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Cosmos Caudatus Kunth: A Traditional Medicinal Herb

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Abstract: *Cosmos caudatus* Kunth is an herb commonly known for its beneficial effects on human health. Nowadays, its popularity is growing in many countries, especially Malaysia, where the use of this herb to treat maladies has recently been increasing. Since its discovery decades ago, *C. caudatus* has been spread to many countries over the world indicating that it has beneficial attributes. Despite this, *C. caudatus* is only being used in traditional and alternative medicine to date. The aim of this review is to summarize the current state of knowledge about this plant, give the reader basic information about this herb as well as phytochemical, ethnobotanical and pharmacological information in order to evaluate its potential.

Key words: Alternative medicine · *Cosmos caudatus* · Biological Activity · Pharmacology

INTRODUCTION

Plants have always been one of the sources of traditional medicine and traditional practices involving plants have been known for centuries all over the world for treatment of various human diseases [1-2]. The healthcare market in Malaysia is full of natural and plant derived medicaments and some of them are used as traditional folk remedies to treat diseases such as high blood pressure, diabetes, arthritis and fever, as well as being used as health tonic [3-5]. A wide variety of biologically active phytochemical constituents has been recently discovered in many of these plants which justifies their traditional use [6-10]. One of these useful plants is *Cosmos caudatus* Kunth.

Cosmos caudatus Kunth *(Asteraceae)* is commonly known as Ulam Raja ("King's Salad") in Malaysia. Traditionally, it is one of the most popular medicinal herbs used to treat human diseases [11-15]. Its appealing smell and unique aroma and taste add diversity to food and the herb is normally eaten raw. It can also be used as a food flavouring agent and as an additive in traditional medicine concoctions. Furthermore, some medicinal and nutritional studies have proven that *C. caudatus* is a rich source of bioactive compounds including flavonoids, carbohydrates, phenolics, minerals, protein and vitamins, increasing its nutritional value [13, 14, 16]. To our knowledge there is no summarized review describing the attributes of this magnificent plant; the goal of this review is to describe the botanical, phytochemical, pharmacological and toxicological properties of this herb.

Botany:

Botanical Names: *Cosmos caudatus* Kunth.

Synonyms: *Bidens artemisiifolia* subsp. *caudata* (Kunth) Kuntze, *Bidens berteriana* Spreng., *Bidens carnea* Heer, *Bidens caudata* (Kunth) Sch.Bip., *Cosmea caudata* (Kunth) Spreng., *Cosmos caudatus* var. *caudatus*, *Cosmos caudatus* var. *exaristatus* Sherff.

Botanical Description and Distribution: *Cosmos caudatus* is a plant usually 30 to 250 cm tall, erect, annual to short-lived perennial. The stem is green and sometimes partially purple in colour with the plant's upper part much more branched in comparison to the lower. Leaves of *C. caudatus* have petioles 1-7 cm, ultimate lobes 2-10 mm with blades of 10-20 cm (Figure 1). These are usually

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Fig 1: *Cosmos caudatus* Kunth.

Table 1: Metabolites identified in *Cosmos caudatus* Kunth.

Plant Part	Compound	Class	References
Whole Plant	(E)-Ocimene	Monoterpenes	[24]
	2,6-Dimethyl-1,3,5,7-octatetraene	Monoterpenes	[24]
	α-Copaene	Sesquiterpenes	[24]
	ß-Elemene	Sesquiterpenes	[24]
	Caryophyllene	Sesquiterpenes	[24]
	α-Humulene	Sesquiterpenes	[24]
	?-Muurolene	Sesquiterpenes	[24]
	?-Cadinene	Sesquiterpenes	[24]
	Bergamotene	Sesquiterpenes	[24]
	ß-Selinene	Sesquiterpenes	[24]
	Bicyclogermacrene	Sesquiterpenes	[24]
	α-Farnesene	Sesquiterpenes	[24]
	ä-Cadinene	Sesquiterpenes	[24]
	Butanedioic acid, methyl- bis(1-methylpropyl) ester	Sesquiterpenes	[24]
	(-)-Spathulenol	Sesquiterpenes	[24]
	Caryophyllene oxide	Sesquiterpenes	[24]
	α-Muurolol	Sesquiterpenes	[24]
	α-Cadinol	Sesquiterpenes	[24]
	Phytol	Diterpenes	[24]
	Quercetin	Flavonoids	[14, 20, 21, 23, 29]
	Luteolin	Flavonoids	[20, 29]
	Naringenin	Flavonoids	[20]
	Quercetin 3-O-β-arabinofuranoside	Flavonoids	[14, 21]
	Quercetin 3-O-α-rhamnoside	Flavonoids	[14, 21]
	Quercetin 3-O-β-glucoside	Flavonoids	[14, 21]
	Rutin	Flavonoids	[11, 14, 21]
	β-glucose	Carbohydrates	[21]
	α-glucose	Carbohydrates	[21]
	Sucrose	Carbohydrates	[21]
	Catechin	Flavonoids	[20, 21]
	Formic acid	Amines	[21]

Table 1: Continue

Plant Part	Compound	Class	References
	Choline	Quaternary Ammonium Salts	[21]
	Alanine	Carboxylic Acids	[21]
	Valine	Carboxylic Acids	[21]
	Kaempferol	Flavonoids	[20, 23, 29]
	Epicatechin	Flavonoids	[20]
	Myricetin	Flavonoids	[11, 20, 29]
	Quercitrin	Flavonoids	[11]
	Apigenin	Flavonoids	[29]
Leaves	Catechin	Flavonoids	[19]
	Chlorogenic Acid	Phenolic Acids	[19, 23]
	Neochlorogenic Acid	Phenolic Acids	[19]
	Cryptochlorogenic Acid	Phenolic Acids	[19]
	Caffeic Acid	Phenolic Acids	[23]
	Ferulic Acid	Phenolic Acids	[23]
	Quercetin 3-O-glucoside	Flavonoids	[19]
	Quercetin pentose	Flavonoids	[19]
	Quercetin deoxyl-hexose	Flavonoids	[19]
Roots	Z-coniferyl alcohol-3'-acetyl-4-*iso*butyrate	Phenylpropane	[25]
	1',2'-dihydroxy-coniferyl alcohol-3'-*iso*butyryl-4-*iso*butyrate	Phenylpropane	[25]
	1'-acetoxy-eugenol-4-*iso*butyrate	Phenylpropane	[25]
	1',2'-epoxy-Z-coniferyi alcohol-3'-(2-methylbutyryl)-4-isobutyrate	Phenylpropane	[25]
	1',2'-epoxy-Z-coniferyl alcohol-3'-acetyl-4-*iso*butyrate	Phenylpropane	[25]
	1',2'-epoxy-Z-coniferyl alcohol-3'-*iso*butyryi-4-*iso*butyrate	Phenylpropane	[25]

arranged in an opposite formation, 2 to 4 pinnate or pinnatipartite, triangular-ovate in outline, coloured dark green above and light green below with tiny hairs. Leaf segments are oblong-lance shaped and measure 1-5 cm x 1-8 mm. The peduncle is 10 to 30 cm. Flowers are 8 ray, sterile; their ligules are linear lance-shaped and measure 1- 1.5 cm x 0.5 cm and are usually violet or reddish, sometimes white or yellow. Tubular flowers are approximately 1 cm long, numerous, yellowish green and bisexual. Fruit of *C. caudatus* is single-seeded, 1-3 cm long, black in colour with a beak ending containing 2-3 unequal awns. It is also 4-angular and linear-spindle-shaped [17].

The plant is native to North America and since its discovery several decades ago it has spread to many parts of the world including subtropical and tropical countries [17].

Ethnobotanical Uses: All parts of *C. caudatus* are used for medicinal purposes. The extracts of this herb have been suggested to be helpful for decreased bone mineral density, blood circulation improvement and also for decreasing high blood pressure (Especially in Eastern Java) [18]. Additionally, salad made of raw stems and leaves of *C. caudatus* is traditionally eaten by Malays to improve and cure ailments such as infectious diseases and as an anti-ageing agent [19].

Phytochemistry: *C. caudatus* is reported to contain a variety of chemicals and possess strong antioxidant activity [20], with over twenty antioxidants discovered to be present in this herb. The major antioxidants belong to a number of proanthocyanidins which, as dimers, exist through numerous compounds such as crypto-chlorogenic acid [19].

In order to distinguish between variations among *C. caudatus* materials processed with a variety of drying techniques, proton nuclear magnetic resonance (1H-NMR) combined with partial least-squares analysis (PLS) and principal component analysis (PCA) was applied [21, 22]. The results discovered β- and α-glucose, catechin, rutin, chlorogenic acid, quercetin, quercetin 3-O-rhamnoside, quercetin 3-O-β-glucoside and quercetin 3-O-β-arabinofuranoside compounds. Furthermore, flavonols, flavones, anthocyanins, phenolic acids, total phenols, ascorbic acid, b-carotene and protein were quantified in *C. caudatus* by Andarwulan *et al.* [23].

Gas chromatography mass spectrometry (GC-MS) was used to analyse essential oils in *C. caudatus*. The study identified 19 of volatile compounds, with α-cadinene as a major volatile haydrocarbon [24]. Additionally, using the roots of *C. caudatus*, one hydroxyeugenol and five coniferyl alcohol derivatives were isolated [25]. The compounds identified in *C. caudatus* are summarized in Table 1.

Pharmacological Reports

Anti-bacteria Activity: An experiment conducted by Rasdi *et al.* [15] aimed to investigate crude n-hexane, diethyl ether (Et_2O), ethanol (EtOh) and phosphate buffered saline (PBS) extracts for their antimicrobial activity against five microbial strains with two Gram positive bacteria. These included *Staphylococcus aureus*, *Bacillus subtilis* and two Gram negative bacteria: *Escerichia coli* and *Pseudomonas aeruginosa* by the disc diffusion method. Using antimicrobial screening, an inhibition by the n-hexane, ethanol extracts and diethyl ether was observed against all of the tested microbes, though the PBS extract was not active for *Bacillus subtilis* nor *Staphylococcus aureus*. According to Lee and Vairappan [24], ethanol extract of *C. caudatus* was found to be active against several strains of human pathogenic bacteria. The tested bacteria were as follows: *Salmonella* sp, *Proteus mirabilis*, *Salmonella typhimurium*, *Listeria monocytogenes*, *Staphylococcus aureus* and *Vibrio cholera*. It can be concluded from all of these findings that *C. caudatus* has an antibacterial potential against the tested microorganisms. The studies also suggest that this herb may be a potential antimicrobial agent and could be used for industrial exploitation.

Antifungal Activity: In order to examine antifungal activity of *C. caudatus* against selected plant pathogens with use of agar cup method, crude leaf extract was separated into hexane, ethyl acetate and aqueous fractions [26]. The EtOAc fraction showed antifungal activity on most of the tested isolates with PIRG values of 4.7 to 52% among the four fractions. Highest inhibition was shown by *P. palmivora* (*Theobroma cacao*) (52%), *C. gloeosporioides* (*Carica papaya*) (23.5%) and *C. gloeosporioides* (*Mangifera indica*) (18%). The remaining fractions (aqueous, hexane and crude) showed low inhibition for all of the tested pathogens. The ethyl acetate (EtOAc) fraction was found to have the highest activity for growth inhibition and spore germination of *Phytophthora palmivora* (Butl.) Butl., the casual pathogen of cocoa that causes black pod disease, with inhibition in radial growth (PIRG) of 52 percent. The EtOAc fraction also showed the lowest level of sporangial germination with 15.62%. These results show that the *C. caudatus* ethyl acetate fraction contains antifungal agents which are effective against *P. palmivora*. The ethyl acetate fraction can, therefore, be potentially used to develop a biopesticide product in order to control black pod disease.

Investigation of crude n-hexane, EtOH, Et_2O and PBS extracts of *C. caudatus* leaves for antifungal potential was conducted by Rasdi *et al.* [15]. Screening for antifungal activity showed inhibition by diethyl ether, n-hexane and ethanol extracts against *Candida albicans* [15].

Antioxidant Effect: *C. caudatus* has been reported to have antioxidant activity potential. An experiment was conducted where 37 raw vegetables extracts were gained using different solvent systems – 70% acetone, 70% methanol, 70% ethanol and distilled water. Highest flavonoid content was gained from 70% methanol extract of *C. caudatus* (27.7 ± 1.0 mg QE/g dry weight basis) [27]. This is expected to have positive effects for degenerative diseases prevention [28].

It was also found that *C. caudatus* does possess the highest total amount of phenols among eleven analysed Indonesian vegetables with 1.52mg GAE/100g of fresh weight [29]. It is believed that phenolic compounds are the main contributor of antioxidant activity in plant extracts. Rafat *et al.* [30] reported that the highest superoxide dismutase assay activity and the highest free radical scavenging potential among five of the most popular Malaysian salad vegetables was obtained from *C. caudatus* – its 86.85% and 98.56% extracts, respectively.

Another study evaluated methanol extracts of 21 tropical plants for free radical scavenging activity with use of 1,1-diphenyl-2-picrylhydrazyl assay (DPPH). *C. caudatus* with IC_{50} 21.3 μg/mL showed the highest potential. It was also observed that *C. caudatus* extract behaved similarly to α-tocopherol or BHA [20]. All of these findings support the rightness of the traditional use of *C. caudatus* for antioxidant effects and suggest its potential use for appropriate drug development.

Anti-osteoporosis Effect: *C. caudatus* can be used as an alternative medicament to treat osteoporosis caused by menopause using cellular and dynamic parameters of bone histomorphometry [31]. An experiment with use of Wistar rats showed that *C. caudatus* caused an increase of double-labeled surface, mineral appositional rate, osteoblast surface and osteoid volume. The herb also produced better results in the osteoid volume compared to 1% calcium. Based on this it can be concluded that *C. caudatus* at 500 mg/kg dose may be an alternative treatment for bone damage which can occur in post-menopausal women.

Mohamed *et al.* [32] determined the beneficial effects of *C. caudatus* as a bone protective agent in an experiment with post-menopausal osteoporosis rats. The experiment proved the potential of *C. caudatus* (500 mg/kg dose) to reverse bone damage induced by ovariectomy.

Antihypertensive Effect: Aqueous extract of wild *C. caudatus* leaves was tested on rats which had undergone sodium chloride and adrenaline treatments in order to attempt antihypertensive effect of this herb [33]. The results demonstrated that this extract, at doses of 500 or 1000 mg kg-1, had beneficial effects on both heart frequency rate and amplitude of stroke volume induced by adrenaline as it blocked the increase of both of these factors. At the same time, the action on the amplitude after sodium chloride induction was only demonstrated.

Diuretic activity of the extract was further revealed in the results, this activity can be synergistic to blood pressure reduction. These findings may, therefore, be a foundation to development of powerful alternative antihypertensive medicaments.

Antidiabetic Activity: In comparison to dichloromethane extract, hexane extracts of *C. caudatus* showed higher inhibitory activity [34]. Furthermore, the dichloromethane extract of *C. caudatus* did not demonstrate any α-glucosidase inhibitory activity. Samples extracted with use of hexane manifested higher inhibitory activity in comparison to the same samples extracted from dichloromethane. It can be concluded that *C. caudatus* has a good inhibitory profile against carbohydrate modulating enzymes which are connected to glucose absorption in the intestine. This herb has also shown a moderate effect against ACE (Angiotensin-converting enzyme) inhibition assay. If correctly combined in a diet, *C. caudatus* can potentially be used to manage glucose-induced hyperglycemia [34].

Toxicology: A study found that the ethanol extracts of *C. caudatus* against P388 murine leukaemia cells with IC_{50} values of 25 μg/ml have weak cytotoxic activity [24]. Furthermore, an acute toxicity study was performed using male rats [35]. It can be concluded that *C. caudatus* can cause acute hepatotoxicity when consumed in high doses.

Concluding Remarks: Use of *C. caudatus* in traditional medicine in countries such as Malaysia is spreading along with increasing popularity of alternative medicine around the world. Recent pharmacological studies confirm that this herb has antibacterial, antifungal, antioxidant, antiosteoporosis, antihypertensive and antidiabetic effects which only support the relevance of its traditional use. Although *C. caudatus* may have many beneficial effects for human health, it can cause acute hepatotoxicity at higher doses. Lower doses of *C. caudatus* are considered as safe to be consumed. Further study on active compounds of this herb is strongly recommended in order to determine the substance responsible for its effects. This is a basic premise for future research and potential industrial use of this herb to treat diseases such as blood pressure issues, bone strength or as antioxidant agents. If this research is successfully conducted, the pharmacological market can have a new powerful drug with variety of uses in the not too distant future.

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