



***Acalypha indica* L. - an Important Medicinal Plant: A Brief Review of Its Pharmacological Properties and Restorative Potential**

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Authors' contributions

This work was carried out in collaboration among all authors. All authors equally contributed in preparing the review article. All authors read and approved the final manuscript.

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ABSTRACT

Medicinal plants are moving from border to mainstream use with a more number of people seeking treatment and health approaches free from side effects caused by synthetic chemicals. India officially recognizes over 3500 plants for their medicinal value. It is generally estimated that over 6000 plants in India are in use in folk, traditional and herbal medicine. This review article aims to provide a comprehensive review on the phytochemical and various pharmacological aspects of *Acalypha indica*. This plant widely used in traditional medicinal system of India and many other countries has been reported to possess anti-cancer, anti-diabetic, anti-oxidant, anti-bacterial, antifungal hepatoprotective, anti-inflammatory, and also used to check anti-ulcers and wounds healing. It is known as a rich source of glycosides, flavanoids and tannins. The medicinal properties and therapeutic uses of *Acalypha indica* and its secondary metabolites investigations prove its importance as a valuable medicinal plant.

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1. INTRODUCTION

Acalypha indica is one of weed plants that contain important medicinal values for human health applications. It can be found commonly in India, Sri Lanka Thailand and Pakistan. The extracts of various parts of the plant, leaves, roots and stem parts are used for medicinal purposes to treat various diseases such as the eye infections, respiratory problems, rheumatism, and skin problems and to decrease blood sugar level. Different extraction methods are used for obtaining active components from *Acalypha indica*. Generally, Soxhlet extraction has a high efficiency and accuracy but the thermal stress might degrade target photochemical components.

Herbal medicines have been playing a vital role in treatment and cure for various diseases and physiological conditions in traditional methods practiced such as Ayurveda, Unani and Siddha. This type of treatment, also known as conventional treatment, was the main source of medical treatment during this time [1]. However, civilization has changed and with it has come the introduction of more advanced techniques and methods, leading the next generations to tend to choose modern treatment over conventional treatments. The information related to conventional treatments are gradually vanishing since the previous generations are getting older and dying without successors. This knowledge is passed on to the next generation, through experiments and observation and oral teaching [2]. Therefore, it is crucial to have proper documentation from the extant practitioners since conventional treatments are an alternative path to treating various types of human diseases [3]. Traditional or conventional medicinal practices based on natural plants have been recognized by the World Health Organization (WHO, 2002) as reliable medicinal sources for therapeutic activities. The medicinal plants are available around backyards, settlements, spreading along roadsides, and house compounds

Medicinal plants are recognized as potential source of bioactive compounds. More than 80% of modern drugs are derived directly from sources of plants and microbes. Natural products derived from medicinal plants have wide range of pharmacological significance. Bioactive compounds as they contain therapeutic and their complex nature will able to interact with

mammalian cell targets. Phytochemicals naturally isolated from the medicinal plants (MAPs) are used specifically in drug industries. However, these Phytochemicals' have certain limitations of low absorption, high toxicity, and other side effects, bioavailability and efficacy. Irrespective of the advantages of synthetic, combinatorial chemistry and molecular modelling, they remain an important source for new drugs discovery.

2. BOTANICAL DESCRIPTION OF *Acalypha indica*

Acalypha indica is a traditional medicinal plant, well-known by older generations in many countries, particularly in Africa and Asia. It grows well in most parts of west and south of Africa northeast, including Somalia, Ethiopia and other regions. The plant can also be found in most wet, tropical and temperate countries in Asia, Europe and both North and South American regions. It grows as a weed in bushes, backyards, alongside roads and other places such as home and crop premises [4]. Many international manuscripts on *Acalypha indica* were published from Indian region because this plant has a close connection with Ayurveda, Sidda and Unani medicinal practices executed by older Indian generations [5].

3. TAXONOMY

The leaves have sub obtuse crenate-serrate and base cuneate and glabrous thin. Their petiolate is usually longer than the slender, blade, and stipulate minute [6]. The leaves of the *Acalypha indica* are simple and arranged spirally; 0.02 – 12.00 cm petiole long; blade broadly ovate to ovate-lanceolate; 2 – 9 cm × 1 – 5 cm; base cuneate; apex acute; margins toothed; membranous; sparingly short hairs to almost glabrous is nature on both surfaces; more hairy along the midrib; 5-veined at base and with 4 to 5 pairs of lateral veins. One month after germination, the stem starts to turn woody as it matures. The stem of the *Acalypha indica* is sparing to densely hairy. The branches are numerous, ascending, long and finely pubescent. The flower of the *Acalypha indica* is arranged in numerous erect, lax, elongated, clusters and auxiliary spikes near the summit of the spikes. The female is in white colour, scattered, and surrounded by a shortly pedunculate large leafy dentate cuneiform with many nerves bract

that is approximately 6 to 8 mm in diameter [6].

4. PLANT PROFILE

Scientific name: *Acalypha indica* (Fig. 1)

Taxonomic Classification

Kingdom : Plantae
Unranked : Angiosperms
Unranked : Eudicots
Order : Malpighiales
Family : Euphorbiaceae
Genus : *Acalypha*
Species : *A. indica*

Vernacular names

Sanskrit : Arittamanjarie.
English : Indian acalypha.
Hindi : Kuppu; Khokali.
Telugu : Kuppichettu; Harita-manjiri;
Kuppinta or Muripindi.

Constituents :Alkaaloids “acalypus” and “acalypine.”

Vernacular names in other countries

Alcalifa : Brazil
Tie Xian : China

Baro , Berbere : Ethiopia
Kuppimani : India
Ricinela : Spain
Kuppameniya : Sri Lanka

5. DISTRIBUTION

Acalypha indica grows naturally in wet, temperate, and tropical areas along the equator cross-continental of Asian, Africa, Europe, Australia and South and North America. The Indian people have the documented records of plant utilization for their traditional medicines as well as conventional medicines [7]. Many Australians recognized this plant in their area but are less inclined to consume it [8]. *Acalypha indica* also can be found in the Arabia Gulf region based on the report that they consumed this plant as a food [9]. *Acalypha indica* is also a common weed found in West Africa and south Nigeria [10].

6. ETHNOMEDICINAL PRACTICES

Most of the practices come from people in the Asian and African regions. Some people in India are regular consumers of this plant leaves since it is a part of the Ayurveda practice. Meanwhile, other countries use this plant as part of their treatment but usage is minimal. The



Fig. 1. *Acalypha indica*

implementation of *Acalypha indica* plant for ethnomedicinal purposes can be divided into three main parts: Roots, stem and leaves. The method of applying this plant for treatment as a single use or in a combination with other ingredients also plays vital role which needs to be discussed. The plant condition during treatment, fresh or dry, could also be an important factor in its therapeutic effectiveness. Even though the plant is known for its therapeutic purposes, even some people who consume this plant as a food prepared either as a green leafy vegetable, soups or a fried flour snack in their daily meal. 64% of ethno medicinal practices consume the leaf of the plant, followed by the whole plant (24%) and the root (12%). The leaves are the most abundant part and easy to be separated, compared to the root, stem, flowers and seeds.

7. PHYTOCHEMICAL STUDY

7.1 Phytochemical and Nutrient Constituent of *Acalypha indica*

The fresh *Acalypha indica* plant has a wide variety of nutrients such as carbohydrates, proteins, vitamins, and lipids. They decided to prepare its documentation with detailed observation of essential and non-essential heavy metals content as a part of the herbal standardization preparation. *Acalypha indica* has high iron content, followed by copper, nickel zinc, and chromium which are useful for patients with mineral deficiencies problems. This plant has a

high moisture content of up to 90% and a total ashes value of 18% [11] suitable for body hydration. As a leafy low-cost vegetable, this plant can provide a more balance in nutrients at minimal costs.

Researchers have studied and listed the secondary metabolites in *Acalypha indica* plant parts as shown in Table 1. These studies show some relevance in the interrelationship between ethnomedicinal practices with the respective parts of the plant. The list of phenolic compounds derived from this plant, corilagin, geraniin, glucogallin and chebulagic acid were useful as antioxidants. Meanwhile [12] stated that there were five compounds from the ethanolic leaf extract of the leaves which acted as antioxidants. Ellagic acid, gallic acid, 16 α , 17-dihydroxy-ent-kauran 19-oic-acid, 4,4',5,5',6,6' hexa hydroxydiphenic acid and kauren- 18-oic-acid can be found inside this plant. [13] Indicated active inhibition of anti-cancer activity against small cell lung and breast cancer by the quebrachitol compound found in leaves. This compound is responsible for healing respiratory problems such as bronchitis and asthma shown in Table 1.

8. PHARMACOLOGY ACTIVITY

8.1 Analgesic

Acalypha indica has analgesic properties as proven by [14] conducting *in vivo* studies on mice. They used a writhing reflex method

Table 1. Phytochemical contents in *Acalypha indica* L. from different parts of the plant (Leaf, root and flower)

Phytochemical	Plant part	References
Acalyphamide	Whole plant	Duke., 2016
Acaindinin	Leaf	Ma et al., 1997
Acetylgeraniin	Whole plant	Ma et al., 1997
Aurantiamide	Leaf	Raj et al., 2000
Caffeic acid	Whole plant	Murugan et al., 2015
Corilagin	Leaf	Ma et al., 1997
Cysteine	Whole plant	Hussain et al., 2013
Ferulic acid	Leaf	Murugan et al., 2015
Gallic acid	Whole plant	Joy et al., 2010
Stigmasterol	Root	Raj et al., 2000
Resin	Leaf	Azmahani et al., 2002
Syringic acid	Root	Murugan et al., 2015
Tectoquinone	Whole plant	Duke., 2016
Triacetnamine	Leaf	Azmahani et al., 2002
3,3' Methylene bis (4-hydroxyl coumarin)	Root	Murugan et al., 2015

developed by [15] to determine the analgesic activity of the *Acalypha indica* hexane extract. Acetic acid was used to induce pain right after the extract was orally administered to the mice. The injection of acetic acid will cause trauma to the whole body in two phases; the first phase will release serotonin and histamine while the second phase will involve prostaglandins in the inflammatory exudates in plant extract [16]. Two kinds of concentrations were tested and compared where amino pyrine was set as a positive control. The results were measured by counting the writhing induced within 20 minutes, immediately after the extract and standard were introduced into the mice. The 100 mg/kg and 200 mg/kg of hexane extractions produced up to 61.1% and 67.2% of writhing inhibition, respectively. The effects showed adequate inhibition activities compared to the use of standard amino pyrine with a 79.9% writhing inhibition [14]. The hexane extract disrupted the first phase of inflammation formation by inhibiting the release of serotonin and histamine. The anti-inflammation, antioxidant and phytochemicals in the fresh plant may be responsible for this inhibition.

8.2 Anthelmintic activity

An anthelmintic is a drug used to expel parasitic worms that usually intrude in the human body parts. The parasitic worm can penetrate animal and human bodies through any available cavities like the skin and mouth. An anthelmintic drug derived from easily available herbal medicine is encouraged since it can save costs in treatment [17]. Both used a similar method to study the anthelmintic activity developed by [18]. From their studies, the extract from methanol and water could kill *Pheretima posthuma* 20 minutes after its introduction and completely killed after 40 minutes. In the [17] study, the concentration of 100 mg/ml methanolic root extract was dissolved and tested in a medium.

8.3 Anti-bacterial Activity

Most therapeutic studies that have been reported on *Acalypha indica* are related to the anti-bacterial activities. There is conflict when identifying the inhibition method, positive and negative controls, and experiment preparation methods because the studies differ from one another. The classification to identify whether the extract is either active or inactive needs a justification. One of the classification methods is through measuring the diameter of the zone of

inhibition. From the diameter, the small number represents slightly active activity while the high number will be noted as very active [19]. Then, the results are expressed in the form of inhibition percentage where between 0 and 30% it is considered weak, 31 to 70% is considered as active and the inhibition over 71% is very active. Thirteen Gram-positive bacteria including *Bacillus*, *Streptococcus*, *Enterococcus*, and *Staphylococcus* species have been tested from those studies. For Gram-negative bacteria only eleven bacteria were tested on the various polarities of *Acalypha indica* extractions at present. In conclusion for anti-bacterial activity, the fresh plant approach is suggested instead of a decoction to treat many diseases related to *Streptococcus* such as pus formation and inflammation. Specific medicinal compounds in *Acalypha indica* responsible for bacterial inhibition are not really discussed by most researchers. They only discussed a certain group of phytochemicals or secondary metabolites in plants, which are responsible for anti-bacterial activities and do not explain the mechanism of inhibition. Besides, the flavonoids, tannins, polyphenol, protein and saponin also play an important role in inhibiting and retarding bacterial growth [20].

8.4 Anti-cancer Activity

Acalypha indica plant extract also has the ability to become an anticancer plant as reported by [21]. Three types of cancer cell lines have been tested with *Acalypha indica* leaf extracts including KB-Oral cavity cancer, MCF7-breast cancer and PC3 human prostate cell cancer. The anti-cancer activity was determined through MTT assay method. The ethanolic extract of *Acalypha indica* inhibited MCF7-breast cancer with an inhibition concentration (IC_{50}) value of 35 $\mu\text{g/ml}$. Two standards have been used in the assay for comparison which was doxorubicin and ellipticine. The IC_{50} value for doxorubicin and ellipticine were 8.8 $\mu\text{g/ml}$ and 0.5 $\mu\text{g/ml}$, respectively. The MCF7- breast cancer and the KB-Oral cavity cancer were considered nonreactive with the methanolic extract since the inhibition concentration exceeded 50 $\mu\text{g/ml}$ [22]. In addition, a recent study has revealed that the quebrachitol could participate in several important mechanisms as potential anti-cancer drugs either via arrest or reverse pathways [23].

8.5 Anti-diabetic Activity

Acalypha indica has potential as an anti-diabetic activity when the plant is used in the treatment.

[24] Indicated the hexane and methanolic extract inhibited alpha amylase activity up to 7.51% and 65.32%, respectively. Amylase is an enzyme that catalyzes and hydrolyses starch into sugars. A continuity of the study has been carried out by through *in vivo tests* on rats. Both of them used the diabetes induction method on rats before the plant extract was introduced via oral the blood glucose levels decreased at least 35% after the administration of different plant extracts, followed by decreases in levels of cholesterol, urea and triglycerides levels after six hours. The streptozotocin drug was used to cause a rapid destruction of pancreatic β cells which led to impaired glucose-stimulated insulin release and resistance. These are the molecular marker features for type II diabetes studies in rats in *in vitro* studies. The plant extract to inhibit the destruction of pancreatic β cells will determine whether the medicine is useful or not. In this case, the whole plant of *Acalypha indica* can be used as an herb for anti-diabetic activity. This data supports the application of *Acalypha indica* plant extract as an agent to lower blood sugar by some people in India [25]. In their practice, the *Acalypha indica* roots alone is used to treat high blood sugar levels whereas, in the studies, the whole plant has proven to be high effective. This is possibly due to the root containing small amounts of cyanogenic secondary metabolites compared to the aerial part [26].

8.6 Anti-fungal Activity

Six kinds of fungi (*Aspergillus flavus*, *Aspergillus niger*, *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, and *Penicillium chrysogenum*) have been used to test whether *Acalypha indica* has an anti-fungal activity or not; these tests were conducted by [27,28]. Six solvents were used including hexane, petroleum ether, chloroform, ethyl acetate, methanol, and water to extract the compounds from *Acalypha indica*. The similar method for anti-bacterial is implemented to categorize the anti-fungal activity of *Acalypha indica*. As a conclusion, there is still little information on anti-fungal activity from this plant those which are currently available [27]. The phenols and flavonoids in *Acalypha indica* are expected to be the source of anti-fungal activity based on the previous studies [29]. For anti-fungal activity, extraction from water like a decoction is recommended since fungi are affected by any photochemical drugs. Raw of the whole plant is suggested to treat fungal infections in the human body.

8.7 Anti-inflammatory Activity

Acalypha indica plant extract can behave as an anti-inflammatory medicine in the human body. [14] Identified this activity of the *Acalypha indica* in the long even rats by using ethanolic extract. They used the anti-inflammation method with minor modifications and selected phenylbutazone as the standard drug for this activity. The anti-inflammation effects were comparable with the standard until five hours after the injection of the carrageenan solution [14]. The anti-inflammation activities from ethanolic extracts are also supported by [30] which resulted in the inhibition of albumin proteinase and denaturation. Both assays showed 85% of inhibition, indicating no protein denaturation when the extract was used. Protein denaturation is one of the indicators for inflammation activity in the human body [31]. The *Acalypha indica* plant extracts stabilized the membrane by inhibiting hypotonicity-induced lysis of an erythrocyte membrane, analogous to a lysosomal membrane.

8.8 Anti-obesity Activity

Obesity is one of the significant peril factors for metabolic disorder and syndrome of energy balance and basically well thought out as a disarray of lipid metabolism, which includes hypertension and hyperlipidaemia potentially leading to type 2 diabetes mellitus, non alcoholic fatty liver disease and cardiovascular diseases [44]. There are two types of methods done to study the anti-obesity of *Acalypha indica* plant extract. Conducted a study using different concentrations of ethanolic extract through a weight assessment for 29 days on Albino swiss mice [32]. They claimed there was no significant increment in mice weight during the experiment. [32] Furthered the study by using a high-fat content diet together with ethanolic extract on Albino Swiss mice. The mean body weight of the rats on the fifteen day was measured to compare between the standard (Simvastatin) and the 300 mg ethanolic extract. Both groups increased by 34.14% and 34.61% after being fed the atherogenic induced diet, while the group of mice who were only fed the atherogenic induced diet had a high value of mean body weight percentage (39.56%). The ethanolic extract exhibited similar results to the standard drug used in the experiment. The flavanols inside *Acalypha indica* like standard drug (quercetin) also played a key role as a potential anti-obesity drug [33].

8.9 Antioxidant Activity

There are three types of assays used for antioxidant measurements for measuring the antioxidant activity. The 2,2-diphenylpicrylhydrazyl (DPPH), 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), and FRAP assays are used to test antioxidant activities from various extracts of *Acalypha indica* extracts from a certain plant part. As a result, these antioxidant studies are quite inconsistent and dubious. For example, the methanolic extract results showed the antioxidant value from poor to very strong activities [34]. The presented antioxidant results in this review are influenced by how the researchers prepared the sample and where the sample came from. The data is reliable but still significant as a reference for future study. The whole *Acalypha indica* plant has antioxidant activities, especially the phytochemicals from semi-polar, polar and non polar groups.

8.10 Anti-ulcer Activity

There are phytochemicals in the methanolic extract of *Acalypha indica* that are capable of inhibiting ulcer activity based on the treatment of the Swiss albino rats [35]. They identified the ulcer inhibition activity by studying the reaction of pylorus ligation and swim stress Swiss albino rats. In their experiment, two concentrations of *Acalypha indica* were administered to the rats; 50 and 100 mg/kg per body weight. The standard drug reference for anti-ulcer activity is famotidine with 10 mg/kg per body weight at 10 ml/kg vehicle (5% w/v of acacia). The 100 mg/kg of extract reduced 67.14% of the volume of gastric juice, 59.29% of total acidity, 53.24% of free acidity, and 37.18% of ulcer index. For famotidine, the standard reduced the volume of gastric juice up to 82.24%, as well as total acidity (70.20%), free acidity (76.26%) and ulcer index (73.34%). The comparison between extract and standard showed that *Acalypha indica* plant extract has anti-ulcerogenic properties since the difference value is small. Major secondary metabolites in the extract such as the alkaloid and steroid provide basic information for anti-ulcer activity [35].

8.11 Anti-venom Activity

Shirwaikar et al. [36] found that the anti-venom derived from *Acalypha indica* can treat with *Daboia russelli* venom. By studying the venom-induced lethality, hemorrhage, necrotizing and

mast cell degranulation in rats, it was found that 500 mg/kg of methanolic extract increased the survival rate up to 100% higher than the anti-venom itself. Later [37] studied other extracts from benzene, petroleum ether, chloroform, and acetone against similar snake venoms. The results showed that 100 mg/kg increased the survival rate of Swiss albino rats. The more polar phytochemical compounds extracted, the higher the survival rate. Meanwhile, benzene, petroleum ether, acetone and chloroform increased the survival rate at 35%, 47%, 47% and 77%, respectively. The antioxidant activity of the different extracts of *Acalypha indica* is one of the mechanisms of venom inactivation and inhibition [38]. The *Daboia russelli* snake is found in Asian countries especially in India, Sri Lanka, Bangladesh, Myanmar and Nepal [39].

8.12 Anti-viral Activity

A study was conducted by [40] to find the growth inhibition activity of a virus from indigenous plant medicines. *Acalypha indica* methanolic extracts were tested against two types of virus that is Herpes simplex virus, Type and Vesicular stomatitis virus on the HeLa cells. They used Minimum Inhibitory Concentration (MIC) to identify the anti-viral growth inhibition activity. From the results, HSV-1 virus was not affected by the *Acalypha indica* methanolic extract, similarly VSV virus was inhibited by methanolic extract with a CD50 value of 0.05 mg/ml. Since Vesicular stomatitis virus is RNA-type virus, they stated the anti-Vesicular stomatitis virus and cytotoxic activities of extract may involve in the mode of action presumably through protein interaction [40]. Further studies are required with different virus species to gather more information related to *Acalypha indica* plant that can act as an anti-viral agent.

8.13 Wound Healing Activity

Reddy et al. [41] confirmed that *Acalypha indica* has wound healing property as well as *Plumbago zeylanica* and *Heliotropium indicum* in their study. The methanolic extract from this plant was experimented on in the Albino Wistar rats by using incision and excision wound models. The 20% w/v concentration of methanolic extract was prepared in a saline for topical application. The ethanolic extract of *Acalypha indica* required 24 days to completely heal a wound and has the lowest breaking strength from incision wound. The extract exhibited a 34.37% healing rate on the excision wound model and 35.93% on

restored incision wound. In their discussion section, they also mentioned the healing mechanism of *Acalypha indica* plant extract which has fair wound healing properties and poor tensile strength, thus lowering the maturation rate of collagen [41]. The other experiments are related to wound healing activity were also carried out by [42]. The plant extract from the mixed solvent (50% water: 50% methanol) was tested on excision and incision wounds on the Swiss albino mice [43]. [44] also used a mixed solvent (70% water: 30% methanol) for extraction at the plant aerial part. The 0.5 mg/ml concentration of ethanolic extract heals scratches 20% faster than the negative control. The methanolic extract has significant wound healing potential by up regulating the genes of TNF- α (Tumour Necrosis Factor - α) and TNF- β (Tumour Necrosis Factor - β) this two cytokines play a very important role in wound healing.

9. CONCLUSION

This review updates the information of *Acalypha indica* studies from several aspects such as phytochemical content, ethno medicinal practice and pharmacological activities, from entire regions. The consumption of *Acalypha indica* as an ethnomedicinal herb has been discussed and identified with relevant pharmacological studies and phytochemical contents. The plant is applicable for treatment depending on the therapeutic activities. The preferred part of the plant for ethnomedicinal practice is its leaves and the root. Studies have identified various 24 pharmacological activities with some positive results. The most potential therapeutic treatments are as anti-cancer, anti-inflammatory, anthelmintic, antibacterial, anti-diabetes, anti-hyperlipidemic, anti-obesity, and anti-venom and wound healing properties.

The present review shows the pharmacological study of the *Acalypha indica* and various phytochemical compounds responsible for it which have been reported. The whole plant of *Acalypha indica* have been used in conventional medicine and traditional medicine for decades and the studies done yet have authenticated the medical practices. However, more clinical and pathological studies is needed to be conducted to investigate the unexploited potential of the plant.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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