6].

Herbal medication is the collection of practices of indigenous systems of medicine and several treatment experiences of many previous generations. This guides the selection, preparation, and application of herbal formulations in the treatment, control, and management of a range of diseases. Plant-based medicinal drugs are reported to be successfully used in curing some diseases such as skin diseases, tuberculosis, diabetes, jaundice, hypertension, mental disorders, cancer, AIDS, and many other infectious diseases. Countries with ancient civilizations like China, South America, India, and Egypt are still using numerous plant-based medicinal drugs for treating such diseases [7].

Martynia annua Linn. is an indigenous plant that is naturally utilized for the self-treatment of a variety of diseases. It is naturally grown to be used as an ornamental and as a medicinal plant. It has a prominent distribution system in the form of seed pods that enable it in spreading by sticking to the legs of large animals and in instantly colonizing new environments as weeds. Hence, the risk of introduction of *Martynia annua* is moderate to high. It is an annual or short-lived perennial herb that belongs to the family Martyniaceae (or Pedaliaceae) [8-11]. Martyniaceae is a small family of flowering plants which includes 12-13 species in five genera [12]. *Martynia* is a monotypic genus that has varying flower sizes, colors, and leaf forms [13].

The seeds of *Martynia annua* germinate in the presence of sufficient moisture [8]. The various pharmacological properties of *Martynia* are due to the presence of some primary metabolites like carbohydrates, proteins, and amino acids and a major component of secondary metabolites such as glycosides, tannins, phenols, flavonoids, steroids, alkaloids, and anthocyanins [14, 15]. These are found abundantly and extracted from the leaves, seeds, fruits, flowers, stems, and roots. The flavonoids and phenolic compounds are responsible for the antioxidant properties of the plant. Additionally, a small percentage of semi-drying oil is found in the seeds while some fatty acids arepresent in the seeds of the plant, and this is used for itchiness and skin affections [16-18].

Martynia annua was first found near Veracruz, Mexico. It is domesticated in Tropical and Subtropical America. Presently, it is reported as invasive in Australia, China, Cuba, India, Indonesia, Malaysia, and New Caledonia. It was inaugurated in areas such as Antilles, Bangladesh, Benin, Burkina, Cambodia, China, India, Jawa, Laccadive Is., Lesser Sunda Is., Mauritius, Myanmar, Nepal, Netherlands, Nigeria, New Caledonia, Togo, Laos, Pakistan, Queensland, Rodrigues, Aruba, Sri Lanka, Thailand, Vietnam, and West Himalaya. In Australia, the species grows as a weed in semi-tropical and semi-humid groves, plain grasslands, landfills, junkheap, and grazing regions [8]. In Guatemala, it is cultivated in damps or dry thickets, open fields, hedgerows, and clearings from sea level to 2400 m. [13]. In India, it is generally distributed in dense clumps on roadsides, degraded moist and dry deciduous forests, and wastelands [19].

In honor of a professor of botany at Cambridge, John Martyn, the plant was named *Martynia*. It was described in Martyn's work *Historia Plantarum Rariorum*, with full demonstrations and illustrations. The following descriptive name of the species was given: *Martynia annua villosa et viscosa, folio subrotundo, flore magno rubro* [20].

Another botanical name of *Martynia annua* is *Martynia diandra* Gloxin. Some common names of the plant are 'Devil's Claw', 'Small Fruit Devil's Claw', 'Unicorn Plant' 'Cat's Claw', 'Tiger's Claw', 'Snake's Head', and 'Ice Plant'. The name 'Ice Plant' should not be confused with the irrelevant family Aizoaceae [8, 21]. 'Kakanasika' is the Ayurvedic name of the plant, and it is a vital ingredient of *Chyavanprasha avaleha* & *Tryushnadi Ghrita* [22].

The leaves are characterized by large, relatively kidney-shaped to circular and 15-23 cm wide or almost circular, broad and round along with the tubular flowers, simple, opposite, green in color, broadly ovate to triangular-ovate, sticky-topped glandular hairs are present on both the upper and lower leaf blade surfaces, cordate at the base with sinuate-dentate margin and apex are acute, chartaceous, palmately 5-nerved from the base. They resemble sticky rhubarb along with the glandular hairs and exude a slimy sap which gives the plant a clammy feel and thus acts as a hindrance against herbivores that would otherwise consume the succulent leaves [11, 14, 15, 23].

The flowers are tubular, trinket, and bell-shaped and produce nectar with the size range, 3-5 cm long, and are pink to whitish with darker purplish markings and a line of yellow spots in the throat [24].

1.1. Exploit and recital of *Martynia annua* herb

Martynia annua is cultivated as an ornamental as well as a therapeutic plant. It is a conventional medicinal plant utilized in wound recoveries and in treating cancer, rheumatism, epilepsy, inflammation, sore throat, burns, itching, respiratory tract, and skin diseases. Many of the

phytoconstituents that have been isolated from the plant exhibit activities like antioxidant, anthelmintic, analgesic and antipyretic, antimicrobial, anticonvulsant, antinociceptive, antifertility, CNS depressant, anti-diabetic, gastroprotective, cytotoxic action, and several other important medicinal properties [25, 26].

Distinct parts of the plant such as leaves, roots, seeds, stems, flowers as well as the whole plant have been used for various medicinal purposes [26]. In folklore and all traditional practices, the decoction of the whole plant is administered in children-especially in infants with pneumonia and other patients with cold fever [19, 27].

The leaves are consumable and demonstrate favorable effects in patients suffering from epilepsy, tuberculous, sore throat [22]. However, *Martynia* is also given for a local sedative effect and the sap of the leaves is employed for the formulation of gargles for sore throat and the paste is exploit in healing wounds with an excellent antiseptic effect along with the leaves and fruits are beneficial as antidote to snake bites, scorpion venomous bites, stings, and insects [17, 19, 28, 29]. It is also used topically on tuberculosis of the lymphatic glands of the neck [30].

For the management of burns, the ash of the fruit of *Martynia* is used with coconut oil. The fruits also exhibit alexiteric, antioxidant, anti-inflammatory effects and deliver salutary effects against asthma [14,15,19,29,31]. The Ayurvedic Pharmacopoeia of India recommends the seeds of *Martynia* for arresting the onset of graying hair for palitya (premature hair graying). Seed oil is used for treating abscesses and skin infections and is applied locally for the treatment of itches and eczema [19, 32].

In the tribal regions of India, the root paste of the plant is utilized to treat cancer and rheumatism [19]. The extract of *Martynia annua* exhibits fungicidal activity against *Alternaria alternata* and *Aspergillus niger, Acaulospora scrobiculata, Sclerocystis sinuosa* [17, 30].

2. PHYTOCONSTITUENTS OF *MARTYNIA ANNUA*

Phytoconstituents are bioactive or inert non-active chemical compounds found in all parts of plants. They are synthesized by primary or secondary synthesis pathways. The bioactive phytoconstituents consist of the pharmacological activity of herbs and spices. The constituents also protect the plants from predators, pests, microorganisms as well as sepsis or outbreaks of diseases. Some of them are also responsible for their appearance, odors, and other morphological properties [33].

Martynia annua is a medicinally significant plant due to its high concentration of phenolic compounds. This is responsible for the plant defense system as well as for its natural antioxidant property which is employed for maintaining good health [34]. From the available literature, it has been observed that the whole plant is used for its medicinal benefits [35]. According to the numerous qualitative and quantitative phytochemical analysis, studies of *Martynia* that have been conducted with the help of phytoconstituent specific test methods in various research, the most recurring constituents detected in the preliminary screening of different extracts across the whole plant are alkaloids, tannins, glycosides, flavonoids, terpenoids, amino acid and protein, phenols, steroids along with the carbohydrates and anthocyanins. The major constituents are shown in Fig. 1 [17, 36-39].

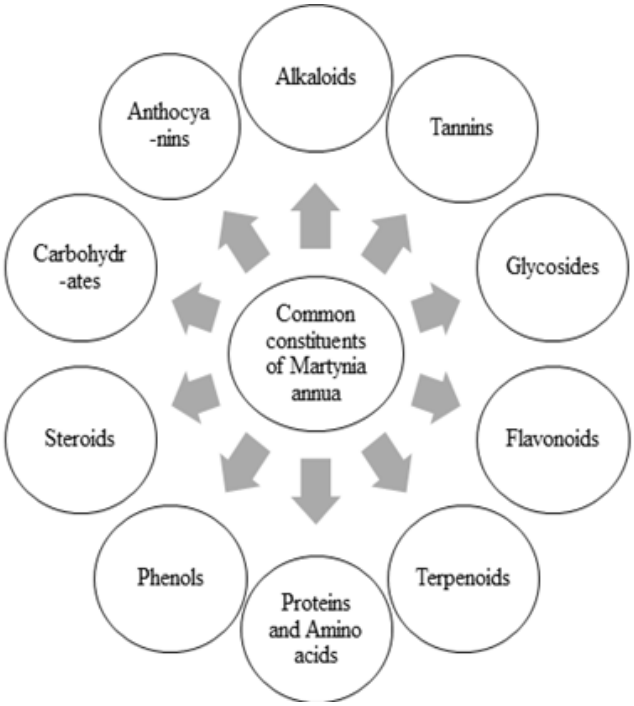

Fig. 1: Common phytoconstituents found across various extracts of all parts of *Martynia annua* Linn.

Different fewer common constituents found across the whole plant were also studied. One such study was done by Gas Chromatography-Mass Spectrometry (GS-MS) on the ethanolic and aqueous extracts of the plant. It exhibited 28 composites for instance pelargonidin-3-5-diglucoside, cyanidin-3-galactoside, p-hydroxybenzoic acid, gentisic acid, arachidic acid, linoleic acid, palmitic acid, stearic acid, apigenin, and apigenin-7-O-

glucuronide. Oleic acid was also present, and it was in a higher amount as compared to the other constituents [40].

Katare and Tyagi identified 11 constituents in the acetonic extracts of the leaves, stems, and roots of *M. annua* with the help of GC-MS analysis. In decreasing order of their occurrence in the extracts, the following compounds were found-2, 5-dihydroxybenzoic acid (36.3%), Cyanidin-3-galactoside (34.14%), 1-Hexyl-2-nitrocyclohexane (31.01%), Oleic acid (30.61%), Apigenin (27.07%), Chlorogenic acid (25.07%), Eicosanoic acid (18.55%), n-Hexadecanoic acid (17.13%), Ethanol, 2-(2-aminoethoxy)- (16.78%), Pelargonidin-3, 5-diglucoside (12.9%) and Apigenin-7-A-D, glucoside (4.4%) [41].

Muazzam et al. conducted a study in which the targeted and untargeted metabolic profiling was performed with the help of UHPLC-MS. The major bioactive compounds that were identified all over the plant were protocatechuic acid, hispidulin, gentisic acid, apigenin, caffeic acid, syringic acid, homovanillic acid, trans-ferulic acid, salicylic acid, and sinapic acid. Along with these, the fruits contained luteolin and hesperetin while the stem contained rutin, p-coumaric acid, and hesperetin. It was observed that the leaves of *Martynia* included major constituents i.e., rutin, p-coumaric acid, kaempferol, luteolin, hesperetin, and isorhamnetin were also found along with the common constituents mentioned above. The flowers of *Martynia* also reported all the above-mentioned constituents except kaempferol, which was only present in the leaves [10].

In another study, Muazzam and Farman investigated the flavonoid glycosides and phenolic acids with the help of HPLC-DAD-ESI-MS fingerprinting of numerous parts of *Martynia*, which were then extracted by ultrasound-assisted solvent extraction. Based on the data obtained, 23 compounds were found which included hispidulin, apigenin, quercetin, and luteolin in significant quantities [42].

The main components of the leaves of *Martynia annua* are sinapic acid, chlorogenic acid, and P-hydroxy benzoic acid [18, 35, 43, 44].

Itankar et al. in their research reported that the medicated oil of leaf extract of *Martynia* contained constituents such as polyphenols, saponins, and steroids which were found to have very good hair growth activity as well as more anti-androgenic and anti-oxidative properties than the medicated oil of fruit extract [32].

It has been reported that the methanolic extract of leaves of *Martynia* comprises the highest quantity of chemical constituents as compared to other leaves extracts because of the higher amounts of terpenoids, alkaloids, glycosides, steroids, tannins, and saponins reported. Considerable numbers of cardiac glycosides, phenols, and anthraquinones were present; however, flavonoids and resins were not present in the methanolic extracts [45].

Kshiragar et al. conducted a study on the methanolic, petroleum ether, and chloroform extracts of *Martynia* leaves and found significant anti-inflammatory activity in the methanolic extract which contained bis (2-ethylhexyl) phthalate. It was also observed that the methanolic extract indicated greater anti-inflammatory activity than other extracts [46].

Lodhi et al. reported presence of the terpenoids, flavonoids, alkaloids, phenols, anthocyanins, carbohydrates, proteins, tannins, and cardiac & saponin glycosides, on the qualitative analysis of the ethanolic extract of *Martynia* leaves [30].

Additionally, presence of the flavonoids in the ethanolic extract of *Martynia annua* leaves are indicated to have antioxidant, free radical scavenging effect as well as antibacterial activities whereas, on HPLC finger-printing, the presence of luteolin was also confirmed. Luteolin is utilized in wound healing and contains antioxidant properties [17, 30].

Sermakkani and Thangapandian reported alkaloids, tannins, saponin, glycosides, flavonoids, anthocyanin, amino acid, steroids, and phenols in the *Martynia annua* acetone leaves extract [45].

The petroleum ether extract of leaves indicated terpenoids and steroids only while the chloroform extract exhibited alkaloids, glycosides, gums and resins, steroids, and flavonoids. The aqueous extract of leaves showed carbohydrates, saponins, gums & resins, tannins, and steroids as well as high amounts of alkaloids [28, 47].

The seeds of *Martynia annua* are found to have pelargonidin-3-5-diglucoside, apigenin, apigenin-7-*O*-beta-D-glucuronide, palmitic acid, malvalic acid, arachidic acid, palmitic acid, stearic acid, cyclo-propenoid, hydrogen cyanide, and linoleic acid. They also contain 10.35% pale yellow semi-drying oil [18, 21, 31, 40, 48, 49].

Alrabie et al. investigated the methanolic extract of *Martynia annua* seeds in which 17 phytoconstituents were found with the help of Gas Chromatography-Mass Spectroscopy (GC-MS). Among them, the most common constituent was 12-Methyl-E, E-2, 13-octa-decadien-1-ol, which is responsible for the antiseptic,

anticonvulsant, allergenic, analgesic, antibacterial, anti-histaminic, anti-salmonella, anesthetic, and antioxidant activities. The next major compound was palmitic acid, which is reported to have pesticidal, antimicrobial, nematicide, antioxidant, anti-inflammatory, cholesterol lowering, anti-androgenic, 5-alpha-reductase inhibitor, hemolytic agent, and dominant mosquito larvicidal activities. The third most common compound was found to be 8, 11-octadecadienoic acid, methyl ester. Isopropyl linoleate was the fourth common compound having anti-cancer, antioxidant, and antimicrobial activities. The fifth common compound was 9, 12-Octadecadienoic acid [Z, Z]- which possesses anti-adherent vegetable, anti-inflammatory, and nematicide activity. Other compounds which showed therapeutic activity were 2-propenoic acid, 3-[4-methoxyphenyl]-, ethyl ester, 2, 3-dihydroxypropyl ester, pentadecane, and flavone. Also, there were reports of the presence of 7 fatty acids which were hexadecanoic acid, methyl ester, 9,12-Octadecadienoic acid, [Z, Z]-, 2,3-dihydroxypropyl ester, palmitic acid, 2-propenoic acid,3-[4-methoxyphenyl]-, ethyl ester, 9,12-octadeca-dienoic acid [Z, Z]-, 8,11-octadecadienoic acid, methyl ester, and isopropyl linoleate [50].

The fruits of *Martynia annua* mainly comprise gentisic acid [44]. Fatty acids such as palmitic acid, stearic acid, linoleic acid, and oleic acid have also been reported to be present in the fruits [18].

On the preliminary qualitative analysis of the fruits, it was found that the ethanolic extract of the fruit of *Martynia* confirmed the presence of terpenoids, phenols, alkaloids, steroids, tannins, and flavonoids while the aqueous extract reported the absence of alkaloids and steroids and the presence of glycosides, anthocyanins, and saponins. In the case of n-hexane extract, alkaloids, saponins, tannins, steroids, and flavonoids were only present while in n-butanol extract flavonoids, tannins, phenols, flavonoids, and glycosides were present. Lastly, in the ethyl acetate extract, all the constituents except alkaloids were present. Amongst these compounds, tannins, and flavonoids are the most substantial compounds as they were found in all the extracts as well as they act as free radical scavengers or primary antioxidants [29, 51].

Additionally, the qualitative analysis conducted by Kaushik et al. revealed the presence of carbohydrates and proteins in the ethanolic extracts. They concluded that it was the ethanolic extract that showed the most total antioxidant and hyaluronidase inhibition activity as well as anti-inflammatory and anti-arthritis activity. The antioxidant property was thought to occur because of the flavonoids and phenolic compounds present [51].

Raipuria et al. revealed in a study that the roots of *Martynia annua* were found to contain saponins, tannins, steroids, phenols in detectable quantity while alkaloids were found in higher quantities in the aqueous extract of the roots. The ethanolic root extract showed the same with the additional presence of a higher number of flavonoids and a detectable number of cardiac glycosides. Tannins and phenols were also found in higher quantities while alkaloids were only just detectable in this extract. In the methanolic root extracts, all of these except steroids were reported with alkaloids, flavonoids, and tannins in higher amounts [47].

Gupta and Deogade mentioned in their study that the aqueous, hydroalcoholic and alcoholic extracts of the roots of *Martynia annua* contained antioxidants which could help in enhancing immunity and may help in reducing the risk for chronic ailments. The antioxidants were evaluated by using the DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical assay method. The water extract exhibited the most numbers of antioxidants followed by ethanol. It was also reported that this antioxidant activity was due to the presence of flavonoids and phenols in the root extracts [52].

Raipuria et al. revealed that the ethanolic extract of the stem of *Martynia annua* contained flavonoids, steroids, cardiac glycosides, and phenols in detectable amounts while alkaloids, saponins, and tannins were found in higher amounts. The methanolic extract exhibited all the above, except the presence of steroids. In this, there was also a higher quantity of flavonoids with tannins and alkaloids. The aqueous extract consisted of terpenoids, flavonoids, phenols, tannins, and alkaloids in lower amounts and saponins in higher amounts [47].

The flowers of *Martynia annua* are reported to have cyanidin-3-galactoside, pelargonidin-3, 5- diglucoside, apigenin-7-O-beta-D-glucuronide, apigenin, luteolin, and luteolin-7-O-beta-D-glucuronide [31, 44].

3. PHARMACOLOGICAL PROPERTIES *MARTYNIA ANNUA*

The major objective of the research of the plant *Martynia annua* is to scrutinize and investigate the pharmacognosy and pharmacological action of drugs or medicaments from several obtainable compositions. Distinct parts of this plant give numerous medicinal properties, for example, the fruits are employed in inflammation, the paste of leaves is used on injuries of animals, and the

paste of nuts is applied to the bites of venomous insects. Also, the leaves of the plant are used in epilepsy and locally used on the tuberculosis of lymphatic glands of camels' necks. The juice of leaves is used for preparing gargles for relief from sore throat [22].

The fruits and leaves are the most bioactive parts of the plant. The seed of *Martynia annua* is indicated for arresting the onset of graying of hairs. According to literature studies, the plant is found to possess anthelmintic properties [53].

3.1. Analgesic and Antipyretic Activity

Kar et al. observed the petroleum ether, ethanol, chloroform, and aqueous extracts of the fruits of *Martynia annua* for analgesic and antipyretic activities. The analgesic activity was performed on Swiss albino mice using Hot Plate and Tail Flick methods. The antipyretic activity was performed on adult Wistar rats by inducing them with hyperpyrexia by brewer's yeast. The results obtained were then compared with the standard drug Diclofenac Sodium. It was observed that all the extracts showed potent analgesic and antipyretic activity when compared with the standard and that the petroleum ether and chloroform extracts showed better results than the ethanolic and aqueous extracts [54].

3.2. Anthelmintic Activity

Nirmal et al., experimented on the petroleum ether, ethyl acetate, and methanolic root extracts of *Martynia annua* and screened them for anthelmintic activity. These extracts were used on *Pheritima posthuma* as they are anatomically and physiologically like the intestinal roundworms found in humans. The time taken by the extracts to cause paralysis and death of the individual worms was recorded. They were then compared with the standard drug Albendazole. It was observed that the petroleum ether extract took the least time to exhibit the anthelmintic activity, followed by ethyl acetate extract and lastly the methanolic extract.

The results obtained reveal similar and potent activity when compared to standard drugs such as Albendazole [53].

3.3. Antifertility Effects

Mali et al. investigated the roots of *Martynia annua* for antifertility effects by studying the reproduction process in male rats. 50% ethanolic extract of *Martynia annua* roots was used for this purpose. The works consist of four groups with five animals in each group. The 1st group received vehicles alone to serve as a control, the 2nd, 3rd, and 4th groups of animals were administered the extract daily at doses of 50 mg/kg body weight, 100 mg/kg body weight, and 200 mg/kg body weight for 60 days.

It was observed that there was an important decline in the weight of testes, epididymides, seminal vesicles, and ventral prostates of the male rats. Reduction in dose-related testicular and epididymal sperm count as well as a decrease in motility was also observed. The reduction in the ratio of delivered and inseminated females and the number of pups were also observed. The number of fertile males also decreased. Between the severity of lesions of seminiferous epithelium and dose, the tests showed a clear correlation.

There was an appearance of a decrease in the size of the seminiferous tubules with consistently filled eosinophilic material. At the secondary spermatocytes stage, spermatogenesis was arrested. Germ cells were evidently immature. The Leydig cells were atrophied, and no morphological changes were reported in Sertoli cells.

While there was a reduction in serum concentration of luteinizing hormone and testosterone, no change in serum FSII concentration was observed. The final body weight of all groups of male rats was elevated. No altercation in general body mechanism was recorded [44].

3.4. Anticonvulsant Activity

Babu et al. studied the methanolic extract of *Martynia annua* leaves (MEMA) for anticonvulsant activity on Maximal Electro Shock (MES) and Pentylenetetrazole (PTZ) in albino rats by inducing convulsions. The MEMA dose of 200mg/kg and 400mg/kg body weight showed anticonvulsant action of 66.31% and 82.73% respectively when induced by MES. In comparison with standard Diazepam, the MEMA of the same dose showed anticonvulsant action of 70.33% and 82.88% respectively. It also showed protection from mortality at 83.33% and 100% respectively from PTZ induced seizures [22].

3.5. Antioxidant Activity

Nagda et al. evaluated the leaves of *Martynia annua* for antioxidant activity. The methanolic and aqueous extracts of *Martynia annua* were studied as *in vitro* system assays namely, Superoxide Radical scavenging assay, DPPH radical-scavenging activity, Reducing Power assay, Nitric Oxide scavenging activity, H_2O_2 Radical scavenging activity, Hydroxyl Radical-scavenging

activity, and Total Antioxidant Capacity. Folin-Ciocalteu reagent was used to measure Total Phenolic Content. Depending on the concentration and the increase in the amount of the extracts, the antioxidant activity increased.

The antioxidant activity reported was due to the presence of flavonoids and phenolic compounds in the extracts. The evaluation also concluded that the methanolic extract exhibited higher antioxidant activity than the aqueous extract [55].

3.6. Antibacterial Activity

Sermakkani and Thangapandian examined the ethyl acetate, chloroform, and methanolic extracts of the leaves of *Martynia annua* for antibacterial activity. Disc Diffusion method in six Gram-positive and nine Gram-negative bacteria was used for this study.

It was observed that the highest activity against *Proteus vulgaris*, *Bacillus subtilis,* and *Bacillus thuringiensis* was shown by the chloroform leaves extract while the methanolic extract resulted in greater antibacterial activity against *Proteus vulgaris, Bacillus subtilis, Salmonella paratyphi B,* and *Pseudomonas aeruginosa*. The ethyl acetate extract showed good activity against *Salmonella paratyphi A, Salmonella paratyphi B,* and *Klebsiella pneumoniae*. The antibacterial effect was immense in only 100% concentration in all the solvent systems [45].

3.7. Anti-Nociceptive Activity and Central Nervous System (CNS) Depressant Activity

Bhalke and Jadhav investigated the petroleum ether, ethyl acetate, and methanolic extracts of roots of *Martynia annua* for antinociceptive and CNS depressant activity. Out of all the extracts, the petroleum ether extract at the dose of 50mg/kg, i.p., showed the most elevation in reaction time in the hot plate method. It also showed a better inhibitory effect on acetic acid-induced writhing when compared to the other extracts as well as the standard drugs like Paracetamol and Pentazocine. A decrease in locomotor activity was also observed by the extract when compared with the standard drug Diazepam. At 30 mg/kg, i.p. dose, it increased the Pentobarbitone Sodium induced sleep up to 215.34% [56].

3.8. Wound Healing Activity

Lodhi and Singhai reported that the leaves of *Martynia annua* were wound to have wound healing activity. This activity was determined with the help of the ethanolic extract of *Martynia annua* leaves using excision and incision models on rats. The *Martynia annua* fraction (MAF-C) of the extract, that they observed, showed the most effectiveness in wound healing activity as it stimulated wound contraction as well as epithelialization. As compared to the control group, better angiogenesis matured collagen fibers, and fibroblast cells were also reported during the histo-pathological study.

Additionally, the phytochemical studies showed that the methanolic extract contains the flavonoid luteolin which is responsible for increasing the wound healing process due to its free-radical scavenging mechanism [17].

3.9. Anti-Diabetic Activity

Saiyad and Gohil evaluated the flowers of *Martynia annua* for antidiabetic activity. The Methanolic Extract of *Martynia annua* (MEMA) flowers was studied with Streptozotocin (STZ) and Streptozotocin- Nicotinamide (STZ-NIC) which is responsible for inducing diabetes in Wistar rats. After 21 days, the results concluded that MEMA showed very good reductions in blood glucose, glycosylated hemoglobin, and triglyceride levels, and an increase in high density lipoprotein (HDL) levels in diabetic rats [57].

3.10. Gastroprotective Activity

Jain and Bhandarkar investigated the ethanolic extract of the leaves of *Martynia annua* for gastroprotective activity. The extract was taken in doses of 200mg/kg and 300mg/kg body weight and used in albino rats with ethanol-induced gastric ulcers.

The observations were made by calculating the ulcer index based on lesion index and pH. It was observed that both the doses of the ethanolic extract of *Martynia annua* showed an important inhibition of ulcer lesion index. The 300mg/kg dose ($p<0.05$) significantly changed the gastric volume, ulcer index, and pH [58].

3.11. Anti-inflammatory Activity

Kaushik et al. reported the *in-vivo* anti-inflammatory activity of the ethanolic fruit extract of *Martynia annua* by using *Calotropis procera* latex (CPL) induced paw edema model in rats. Results showed that *Martynia annua* treated groups showed very good anti-inflammatory activity at a higher dose when compared with the control group, but in comparison with

standard drug Ibuprofen, the extract showed lesser action [51].

3.12. Anti-Arthritic Activity

Kaushik et al. examined the anti-arthritic activity of the ethanolic fruit extract of *Martynia annua* by inducing paw edema by injecting Complete Freund's Adjuvant (CFA) intra-articularly and hence inducing arthritis in rats. It was observed that the extract exhibited an important reduction in arthritis in the animals when compared with the control group although the activity was minor as indicated by the standard group [51].

3.13. Anti-muscular activity

Vinnarasi and Raj showed that various parts of *Martynia annua* (leaves, roots, stem, and seeds) consist of anti-muscular activity by using Wistar albino rats in a Rotarod test. A Rotarod test is used to evaluate muscle relaxant properties. The time spent by the animals on the revolving rod and the amount of time taken indicated the potential of the experimental drug.

All parts of *Martynia annua* acetone extract showed significant skeletal muscle relaxant property by reducing the time taken by the animals to stay on the revolving rod by 70%. The leaves showed the highest skeletal muscle relaxant activity at 89.48%. The percentage of decrease in time taken by the animals by the various parts of *Martynia* followed this order -

Leaves > Seeds > Stem > Root

The results obtained from this experiment were found like that of the standard drug Diazepam [59, 60].

3.14. Immunomodulatory Activity

Katare and Tyagi experimented on the bark of *Martynia annua* for the determination of immunomodulatory activity. For the study, healthy mice were selected and were divided into 6 groups containing six in each. The mice were included in the following groups - control animals in group 1 which received normal saline for 7 continuous days, animals in group 2 were injected with cyclophosphamide (CP) on the 6th day of the beginning of the experiment, group 3 consisted of Methanolic Extract of *Martynia Annua* (MEMA) animals in MEBC (methanolic extract of *Martynia* annua Bark) treatment and group 3, 4 (MEAC and MEAC 2) animals in MEAC (Methanolic extract of *Martynia annua* leaves) treatment got plant extract for 7 continuous days, group 5,6 animals (MEBC 1+CP and MEBC 2+CP) in MEBC treatment, and group 5,6 animals in MEAC treatment (MEAC 1+ CP, and MEAC 2 + CP), were given plant extract treatment for 7 continuous days along with a single dose of CP on 6th day of starting of the experiment.

On the 5th day for humoral response activity, the animals of all groups were given 0.2ml of 10% Sheep Red Blood Cells (SRBC) i.p. A modified version of Bin-Hafeez et al. method was used for the purpose [61]. For examining Cell-Mediated Immunity, the footpad reaction method was used. For the evaluation of blood parameters, blood was extracted from the tail vein. 24 hours after the last dose, the mice were sacrificed for body weight determination.

For humoral response activity, hemagglutination reaction (H.A.) was carried out by measurement of antibody titer. MEMA showed that in the 3rd and 4th group animals, H.A. increased with increase in dose when compared with the control group. In negative control group animals, CP treatment gave a decreased titer value. When CP treatment with different concentrations of plant extract was given to the 5th and 6th groups, important ($P<0.001$) recovery of immunosuppressant activity was observed, more than that of only the CP treated group. This proved that the plant extract has good humoral response activity.

Footpad reaction test was done for cellular immune response or delayed-type hypersensitivity (DTH). The important activity was seen in groups 3 and 4 animals where the different plant extract doses increased the DTH reactivity. MEBC treatment and CP treatment (group 5) animals were compared; there was an increase in DTH reactivity. When group 6 animals got the extract treatment at a higher concentration with CP, the increase in DTH reactivity was similar to that when compared with only CP treatment. Group 5 and 6 showed no important increase in DTH reactivity when compared to only the CP-treated group. This proved that changes in DTH reactivity in mice in response to SRBCs showed a stimulatory effect on the MEBC and MEAC extracts on T cells.

For the evaluation of the blood parameters, at a dose of 150 mg/kg and 300mg/kg, the plant extract caused an increase in the WBC count of MEBC treatment when compared to the control group. MEAC treatment also showed an increase in WBC counts at doses 800mg/kg and 1200mg/kg whereas CP treated animals showed a decrease in WBC count. CP+MEBC (150mg/kg) and MEBC (300mg/kg) showed good recovery in bone marrow activity when compared to only the CP-treated animals. CP+MEAC (800mg/kg) and MEAC (1200mg /kg) also showed increased bone marrow recovery.

For body weight determination, groups 3 and 4 animals showed no important reduction in relative weight difference on liver, kidney, and spleen of the animals when compared to the control group, and groups 5 and 6 showed no important recovery of spleen weight. Group 2 animals showed an important decrease in the relative organ weight of the spleen [62].

3.15. Cytotoxic Activity

Vinnarasi et al. reported by bioassay of brine shrimp lethality, the alcoholic and acetone extract of leaves of *Martynia annua* showed cytotoxic activity. The extracts of *Martynia annua* were observed to be mainly effective at which half mortality of brine shrimp nauplii occurred [63].

3.16. *Hepatoprotective activity*

Dhingra and Chopra studied the methanol extract of *Martynia annua* L. leaves on Albino rats for hepato-protective activity. The CCl_4 induced hepatotoxic model was used to cause hepatic injury to the animals. Biochemical parameters like Serum Glutamate Oxalo-acetate Transaminase (SGOT) and Serum Glutamate Pyruvate Transaminase (SGPT) were estimated by Reitman and Frankel's method. Assessment of Alkaline Phosphatase (ALP) and serum bilirubin was carried out by Kind King's method. Total bilirubin was determined by Jendrassik and Grof method while total protein was determined by cholesterol oxidase/peroxidase method [64-67].

Daily oral administration of the methanolic extract of the leaves of *Martynia* was given at 200 and 400mg kg^{-1}doses.

The CCl_4 treated group of rats showed significant increase in the concentrations of SGPT, SGOT, ALP and serum bilirubin as compared to the control group. The plant extract at the dose of 400 mg kg^{-1}, showed a more considerable decline in the increased levels of the enzymes when compared to the 200 mg kg^{-1} dose. Similar decline in the enzyme level was observed when treated with the standard drug Silymarin. Additionally, histopathological observations showed that the *Martynia annua* extract treatment reduced the abnormalities and restored the morphological changes caused by the CCl_4 induced hepatotoxicity [68].

3.17. *Anticancer Activity*

Gupta and Rathi examined the ethanolic, aqueous and hydro-ethanolic root extracts of *Martynia annua* for anticancer activity. The *in vitro* cytotoxic activity was examined by using human lung cancer cell lines (A549), human leukemia cancer cell lines (K-562), human oral cancer cell lines (SCC-40), human breast cancer cell lines (MCF-7) and human cervix cancer cell lines (SiHa) and experimented on the extracts. Sulforhodamine B (SRB) estimation method was exercised, where the growth inhibition of 50% (GI_{50}) was evaluated with standard drug Adriamycin (ADR) (Doxorubicin).

It was observed that the *Martynia* extracts exhibited very favorable activity against Human Leukemia Cell Line K-562 when compared to the other cell lines. The aqueous and ethanolic extracts of *Martynia* indicated elevated anticancer activity with GI_{50} value 11.3µg/ml and 20.4µg/ml respectively on leukemia cell line K-562 with aqueous extract showing superior activity than the ethanolic extract. At more than 80µg/ml, the extracts also exhibited activity against breast cancer cell line MCF-7, lung cancer cell line A549, squamous cell carcinoma SCC-40 and cervical cancer cell line SiHa [69].

3.18. *Toxicity study*

Kaushik et al. performed an acute toxicity study for observing the potential toxicity of the ethanolic extract of the fruit of *Martynia annua* by evaluating according to OECD guideline 423. They reported that the extract was non-toxic to the albino Wistar rats up to 2000mg/kg dose. These animals were under 14 days of observations and no signs of changes in their fur color, behavior, lethargy, writhing response, micturition, and feeding habits were observed [51].

Another acute toxicity study was performed by Vinnarasi and Raj in Wistar Albino rats for testing the toxicity potential of the acetone extract of various parts of *Martynia annua*. The animals were made to starve overnight. The extract was administered orally to the animals in graded doses. After the treatment, they were observed for 30 minutes. This was followed by close observation every hour for 8 hours and once everyday up to the next 13 days. Observations were made for mortality, moribund, coma, adverse reactions, changes in the skin, fur, eyes, mucus membrane, salivation, behavior, lethargy, micturition, sleep cycle, illnesses like convulsions, tremors, and diarrhea. This experiment determined that the acetone extract of *Martynia annua* parts was non-toxic up to a dose of 2000 mg/Kg body weight (LD50>2000 mg/Kg) [59].

The various pharmacological properties of *Martynia annua* are summarized in the table 1.

Table 1: Pharmacological properties of *Martynia annua* Linn.

S. No.	Type of Activity	Part used	Researchers	Year of Research Conducted
1.	Anti-inflammatory activity	Fruits	Kaushik et al. [51]	2021
2.	Anticancer activity	Root	Gupta and Rathi [69]	2021
3.	Anti-arthritic activity	Fruits	Kaushik et al. [51]	2021
4.	Immunomodulatory activity	Bark	Katare and Tyagi [62]	2020
5.	Hepatoprotective activity	Leaves	Dhingra and Chopra [68]	2020
6.	Anti-muscular Activity	Leaves, roots, stem, seed	Vinnarasi and Raj [59]	2017
7.	Gastroprotective Activity	Leaves	Jain and Bhandarkar [58]	2016
8.	Cytotoxic Activity	Leaves	Vinnarasi et al. [63]	2014
9.	Anti-Diabetic Activity	Flowers	Saiyad and Gohil [57]	2013
10.	Wound Healing Activity	Leaves	Lodhi and Singhai [17]	2011
11.	Anticonvulsant activity	Leaves	Babu et al. [22]	2010
12.	Antibacterial Activity	Leaves	Sermakkani and Thangapandian [45]	2010
13.	Antinociceptive activity and CNS depressant activity	Roots	Bhalke and Jadhav [56]	2009
14.	Antioxidant Activity	Leaves	Nagda et al. [55]	2009
15.	Anthelmintic Activity	Roots	Nirmal et al. [53]	2007
16.	Analgesic and Antipyretic Activity	Fruits	Kar et al. [54]	2004
17.	Antifertility effect	Roots	Mali et al. [44]	2002

4. CONCLUSION AND PROSPECT REACH

Martynia annua Linn. is a medicinal and an ornamental plant. It has been naturalized and integrated in numerous countries with warm climates in the form of weeds [8, 9]. Many literature reviews performed on the herb describe its various medicinal uses. The entire plant contains important bioactive constituents and so it exhibits many pharmacological activities [35]. Therefore, *Martynia* is traditionally used in folk medicine. The modern healthcare industry can hence explore its health benefits as there is a potentially growing market for the use of *Martynia*.

The reviews investigated exhibit that the greatest number of phytoconstituents and therapeutic benefits are shown by the leaves of *Martynia*. Moreover, the methanolic extract of the leaves of the plant indicates the most amounts of phytoconstituents while other extracts of different parts of the plant such as fruits, roots, stem, flowers, and seeds exhibit few to significant amounts of constituents [45]. All of these are responsible for many of the potentially effective therapeutic activities reported to be indicated by the plant and in this article which includes antipyretic and analgesic activity, anthelmintic activity, antifertility effect, anticonvulsant activity, antioxidant effect, antibacterial effect, antinociceptive activity and CNS depressant activity, wound healing activity, anti-diabetic activity, gastroprotective activity, anti-inflammatory activity, anti-arthritic activity, anti-muscular activity, immunomodulatory activity, hepatoprotective activity, anticancer activity and cytotoxic activity [17, 22, 44, 45, 51, 53-59, 62, 63, 68, 69].

The studies conducted on the health benefits of *Martynia* are limited. Many of the researchers reported the health benefits on animal-based studies. Moreover, these studies used different types of solvents, methods of preparation, and different instruments for isolation, identification, and quantification, so this may result in the evaluation of the activity of *Martynia* to be difficult. This diversified type of research is inadequate to show its proper benefit for human healthcare. Therefore, future studies in larger, well-designed, and randomized controlled trials must be conducted to study the importance of *Martynia* for benefits and consumption on human health just as its importance in animal-based studies were reported. Much like with different plant-based products, the future of several active constituents found in *Martynia* should be addressed for their positive

as well as their negative or toxic actions in the human body. Additionally, the details of those constituents and the mechanisms of their promotion of pharmacological properties should also be worthy of further exploration.

Conflict of interest

Authors don't have any conflict of interest.

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