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Santosh Kumar Singh
Ph.D. Scholar, Pacific college of
Pharmacy, Pacific University,
P.B. – 12 Pacific Hills, Airport
Road, Pratap Nagar Extension,
Debari, Udaipur, Rajasthan,
India

Dr. Jay Ram Patel
Oriental College of Pharmacy,
Patel Nagar, Raisen Road,
Bhopal, Madhya Pradesh, India

Arvind Dangi
IES College of Pharmacy,
Kalkheda, Ratibadh Bhopal,
Madhya Pradesh, India

Deepak Bachle
Radharaman Institutes of
Pharmaceutical Sciences,
Ratibarh, Bhadbhada Road,
Bhopal, Madhya Pradesh, India

Rahul Kumar Kataria
Mittal Institutes of Pharmacy,
Opp. Bhopal Memorial Hospital
and Research Centre (BMHRC),
Bypass Road, Nabibagh,
Bhopal, Madhya Pradesh, India

Correspondence
Santosh Kumar Singh
Ph.D. Scholar, Pacific college of
Pharmacy, Pacific University,
P.B. – 12 Pacific Hills, Airport
Road, Pratap Nagar Extension,
Debari, Udaipur, Rajasthan,
India

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A complete over review on *Adhatoda vasica* a traditional medicinal plants

Santosh Kumar Singh, Dr. Jay Ram Patel, Arvind Dangi, Deepak Bachle and Rahul Kumar Kataria

Abstract

Adhatoda vasica plant has a vital medicinal role in our country (India) as well as other country. This plant has been used commonly in Ayurvedic System of medicine. The present paper gives an account of updated information on its phytochemical and pharmacological activities. The review reveals that wide range of phytochemical constituents isolated from the vasaka plants and its possesses various activities like antifungal, antiviral, hepatoprotective, antitussive, antibacterial, anti-inflammatory and antiulcer, abortifacient, thrombolytic, radiomodulation, cardiovascular protection, hypoglycaemic, antitubercular, antioxidant, antimutagenic, reproductive action have been reported.

Keywords: *Adhatoda Vasica*, Vasaka, phytoconstituents, pharmacological activity

1. Introduction

Adhatoda vasica (AV) belong to the family *Acanthaceae*. The leaves, roots and young plants of AV contain the quinazoline alkaloids vasicine, 7- hydroxyvasicine, vasicinolonone, 3-deoxyvasicine, vasicol, vasicoline, vasicolinone, triterpenes, anisotine) betaine, steroids carbohydrate and alkanes. In the flowers triterpenes (a-amirine), and flavonoids (Apigenin, astragaline, kaempferol, quercetin, vitexin) have been found [1, 2] *Adhatoda vasica*, also known as Malabar nut tree is part of the *Acanthaceae* plant family. It is a common small evergreen, sub-herbaceous bush distributed throughout India, especially in the lower Himalayas (up to 1300 meters above sea level), India, Sri Lanka, Burma and Malaysia. In Ayurveda, the ancient system of Indian medicine it is commonly known as vasaca [3] which is a well-known plant in indigenous system of medicine. It grows to about a height of 1.5-2.0m with leaves about 10-15cm long & 5.0cm wide & white or purple flowers & 4-seeded fruits. The leaves are of dark green colors above & pale yellow below. Flowers are typical, white arranged in pedunculated spike. *Adhatoda* leaves have been used extensively in Ayurvedic Medicine for over 2000 years primarily for respiratory disorders. It is propagated by tender stem cuttings. Stem cuttings of 15-20cm long & 3-4 nodes are ideal for planting. *Adhatoda* is obtained from commercial sources or collected from open fields. Propagation is primarily by means of seeds, can also propagate from cuttings in springs early summer with hardwoods cuttings [4]. Medicinal plants play a key role in world health care systems [5]. Charaka Samhita has classified the drug under mucolytic and expectorant drug. The roots, leaves & flowers are active principles of the plant possess a number of pharmacological properties & are used in cough, chronic bronchitis, rheumatism, asthma & bronchial asthma. Majority of medicinal plant species are rich in biomolecules contents which can cope with health hazards and recently, antibacterial activity of many plant species has been reported [6]. The leaves and roots contain several alkaloids (chief principle being quinazoline alkaloid, vasicine and vasicinone, vasicinolonone and vasicol), which may have a bronchodilator effect of the bronchii. These alkaloids are said to exist in combination with an acid that has been named *adhatoda* acid. It acts as a sedative, expectorant, antispasmodic, anthelmintic, bronchial antiseptic and bronchodilator. The leaf extract has been used for the treatment of bronchitis and asthma for many centuries. It relieves cough and breathlessness. It is also prescribed commonly for bleeding due to idiopathic thrombocytopenic purpura, local bleeding due to peptic ulcer, piles, menorrhagia. Its local use gives relief in pyorrhoea and in bleeding gums [7]. As the alkaloid content of plant varies with genotype therefore, it is recommended to propagate *A. vasica* plant using vegetative method [8]. *Adhatoda zeylanica* Medicus also known as *A. Vasica* Nees. *Justicia adhatoda* Linn.

It is a dense shrub 1.2-2.4 m. sometime arborescent, 6m. High with many long opposite ascending branches; stem with yellowish bark, terete, glabrous. Leaves 10-20 by 9-8 cm. elliptic-lanceolate, acuminate, minutely puberulous when young, glabrous when mature, entire, dark green above, paler beneath, base tapering; main nerves 10-12 pairs with reticulate venation between; petioles 1-2.5 cm. long. Flowers in short dense axillary pedunculate spikes 2-8 cm. long, towards the end of the branches; peduncles 3-10 cm., stout, shorter than the leaves; bracts reaching 1-2 by 0.5-1.2 cm, elliptic subacute, glabrous or nearly so, 5-7 nerved, closely reticulately veined; bracteoles 1.5-2 by 0.3-0.4 mm., oblong-lanceolate, acute, with ciliolate margins, 1-nerved, reticulately veined. Calyx rather less than 1.3 cm. long, glabrous or slightly pubescent, divided to within 2 mm. of the base; sepals imbricate, oblong-lanceolate, acute, 3-nerved, reticulately veined. Corolla white, with a few irregular pinkish coloured bars in the throat, 2.5-3 cm. long, pubescent outside; tube 1-2 cm. long, the lower half cylindrical, 4mm. diam., the upper half much laterally inflated; upper lip 2 by 1.3 cm. long, ovate-oblong, curved, obtuse, notched; lower lip as long as the upper, the lobes 1.3 cm. deep, ablong, rounded, the middle lobe the broadest. Filaments hairy at the base, long, stout, curved; lower anther-cells minutely apiculate (not white-apurred) at the base. Ovary pubescent; lower part of style pubescent, Capsules 1.5-2 by 0.6-0.8 cm. clavate, subacute, shortly and bluntly pointed, pubescent; solid stalk flattened, 1 cm. long. Seeds 5-6 mm. long, orbicular-oblong, tubercular-verrucose, glabrous [9]. Man and animals depend on the plants for their very existence our environment is characterized by richly diversified plant life. Plant diversity is composed of more than 5,00,000 botanical species, Plants constitute a vital component of the biodiversity as they play a key role in maintaining earth's environmental equilibrium and ecosystem stability. Herbal medicine is known to be the oldest form of healing. It originated from ancient Greek as far back as 1600 BC1. With Herbal Renaissance happening all over the globe, medicinal herbs are staging a phenomenal comeback. Ethno botanical information from India estimates that more than 6000 higher plant species forming about 40 % of the higher plant diversity are used in its codified and folk healthcare traditions [10]. The individual extract was subjected to the qualitative phytochemical screening for the presence of some chemical constituents. Phytochemical test were carried out adopting standards procedure [11, 12, 13].

2. Pharmacological activity

2.1 Uterine activity

The uterotonic activity of vasicine was studied in detail both by *in vitro* and *in vivo* methods employing the uteri under different hormonal influences and of different species of animals. The uterotonic activity seemed to be similar to that of oxytocin and methyl ergometrine. The abortifacient effect of vasicine like its uterotonic effect was more marked under the priming influence of oestrogens [14, 15]. Vasicine-induced abortion was studied in rats, guinea pigs, hamsters and rabbits. Study showed that vasicine acted through the release of PGs Synthesized vasicine and vasicinone derivatives in *in vitro* studies were found to have oxytocic activity at the dose above 1 mg/ml [16].

2.2 Antibacterial

Preliminary phytochemical and antibacterial investigations were carried out of the crude extracts obtained from the leaf of *Adhatoda vasica*, using solvents of varied polarity. The

presence of phenols, tannins, alkaloids, anthraquinones, saponins, flavanoids, amino acids and reducing sugars was indicated by the tests conducted. The effect of ethanol, petroleum ether and water extracts were tested on *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Klebsiella pneumoniae* and *Candida albicans*. The minimum inhibitory concentration of the crude extracts was determined for various organisms [17].

2.3 Antimicrobial Activity

Adhatoda vasica leaves for its phytochemical composition and antioxidant activity. Antioxidant activity of methanol extract of *A. Vasica* was estimated by total antioxidant activity, 2, 2 diphenyl-1-picrylhydrazyl radical scavenging activity, reducing power potential and iron chelating activity. Antimicrobial activity was performed by agar well diffusion method. Estimation of total phenolic content was measured by Folin-Ciocalteu reagent method and estimation of total flavonoid content was performed by aluminum chloride method. Leaves of *A. Vasica* were found to possess saponins, oils and fats, phytosterol, phenolic compounds, tannins, carbohydrate, alkaloids, flavanoids and proteins. Extract showed high antioxidant activity in various antioxidant experiments. The extract of *A. Vasica* showed presence of high levels of polyphenolic compounds (phenolic compounds and flavonoids), which could be the possible reason behind the antioxidant activity of the plant. In addition extract demonstrated moderate antimicrobial and cytotoxic activity (brine shrimp lethality) [18].

2.4 Antioxidant activity

Adhatoda vasica Nees and *Sesbania Grandiflora* (L.) Pers are the two important medicinal plants native to India. The aqueous leaf extracts of these two plants have been analysed for their free radical-scavenging activity in different *in vitro* systems, e.g. DPPH radical scavenging activity, hydroxyl radical-scavenging activity in Fe³⁺/ascorbate/EDTA/H₂O₂ system, inhibition of lipid peroxidation induced by FeSO₄ in egg yolk, metal chelating activity. The free radical scavenging activities were compared with standard antioxidants like butylated hydroxy toluene (BHT), ascorbic acid and EDTA. Total antioxidant activity was measured, based on the reduction of Mo (VI) to Mo (V) by the extract and subsequent formation of green phosphate/Mo (V) complex at acid pH and reducing power by Fe³⁺ - Fe²⁺ transformation in the presence of extracts. The content of total phenolics (expressed as mg of gallic acid equivalents/gm) and total flavonoids (expressed as mg of quercetin equivalent/gm) and ascorbic acid were determined along with antioxidant enzymes. The results indicated that *A. vasica* and *S. Grandiflora* showed significant antioxidant activity *in vitro*. The enzymatic and non-enzymatic antioxidants in *A. Vasica* were found to be more than that of *S. grandiflora*, similarly the antioxidant and radical scavenging activities of *A. vasica* were found to be more significant than *S. Grandiflora* [19].

2.5 Anti-inflammatory

Adhatoda vasica (L.) Nees is a well-known plant drug in Ayurvedic and Unani medicine. It has been used for the treatment of various diseases, particularly for the treatment of inflammatory and cardiovascular diseases. However, the scientific rationale and mechanisms by which it functions in these diseases is not known. This study was designed to

explore the inhibitory activity of *Adhatoda vasica* aqueous and butanolic fractions on arachidonic acid (AA) metabolism. For this purpose aqueous and butanolic fractions of *Adhatoda vasica* were screened for the presence of activities against arachidonic acid (AA) metabolites and their effectiveness was further evaluated by studying platelet aggregation induced by a AA, adenosine diphosphate (ADP), platelet activating factor (PAF), and collagen. AA metabolism was studied by thin layer chromatography system while platelet aggregation was measured by dual channel Lumiaggrego meter. Aqueous fraction of *Adhatoda vasica* but not of butanolic fraction inhibited the AA metabolites through COX pathway (TXB2) and LOX pathway (LP1 and 12-HETE). However, in platelet aggregation studies butanolic extract of *Adhatoda vasica* showed strong inhibition against AA, PAF and collagen induce aggregation but not against ADP [20].

2.6 Antitussive

The effect of the ethanol extracts of *Glycyrrhiza glabra* and *Adhatoda vasica* on SO₂ gas induced cough in experimental animals have very significant effects at the level of $P < 0.01$ in inhibiting the cough reflex at a dose of 800 mg/kg and 200 mg/kg body wt. p.o., in comparison with the control group. Mice showed an inhibition of 35.62%, in cough on treatment with *Glycyrrhiza glabra* and 43.02% inhibition on treatment with *Adhatoda vasica* within 60 min of the experiment. The antitussive activity of the extract was comparable to that of codeine sulphate (10, 15, 20 mg/kg body wt.), a standard antitussive agent. Codeine sulphate, as a standard drug for suppression of cough, produced 24.80%, 32.98%, and 45.73% inhibition in cough at a dose of 10 mg/kg, 15 mg/kg and 20 mg/kg respectively, whereas, codeine sulphate (20 mg/kg) showed maximum 45.73% ($P < 0.001$) inhibition at 60 min of the experiment [21].

2.7 Hepatoprotective Activity

The hepatoprotective activity of Ethyl acetate extract of *Adhatoda vasica* was investigated against CCl₄ induced liver damage in Swiss albino rats. At the dose of 1ml/kg, CCl₄ induced liver damage in rats as manifested by statistically significant increase in serum Alanine aminotransferase, (ALT), Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP) and also in serum Bilirubin. Pre-treatment of rats with the ethyl acetate Extract of *Adhatoda vasica* (100mg/kg and 200mg/kg) prior to the CCl₄ dose at 1ml/kg statistically lowered the three serum level enzymes and also Bilirubin. Histopathological observations also coincided with the above results, however 200mg/kg dose was found to be more active. Current results suggest that Ethyl acetate extract of *Adhatoda vasica* has potent hepatoprotective effect against CCl₄ - induced liver damage [22].

2.8 Antiviral activity

The influenza viruses are major etiologic agents of human respiratory infections, and inflict sizable health and economic burden. The present study reports the *in vitro* antiviral effect of *Justicia adhatoda* crude extracts against influenza virus by Hemagglutination (HA) reduction in two different layouts of simultaneous and post treatment assay. The aqueous and methanolic extracts were used for antiviral activity in the non-cytotoxic range. Methanolic extract showed 100% reduction in HA in the simultaneous and post treatment assays at the concentration of 10mg/ml. The aqueous extracts at concentrations of 10mg/ml and 5mg/ml reduced the HA to 33% and 16.67%, respectively, in the simultaneous assay.

These results suggest that extracts have strong anti-influenza virus activity that can inhibit viral attachment and/or viral replication, and may be used as viral prophylaxis [23].

2.9 Thrombolytic Activity

As a part of discovery of cardio-protective drugs from natural sources the extractives of *Adhatoda vasica* were assessed for thrombolytic activity and the results are presented in Table 1. Addition of 100µl SK, a positive control (30,000 I.U.), to the clots and subsequent incubation for 90 minutes at 37°C, showed 80.65% lysis of clot. At the same time, distilled water was treated as negative control which exhibited negligible lysis of clot (4.08%). In this study, the methanolic fraction (MF) exhibited highest thrombolytic activity (53.23%) [24].

2.10 Antifungal Activity

Plants have been proven as promising sources of new and biologically active natural products exhibiting higher activity in medicinal applications. The usage of natural products and active plant extracts has been increased recently and new drugs are discovered using new technological advancements. The present elucidates the phytochemical constituents of *Adhatoda vasica* and their effective agent's human pathogenic fungus. The minimum inhibition activity of the phytochemical extract is identified. Further study is carried out with the extract for the partial characterization by TLC and antifungal determined by agar disc diffusion and germ tube formation inhibition activity. The aim of the current study on the effect of *A. Vasica* on *Aspergillus ruber* and *Trichophyton rubrum* pathogenic fungus was to conclude the antifungal activity of the *A. Vasica* [25].

2.11 Anthelmintic activity

The main objective of this study was to evaluate the anthelmintic activity of *Adhatoda vasica* (Acanthaceae) *in vitro* against the gastrointestinal nematodes of sheep. The aqueous and ethanolic extracts of *Adhatoda vasica* aerial parts were evaluated by egg hatching and larval development assays. The aqueous and ethanolic extracts at 25-50 mg/ml concentrations exhibited ovicidal and larvicidal ($P < 0.05$) activity against gastrointestinal nematodes. The plant extracts showed dose-dependent inhibition ($P < 0.05$). The ethanolic extract at the concentration of 50.0 mg/ml was more effective in inhibiting egg hatching and larval development of gastrointestinal nematodes. The effective dose (ED₅₀) of aqueous and ethanolic extracts were determined graphically from linear regression equation with probit scale, $y = 5$. The results of this study suggested that *Adhatoda vasica* extracts may be useful in the control of gastrointestinal nematodes of sheep [26].

2.12 Antidiabetes activity

'Diabetic encephalopathy' refers to diabetes associated cognitive decline (DACD), which involves oxidative-nitrosative stress, inflammation and cholinergic dysfunction. Current study was designed to investigate the effect of *Adhatoda vasica*, a known anti-inflammatory, antioxidant, anti-cholinesterase and anti-hyperglycemic plant, on diabetic encephalopathy. Streptozotocin (STZ)-induced diabetic Wistar rats were treated with *Adhatoda vasica* leaves ethanolic extract (AVEE) for 6 weeks at 100, 200 and 400 mg/kg/day dose. During fifth week of treatment, learning and memory was investigated in single Y-maze and passive avoidance test. At the end of the study biochemical parameters like acetylcholinesterase (AChE) activity, nitrite

levels, tumor necrosis factor-alpha (TNF- α) and oxidative stress was measured from cerebral cortex and hippocampus regions of brain. AchE activity was found increased by 70% in the cerebral cortex of diabetic rat brain. Lipid peroxidation (LPO) levels were increased by 100% and 94% in cerebral cortex and hippocampus of diabetic rats, respectively. Non-protein thiol levels, enzymatic activities of superoxide dismutase and catalase were found decreased in cerebral cortex and hippocampal regions of diabetic rat brain. Nitrite levels in both regions of diabetic brain were increased by 170% and 137% respectively. TNF- α , a pro-inflammatory cytokine, was found significantly increased in diabetic rats. Conversely, animal groups treated with AVEE significantly attenuated these behavioral and biochemical abnormalities. The results suggest a protective role of *Adhatoda vasica* Nees against diabetic encephalopathy, which may be sum of its anti-oxidant, anti-cholinesterase, anti-inflammatory and glucose lowering action [27].

2.13 Anti-tuberculosis Activity

The extraction and determination of alkaloids was performed and confirmed by phytochemical analysis. Six different quinazoline alkaloids (vasicoline, vasicolinone, vasicinone, vasicine, triterpenes and anisotine) were found in the leaf of *Justicia adhatoda* (*J. adhatoda*). The presence of the peaks obtained through HPLC indicated the diverse nature of alkaloid present in the leaf. The enzyme β -ketoacyl-acyl-carrier protein synthase III that catalyses the initial step of fatty acid biosynthesis (FabH) via a type II fatty acid synthase has unique structural features and universal occurrence in *Mycobacterium tuberculosis* (*M. tuberculosis*). Thus, it was considered as a target for designing of anti-tuberculosis compounds. Docking simulations were conducted on the above alkaloids derived from *J. adhatoda*. The combination of docking/scoring provided interesting insights into the binding of different inhibitors and their activity. These results will be useful for designing inhibitors for *M. tuberculosis* and also will be a good starting point for natural plant-based pharmaceutical chemistry [28].

2.14 Anticestodal activity

The result indicated 800 mg/kg double dose of extract has profound efficacy against mature worms, where the EPG count was reduced by 79.57% and percentage worm recovery rate by 16.60%. These effects were better than treatment with 5 mg/kg single dose of praziquantel, the standard drug. In case of efficacy against immature worms, the extract showed a significant reduction in worm recovery rate (from 100% in control to 20.00% at 800 mg/kg dose of extract) [29].

2.15 Electrophoresis

A new method of capillary electrophoresis was developed for the quantitative determination of vasicine and vasicinone from *Adhatoda vasica* (L.) Nees. The electrophoretic separation was performed using a 47cm_50 mm ID (38.5 cm effective length) fused silica capillary. The samples were injected by pressure for 3 s at 50 mbar and the running voltage was 19 kV at the injector end of the capillary. The capillary temperature was maintained at 40 °C. The separation of the two alkaloids has been achieved within 11 min with good repeatability. The method was validated in terms of reproducibility, linearity, accuracy and applied for the quantitative determination of vasicine and vasicinone in *A. vasica* plant samples/extracts. Parameters affecting the resolution such as pH, temperature, organic modifier, buffer concentration and capillary dimensions were reported [30].

2.16 Hepato suppression

Liver disorder is one of the common thrust area declared by the Indian Council of Medical Research, New Delhi in the reviewed research on traditional medicine. *Adhatoda vasica* have been reported to exhibit varying degrees of hepatoprotection against the CCl₄ induced liver dysfunction in rats. The present work was carried out to investigate the potential hepatoprotective action of *Adhatoda vasica* whole plant powder against CCl₄ induced liver damaged Wister rat model. Blood and tissue biochemical parameters of liver have been examined for evaluating the hepatoprotection action. These biochemical markers are GOT, GPT, Alkaline phosphate, glucose, bilirubin, Triglycerides, γ GT, cholesterol, DNA, RNA, total protein, The effect of *Adhatoda vasica* whole plant powder is compared with Silymarin by standard protocol and is found to have better hepatoprotective action, thus *Adhatoda vasica* indicating protection in liver may prove promising effect against liver disorders. Thus it may act even in humans as a potent liver tonic [31].

2.17 Radio modulatory

The radiomodulatory influence of ethanolic extract of *Adhatoda vasica* Nees leaf extract against radiation-induced hematological alterations in peripheral blood of Swiss albino mice was studied at various post-irradiation intervals between 6 h to 30 days. Conversely, animals pre-treated with *A. vasica* leaf extract showed 81.25% survival till 30 days after exposure and a gradual recovery was noted in the hematological values. However, these hematological values remained significantly below the normal even till day 30. A significant decrease in blood reduced glutathione (GSH) content and increase in lipid peroxidation (LPO) level was observed in control animals (Radiation alone). However, *A. vasica* leaf extract pretreated irradiated animals exhibited a significant increase in GSH content and decrease in LPO level. A significant increase in the serum alkaline phosphatase activity and decrease in acid phosphatase activity was observed in *A. vasica* leaf extract pretreated irradiated animals during the entire period of study [32].

2.18 Immunomodulatory activity

Methanolic, chloroform and diethyl ether extracts of leaves of Indian medicinal plant *Adhatoda vasica* Linn. Were pharmacologically validated for its immunomodulatory properties in experimental animals. Oral administration of extracts at a dose of 400 mg/kg in adult male Wister rats significantly increased the percentage neutrophil adhesion to nylon fibers ($P < 0.001$). It extracts were also found to induce Delayed Type Hypersensitivity reaction by sheep erythrocytes ($P < 0.001$). The observed results at different doses were significant when compared to control groups. These findings suggested that the extracts of this plant, *A. vasica* Linn positively modulates the immunity of the host [33].

2.19 Effect on reproductive organs

The possible abortive effect of an extract of *Adhatoda vasica* leaf spissum, was studied in rats. The principal alkaloid detected in the extract was vasicine ($0.85 \pm 0.03\%$). The extract (325 mg/kg/day) was administered with a gastric cannula to a group of 5 pregnant females between day 1 and 9 of pregnancy. In another experiment 9 pregnant females received in the water 0.25 and 2.5% of *Adhatoda vasica* between day 1 and 9 of pregnancy. It was concluded that the administration of *Adhatoda vasica* did not produce abortion in any of the treated groups [34].

3. Conclusion

The literature survey revealed that *Adhatoda vasica* has been widely studied for its phytochemical and pharmacological activities. It is present in class of herbal drug with very strong conceptual or traditional base. *Adhatoda vasica* is an important source of vasicine, vasicinone, vasicolone and some other alkaloids. In this review some pharmacological studies have been concluded like antibacterial, antifungal, hepatoprotective, antitussive, radiomodulation, anti-inflammatory and antiulcer, abortifacient, antiviral, thrombolytic, antimutagenic, cardiovascular protection, hypoglycaemic, antitubercular, antioxidant and some more studies are done. Furthermore studies are summarized in mentioned review papers.

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