JOURNAL OF AMASYA UNIVERSITY THE INSTITUTE OF SCIENCES AND TECHNOLOGY (JAUIST)

BIOACTIVITIES OF ISOLATED PHYTOCHEMICAL CONSTITUENTS AND EXTRACTS OF *Crateva adansonii.*

Vinujan Shanmugalingam[1], Saravanan Vivekanandarajah (✉)[2,3], [4]Pholtan Rajamanoharan[4]

[1]Palmyra Research Institute, Jaffna 40000, Sri Lanka
[2]KnowledgeLink Group, Inc., Waltham, MA 02451, USA
[3]Poigai Institute, Batticaloa 30000, Sri Lanka
[4]Provincial Herbal Garden Management Center, Trincomalee 31000, Sri Lanka

[1]ORCID: 0000-0002-9208-4090
[2,3]ORCID: 0000-0002-5938-0509
[4]ORCID: 0000-0001-9341-5843

A Review Article
Received: 11.06.2021/Accepted: 29.06.2021
(✉) Corresponding author: vivekanandarajahs@yahoo.co.uk

ABSTRACT

Crateva adansonii DC. is a tree belonging to the Capparaceae family. In traditional medicine, it is used to cure several disorders including constipation, earache, fevers, itch, malaria, rheumatic pains, and snakebites. Furthermore, phytochemicals including daucosterol, phytol, pyropheophorbide A, suramin, and ψ-taraxasterol have been isolated from different parts of *C. adansonii.* This review paper objects to scrutinize, recap, and document the reported bioactivity studies of *C. adansonii*. ScienceDirect, Web of Science, Semantic Scholar, Scopus, and PubMed were utilized to detect the applicable published works from 1900 to June 2021. Up to now, *in vivo* and *in vitro* scientific evidence is available for various bioactivities. In addition, analgesic, antiarthritic, antibacterial, anticancer, antifungal, antiinflammatory, antimalarial, antioxidant, and antiprotozoal activities have been observed for various parts of this plant. This work supports a detail information related to this plant for further studies in the future.

Keywords: Capparaceae, *Crateva adansonii.*, Ethnobotany, Siddha Medicine, Sri Lanka.

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ÖZET

Crateva adansonii DC. Capparaceae familyasına ait bir ağaçtır. Geleneksel tıpta kabızlık, kulak ağrısı, ateş, kaşıntı, sıtma, romatizmal ağrılar ve yılan sokması gibi çeşitli rahatsızlıkları tedavi etmek için kullanılır. Ayrıca, daukosterol, fitol, pirofeoforbit A, suramin ve ψ-taraksasterol gibi fitokimyasallar *C. adansonii*'nin farklı kısımlarından izole edilmiştir. Bu inceleme makalesi, *C. adansonii*'nin yapılan biyoaktivite çalışmalarını incelemeyi, özetlemeyi ve belgelemeyi amaçlamaktadır. 1900'den Haziran 2021'e kadar yayınlanmış çalışmaları tespit etmek için ScienceDirect, Web of Science, Semantic Scholar, Scopus ve PubMed kullanıldı. Şimdiye kadar çeşitli biyoaktiviteler için *in vivo* ve *in vitro* bilimsel kanıtlar mevcuttur. Ayrıca bu bitkinin çeşitli kısımlarında analjezik, antiartritik, antibakteriyel, antikanser, antifungal, antiinflamatuar, antimalaryal, antioksidan ve antiprotozoal aktiviteleri gözlemlenmiştir. Bu çalışma, gelecekte yapılacak çalışmalar için bu bitki ile ilgili ayrıntılı bir bilgiyi sağlamaktadır.

Anahtar Kelimeler: Capparaceae, *Crateva adansonii.*, Etnobotanik, Siddha Tıbbı, Sri Lanka.

1. INTRODUCTION

Crateva adansonii DC. [synonyms: *Crateva guineensis* Schumach. & Thonn. and *Crateva laeta* DC.; Accepted infraspecific: *Crateva adansonii* subsp. odora (Buch. -Ham.) Jacobs] is a tree (6 to 15 m tall) belonging to *Capparaceae* family. *C. adansonii* is also called மாவிலங்கு (Maavilangu) in Tamil. This plant species is native to Asia (Sri Lanka and India) and Africa (Benin, Zaïre, Burkina, Zambia, Cameroon, Uganda, Chad, Tanzania, Eritrea, Sudan, Ethiopia, Senegal, Gambia, Rwanda, Ghana, Nigeria, Guinea, Niger, Mali, Guinea-Bissau, Mauritania, Ivory Coast, and Kenya) (Kew Science, 2021). Furthermore, *C. adansonii* is widely used to heal several disorders including asthma, constipation, diabetes, earache, epilepsy, fevers, headache, inflammations, itch, jaundice, malaria, rheumatic pains, snakebites, swellings, syphilis, toothache, urinary tract, bladder, and skin disorders, and eye and ear infections in traditional medicines globally (Sivarajan & Balachandran, 1994; Gitte et al., 2012; Temitope & Felix, 2010; Burkill, 1985; Ogunwade et al., 2009; Sathasivampillai et al., 2015, 2016, 2017, 2018). Phytochemicals including 17-pentatriacontene; 2,6,10-trimethyl tetradecane; 6,10,14-trimethyl-2-pentadecanone; aurantiamide acetate; daucosterol; erucic acid; ethyl pyropheophorbide A; heptacosane; hexatriacontane; lupanol; lupenone; lupeol; nonacosane; oleanolic acid; pentadecane; phytol; purpurin-18 ethyl ester; pyropheophorbide A; suramin; tetratriacontane; γ-sitosterol; and ψ-taraxasterol have been isolated from different parts of *C. adansonii* (Igoli et al., 2014; Nguedia et al., 2020; Michel et al., 2016; Pervaiz et al., 2019).

This review paper objects to scrutinize, recap, and document the reported bioactivity studies of *C. adansonii*. For this purpose, ScienceDirect, Web of Science, Semantic Scholar, Scopus, and PubMed were utilized to detect the applicable published works from 1900 to June 2021. Search terms ("*Crateva adansonii*", "*Crateva guineensis",* and "*Crateva laeta")* were applied and only bioactivities connected to published works were taken into account in this work.

2. REPORTED BIOACTIVITIES of *C. adansonii*

The details of reported studies of bioactivities including the level of scientific evidence, part used, extract/fraction/compound, assay/model, dose/concentration, and reference were shown in Table 1. Up to now, *in vivo* and *in vitro* scientific evidence are available for various bioactivities but *in vitro* studies lead in position among these investigations. In addition, analgesic, antiarthritic, antibacterial, anticancer, antifungal, antiinflammatory, antimalarial, antioxidant, and antiprotozoal

activities have been observed for various parts of this plant species (Udeh & Onoja, 2015; Rathinavel et al., 2021; Abdullahi et al., 2012; Ahama-Esseh et al., 2017; Agboke Ayodeji et al., 2011; Nguedia et al., 2020; Zingue et al., 2016, 2018, 2020; Thirumalaisamy et al., 2020; Tsado et al., 2020; Michel et al., 2016; Igoli et al., 2014). There is *in vivo* scientific evidence for analgesic and antimalarial activities, whereas there is *in vitro* scientific evidence for antiarthritic, antibacterial, antifungal, and antiprotozoal activities. Anticancer, antiinflammatory, and antioxidant activities have both *in vitro* and *in vivo* scientific evidence. Moreover, antioxidant activity has been identified in a higher number of studies. Leaf and bark exhibited different bioactivities, while, leaves were employed in a higher number of studies. Acetone, aqueous, chloroform, dichloromethane, ethanol, ethyl acetate, hexane, methanol, and petroleum ether extracts were utilized to study the various bioactivities of this plant species. Well, methanol was used in the highest number of studies. Up to now, only two bioactive compounds have been isolated from *C. adansonii*. Daucosterol isolated from bark showed anticancer activities and lupeol isolated from leaves showed antioxidant activities (Michel et al., 2016; Thirumalaisamy et al., 2020; Zingue et al., 2019; Nguedia et al., 2020). At present, traditional medicinal utilization to cure disorders including malaria, swellings, rheumatic pains, and inflammations have scientific evidence (Zingue et al., 2020; Rathinavel et al., 2021; Udeh & Onoja, 2015). On the other hand, traditional medicinal using to cure asthma, diabetes, fevers, snakebites, and urinary tract disorders have no scientific evidence at the moment. Only remarkable studies with the highest level of scientific evidence available, the lowermost concentration/dose used, and bioactive compounds identified are detailed underneath.

2.1 *Reported in vivo studies*

2.1.1 *Analgesic activity*

The methanol bark extract was used to investigate the analgesic property of *C. adansonii* using the acetic acid-induced writhing inhibition method. The extract orally administered (100 mg/kg) produced a significant effect in the reduction in the number of writhing in treated rats. In this study, aspirin was used as a standard drug at a dose of 100 mg/kg (Udeh & Onoja, 2015).

In another study, the lupeol fraction from leaf extract was again orally administered to rats and the acid-induced writhing inhibition method was analyzed. The results revealed that a there was a significant analgesic activity was observed with the reduced writhing count. Pentazocine (10 mg/kg) was used as a standard drug (Rathinavel et al., 2021).

Table 1. Reported bioactivities of *C. adansonii*

Level of scientific evidence	Bioactivity	Part used	Extract / Fraction / compound	Assay / Model	Dose / Concentration	Reference
In vivo	Analgesic	Bark	Methanol	Acetic acid-induced writhing inhibition method	100 mg/kg	(Udeh and Onoja., 2015)
In vivo	Analgesic	Leaf	Lupeol fraction	Acetic acid-induced writhing inhibition method	100 mg/kg	(Rathinavel et al., 2021)
In vivo	Anticancer	Bark	Daucosterol	DMBA-induced breast tumor	2.5 mg/kg	(Nguedia et al., 2020)
In vivo	Anticancer	Bark	Dichloromethane: Methanol (1:1)	DMBA-induced breast tumor	75 mg/kg	(Zingue et al., 2018)
In vivo	Antiinflammatory	Leaf	Lupeol fraction	Carrageenan-induced rat paw edema, Cotton pellet-induced granuloma	100 mg/kg	(Rathinavel et al., 2021)
In vivo	Antiinflammatory	Leaf	Methanol, Chloroform	Carrageenan-induced rat paw edema, Cotton pellet-induced granuloma	200 mg/kg	(Rathinavel et al., 2021)
In vivo	Antimalarial	Leaf	Hexane, Ethyl acetate, Methanol	Mouse	600 mg/kg	(Tsado et al., 2020)
In vivo	Antioxidant	Leaf	Lupeol	Mouse	15 mg/kg	(Michel et al., 2016)
In vitro	Antiarthritic	Leaf	Methanol (70 %)	Xanthine oxidase inhibitory	5 µg/ml	(Abdullahi et al., 2012)
In vitro	Antibacterial	Leaf	Acetone, Ethyl acetate, Petroleum ether, Aqueous, Methanol, Ethanol	*Staphylococcus aureus*	100 µg/ml	(Ahama-Esseh et al., 2017)

In vitro	Antibacterial	Leaf	Methanol	*Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Bacillus subtilis*	50 mg/ml	(Agboke Ayodeji et al., 2011)
In vitro	Anticancer	Bark	Daucosterol	Human prostate cancer cell	1 µg/ml	(Zingue et al., 2018)
In vitro	Anticancer	Bark	Dichloromethane: Methanol (1:1)	Human breast cancer cell	75 mg/kg	(Zingue et al., 2016)
In vitro	Antifungal	Leaf	Methanol	*Aspergillus niger*, *Candida albicans*	50 mg/ml	(Agboke Ayodeji et al., 2011)
In vitro	Antiinflammatory	Leaf	Acetone, Ethyl acetate, Petroleum ether, Aqueous, Methanol, Ethanol	Human epidermis keratinocyte cell	5 µg/ml	(Ahama-Esseh et al., 2017)
In vitro	Antiinflammatory	Leaf	Lupeol, Methanol, Chloroform	Albumin denaturation inhibitory	NS	(Thirumalaisamy et al., 2020)
In vitro	Antiinflammatory	Leaf	Lupeol, Methanol, Chloroform	Antilipoxygenase, Protease inhibitory	NS	(Thirumalaisamy et al., 2020)
In vitro	Antiinflammatory	Leaf	Lupeol, Methanol, Chloroform	Membrane stabilization	125 µg/ml	(Thirumalaisamy et al., 2020)
In vitro	Antioxidant	Bark	Methanol	DPPH radical scavenging	25 µg/ml	(Udeh and Onoja, 2015)
In vitro	Antioxidant	Leaf	Acetone, Ethyl acetate, Petroleum ether, Aqueous, Methanol, Ethanol	DPPH radical scavenging	0.1 mg/ml	(Ahama-Esseh et al., 2017)
In vitro	Antioxidant	Leaf	Aqueous, Methanol, Petroleum ether	DPPH radical scavenging	10 µg/ml	(Thirumalaisamy et al., 2018)

In vitro	Antioxidant	Leaf	Lupeol	ABTS radical scavenging, Antilipid peroxidation scavenging, DPPH radical scavenging, FRAP, H2O2 scavenging, Hydroxyl radical scavenging, Superoxide radical scavenging, β-Carotene bleaching	25 µg/ml	(Michel et al., 2016)
In vitro	Antiprotozoal	Leaf	Hexane, Ethyl acetate	*Trypanosoma brucei*	10 mg/ml	(Igoli et al., 2014)

Abbreviations:

NS: Not stated; DPPH: 2,2-diphenyl-1-picrylhydrazyl; FRAP: Ferric Reducing Antioxidant Power; H_2O_2: Hydrogen peroxide; BHT: Butylated hydroxytoluene; DMBA: 7,12 dimethylbenz(a)anththracene; ABTS: 2,2-Azinobis (3-ethyl-benzothiozoline-6-sulfonic acid)

2.1.2 *Anticancer activity and antiinflammatory activities*

In an investigation conducted by Nguedia et al. (2020), daucosterol (isolated from bark) was orally administered to the animals have DMBA-induced breast tumors. The results showed that there was a reduction in tumor volume at a dose of 2.5 mg/kg. Doxorubicin (5 mg/kg) was employed as a standard drug in this study (Nguedia et al., 2020).

Rathinavel et al. (2021) studied the antiinflammatory activity of lupeol fraction of leaf using carrageenan-induced rat paw edema and cotton pellet-induced granuloma models at a dose of 100 mg/kg. The lupeol fraction acted as a promising antiinflammatory agent and exhibited significant inhibition of rat paw edema at time intervals measured (Rathinavel et al., 2021).

2.1.3 *Antioxidant and antimalarial activities*

Michel et al. (2016) exhibited the antioxidant activity of lupeol (15 mg/kg) isolated from leaves in mice. The outcomes revealed that the fraction may act preventing reactive radicals from damaging. The authors did not mention the standard drug used in this study (Michel et al., 2016).

Leaf extracts prepared using hexane, ethyl acetate, and methanol solvents were utilized to study the antimalarial activity. The extracts were orally administered at a dose of 600 mg/kg to mice. The extracts significantly inhibited the parasite and chloroquine was used as a standard drug in this study (Tsado et al., 2020).

2.2 *Reported in vitro studies*

2.2.1 *Antiarthritic activity*

Methanol extract of the leaf at a concentration of 5 µg/ml showed promising xanthine oxidase inhibitory activity and the results were compared with allopurinol (positive control) at a concentration of 5 µg/ml (Abdullahi et al., 2012).

2.2.2 *Antibacterial and antifungal activities*

Leaf extracts (100 µg/ml) obtaining from acetone, ethyl acetate, petroleum ether, aqueous, methanol, and ethanol solutions exhibited significant antibacterial activity against *Staphylococcus aureus*. However, the authors did not mention the positive control and its concentration used in this study (Ahama-Esseh et al., 2017).

Agboke Ayodeji et al. (2011) investigated the antifungal activity of methanol leaf extract. They used the agar dilution method to study the antifungal activities against *Aspergillus niger* and *Candida albicans* at a 50 mg/ml concentration. The results revealed that the extract has exhibited promising antifungal activities compared with the positive control (Nystatin). The authors did not state the concentration of the positive control used in this study (Agboke Ayodeji et al., 2011).

2.2.3 *Antiprotozoal activity and toxicity study*

Hexane and ethyl acetate extracts of the leaf (10mg/ml) unveiled possible antiprotozoal activity against *Trypanosoma brucei*. The results revealed that the extract has a strong antiprotozoal activity and it was compared with suramin (10 µM) (Igoli et al., 2014).

Methanol and chloroform extracts of leaf were orally administered to rats at a dose of 2000 mg/kg. It was observed that there was no behavioral change and mortality (Rathinavel et al., 2021). Hence, this study shows that up to 2000 mg/kg dose of methanol and chloroform extracts of the leaf is safe.

3. CONCLUSION

Only two parts of this plant have been investigated for various bioactivities and it has huge potential to be explored as a significant source in traditional medicinal uses. Clinical studies should be designed to make sure the better use of different extracts of this plant species. These extracts need to be scientifically evidenced by academics from different disciplines. It will be valuable to isolate the bioactive compounds responsible for different bioactivities from *C. adansonii*. This work supports put a basis for further studies associated with this plant species in the future. This work scrutinized, recapped, and documented the pieces of scientific evidence for bioactivities from published articles of *C. adansonii*.

Conflicts of interest

The authors declare that there are no potential conflicts of interest relevant to this article.

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