

ANTI-INFLAMMATORY AND ANTI-ANALGESIC ACTIVITY, ACUTE TOXICITY STUDIES *AILANTHUS EXCELSA*Satya Pal Singh Verma*¹, Dharam Pal Singh² and Pankaj Kumar Kashyap³¹Assistant Professor ACME INSTITUTE of Pharmacy Bareilly U.P. INDIA.²Assistant Professor, Jyoti College of Pharmacy Bareilly U.P.³Assistant Professor, Lotus Institute of Pharmacy, Bareilly.Article Received on
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Corresponding Author*Dr. Satya Pal Singh Verma**Assistant Professor ACME
INSTITUTE of Pharmacy
Bareilly U.P. INDIA.**ABSTRACT**

This plant study in the present chemical constituent deferent study plant activity of the plant, Pharmacological studies were also performed *ie.* Analgesic and anti-inflammatory Acute oral toxicity. These studies will be useful for establishing parameters for the standardization of drugs *Ailanthus excelsa*.

INTRODUCTION

Deferent species of the genus are *Ailanthus glandulosa* in China and the Malay Peninsula, (leaflets very coarsely toothed at the base and filaments several times exceeding the anther), *Ailanthus malaria* in Indo-China (leaflets entire and filaments larger than anther), and *Ailanthus excelsa* in India (leaflets very coarsely toothed and filaments shorter than anther) *Ailanthus excelsa*. Belonging to the family Simaroubaceae which is defined in Engler's Syllabus consists of six subfamilies with 32 genera and over 170 arboreous or shrubby species. The largest genus is *Picromnia* with ca 40 species native to the new world tropics. Indeed the entire family is of pantropical occurrence except for the genera *Picrasma* and *Ailanthus* which extend to temperate Asia. The genera of Simaroubaceae are mostly well defined, but the family is only loosely knit. A large botanical literature has accumulated on the question of affinity and the five subfamilies Surianoideae (four genera), Kirkioideae (monogeneric), Irvingioideae (three genera), Picramnioideae (monogenetic) and Alvaradoideae (monogenetic) have all been removed from the Simaroubaceae at one time or another. This would leave only the Simarouboideae within the Simaroubaceae. This family contains the following species which are rich in quassinoids and other important constituents.

Ailanthus is found generally around villages and old forts and in forests. The plant is identified by light grey bark with large conspicuous leaf scars and long peri-pinnate leaves crowded at the end of the branches. The bark of the plant was bitter, refrigerant, astringent, and appetizer. The juice of the bark is used for local applications like diarrhea, and dysentery and it is used for the treatment of the skin diseases and troubles of the rectum. The bark is aromatic and used for dyspeptic complaints and it is also regarded as a tonic and febrifuge in cases of debility, expectorant and antispasmodic, given in chronic bronchitis and asthma. Also used as an astringent in diarrhea and dysentery. A novel triterpenoid isolated from the root bark of *Ailanthus excelsa* (Tree of Heaven), AECHL-1 is a potential anticancer agent. The stem of *Ailanthus excelsa* (Simaroubaceae) may develop vascular occlusions and gum-resin cavities in the xylem as a response to injury and infection.

Ailanthus excelsa (Simaroubiaceae) is commonly known as Mahanaim. *Ailanthus excelsa* is a large tree originally from China. Different parts of this plant are used widely in traditional medicine for a variety of diseases. The bark is used as bitter, refrigerant, astringent, appetizer, anthelmintic, febrifuge, dysentery, skin disease, troubles of the rectum, and fever due to tridosha and allays thirst. It is also used in gout, rheumatism, dyspepsia, bronchitis, and asthma. *Ailanthus* is used to cure wounds and skin eruptions as mentioned in traditional medicine. Stem bark extracts showed potent antibacterial and antifungal activities. The alcohol extract from leaf and stem bark exhibits remarkably high anti-implantation and early abortifacient activity. The plant reported containing chemical Constituents like Quassinoids, excelsin, glaucarubin, ailanthone, glaucarubinone, and Glaucarubilone. Quassinoids compounds were reported from *Ailanthus excelsa* leaves A new quassinoids, 13, 18-dehydroexcelsin and glaucarubol have been isolated by Khan *et al.* New dammarane-type triterpenes, ailexcelone and ailexcelol, together with ocotillo, malabaricol, epoxymarabicol, and lupeol were reported by Shrinivas *et al.* The present study is intended to explore the antifungal activity of Methanolic extract of *Ailanthus excelsa*. The whole plant was tested against selected human pathogenic fungi.

The use of medicinal plants for the treatment of human diseases has increased considerably worldwide. Evaluation of the effects of these plants on organs and systems has contributed to the development of the scientific basis for their therapeutic application and also has enriched considerably the therapeutic arsenal for the treatment of several diseases (Elizabetsky, 1986). *Ailanthus excelsa* is a tree belonging to the family Simaroubaceae, indigenous to central and

southern India. Commonly it is known as Mahanimba. The traditional claims, phytochemical investigations, pharmacological evaluation, and some Ayurvedic formulations provide the backbone to make this tree a Mahanimba. This is not wrong to say that it is largactil because it has several activities. In the Indian system of medicine, it is used in panic diarrhea, bronchitis, and dysentery (Nadkarni, 2000). In addition, *Ailanthus excelsa* was shown to have antipyretic activity. Even though *Ailanthus excelsa* was reported to be useful in many ailments like stem bark of *Ailanthus excelsa* was a potent antiasthmatic, bronchodilator. From a pharmaceutical perspective flavonoids possess a remarkable spectrum of biochemical and pharmacological activities. The leaves were reported to contain different flavonoids like kaempferol (5,4',5,7-tetrahydroxy flavone), luteolin (3',4',5,7-tetrahydroxy flavone), apigenin (4',5,7- trihydroxy flavone) (Lavhale & Mishra, 2007). Thus, drug development has been encouraging researchers to find strategies to treat allergic diseases, and the medicinal plants have been the target of these studies and an important tool to treat immediate-type allergic responses.

Inflammatory diseases are still one of the most important health problems in the world. Inflammation is initiated as a healing process by the tissue in response to an injury pathogens, irritants, or cell damage. It is believed that current drugs available such as opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are not useful in all cases of inflammatory disorders, because of their side effects and potency. The screening and development of drugs for their anti-inflammatory activity is still in progress and there is hope for finding anti-inflammatory drugs from indigenous medicinal plants. *Ailanthus excelsa* (Family-Simaroubaceae) is a large deciduous tree. It is commonly known as the Tree of Heaven as well as Mahanimba. *Ailanthus excelsa* is widely used in several indigenous systems of medicine for the treatment of various ailments viz. asthma, inflammatory diseases, ulcer and stomach problems, cancer, cardiac and hepatic disorders, etc.

During the past decade, traditional systems have gained importance in the field of medicine. In many developing countries, a large proportion of the population relies heavily on traditional practitioners, who are dependent on medicinal plants to meet their primary health care needs. Although modern medicines are available, herbal medicines have often retained popularity for historical and cultural reasons. Since the usage of these herbal medicines has increased, the issues regarding their safety, quality, and efficacy in industrialized and developing countries are cropped up. Growing interest has also prompted the researcher to

screen scientifically various claims regarding the properties and uses of medicinal plant materials. Presently, both, common consumers and healthcare professionals seek updated, authoritative information on the safety and efficacy of any recommended medicinal plant as a drug before its use. The present attempt is to review and compiles updated information on various aspects of *Ailanthus excelsa* a plant used in the Indian system of medicine for a variety of purposes. *Ailanthus* is a genus of tall, lofty trees, distributed in Indo-Malaya, China, Japan, and Australia. The genus is noted for its antidiarrhoeal and antidysenteric properties (Jaccard P-1908) Different species of the genus are *Ailanthus glandulosa* in the Malay Peninsula and China, (leaflets very coarsely toothed at the base and filaments several times exceeding the anther), *Ailanthus excelsa* in India (leaflets coarsely toothed and filaments shorter than anthers) and *Ailanthus malaria* in Indo-china (leaflets entire and filaments larger than anthers). *Ailanthus excelsa* (Simaroubaceae) is commonly known as “Mahanimba” due to its resemblance with the neem tree (*Azadirachta indica*). The plant is known by different names like, tree of heaven in English, Carducci, aralavo in Gujarati, mark, Ghoda karanji, aakashneem, and are in Hindi, peruvagai in Tamil, and peddamanu in Telgu. It is a fast-growing tree extensively cultivated in many parts of India in the vicinity of villages. The tree is indigenous to central and southern India and is distributed in Madhya Pradesh, Gujarat, some coastal districts of Andhra Pradesh, Ganjam, and Puri districts of Orissa. The plant is known for its high commercial and economic importance.

Herbal medicines are being increasingly utilized to treat a wide variety of diseases, though the knowledge about their mode of action is relatively scanty. There is a growing interest in the pharmacological evaluation of various plants used in traditional systems of medicine. Allergies occur when a hypersensitive immune system reacts to a common or unusual substance. The number of individuals suffering from allergic illnesses is increasing in the industrialized, as well as in large cities of developing countries. Allergies also have reached high prevalence and incidence all over the world. Most allergic diseases are due to allergens like airborne pollens (grass, trees, and weeds), house dust, mites, animal dander, cockroaches, fungal spores, etc. Overproduction of histamine in the body triggers allergic and inflammatory responses. Drugs always exist in nature to prevent the effect of histamine. *Ailanthus excelsa* is a tree belonging to the family Simaroubaceae, indigenous to central and southern India. Commonly it is known as a Tree of Heaven. In the Indian system of medicine, it is used in panic diarrhea, bronchitis, and dysentery. In addition, *Ailanthus excelsa* was shown to have antipyretic activity Even though *Ailanthus excelsa* was reported to be useful in

many ailments like bronchodilatory, antiasthmatic, antiallergic, etc., scientific evaluation of the plant was not reported for its antihistaminic activity. Plants containing flavonoids have been reported to possess antihistaminic, antiallergic, and mast cell degranulation properties.

Ailanthus excelsa is an exotic fast-growing deciduous tree. It belongs to the Simaroubaceae family it is native to India. This hardwood tree reaches up to 35m high and 90cm in diameter. Ailanth tree is used as an ornamental tree, shelterbelts, afforestation, and reforestation, for cultures of silkworms, and biomass production for fuelwood and as fodder for goats and cattle. *Ailanthus excelsa* was investigated previously to prove antibacterial, antifungal, antiviral Antifertility, and anticancer this tree species was first introduced in Sudan from India in 1960. Plantations were made at Kunduwa Central Forest Reserve (Southern Darfur), Asian, and Andraberu forests (Western Darfur) in 1970.

During the past years, the indigenous system of medicine has gained importance in procuring the life of mankind. The use of herbal medicines has increased with the issues and aim regarding their quality, safety, and efficacy in industrialized and developing countries (WHO Monographs on Selected Medicinal 1999). There is a need for screening their traditional claims because in this scientific era and everyone wants scientific support and proof before using the traditional medicines for the desired therapeutic effect. In this review article, an attempt has been made to compile the scientific survey until the date of *Ailanthus excelsa* which is widely used in the Indian traditional system of medicine for various medicinal purposes. Different species of *Ailanthus* are present in the form of *Ailanthus glandulosa* which is present in China and the Malay Peninsula and *Ailanthus malaria* in Indo-China, and *Ailanthus excelsa* in India. *Ailanthus excelsa* belongs to the family Simaroubaceae, which consists of six subfamilies with 32 genera and over 170 shrubby species. *Ailanthus excelsa* resembles to the neem tree (*Azadirachta indica*) and Maharukha due to its large size. The plant is known by different names like the tree of heaven in English, and other Indian local names are: Araluka, Aralu, Katvanga, Deerghavrinta, Putiveriksha, Mahanaim.

The tree is indigenous to central and southern India and is found across Madhya Pradesh in Panchmahal and Bharuch districts in Gujarat, some coastal districts in Andhra Pradesh, Ganjam, and Puri districts in Orissa. It also grows in Sri Lanka, Japan, China, and Australia. It occurs in dry deciduous forests. It can be seen planted along the roadsides. The tree is known for its high economic and commercial importance.

Plants are the richest sources of organic chemicals on the earth. Most of the medicinal plants were used in Indian traditional medicine to cure various diseases. The indigenous system of medicine namely Ayurveda, Unani, and Siddha has been in existence for several centuries. In India, about seventy percent population resides in the villages and these people depend on herbal medicine to cure ailments. Nature has bestowed a rich botanical wealth with its diversity in varied topography and changed agro-climatic conditions in different parts of the country (Chaudhari, 1980). The world is looking towards India for new drugs to manage various challenging diseases because of its rich biodiversity of medicinal plants and abundance of traditional knowledge to cure different diseases.

Ailanthus excelsa is a multipurpose, deciduous, fast-growing tree species that belongs to the family Simaroubaceae. It grows well in arid and semi-arid regions and is suitable for planting in dry areas with an annual rainfall of about 400 mm. It avoids moist areas having high rainfall. It grows in a broad range of soil types including sandy soils, adapts to drought stress, and tolerates a dry season of 4 to 6 months. Concerning Tamil Nadu, *Ailanthus excelsa* is widely distributed in four agro-climatic zones *viz.*, Western zone, North Western zone, Cauvery delta zone, and Southern zone (Rajasugunasekar, 2014). Because of land degradation and unavailability of the intensive agricultural system, *Ailanthus excelsa* became an important agroforestry tree species and was popularized under the social forestry system. The demand for *Ailanthus excelsa* is increasing in recent years due to its multipurpose uses. Owing to such importance as a multipurpose tree, it is a matter of concern to keep these trees healthy from the damages caused by arthropod pests. All the parts of the tree *viz.*, foliage, shoots, stem, terminal leaders, and roots are vulnerable to pest infestation. The damage due to arthropod pests ranges from a minimum of less than 10 percent which does not affect the value of the harvested produce to severe that stunts or kills the tree or reduces the market value. Mirid bugs of the genus *Helopeltis* are serious pests of various cultivated plants in the OldWorld Tropics. The damaging effect of these insects on tea plants in India was documented over a century ago. It was in these early accounts that the common names 'tea bug' and 'tea mosquito' were established. Since the late 1800s, over 100 species of plants have been reported as hosts for *Helopeltis* spp. including several major commercial crops such as cashew, black pepper, cocoa, cinchona, and tea. Of the 40 recognized species of *Helopeltis*, 26 are restricted to Africa and 14 are distributed in Oriental and Australasian regions (Stonedahl, 1991). In South India, earlier records indicated the occurrence of two species of *Helopeltis*, *viz.*, *H. antonii* Signoret and *H. the ivory* Waterhouse (Fletcher, 1914;

Ballard, 1921). Later, three species of tea mosquito bug (TMB), viz. *H. antonii* Signoret, *H. Brady* Waterhouse, and *H. the ivory* Waterhouse were recorded (De Silva, (De Silva, 1957; Stonedahl, 1991; Sundararaju, 1996]. Among them, *H. antonii* was recorded as the dominant species (Sundararaju and Bakthavatsalam, 1994; Sundararaju, 1996). (Satapathy, 1993) and (S

The extreme scarcity of water, sandy dunes terrain, wind erosion, and recurring droughts have been driving farmers to despondency. In absence of favorable conditions for intensive agriculture, livestock rearing is an alternative source of livelihood for the majority of the rural population in arid ecosystems of different states of India. To meet the increasing demand for fodder for livestock and food, fuelwood and timber, etc. for the human population on a sustainable basis without degradation of land resources, the only alternative is parallel advancement in land productivity and agroforestry (Gupta, 1980). *Ailanthus excelsa* is a lofty deciduous tree, though it is widely distributed in the country, it grows In the semi-arid and semi-moist regions. In its natural habitat, the absolute maximum shade temperature varies from 45°C to 47.5°C and the absolute minimum from 00 to 12.5°C. The mean maximum temperature in May is generally the highest. The temperature varies from 30 to 42.5°C. The mean daily minimum temperature in January, the coldest month of the year varies from 4 to 21°C. The mean annual rainfall ranges from 500 –1900 mm, sometimes even up to 2500 mm. The mean relative humidity ranges from 40-80 percent in January and from 60-90 percent in July. It is a suitable species for planting in dry areas of Rajasthan with an annual rainfall of about 400 mm. It avoids moist areas having high monsoon rainfall. It can grow on a variety of soils but thrives best on porous sandy loams. It avoids clayey soils with poor drainage and waterlogged areas. It can grow even on shallow dry soils but the growth is poor. *Ailanthus excelsa* has given better performance as compared to other species in lateritic soils. The tree can be seen growing up to an elevation of 900 meters.



Fig of plant.

Ailanthus excelsa is a multipurpose, deciduous, fast-growing tree species belonging to the family Simaroubaceae. It grows well in arid and semi-arid regions and is suitable for planting in dry areas experiencing annual rainfall of 400 mm. In India, the tree is indigenous to southern and central India and also distributed in Western Peninsula, Rajasthan, Bihar, Orissa, Bundelkhand in Madhya Pradesh, Broach, and Panchamal districts of Gujarat, in dry deciduous forests of Maharashtra, and scarce in Deccan and Karnataka. It avoids moist areas having high rainfall. It grows in a broad range of soil types including sandy soils, adapts to drought stress, and can tolerate a dry season of 4 to 6 months (Rajasugunasekar, 2014). The demand for *Ailanthus excelsa* is increasing due to its multipurpose uses *viz.*, leaves as fodder and stem in the production of matchwood, box plank, packing cases, sword sheath, paper, toys, plywood veneers pencil, and fuelwood. Among the various pests, *Eligma narcissus*, and *Atteva fabriciella* are the major pests of *Ailanthus excelsa*. *Eligmanarcissus* causes complete defoliation of seedlings in the nursery and up to 95% defoliation in the young plantations up to 5 years old, resulting in loss of growth increment. Defoliation by *Atteva Gabriella* leads to

a reduction in growth increment due to defoliation of tender leaves, forking off the tree due to terminal bud damage, and loss of seed production due to damage of inflorescence and fruits reported that the common phenomenon for the abundance of tropical insect is seasonal variation. Change in insect abundance occurs over time for various reasons such as micro and macro climate change and variation in the availability of food resources. Insects can operate faster and more efficiently at higher temperatures and can also feed, develop, reproduce and disperse once the climate is warm, although they live for a short period (Drake, 1994). Information on weather parameters of standard weeks is important compared to the annual mean to analyze the population dynamics of pests and natural enemies about changing environmental conditions. Understanding the impact of native weather variables on insect population dynamics is vital for managing pests of tropical crops.

EXPERIMENTAL WORK

PHARMACOLOGICAL STUDIES

Acute toxicity studies

Acute oral toxicity is the adverse effects occurring within a short time of oral administration of a single dose of a substance or multiple doses given within 24 hours. The highest attainable dose 2000 mg/kg will be used as per as Organization for Economic Cooperation and Development (OECD) guidelines 423. Three rats, each sequentially dosed at interval of 48 hours, will use for test. Once daily cage side observations include changes in skin, fur, mucus membrane (nasal), eyes, autonomic salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation) and central nervous system (drowsiness, gait, tremors, and convulsion) changes. Mortality, if any, will be determined over a period of 2 weeks.

Analgesic studies

Eddy's hot plate method

This protocol describes the use of a hot plate to measure the potential analgesic effect of test compound to an acute thermal stimulus. The hot plate consists of an electrically heated surface, the temperature of which is maintained at 55°C to 56°C. Healthy young albino of either sex weighing 150-250g and showing a normal reaction time of 3 seconds were used for the study. They were divided into four groups of six animals each. Group 1: Control rats-received vehicle only (distilled water) Group II: Standard rats received Indomethacin 25 mg/kg Group III: Test rats-received AB 200 mg/kg Group IV Test rats-received AE 400 mg/kg. The paws of rats are very sensitive to heat at temperatures which are not damaging

the skin. The responses are jumping, withdrawal of the paws and licking of the paws. The time until these responses occur is prolonged after administration of centrally acting analgesics, whereas peripheral analgesics of the acetylsalicylic acid or phenyl-acetic acid type do not generally affect these responses. The rats were placed individually on the hot plate and the reaction time between placing the animal on the hot plate and licking of fore or hind limb (paw response) or the jump response recorded by a stop-watch. In order to avoid thermal injury to the paws a cut off time of 30secs was followed. The latencies were recorded before and after 20, 60 and 90mins following drug administration. The results were expressed as mean+SEM and data analysed statistically.

Anti-inflammatory studies

Mercury displacement method

The anti-inflammatory activity was studied by carrageenan induced rat hind paw edema measured by plethysmograph (mercury displacement method) Wistar strain rats of either sex weighing between 150-200 gm. were divided into four groups of six animals each. The first group served as the control and received the vehicle i.e., Tween 80, second group of animals was administered with standard drug diclofenac sodium, 10 mg/kg body weight, (subcutaneous). The third and fourth groups of animals were treated with crude extracts of *Ailanthus excelsa* leaf at a dose of 200 and 400 mg/kg body weight, orally. The volume of paw oedema was measured in control and standard and treated groups accordingly 1, 2, 3, and 4 h after carrageenan injection. The percent inhibitions of oedema were calculated and are tabulated in.

MATERIALS AND METHODS

CHEMICALS

Organic solvent Ethyl Acetate, Chloroform, Water, Methanol, Hydro Alcoholic etc. and very type chemical use as a working time of activity.

PREPARATION OF EXTRACTS

The plant *Ailanthus excelsa* has been selected and the plant collected leaf and dried at room temperature without sunlight and ground powder is used in the grinder, the powder was extracted hydrochloric were evaporate and used rotary evaporator and hot air oven used dried, and resulted in crud extract preserved in packed containers and tightly closed container cap and then further analysis.

PHARMACOLOGICAL STUDY

Acute toxicity studies

No signs and symptoms of acute toxicity and mortality up to 2000mg/kg body weight were observed during the whole experimental period. The body weight and food consumption were normal compared to vehicle-treated rats.

Analgesic activity

AE 400 mg/kg was found to be better than AE 200 mg/kg during an entire test period of 90 minutes. However, both AE 200 mg/kg and 400 mg/kg were found not to be better than the standard drug I.e Indomethacin during an entire test period of 90 minutes.

Table: Analgesic activity of extract of *Ailanthus excelsa* leaf.

Treatment Groups	Dose	Pre drug reaction time in sec (mean±SD)	Post drug time (minutes) reaction time in sec (mean±SD)			
			30 min	60 min	90 min	P-value
Control (Group-I)	D/W 2 ml/kg	3.38±0.416	3.35±0.260	3.62±0.496	3.47±0.381	0.660
Standard (Group-II)	IND 25 mg/kg	3.54±0.636	4.48±0.869	8.68±1.754	11.18±1.696	0.00001
Hydroalcoholic Extract (Group-III)	AE 200 mg/kg	3.27±0.526	4.10±0.457	5.49±1.028	7.89±1.577	0.00001
Hydroalcoholic Extract (Group-IV)	AE 400 mg/kg	3.6±1.420	4.54±0.898	6.59±1.386	9.43±1.376	0.00001

Results expressed as mean±SD, n=6, P value < 0.05 is significant, < 0.001 is highly significant.

Anti-Inflammatory Activity

Table: Anti-inflammatory activity of extract of *Ailanthus excelsa* leaf.

Effect of Hydroalcoholic extract of AE leaves at a dose of 200 and 400 mg/kg, and diclofenac sodium as compared to the carrageenan control group at different hours in carrageenan-induced paw edema measured by plethysmograph					
Groups	Dose(mg/kg)	Paw volume (ml)			
		1 st h	2 nd h	3 rd h	4 th h
Control (Group-I)	-	0.411 (±0.018)	69.96** (±0.015)	0.449 (±0.0139)	0.45 (±0.041)
Standard (Group-II)	10	48.89* (±0.012)	0.418 (±0.0474)	77.60** (±0.017)	69.74** (±0.014)
Hydroalcoholic extract (Group-II)	200	18.1 (± 0.010)	22.88* (± 0.011)	35.57* (± 0.119)	28.78** (±0.124)
Hydroalcoholic extract	400	18.9(+0.016)	23.68* (±0.019)	36.27* (±0.149)	29.29** (±0.174)

(Group-IV)					
Standard: diclofenac sodium, Control 1% Tween 80, *indicates significance difference at $p < 0.05$ compared to control, ** indicates significance difference at $p < 0.01$ compared to control					

CONCLUSION

In the acute toxicity study, no signs and symptoms of acute toxicity and mortality up to 2000mg/kg body weight.

In analgesic activity, hydroalcoholic extract of leaf of *Ailanthus excelsa* 400ml/kg was found to be more significant as compared to another dose.

In anti-inflammatory activity, the result showed a hydroalcoholic extract of 400 ml/kg of leaf showed significant anti-inflammatory action.

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