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Review Article

Pharmacological activities of extracts and isolated compounds of *Acalypha Fruticosa* Forssk. (Euphorbiaceae)

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Abstract: *Acalypha fruticosa* Forssk is a shrub belonging to the family Euphorbiaceae. *A. fruticosa* has a wide adaptation through traditional medicinal uses to cure several disorders such as dermatitis, diarrhea, dyspepsia, eye infection, inflammations, and stomachache. This article objects to identify, analyze, and document the reported pharmacological activities of *A. fruticosa*. Electronic databases namely, PubMed, ScienceDirect, Scopus, and Web of Science were employed to identify the related publications from 1900 to August 2021. Compounds such as 1, 2-benzene dicarboxylic acid diisooctyl ester, and eicosyltrichlorosilane were recognized from different parts of this plant species. Until now, only *in vivo* and *in vitro* scientific evidence is available for several pharmacological activities for *A. fruticosa*. Various parts of this plant species have anticancer, antidiabetic, anthelmintic, antibacterial, antileishmanial, and antiplasmodial properties. This work will benefit the investigators on pharmacological and phytochemical investigations of this plant species in the future.

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Anticancer,
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1. INTRODUCTION

Acalypha fruticosa Forrssk is known as a shrub, and it belongs to the Euphorbiaceae family (Figure 1). *A. fruticosa* tends to grow up to 4 m in height, and it is generally a densely branched plant. Further, this plant species is commonly known as Kadukkan (கடுக்கன்) in Tamil, and it is native to Eritrea to South Africa, Myanmar, South India, Sri Lanka, and Yemen. *A. fruticosa* has a wide range of adaptation on ecology from 4 m up to 230 m altitudes (Kewscience, 2021). This plant species is used to treat chest problems, cholera, colds, conjunctivitis, constipation, convulsions, cough, dermatitis, diarrhea, epilepsy, eye infection, fevers, gonorrhea, indigestion, inflammations, rheumatism, scabies, snake bites, sores, stomachache, toothache, and venereal diseases in various traditional medicinal systems

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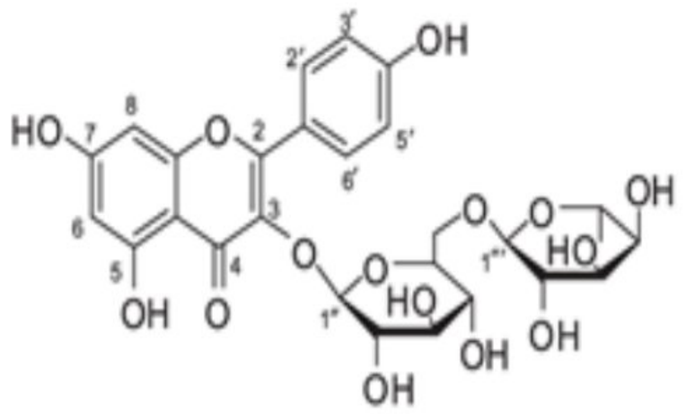
(Ambasta, 1986; Anonymous, 1988; Ruffo *et al*., 2002; Kirtikar & Basu, 2003; Senthilkumar *et al*., 2006; Khare, 2007; Gopalakrishnan *et al.,* 2010; Mothana *et al*., 2010).

The shoot of *A. fruticosa* is utilized to heal the injuries, toothache, and the aerial part is applied to heal cuts, skin infections, and malaria. Similarly, the root of this plant species is employed to cure gonorrhea. In addition, the decoction and infusion prepared using leaf are applied to cure stomach issues and body swellings, eye infections, epilepsy, cough, and chest problem (Gopalakrishnan *et al.,* 2010; Thambiraj & Paulsamy, 2011; Deepa *et al*., 2012; Fawzy *et al*., 2016; Al-Massarani *et al.,* 2019). Compounds such as eicosyltrichlorosilane, 9,12-octadecadienoic acid (Z, Z), acalyphin, α-D-glucopyranoside, apigenin, diisooctyl phthalate, α-humulene, isocaryophyllene, caryophyllene, 5-O-β-D-glucopyranoside, kaempferol 3-orutinoside, 2–methyl–5,7-dihydroxychromone, and n-hexadecenoic acid were isolated from aerial parts of this plant species (Gopalakrishnan *et al.,* 2010; Deepa *et al*., 2012; Fawzy *et al*., 2016) (Figure 2).

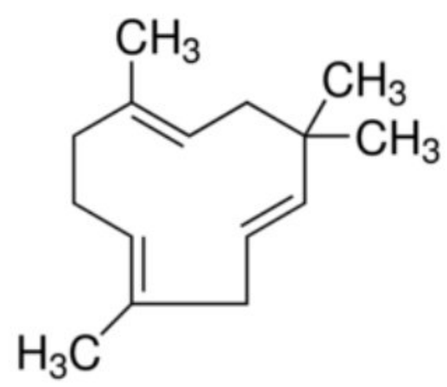
Figure 1. *Acalypha fruticosa* Forssk.

Source: Tropical Plants Database, 2021.
http://tropical.theferns.info/viewtropical.php?id=Acalypha+fruticosa

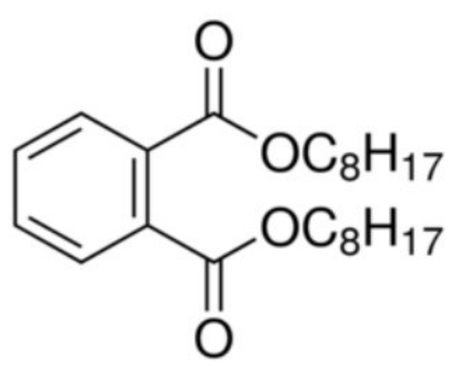
Figure 2. Some of the isolated compounds from *A. fruticosa*.



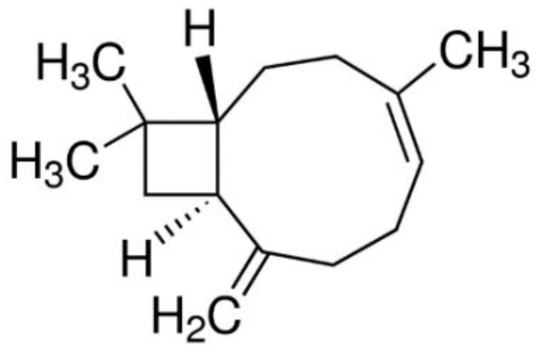
Kaempferol 3-O-rutinoside



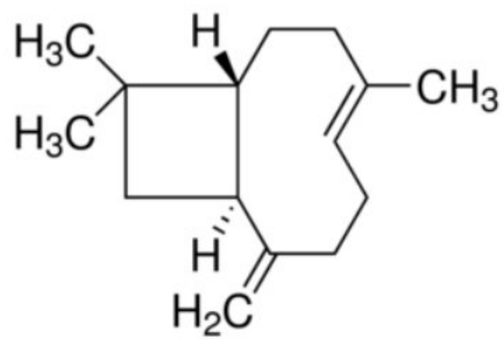
α-humulene



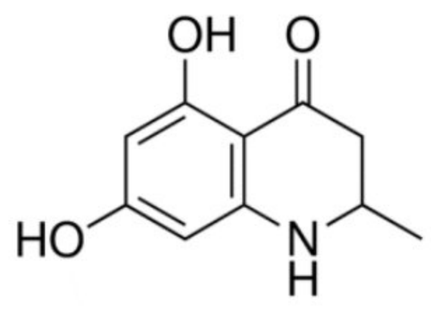
Diisooctyl phthalate



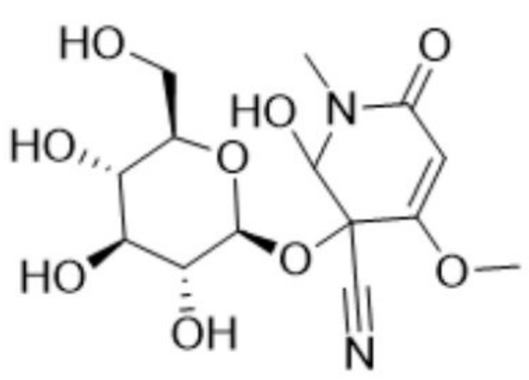
Isocaryophyllene



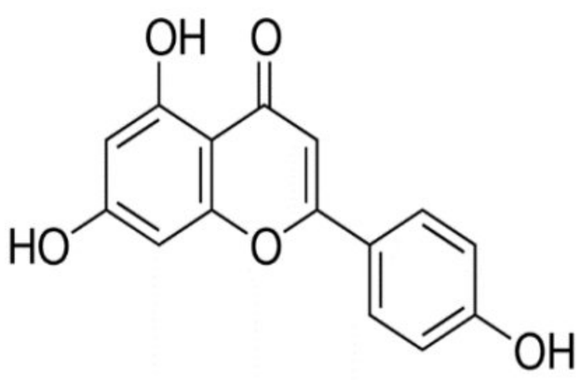
Caryophyllene



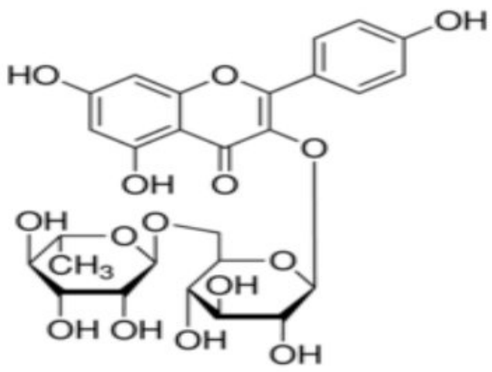
2–methyl–5,7-dihydroxychromone



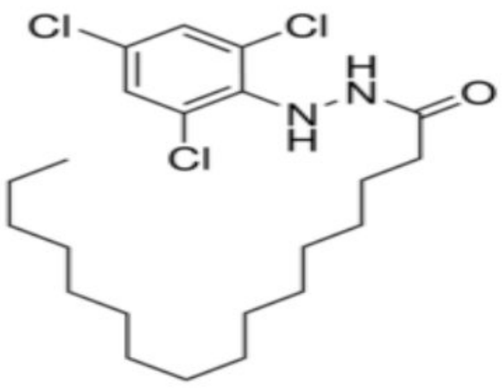
Acalyphin



Apigenin



Kaempferol 3-orutinoside



n-hexadecenoic acid

This systematic review aims to analyze, recap, and document the pharmacological activities of published research studies using various parts of *A. fruticosa*. This review article will be valuable for the researchers who are concerned to perform future pharmacological and phytochemical studies of this plant species.

2. MATERIAL and METHODS

Electronic records (PubMed, ScienceDirect, Scopus, and Web of Science) were utilized to identify the more suitable existing published articles from 1900 to July 2021. The search terms "*Acalypha fruticosa*" and "*Ricinocarpus fruticosus*" were engaged, and accompanied pharmacological properties were considered in this work.

3. RESULTS

3.1. Reported Pharmacological Activities of *A. fruticosa*

Table 1 displays the details on reported pharmacological activity studies (the level of scientific evidence, plant part employed, extract/fraction/compound, assay/model, dose/concentration, and reference). Until now, *in vivo* and *in vitro* scientific evidence is available for several pharmacological activities. Then, *in vitro* studies stand in the lead position amongst these investigations. In addition, various parts of this plant species exhibited anticancer, antidiabetic, antiepileptic, anthelmintic, antibacterial, antifungal, antiinflammatory, antileishmanial, antimalarial, antioxidant, antiplasmodial, and antitrypanosomal activities (Duraipandiyan *et al*.,

2006; Alshawsh *et al*., 2007; Sivakumar *et al*., 2010; Raj *et al*., 2012; Govindu & Adikay, 2014; Mothana, 2014; El-shaibany *et al*., 2015; Fawzy *et al*., 2016; Chellapandian *et al*., 2018; Al-Massarani *et al*., 2019). Among the reported studies, *in vitro* evidence is available for anthelmintic, antibacterial, antifungal, antiinflammatory, antileishmanial, antimalarial, antioxidant, antiplasmodial, and antitrypanosomal activities, while *in vivo* evidence is available for anticancer, antidiabetic, and antiepileptic activities. Furthermore, the greatest number of researches revealed the antibacterial activities of this plant species. Plant parts like aerial, bark, leaf, stem, and whole plant showed different bioactivities, while the leaf was used in a greater number of studies. Extracts of acetone, aqueous, chloroform, ethanol, ethyl acetate, hexane, methanol, and petroleum ether were used to prepare different extracts. Anyway, methanol has been accompanied in the majority of the studies. Until now, four active compounds were isolated, and they were acalyphin, 2–Methyl–5, 7-dihydroxychromone5-O-b-D-glucopyranoside, kaempferol 3-orutinoside and apigenin exhibited antiinflammatory activities (Fawzy *et al*., 2016). At present, traditional medicinal utilizations to heal epilepsy, malaria, pain, and swelling have scientific evidence (Fleurentin & pelt, 1982; Muthukumarasamy *et al*., 2003; Schmelzer, 2007; El-Shaibany *et al*., 2015). On the other hand, there is no scientific evidence for the traditional medicinal uses for the treatments including toothache, diarrhea, snake bites, cough, constipation, rheumatism, and liver disorders. Surprisingly, the same plant parts used in traditional medicine to treat certain illnesses were not employed in the published studies. As a result, using the same plant parts to treat the same illnesses as indicated in traditional medicinal usage is more beneficial. The related studies with the highest levels of scientific evidence with the lowermost concentration/dose applied and bioactive compounds recognized are comprehended beneath.

3.2. Reported *In Vivo* Studies

3.2.1. *Anticancer activity*

The methanol leaf extract showed anticancer activity in Ehrlich's Ascites Carcinoma bearing model was used in this investigation. To study this potent activity, the plant extract was intraperitoneally administered for 14 days to see the effect at the dose of 250 mg/kg. In respect of comparing the effectiveness of the extract with a standard drug, 5-Fluorouracil, was used at a 20 mg/kg dose. In this study, the effect of the extract on the increase in rise in life expectancy, survival period, tumor size, and the amount of viable and non-viable tumor cells were assessed. Thus, the results explored that methanol leaf extract exhibited a significant decrease in tumor cell size and viable tumor cell number, as well as tumor-bearing animals' longevity (Sivakumar *et al*., 2010).

3.2.2. *Antidiabetic activity*

In a study conducted by El-Shaibany *et al.* (2015), the effect of aqueous extract of aerial part of *A. fruticosa* was investigated in reducing serum glucose level. In this study, randomly assigned animals were orally administered the plant extract at the dose of 600 mg/kg. After the administration, the serum glucose level was examined up to 12 hours by a glucose analyzer to study the effect and the results explored that water extract of the plant's aerial portion significantly lowered the fasting blood glucose level and the effects were matched with standard medication, metformin, administered at the dose of 300 mg/kg (El-Shaibany *et al*., 2015).

3.2.3. *Antiepileptic activity*

This research was aimed to reveal the potential antiepileptic property of aerial parts of chloroform extract in mice and in this study, the specified activity of this orally treated plant extract was evaluated at the dose of 300 mg/kg by maximum electroshock, pentylenetetrazol, and isoniazid-induced convulsion *in vivo* assays. The standard drugs, diazepam, and phenobarbitone sodium were administered to an assigned group of animals at different levels

of 3 and 4 mg/kg correspondingly. After the administration, the inactivity of convulsions was registered during the next 2 hours period. The convulsions induced by a dose-dependent electroshock method were potentially protected and exhibited more activity at the stated dose (Govindu *et al*., 2014).

3.3. Reported *In vitro* Studies

3.3.1. *Anthelmintic activity*

Raj *et al.* (2012) studied the possible anthelmintic activity of methanol extract of the whole plant of *A. fruticosa* and an *in vitro* assay using Indian earthworm was designed to investigate this effect. In this investigation, the plant extract at the concentration of 25 mg/kg was used and after the administration, a dose-dependent vermicidal activity was noticed. Results were expressed by the time after the observation made with death and paralysis and the significant results of the plant extract were comparable with the piperazine, a positive control, at the concentration of 10 mg/ml (Raj *et al*., 2012).

3.3.2. *Antibacterial activity*

Altogether, the nine isolated bacterial strains including *Staphylococcus aureus, Escherichia coli, Ervinia* sp, *Enterococcus faecalis, Staphylococcus epidermidis, Pseudomonas aeruginosa, Bacillus subtilis, Proteus vulgaris,* and *Klebsiella pneumonia* were used in this study. A standard disc diffusion method was performed and the extract at 1.25 mg/disc concentration was applied. The antibacterial activity of hexane extract of leaf exhibited the potential growth inhibition activity against the four bacterial strains such *Staphylococcus epidermidis, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Bacillus subtilis*. The positive control employed in this investigation was not mentioned (Duraipandiyan *et al*., 2006).

3.3.3. *Antifungal activity*

The potential antifungal activity of ethanolic leaf extract was studied by Chellappandian *et al.* (2018). In this study, the *Trichophyton rubrum* (CI-1) and (CI-2) *in vitro* assays were used to see the significant effect. To study the ability of inhibition of growth, the plant extract at 125 µg/ml concentration was employed and the effects were compared with standard known fungicide, Fluconazole (35 mg/ml). After the inhibition period, the results showed that the plant extract exhibited selective and promising antifungal activity against the investigated fungal strains (Chellapandian *et al*., 2018).

3.3.4. *Antiinflammatory activity*

In this study, Fawzy *et al.* (2016) isolated four bioactive compounds and subjected the plant extract and compounds into an *in vitro* bioassay to screen the antiinflammatory activity using NF-kB inhibitory assay. The aerial part of *A. fruticosa* was used in this study and methanol was practiced to isolate those bioactive compounds. The results explored that, among the four isolated compounds, acalyphin exhibited promising anti-inflammatory activity with 3.9 µg/ml (IC_{50}). The activity was compared with the positive control, Parthenolide, and the concentration used was not mentioned (Fawzy *et al.*, 2016).

Table 1. Pharmacological properties of *A. fruticose*.

Level of scientific evidence	Bioactivity	Part used	Extract / fraction / compound	Assay / model	Dose / concentration	Reference
In vivo	Anticancer	Leaf	Methanol	Ehrlich's Ascites carcinoma	250 mg/kg	(Sivakumar *et al*., 2010)
In vivo	Antidiabetic	Aerial	Aqueous	Rabbit	600 mg/kg	(El-Shaibany *et al*., 2015)
In vivo	Antiepileptic	Aerial	Chloroform	Maximum electroshock test, Pentylenetetrazole-induced convulsions, Isoniazid-induced convulsions	300 mg/kg	(Govindu *et al*., 2014)
In vitro	Anthelmintic	Whole plant	Methanol	*Pheretima posthuma*	25 mg/ml	(Raj *et al*., 2012)
In vitro	Antibacterial	Bark	Petroleum ether, Ethyl acetate, Methanol	*Pseudomonas aeruginosa, Pseudomonas stutzeri, Escherichia coli, Micrococcus* sp., *Lactobacillus* sp., *Servatia* sp., *Moraxetta* sp., *Bacillus subtilis, Bacillus thuringiensis, Klebsiella pneumoniae*	NS	(Thambiraj & paulsamy, 2011)
In vitro	Antibacterial	Leaf	Acetone	*Staphylococcus aureus, Enterococcus faecalis, Escherichia coli*	NS	(Alasbahi *et al*., 1999)
In vitro	Antibacterial	Leaf	Chloroform, Hexane	*Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa*	NS	(Alasbahi *et al*., 1999)
In vitro	Antibacterial	Leaf	Ethanol	*Staphylococcus aureus*	NS	(Alasbahi *et al*., 1999)
In vitro	Antibacterial	Leaf	Hexane	*Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis*	1.5 mg/disc	(Duraipandian *et al*., 2006)
In vitro	Antibacterial	Leaf	Methanol	*Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis*	5 mg/disc	(Duraipandian *et al*., 2006)
In vitro	Antibacterial	NS	Methanol	*Staphylococcus aureus, Bacillus subtilis, Micrococcus flavus, Staphylococcus epidermidis, Staphylococcus aureus* (multidrug-resistant)	NS	(Mothana *et al*., 2010)

Level of scientific evidence	Bioactivity	Part used	Extract / fraction / compound	Assay / model	Dose / concentration	Reference
In vitro	Anticancer	Aerial	Aqueous fraction [Methanol (85%) extract]	Human cancer cell (HCT-116)	48.6µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Aqueous fraction [Methanol (85%) extract]	Human cancer cell (HepG-2)	77.7 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Aqueous fraction [Methanol (85%) extract]	Human cancer cell (MCF-7)	62.6 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Chloroform fraction [Methanol (85%) extract]	Human cancer cell (HCT-116)	4.81 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Chloroform fraction [Methanol (85%) extract]	Human cancer cell (HepG-2)	5.21 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Chloroform fraction [Methanol (85%) extract]	Human cancer cell (MCF-7)	12.2 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Methanol (85%)	Human cancer cell (HCT-116)	37.6 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Methanol (85%)	Human cancer cell (HepG-2)	73.9 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	Methanol (85%)	Human cancer cell (MCF-7)	84.9µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	n-butanol fraction [Methanol (85%) extract], Ethyl acetate fraction [Methanol (85%) extract]	Human cancer cell (HCT-116)	100 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	n-butanol fraction [Methanol (85%) extract], Ethyl acetate	Human cancer cell (HepG-2)	100 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)

Level of scientific evidence	Bioactivity	Part used	Extract / fraction / compound	Assay / model	Dose / concentration	Reference
			fraction [Methanol (85%) extract]			
In vitro	Anticancer	Aerial	n-butanol fraction [Methanol (85%) extract], Ethyl acetate fraction [Methanol (85%) extract]	Human cancer cell (MCF-7)	100 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	n-Hexane fraction [Methanol (85%) extract]	Human cancer cell (HCT-116)	10.1 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	n-Hexane fraction [Methanol (85%) extract]	Human cancer cell (HepG-2)	15.4 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Aerial	n-Hexane fraction [Methanol (85%) extract]	Human cancer cell (MCF-7)	23.1 µg/ml (IC_{50})	(Al-Massarani *et al*., 2019)
In vitro	Anticancer	Leaf, Stem	Chloroform	Human lung cancer cell (A-427), Human lung cancer cell (LCLC-103H), Human urinary bladder cancer cell (5637), Human urinary bladder cancer cell (RT-112), Human breast cancer cell (MCF-7)	50 µg/ml (IC_{50})	(Mothana *et al.,* 2006*)*
In vitro	Anticancer	Whole plant	Aqueous	Human breast carcinoma cell	630.75 µg/ml (LC_{50})	(Rajkumar *et al*., 2010)
In vitro	Anticancer	Whole plant	Aqueous	Human hepatocellular carcinoma cell	538.30 µg/ml (LC_{50})	(Rajkumar *et al*., 2010)
In vitro	Anticancer	Whole plant	Methanol	Human breast carcinoma cell	212.72 µg/ml (LC_{50})	(Rajkumar *et al*., 2010)
In vitro	Anticancer	Whole plant	Methanol	Human hepatocellular carcinoma cell	322.80 µg/ml (LC_{50})	(Rajkumar *et al*., 2010)
In vitro	Antifungal	Bark	Petroleum ether, Ethyl acetate, Methanol	*Aspergillus niger, Aspergillus flavus, Aspergillus baumannii, Fusarium oxysporum, Fusarium solani, Mucor*	NS	(Thambiraj & Paulsamy 2011)

Level of scientific evidence	Bioactivity	Part used	Extract / fraction / compound	Assay / model	Dose / concentration	Reference
				rouxii, Alternaria alternata, Candida albicans, Cladosporium sp., *Rhizopus* sp.		
In vitro	Antifungal	Leaf	Acetone, Chloroform, Hexane	*Candida albicans*	NS	(Alasbahi *et al*., 1999)
In vitro	Antifungal	Leaf	Ethanol	*Trichophyton mentagrophytes* (CI-1), *Trichophyton simii*, *Trichophyton mentagrophytes* (CI-2)	250 µg/ml	(Chellapandian *et al., 2018)*
In vitro	Antifungal	Leaf	Ethanol	*Trichophyton rubrum* (CI-1), *Trichophyton rubrum* (CI-2)	125 µg/ml	(Chellapandian *et al., 2018)*
In vitro	Antifungal	Leaf	Ethanol	*Trichophyton tonsurans*	1000 µg/ml	(Chellapandian *et al., 2018)*
In vitro	Antifungal	Leaf	Ethyl acetate	*Magnaporthe grisea*	0.25 mg/ml	(Duraipandiyan & Ignacimuthu, 2011)
In vitro	Antifungal	Leaf	Ethyl acetate, Methanol	*Trichophyton rubrum*	1 mg/ml	(Duraipandiyan & Ignacimuthu, 2011)
In vitro	Antifungal	Leaf	Hexane	*Epidermophyton floccosum, Magnaporthe grisea*	1 mg/ml	(Duraipandiyan & Ignacimuthu, 2011)
In vitro	Antifungal	Leaf	Hexane	*Trichophyton mentagrophytes*	0.125 mg/ml	(Duraipandiyan & Ignacimuthu, 2011)
In vitro	Antiinflammatory	Aerial	2-methyl-5,7-dihydroxychromone 5-O-β-d-glucopyranoside	NF-kB inhibitory	29.5 µg/ml (IC_{50})	(Fawzy *et al*., 2016)
In vitro	Antiinflammatory	Aerial	Acalyphin	iNOS inhibitory	15.5 µg/ml (IC_{50})	(Fawzy *et al*., 2016)
In vitro	Antiinflammatory	Aerial	Acalyphin	NF-kB inhibitory	3.9 µg/ml (IC_{50})	(Fawzy *et al*., 2016)
In vitro	Antiinflammatory	Aerial	Apigenin	iNOS inhibitory	50.0 µg/ml (IC_{50})	(Fawzy *et al*., 2016)
In vitro	Antiinflammatory	Aerial	Apigenin	NF-kB inhibitory	17.0 µg/ml (IC_{50})	(Fawzy *et al*., 2016)
In vitro	Antiinflammatory	Aerial	Kaempferol 3-O-rutinoside	NF-kB inhibitory	100 µg/ml (IC_{50})	(Fawzy *et al*., 2016)

Level of scientific evidence	**Bioactivity**	**Part used**	**Extract / fraction / compound**	**Assay / model**	**Dose / concentration**	**Reference**
In vitro	Antileishmanial	Leaf	Methanol	*Leishmania infantum*	64.0 µg/ml (IC_{50})	(Mothana *et al.*, 2014)
In vitro	Antimalarial	Aerial	Aqueous	*Plasmodium falciparum*	1.6 µg/ml (IC_{50})	(Alshawsh. *Et al.*, 2007)
In vitro	Antimalarial	Aerial	Methanol	*Plasmodium falciparum*	10.7 µg/ml (IC_{50})	(Alshawsh. *Et al.*, 2007)
In vitro	Antioxidant	Aerial	Aqueous fraction [Methanol (85%) extract]	DPPH free radical scavenging	84.5 µg/ml (IC_{50})	(Al-Massarani *et al., 2019*)
In vitro	Antioxidant	Aerial	Chloroform fraction [Methanol (85%) extract]	DPPH free radical scavenging	117.6 µg/ml (IC_{50})	(Al-Massarani *et al.*, 2019)
In vitro	Antioxidant	Aerial	Ethyl acetate fraction [Methanol (85%) extract]	DPPH free radical scavenging	14 µg/ml (IC_{50})	(Al-Massarani *et al.*, 2019)
In vitro	Antioxidant	Aerial	Methanol (85%)	DPPH free radical scavenging	75.6 µg/ml (IC_{50})	(Al-Massarani *et al.*, 2019)
In vitro	Antioxidant	Aerial	n-butanol fraction [Methanol (85%) extract]	DPPH free radical scavenging	23 µg/ml (IC_{50})	(Al-Massarani *et al.*, 2019)
In vitro	Antioxidant	Aerial	n-Hexane fraction [Methanol (85%) extract]	DPPH free radical scavenging	138.9 µg/ml (IC_{50})	(Al-Massarani *et al.*, 2019)
In vitro	Antioxidant	Leaf	Methanol	DPPH free radical scavenging	92 µg/ml (IC_{50})	(Thambiraj *et al*., 2012)
In vitro	Antioxidant	Leaf	Methanol	Hydroxyl radical scavenging	290 µg/ml (IC_{50})	(Thambiraj *et al*., 2012)
In vitro	Antioxidant	Leaf	Methanol	Metal chelating	287 µg/ml (IC_{50})	(Thambiraj *et al*., 2012)
In vitro	Antioxidant	NS	Methanol	DPPH free radical scavenging	70 µg/ml (IC_{50})	(Mothana *et al*., 2010)
In vitro	Antioxidant	Whole plant	Aqueous, Methanol	DPPH free radical scavenging	500 µg	(Rajkumar *et al.*, 2010)
In vitro	Antioxidant	Whole plant	Aqueous, Methanol	Ferric reducing antioxidant property	200 µg	(Rajkumar *et al.*, 2010)
In vitro	Antioxidant	Whole plant	Aqueous, Methanol	Thiobarbituric acid, Hydroxyl radical scavenging	100 µg	(Rajkumar *et al.*, 2010)

Level of scientific evidence	**Bioactivity**	**Part used**	**Extract / fraction / compound**	**Assay / model**	**Dose / concentration**	**Reference**
In vitro	Antiplasmodial	Leaf	Methanol	Chloroquine-resistant *Plasmodium falciparum*	27.1 µg/ml (IC_{50})	(Mothana *et al*., 2014)
In vitro	Antitrypanosomal	Leaf	Methanol	*Trypanosoma brucei*	32.9 µg/ml (IC_{50})	(Mothana *et al*., 2014)
In vitro	Antitrypanosomal	Leaf	Methanol	*Trypanosoma cruzi*	35.7 µg/ml (IC_{50})	(Mothana *et al*., 2014)

Abbreviations:
NS: Not Stated; IC_{50}: The half-maximal inhibitory concentration; LC_{50}: Median lethal dose; DPPH: 2,2-diphenyl-1-picrylhydrazyl; iNOS: Inducible nitric oxide synthase; NF-κB: Nuclear Factor - κ-light-chain-enhancer of activated B cell.

3.3.5. *Antileishmanial activity*

In a study conducted by Mothana *et al.* (2014), the methanol leaf extract was prepared to investigate the potential antileishmanial activity. The *Leishmania infantum* was collected from the spleen of an infected hamster and used to infect the primary macrophages. In this study, Miltefosine was used as the reference standard to compare the effect of methanolic plant extract (64 µg/ml), but the concentration of positive control used was not mentioned. The investigators microscopically assessed the Intracellular amastigotes burdens and stated as a percentage of the burdens. Results supported that the plant extract exhibited promising stated activity (Mothana *et al*., 2014).

3.3.6. *Antimalarial activity*

An *in vitro* duplicate assay using *Plasmodium falciparum* was performed by Alshawsh *et al.* (2007) to study the antimalarial activity of aqueous leaf extract of *A. fruticosa.* The plant crude extract at the concentration of 1.6 µg/ml (IC_{50}) was administered to see the effect. The chloroquine phosphate was selected as positive control and the concentration used was not mentioned in this study. This work represented the first investigation of the antimalarial property of *A. fruticosa* and supported its therapeutic potential use as an antimalarial agent in traditional medicine (Alshawsh *et al*., 2007).

3.3.7. *Antioxidant activity*

This study was aimed by Al-Massarani *et al.* (2019) to study the significant property of *A. fruticosa* as an antioxidant agent. The methanolic aerial plant extract was prepared by cold maceration method and subjected to fraction by ethyl acetate and used in this investigation. The plant extract at 14 µg/ml (IC_{50}) was used and the scavenging activity was compared with standard ascorbic acid (5 mg/ml). The 2,2-diphenyl-1-picrylhydrazyl free radical scavenging activity was used for the different fractions and absorbance was measured after 30 min intervals. A significant dose-dependent inhibition scavenging activity was observed against the DPPH radicals (Al-Massarani *et al*., 2019).

3.3.8. *Antiplasmodial activity*

Mothana *et al.* (2014) used the leaf extract of *A. fruticosa* to support its traditional use as an antiplasmodial agent. In this evaluation, methanol leaf extract was used to study the effect using the chloroquine-resistant *Plasmodium falciparum in vitro* assay. The plant extract at the concentration of 27.1 µg/ml (IC_{50}) exhibited an interesting activity against the selected assay. Chloroquine was applied as the reference standard in this study and the concentration used was not mentioned (Mothana *et al*., 2014).

3.3.9. *Antitrypanosomal activity*

The potential antitrypanosomal activity was investigated against the *Trypanosoma brucei* strain in a study conducted by Mothana *et al.* (2014). In this investigation, methanol leaf extract was prepared and applied at 32.9 µg/ml (IC_{50}) concentration to study the activity. The Suramin was applied as a reference standard to compare the effect of plant extract whereas the concentration of positive control used was not mentioned by the authors. The parasite growth was assessed by measuring the absorbance value and the potential *in vitro* antitrypanosomal activity of plant extract was supported by inhibition of proliferation of parasites (Mothana *et al*., 2014).

4. CONCLUSION

The available scientific evidence for traditional medicinal uses of *A. fruticosa* represents a valuable contribution to the phytotherapy of this plant. However, only limited evidence is available to support the wide uses of this plant species in traditional medicinal uses. Through this systematic review, it is proposed to carry out more research activities related to the

pharmacological properties of *A. fruticosa* employing *in vitro, in vivo,* and clinical studies. Furthermore, only a few pharmacologically active compounds were only isolated and proved their capability. There is a huge potential in the isolation and characterization of compounds that have biological properties. These compounds would be used as key elements in modern medical industries in the future. This review investigated, briefed, and documented the reported pharmacological properties of *A. fruticosa*.

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Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

Authorship Contribution Statement

Author 1: Investigation, Resources, and Writing- original draft. **Author 2**: Methodology, Supervision, and Validation. **Author 3**: Original draft, and Formal Analysis.

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