### **REVIEW ARTICLE**

# Tasty Herb that Heals: A Review of *Cosmos caudatus* (Ulam Raja) and its Potential Uses in Dentistry

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### **A**BSTRACT

Aim: In recent years, there has been an increase in research on herbal derivatives with regards to their medicinal use. This review aims to summarize the scientific reports on one such herb, *Cosmos caudatus*. Our primary focus is to highlight its pharmacological properties and their potential applications in the field of dentistry.

Background: The vascular plant biodiversity of Southeast Asia is second to that of South America, with many of these plants being used for their traditional medicinal benefits. One such herb that is popular in Malaysia is *C. caudatus*, locally referred to as ulam raja. It is an edible herb, commonly served in the form of a salad and is also used in traditional medicine practices to boost blood circulation, increase strength of bones, reduce fever, treat infections, and improve skin texture. Recent scientific studies have reported numerous pharmacological benefits of *C. caudatus* ranging from being an antioxidant agent to having bone-protective properties. These properties are attributed to a rich source of biochemical compounds found in the herb. A PubMed and Science Direct database search was conducted revealing 25 papers relevant to our review of *C. caudatus*, describing its traditional uses, pharmacological uses, botanical description, and phytochemical description.

**Review results:** Published studies have reported that *C. caudatus* has potent antioxidant properties. It has shown both antibacterial and antifungal activities. Extracts of *C. caudatus* are capable of acting as an antihypertensive and antidiabetic agent, in both human and animal models. It also plays a role as a bone-protective and bone-proliferative agent.

**Conclusion:** *C. caudatus* has the potential of being greatly beneficial in treating various dental diseases due to its pharmacological properties. **Clinical significance:** There is need for further research into this abundant natural resource in order to explore its potential uses in clinical dentistry. **Keywords:** *Cosmos caudatus*, Pharmacological use, Traditional medicine, Ulam raja.

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#### Introduction

In Malay culture, the word "ulam" refers to certain plants found locally that are consumed as green salads either on their own or served up together with certain spices and fermented sauces to be eaten with rice. The word "ulam" is a broader term encompassing more than 100 different species of traditional herbs and vegetables found locally in Southeast Asia. In Malaysia, one such plant consumed widely as a side dish is Cosmos caudatus. The local name for this plant is ulam raja, which translates to king's salad as the word "raja" means king. In traditional medicine, C. caudatus is applied to individuals with burns to prevent infection. It is also used to treat muscular injuries such as spasms and strains.<sup>2</sup> One of its popular uses in Malaysia is to cure infections caused by both bacteria and fungus.<sup>3</sup> It is also given to people with high blood pressure, a practice popular in eastern Java. 4 It is also marketed as an antiaging supplement, believed to improve blood circulation, improve bone strength, and as a dental remedy to cure halitosis.<sup>5</sup> Apart from these traditional uses, there exist scientific data on the pharmacological properties of C. caudatus as a rich antioxidant source and an antidiabetic, antihypertensive, antibacterial, antifungal, and bone-protective agent. Our review aims to highlight these pharmacological reports alongside its botanical description and phytochemical components.

# **BOTANICAL DESCRIPTION**

C. caudatus is an aromatic plant from the Asteraceae family (Fig. 1). It produces flowers and fruits and grows between 1 meter and 2 meters tall. The plant can be seen growing alone or in clusters.

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Its leaves and leaflets are variably lobed and also show a variation in size. The plant produces flowers that may be pink, yellow, or white in color. The plant neither requires fertilizer nor a rich soil to grow, and the ideal growing temperature is between 50°C and 55°C. If the shoots are picked 8 weeks after planting, this causes an increase in height and branching of the plant.<sup>6</sup>

#### **PHYTOCHEMISTRY**

Phytochemical studies have shown that the *C. caudatus* plant contains various bioactive compounds. These include a large group of flavonoids such as quercetin and proanthocyanidin, out of which quercetin is found to be the most abundant flavonoid in the plant leaves. These flavonoids are considered to be potent antioxidants.<sup>7,8</sup> Other major bioactive compounds found are carbohydrates, phenolic acids, amino acids, and essential oils.<sup>9</sup> Certain other miscellaneous elements like calcium, organic acids, vitamins,

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Fig. 1: C. caudatus plant in Kota Bharu, Malaysia. Photographed by author, June 2019

mineral quaternary ammonium salt, sugar acids, and carotenoids are also present.<sup>3</sup>

# PHARMACOLOGICAL REPORTS

# **Antioxidant Activity**

Studies have shown that *C. caudatus* contains a variety of bioactive chemicals with strong antioxidant properties. Over 20 antioxidants are discovered to be present in this herb. The major antioxidants belong to a number of proanthocyanidins, classified as flavonoids, which, as dimers, exist through numerous compounds. 9,10 Apart from flavonoids, phenolic compounds are present in *C. caudatus*, which are also antioxidants. 8 In a comparative study, *C. caudatus* showed the highest antioxidant activity among five of the most widely consumed ulam in Malaysia that were "selom" (*Oenanthe javanica*), curry leaf (*Murraya koenigii*), "pegaga" (*Centella asiatica*), ulam raja, and the seeds of "petai" (*Parkia speciosa*). 1 In a similar study, *C. caudatus* was ranked highest in antioxidant activity among three other local herbs, *Persicaria hydropiper*, *Centella asiatica*, and *Artemisia argyi*, which was evaluated by ferric reducing antioxidant power (FRAP) assays. 8

The antioxidant capacity of a fresh sample of a 100 g *C. caudatus* was reported to have 2,400 mg L-ascorbic acid equivalent antioxidant capacity (AEAC), which is considered to be extremely high.<sup>11</sup>

As the name implies, a molecule that can inhibit the oxidation of another molecule is termed as an antioxidant. Free radicals are produced as result of molecule oxidation, accumulation of which can cause cell damage or cell death by damaging the cellular RNA, DNA, and proteins. Majority of these free radicals are unstable molecules that contain oxygen and are termed as "reactive oxygen species" (ROS). By reacting with the oxygen of these free radicals, the antioxidants cause their deactivation, thus preventing them from attacking human cells. Hence, these antioxidants play a pivotal role in disease prevention and control. Therefore, C. caudatus as a pharmacological agent can play a significant role in the potential reduction of oxidative damage that occurs in dental conditions such as gingivitis, periodontitis, and peri-implantitis. Similarly, many commonly used dental restorative materials produce free radicals like bleaching agents, composite fillings, ceramic restorations,

intracanal medicaments, and dental implants.<sup>14</sup> Therefore, the antioxidant potential of *C. caudatus* carries great value in the field of restorative dentistry. Another potential application of the antioxidant property of *C. caudatus* can be applied in the case of oral cancers. It has been reported that antioxidant flavonoids present in *C. caudatus* have the ability to reduce cell growth and proliferation of oral carcinomas, a benefit that can be applied in treating oral cancer.<sup>15</sup>

# **Antibacterial Activity and Antifungal Activity**

A study conducted by Rasdi et al.<sup>5</sup> tested *n*-hexane, diethyl ether, and ethanol extracts of *C. caudatus* against the fungus, *Candida albicans*; gram-positive bacteria, *Bacillus subtilis* and *Staphylococcus aureus*; and gram-negative bacteria, *Escherichia coli* and *Pseudomonas aeruginosa*, utilizing the method of disk diffusion. The extracts demonstrated a significant inhibitory action against all five microorganisms at minimal inhibitory concentrations of 25 mg/mLfor*n*-hexane, 6.25 mg/mLfor diethyl ether, and 6.25 mg/mL for ethanol.

In a separate study, ethanol extract of *C. caudatus* was found to be active against *Proteus mirabilis* Salmonella species, *Listeria monocytogenes*, *Salmonella typhimurium*, *Staphylococcus aureus*, and *Vibrio cholera*. Microorganisms such as *Lactobacillus acidophilus*, *Pseudomonas aeruginosa*, *Streptococcus mutans*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Escherichia coli* are responsible for causing dental caries and periodontal disease. He tated studies indicate that *C. caudatus* possesses the potential of fighting and controlling microbial plaque that lies at the root of dental caries, gingivitis, and periodontitis.

Candida species has been identified as the normal flora of the oral and gastrointestinal tract.<sup>17</sup> The principal most virulent species responsible for human oral mycoses is *C. albicans*, which manifest as opportunistic infections in immunocompromised patients. Treatment comprises oral antifungal drugs in the form of lozenges, pastilles, and oral suspensions, which act locally.<sup>18</sup> *C. caudatus* is mostly consumed orally in Southeast Asia,<sup>1</sup> which is the same route as the antifungal drugs described above. Therefore, keeping this common factor in view, there is a need to study the antifungal effects of *C. caudatus* preparation locally in the oral cavity.

#### ANTIDIABETIC EFFECTS

*C. caudatus* extract-treated obese rats demonstrated a marked decrease in plasma blood glucose levels in comparison to that of the control group over a period of 1 month. <sup>19</sup> Loh et al. <sup>20</sup> reported inhibitory activity of the *C. caudatus* extract against the enzymes  $\alpha$ -glucosidase and  $\alpha$ -amylase, with higher inhibitory levels seen in the former.

A 8-week randomized controlled study reported an improvement in plasma blood glucose of type II diabetic patients who were given supplements of *C. caudatus*. In this study, a reduction was also seen in the level of serum fasting insulin. An improvement in insulin resistance was denoted by a decrease in HOMA-IR and an increase in QUICKI, which denoted an improvement in insulin sensitivity. These results indicate a positive antidiabetic effect of *C. caudatus* over a short period of time. This study also concluded that *C. caudatus* was safe to consume as no side effects were reported.<sup>21</sup>

The dental implications of having high blood sugar level put an individual at risk of developing dental caries, gingivitis, periodontitis, thrush, and xerostomia. <sup>22</sup> As dental professionals we



frequently deal with diabetic patients, thus there is a need to find new treatment modalities such as *C. caudatus* supplements to help control diabetes and its negative oral implications.

#### **Antihypertensive Effects**

The antihypertensive effects of C. caudatus as an aqueous extract were reported in a study carried out on rats that were given sodium chloride treatment and an adrenaline treatment. In the sodium chloride-treated rats (500 mg/kg and 1,000 mg/kg). there was a decrease in the stroke volume similar to that which is seen in treatment with antihypertensive drugs captopril and hydrochlorothiazide. In the adrenaline-treated cases (500 mg/ kg and 1,000 mg/kg), inhibition of adrenaline induced increase of heartbeat and stroke volume was reported.<sup>23</sup> Separately, the dichloromethane extract of C. Caudatus in vitro demonstrated a moderate suppression of the angiotensin-converting enzyme.<sup>20</sup> These results are indicative of the potential of C. caudatus as an antihypertensive agent. Antihypertensive drugs such as ACE inhibitors can cause xerostomia, and calcium channel blockers can cause gingival hyperplasia. Similarly, oral lichenoid reactions are seen with captopril and propranolol. Furthermore, local anesthetic toxicity and cardiovascular changes with the epinephrinecontaining local anesthetics are seen with nonselective  $\beta$  -blockers.  $^{24}$ Dentists' management of hypertension encompasses recognizing the disease, knowing its various treatment options, and fully assessing the risks posed during dental treatment. C. caudatus promises an adjunct treatment modality for this condition that needs to be explored further.

# **Antiosteoporotic Effect**

Two studies published a year apart from the same authors used *C. caudatus* as an aqueous extract on ovariectomized rats, a model that is used to depict bone loss in postmenopausal women.<sup>25,26</sup>

The first study reported an improvement in bone volume, trabecular number, and separation to levels prior to removal of the ovaries. This result is superior in comparison to the treatment with 1% calcium in term of trabecular separation and trabecular number. In the latter study, treatment with the C. caudatus extract exhibited an increased volume of osteoid, a higher labeled surface, an increased mineral oppositional rate, and a higher surface value of osteoblasts. This study concluded that C. caudatus had a better effect on osteoid volume compared to 1% calcium. These studies indicate valuable potential of C. caudatus as a boneprotective and bone-proliferative resource. This knowledge can be applied in today's dental practice as evidence exists that osteoporosis is associated with oral conditions such as tooth loss, periodontal disease, difficulty in creation of dental prosthesis, temporomandibular joint disorders, and an increase in fracture risk. This option may also be of great value to explore with regards to approaching the bisphosphonate-related osteonecrosis of jaws, a difficult and complex disease to treat by dentists.<sup>27</sup>

#### Conclusion

Dentistry of today requires a multidisciplinary approach in treating oral diseases. Naturally derived plant products are gaining traction worldwide as a new avenue for treating various diseases. One such natural herb popular for its medicinal use locally in Malaysia is *C. caudatus* or ulam raja. Various scientific studies have reported on the pharmacological benefits of *C. caudatus*, which carry great potential value for application in clinical dentistry.

Due to the abundance of this natural resource, there is a necessity to exploit its potential benefits through further research. The compounds contained within this resource show great promise for it to emerge as a new and novel treatment option. Therefore, today's dentists need to explore all such options so as to offer the most optimum treatment regimen to the patients.

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