JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2016/8370

Ulam Herbs of *Oenanthe javanica* and *Cosmos caudatus*: An Overview on their Medicinal Properties

Eric Wei Chiang Chan[1*], Siu Kuin Wong[2], Hung Tuck Chan[3]

[1]Faculty of Applied Sciences, UCSI University, Cheras - 56000, Kuala Lumpur, Malaysia; chanwc@ucsiuniversity.edu.my, erchan@yahoo.com
[2]School of Science, Monash University Sunway, Petaling Jaya - 46150, Selangor, Malaysia
[3]International Society for Mangrove Ecosystems, Faculty of Agriculture, University of the Ryukyus, Okinawa 903-0129, Japan

Abstract

In Southeast Asia, ulam herbs are consumed raw as a condiment. It is believed that these herbs have medicinal benefits and their regular intake can prevent degenerative diseases, delay aging and improve overall health. In this review, the current knowledge on the phytochemistry and pharmacology of *Oenanthe javanica* (water dropwort) and *Cosmos caudatus* (wild cosmos) is updated with some descriptions of their botany and uses. Water dropwort has constituents of phenylpropanoids, flavonoids and phenolic acids, notably, persicarin and isorhamnetin. Antioxidant, anti-quorum sensing, melanogenic, anti-diabetic, anti-arrhythmic, anti-inflammatory, neuroprotective, neurogenesis, alcohol detoxification, antitoxic, anti-coagulant, hepatoprotective, anti-hepatitis B virus and memory improvement are pharmacological properties of water dropwort. Wild cosmos, with flavonoids, phenolic acids and diterpenoids as major metabolites, possesses antioxidant, antibacterial, anti-quorum sensing, antifungal, anti-inflammatory, anti-diabetic, anti-hypertensive, hepatoprotective, detoxification, anti-osteoporosis and anti-hyperlipidemic activities. There are several patents on some of the pharmacological properties of water dropwort while a clinical trial has been conducted on the anti-diabetic effects of wild cosmos. Both these ulam herbs possess a wide array of pharmacological properties, which confer their traditional uses as food and medicine.

Keywords: Pharmacology, Phytochemistry, Toxicity, Water Dropwort, Wild Cosmos

1. Introduction

In Southeast Asian countries, particularly Malaysia, Thailand and Indonesia, ulam herbs are consumed raw as condiments, and they form an important component of the traditional diet. Dipped in a hot and spicy sauce made from shrimp or fish paste, these herbs would whet the appetite during meals. Ulam herbs are believed to have health-promoting properties, and their regular intake can assist in preventing degenerative diseases, delaying aging and improving overall health[1]. Herbs commonly consumed as ulam include young leaves of *Anacardium occidentale* (cashew), *Barringtonia racemosa* (common putat), *Centella asiatica* (pennywort), *Cosmos caudatus* (wild cosmos), *Oenanthe javanica* (water dropwort), *Piper sarmentosum* (wild pepper) and *Persicaria hydropiper* (water pepper).

*Author for correspondence
Email: chanwc@ucsiuniversity.edu.my

In this review, two ulam herbs of *O. javanica* (water dropwort) and *C. caudatus* (wild cosmos) are updated with descriptions of their botany and ethnopharmacological uses. The focus is on their leaves and aerial parts. To date, this is the first review on *O. javanica* as its information has not been documented. There are two reviews on *C. caudatus* i.e. *Cosmos caudatus* Kunth: A traditional medicinal herb[2] and Potential medicinal benefits of *Cosmos caudatus* (ulam raja): A scoping review[3].

2. *Oenanthe javanica*

2.1 Botany and Uses

Oenanthe javanica (Blume) DC or water dropwort of the family Apiaceae is an aromatic perennial herb with root tubers[4]. The plant grows up to a metre in height, often forming pure stands. Leaves are variable in shape and resemble those of celery (Fig. 1). The leaf axis branches several times, bearing ovate leaflets that are coarsely dentate or serrate at the terminal. Inflorescences form umbels bearing 5–15 white fragrant florets.

Fig. 1. Plants of *Oenanthe javanica*.

In Southeast Asia, the strongly celery-flavoured leaves of *O. javanica* or selum are consumed raw as ulam during meals. Known as shui qin in China, minari in Korea and seri in Japan, *O. javanica* is cultivated in early spring, and its aerial parts are consumed for their distinctive aroma and taste. In Korea, *O. javanica* is consumed as salad or seasoning, and its soup is drunk to clear hangovers from alcohol intoxication[5]. In Chinese and Korean traditional medicine, the herb is used for treating jaundice, hypertension, polydipsia, fever, cold, abscesses, swellings, abdominal pain, leucorrhea, mumps and difficulty in urination[6].

2.2 Phytochemistry

From plants of *O. javanica*, three glucosides (oenanthoside A, pinoresinol-β-D-glucopyranoside and eugenyl-β-D-glucopyranoside) have been isolated along with known phenylpropanoids (ferulic acid, *p*-coumaric acid, and 4-hydroxyphenethyl *trans*-ferulate), and polyacetylenes (falcarinol and falcarindiol)[7]. Persicarin and isorhamnetin are the main components isolated from the methanol extract[8-10]. Analysed using HPLC, chlorogenic acid (227 mg/g) is the dominant phenolic compound in the ethanol extract of *O. javanica*[11]. The hydrophilic extract contains chlorogenic acid, quercetin rhamnosyl galactoside, rutin, hyperoside and isoquercitrin, while lutein, γ-tocopherol and α-tocopherol have been identified in the lipophilic extract[12]. Major chemical constituents of the essential oil from *O. javanica* are incensole (26%), α-copaene (18%) and n-nonylacetate (18%)[13]. α-Terpinolene is the dominant aromatic compound with *p*-cymene, α-terpinene, γ-terpinene, hexanal, (*Z*)-3-hexenol, (*E*)-cayophyllene, (*E*)-2-nonenal, (*Z,E*)-α-farnesene, phenylacetyaldehyde and bornyl acetate also reported[14].

2.3 Pharmacological Properties

2.3.1 Antioxidant

Among 10 ulam herbs studied, *O. javanica* ranked seventh suggesting that its antioxidant properties are moderately low[15]. Total phenolic content, free radical scavenging and ferric reducing power of *O. javanica* were 3.0, 11 and 5.4 times lower than those of *C. caudatus*, respectively. However, the contents of carotenoid, lutein and β-carotene of *O. javanica* were 2.5, 1.9 and 2.8 times higher than those of *C. caudatus*[16]. The lutein content of *O. javanica* was the highest among 13 vegetables grown in Thailand[17]. Results of a study on the antioxidant activities of ethanol extract of *O. javanica*, and its hexane, chloroform, ethyl acetate, butanol and aqueous fractions showed that the ethyl acetate fraction had the highest total phenolic and flavonoid contents, and the strongest free radical scavenging, reducing power and iron-chelating abilities[18]. The benefits of an *O. javanica* extract in enhancing the activities of

endogenous antioxidant enzymes in the rat kidney has been reported[19]. Immunoreactivities of the enzymes increased two-fold in the group treated with the extract.

2.3.2 Anti-quorum Sensing

Leaves of *O. javanica* did not exhibit any antibacterial activity against Gram-positive bacteria of *Brevibacillus brevis*, *Micrococcus luteus* and *Staphylococcus cohnii*, and Gram-negative bacteria of *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella enterica*[20]. However, the plant has been reported to possess anti-quorum sensing activity against *Chromobacterium violaceum* with a Diameter of Inhibition Zone (DIZ) of 20.5 mm and Minimum Inhibitory Concentration (MIC) of 15.6 mg/ml[21].

2.3.3 Melanogenic

Unlike most plants, *O. javanica* is one of the few plants that enhances tyrosinase activity and have melanogenic effects. The ethanol extract (50 µg/ml) enhanced tyrosinase activity and melanin synthesis in B16F1 melanoma cells[22]. The study suggested that *O. javanica* can be used to promote the growth of black hair and to protect the skin from oxidative stress. Other species with similar properties as *O. javanica* included *Piper betle*[23] and *Salvia miltiorrhiza*[24].

2.3.4 Anti-diabetic

The anti-diabetic effect of *O. javanica* flavones on alloxan-induced hyperglycaemic mice has been reported[25]. Daily doses of 200 and 400 mg/kg for 10 days decreased blood glucose level in hyperglycaemic mice. The compounds stimulated the secretion of insulin in both normal and diabetic mice, and decreased serum triglyceride and ameliorated the activity of pancreatic amylases in diabetic mice. Oral administration of the *O. javanica* extract containing falcarindiol (15 mg/kg) significantly decreased the blood glucose level in rats[26]. Falcarindiol was found to inhibit glycogen synthase kinase-3β with an inhibitor constant (Ki) of 87 µM.

2.3.5 Anti-arrhythmic

The anti-arrhythmic activity of *O. javanica* extract was demonstrated in experimental rats[27]. Intravenous injection of 3.0 ml/kg significantly antagonized arrhythmia induced by aconitine and $BaCl_2$, and decreased the rate of ventricular fibrillation induced by $CaCl_2$.

2.3.6 Anti-inflammatory

Active compounds isolated from *O. javanica* have been reported to possess potent anti-inflammatory properties[28,29]. Persicarin and isorhamnetin effectively inhibited the release of High Mobility Group Box 1 (HMGB-1) protein and down-regulated inflammatory responses in human endothelial cells and inhibited hyperpermeability and leukocyte migration in mice. Studies have been conducted on the anti-inflammatory roles of *O. javanica* extract and isolated isorhamnetin using lipopolysaccharide (LPS)-activated RAW 264.7 murine cells. Expression of cyclooxygenase (COX)-2, and activation of nuclear factor-kappa B (NF-κB) and activator protein-1 were significantly inhibited by the extract at 400 and 600 µg/ml concentration[30]. This suggested that inhibition of LPS-stimulated COX-2 expression by the extract is due to inhibition of NF-κB activation. Isorhamnetin has also been reported to inhibit the inflammatory response by blocking NF-κB activation[31].

2.3.7 Neuroprotective

The *O. javanica* extract and persicarin showed significant neuroprotective activity in glutamate-injured rat cortical cells[10]. Persicarin diminished calcium influx and inhibited over-production of nitric oxide and intracellular peroxide. It also restored the reduced activities of glutathione reductase and glutathione peroxidase, and the content of glutathione. In another related study, the neuroprotective effect of *O. javanica* extract in the hippocampal region of gerbils subjected to transient cerebral ischemia was investigated[32]. Results showed that the extract can protect neurons from transient ischemic damage and that the neuroprotective effect may be attributed to increased or maintained intracellular antioxidant enzymes.

2.3.8 Neurogenesis

Besides protection against glutamate-induced neurotoxicity, *O. javanica* has neurogenesis effects based on a study on cell proliferation and neuroblast

differentiation in the hippocampal dentate gyrus of adolescent rats[33]. Rats with a diet containing the ethanol extract of *O. javanica* had more immunoreactive cells and neuroblasts, and the immunoreactivity of brain-derived neurotrophic factor was enhanced.

2.3.9 Alcohol Detoxification

The ability of *O. javanica* to detoxify the harmful effects of alcohol has been reported. The methanol plant extract and persicarin enhanced the activities of alcohol dehydrogenase, microsomal ethanol oxidizing system and aldehyde dehydrogenase in the liver of rats intoxicated with ethanol[34]. In another related study, the effects of *O. javanica* were investigated in ethanol-injected rabbits and ethanol-fed mice[5]. When the extract and ethanol were injected into rabbits, the plasma ethanol level was rapidly reduced from 215 to 50 mg/dL several hours later. When ethanol was orally ingested, the *O. javanica* extract eliminated up to 44% of the plasma ethanol while the butanol fraction (50–200 mg/kg) of the extract eliminated up to 70% in mice.

2.3.10 Antitoxic

A study on the antitoxic effects of orally administered *O. javanica* extract was conducted on mice exposed to methyl mercuric chloride through the drinking water[35]. The control, mercury treated and extract groups did not reveal any significant differences in mean body and organ weights. Examinations of the distribution of mercury in the cerebellum, kidney, liver, and spleen of the mice showed much less staining intensity of mercury in the cerebellum and liver of the extract group.

2.3.11 Anti-coagulant

Persicarin and isorhamnetin isolated from *O. javanica* displayed anti-coagulant activities[36]. The anti-coagulant and profibrinolytic effects of persicarin were stronger than those of isorhamnetin, suggesting that the sulphonate group of persicarin may be responsible for the anti-coagulatory function. The antithrombotic and profibrinolytic activities of isorhamnetin-3-*O*-galactoside (IMG) were found to be stronger than those of hyperoside, indicating that the methoxy group in IMG may be responsible[37].

2.3.12 Hepatoprotective

The hepatoprotective effects of *O. javanica* extracts in rats with liver damage have been demonstrated. The extracts enhanced hepatic lipid peroxide content markedly decreased by carbon tetrachloride (CCl_4)[38], bromobenzene[39] and acetaminophen[40]. The extracts also increased the expression of enzymatic antioxidants in the rat liver cells, which decreases oxidative stress in the liver[41], and protects against liver damage by scavenging free radicals, boosting endogenous antioxidants and inhibiting pro-inflammatory mediators[42]. The hepatoprotective ability of *O. javanica* extracts have been attributed to chlorogenic acid and caffeic acid[43]. Chlorogenic acid protected against CCl_4-induced liver damage in rats[44] while caffeic acid protected against H_2O_2-induced cell death in HepG2 human liver cancer cells[45]. Isorhamnetin inhibited reactive oxygen species, reduced glutathione levels and maintained mitochondria membrane potential in treated HepG2 cells possibly *via* the AMP-activated protein kinase pathway[46], and inhibited fibrosis in rat hepatic stellate cells partly *via* inhibition of the extracellular signal-regulated kinase signalling pathway[47]. The hepatoprotective effect of persicarin against inflammatory response in type-1 diabetes probably involved hyperglycemia-activated NADPH oxidase activation[48].

2.3.13 Anti-HBV

The activity of *O. javanica* flavones (OJF) against hepatitis B virus (HBV) was investigated using human hepatoma HepG2.2.15 cell culture and ducklings[49,50]. In the cell culture, OJF inhibited the production of HBeAg (70%) and HBsAg (73%) on day 9. In HBV-infected ducklings, HBV-DNA levels decreased significantly. At 0.2 g/kg/day, inhibition was 64% on day 5 and 67% on day 10. Reviews on the role of traditional Chinese medicines and their related compounds on HBV infection[51] and on anti-HBV agents of botanical origin[52] had included *O. javanica* amongst them. Both reviews acknowledged the need to determine the flavones responsible for the anti-HBV activity and their mechanisms of action.

2.3.14 Memory Improvement

A collaborative research project conducted by universities and the private sector in Korea has reported

on the memory improvement properties of *O. javanica*. Screening of seven herbs for acetylcholinesterase (AChE) inhibitory activity showed that the extract of *O. javanica* had the strongest inhibition of 18.6% and IC_{50} value of 992 μg/ml[53]. When treated with the extract, Tg2576 transgenic mice displayed longer latency period in the passive avoidance test and showed a significant reduction in cortical amyloid-β concentration. The neuroprotective properties of the extract were evident by the significant reduction in hydrogen peroxide (H_2O_2)-induced cell death of SH-SY5Y neuroblastoma cells and in H_2O_2-induced neurotoxicity[54]. In addition, treatment with the extract at 1.0 mg/kg slightly improved scopolamine-induced memory impairment in rats.

3. Patents

In view of the convincing pharmacological properties of *O. javanica*, scientists in Korea have published several patents. They include three related to alcohol and carcinogen detoxification[55-57], and another three on brain functioning and memory improvement[58-60].

4. Cosmos caudatus

4.1 Botany and Uses

Cosmos caudatus Kunth. or wild cosmos of the family Asteraceae is native to Central America. The species is a short-lived, 1–2 m tall, perennial aromatic herb[61]. Leaves are opposite, pinnate and dissected into five leaflets (Fig. 2). The upper surface of leaf lamina is dark green while the lower surface is light green with minute hairs. The pinkish or violet daisy-like flowers are composite with a cluster of yellow florets at the centre.

Fig. 2. Plants of *Cosmos caudatus*.

In Malaysia, *C. caudatus* or ulam raja is a popular herb that is consumed raw during meals. Its leafy aroma adds diversity and taste to the main dishes. Health benefits include reducing body heat, slowing down aging, improving blood circulation, promoting fresh breath, strengthening bone marrow and treating infections[62]. In Bangladesh, flowers of *C. caudatus* are used as ornaments during Hindu religious ceremonies[63]. Aerial parts are used to treat skin diseases such as leprosy and are prescribed in herbal bath for patients with skin infections.

4.2 Phytochemistry

From the leaves of *C. caudatus*, phenolic compounds of caffeoylquinic acids, quercetin glycosides, catechin, and proanthocyanidins have been identified[64]. The caffeoylquinic acids are those of chlorogenic, neo-chlorogenic and crypto-chlorogenic. Quercetin glycosides include those of arabinofuranoside, glucoside, rhamnoside, and rutinoside[65,66]. Quercetin (51%) is the dominant flavonoid in the leaves of *C. caudatus*, and major phenolic acids are chlorogenic acid (4.5%), caffeic acid (3.6%) and ferulic acid (3.1%)[67,68]. The essential oil of *C. caudatus* contains γ-cadinene (33%) and caryophyllene (10%) as major components[69].

4.3 Pharmacological Properties

4.3.1 Antioxidant

Among the leaves of 10 ulam herbs screened for phenolic contents and antioxidant activities, *C. caudatus* ranked third suggesting its strong antioxidant properties[15]. Analysis of the antioxidant properties of herbal teas prepared from *C. caudatus* leaves of different ages showed that teas from young leaves possessed significantly higher phenolic contents and antioxidant activities than teas from mature and old leaves[70]. Another study on the antioxidant properties of *C. caudatus* leaves reported that the aqueous extract yielded the highest phenolic content while the methanol and ethanol extracts had the strongest antioxidant properties[71]. Among the chemical constituents of *C. caudatus*, free radical scavenging of quercetin and quercetin 3-*O*-β-D-arabinofuranoside was the most potent with IC_{50} values of 18 and 19 μM, respectively[66].

4.3.2 Antimicrobial

Hexane, diethyl ether and ethanol leaf extracts of *C. caudatus* have been reported to inhibit the growth of Gram-positive bacteria of *Bacillus subtilis* and *Staphylococcus aureus*, and Gram-negative bacteria of *Escherichia coli* and *Pseudomonas aeruginosa* with MIC values ranging from 6.3–25 mg/ml[72]. The plant has also been reported to possess anti-QS activity against *C. violaceum* with DIZ of 21 mm and MIC of 31 mg/ml[20]. Sequential leaf extracts of *C. caudatus* screened for antifungal activity using the agar cup method showed that the ethyl acetate extract was most effective in inhibiting fungal growth and spore germination[73].

4.3.3 Anti-inflammatory

The anti-inflammatory activity of *C. caudatus* against carrageenan-induced paw oedema in mice has been reported[74]. Petroleum ether, chloroform, methanol and aqueous leaf extracts, orally administered at 200 mg/kg, significantly reduced paw oedema. Methanol and aqueous extracts showed significant anti-inflammatory activity, comparable to diclofenac sodium, the standard drug.

4.3.4 Anti-hypertensive

The aqueous extract of *C. caudatus* leaves was assessed for anti-hypertensive effect using rats treated with adrenaline and sodium chloride, and results showed that the extract (500 and 1000 mg/kg) lowered the heart beat frequency and stroke volume amplitude[75]. Together with its diuretic activity, the extract can have a synergistic effect in reducing blood pressure.

4.3.5 Hepatoprotective

The aqueous extract of *C. caudatus* was administered orally to mice at doses of 100, 500 and 1000 mg/kg with control mice given a diet containing 0.5% butylated hydroxyanisole[76]. After 21 days, lactate dehydrogenase levels, which indicated the extent of liver damage caused by oxidative stress, were significantly reduced in all the extract groups.

4.3.6 Detoxification

The effects of *C. caudatus* extract on detoxifying enzymes in lungs, kidneys and stomachs of mice have been reported[77]. Thirty adult male white mice were fed with 100, 500 and 1000 mg/kg of the aqueous extract for 21 days. In lungs of the treated group, all doses resulted in significant increase in catalase (CAT), superoxide dismutase and glutathione S-transferase activities. The activity of DT-diaphorase (DTD) increased significantly in mice treated with 1000 mg/kg. Lipid peroxidation levels based on malondialdehyde concentration were significantly decreased in mice fed with 100 and 500 mg/kg of the extract but was significantly increased with 1000 mg/kg. In stomachs and kidneys of the treated groups, CAT and DTD activities were significantly increased in mice fed with 1000 mg/kg, respectively. Results suggested that *C. caudatus* supplementation in mice could protect extra-hepatic organs from xenobiotic and oxidative injury.

4.3.7 Anti-diabetic

The hexane extract of *C. caudatus* inhibited α-glucosidase activity, but not the dichloromethane extract, and both extracts inhibited α-amylase activity[78]. The ethanol extract of *C. caudatus* inhibited α-glucosidase activity with an IC_{50} value of 58 ppm[79]. The α-glucosidase inhibitory activity of aqueous and ethanol extracts was attributed to catechin, α-linolenic acid, α-D-glucopyranoside and vitamin E[80].

4.3.8 Anti-osteoporosis

The effectiveness of *C. caudatus* in the bone protection of post-menopause osteoporosis has been studied in rats[81]. Four groups of eight female rats were ovariectomized, and treatments of 1% calcium and 500 mg/kg of *C. caudatus* extract were given six days a week for eight weeks. Results showed that ovariectomy decreased trabecular bone volume and number, and increased trabecular separation. Both 1% calcium and 500 mg/kg of extract reversed structural bone histomorphometry to normal level with *C. caudatus* showing better effects on trabecular number and separation. The effectiveness of *C. caudatus* as treatment for post-menopause osteoporosis in rats were further evaluated based on dynamic and cellular parameters of bone histomorphometry[82]. Results showed that the extract increased double-labelled surface, mineral appositional rate, osteoid volume and osteoblast surface, supporting its role in bone protection. It was also reported that supplementation of *C. caudatus*

can prevent the increase of interleukin-1, pyridinoline and bone resorption in ovariectomized rats[83]. In a follow-up study, *C. caudatus* extract (500 mg/kg) was found to enhance fracture healing in ovariectomized rats with fractured tibia[84].

4.3.9 Anti-hyperlipidemic

In a recent study, the anti-hyperlipidemic effects of *C. caudatus* extract on obese rats were evaluated[85]. Rats were given a high-fat diet for three months and those administered with 200 mg/kg of the extract for four weeks showed a significant reduction in plasma triglycerides, total cholesterol, low-density lipoprotein cholesterol and plasma glucose, and significant increase in high density lipoprotein-cholesterol and atherogenic index values. Compared to obese rats, declines in plasma glucose (38%) and total cholesterol (28%) of treated rats were significant at week 17.

4.4 Toxicity Studies

An acute toxicity study on *C. caudatus* extract was conducted in male rats with single doses of 50, 500 and 2000 mg/kg given to the respective groups[86]. Changes in biochemical parameters included increase in the levels of liver enzymes and lower creatinine levels in the 500 and 2000 mg/kg groups, and lower albumin levels in the 2000 mg/kg group. The study showed that the extract may cause acute toxicity at high doses. Concurrently, another toxicity study on *C. caudatus* appeared to yield contradictory results[62]. Single doses of 2000 and 5000 mg/kg of aqueous extract showed no evidence of toxicity based on behavioural pattern, haematological evaluation and organ weight of rats. Although there was significant weight gain in the 5000 mg/kg group, the organs showed no detectable inflammation. However, the sub-acute toxicity study (single doses of 125, 250 and 500 mg/kg of aqueous extract) yielded variable results indicating that different extract concentrations could have different toxicity effects in rats.

4.5 Clinical Trial

In August 2014, the first randomized and controlled clinical trial to assess the effectiveness and safety of *C. caudatus* in patients with type-2 diabetes (ClinicalTrials.gov ID: NCT 02322268) was conducted in a tertiary hospital in Serdang, Malaysia[87]. In this study, 100 patients with type-2 diabetes and who met the eligibility criteria were divided into two groups (treated and control). Primary and secondary outcomes of serum and urine of the patients were examined at 4, 8 and 12 weeks. The trial was completed in November 2015, and preliminary findings showed that, after eight weeks of supplementation, *C. caudatus* significantly reduced serum insulin, reduced homeostatic model assessment-insulin resistance and increased quantitative insulin sensitivity check index in the diabetic treated group[88]. The study concluded that *C. caudatus* was safe to consume and that its supplementation significantly improved insulin resistance and sensitivity in patients with type-2 diabetes.

5. Conclusion

Both ulam herbs reviewed possess a wide array of biological and pharmacological properties, which confer their traditional uses as food and medicine. Properties of water dropwort are anti-diabetic, anti-arrhythmic, anti-inflammatory, neuroprotective, alcohol detoxification, antitoxic, anti-coagulant, hepatoprotective, anti-HBV and memory improvement. Wild cosmos possess properties such as antioxidant, antibacterial, antifungal, anti-inflammatory, anti-diabetic, anti-hypertensive, hepatoprotective, detoxification, anti-osteoporosis and anti-hyperlipidemic activities. Some of the pharmacological properties of water dropwort have been patented while a clinical trial has been conducted on the anti-diabetic properties of wild cosmos. Further studies can be conducted on the pharmacological properties of these two ulam herbs. They include isolating and identifying bioactive compounds; assessing the properties and elucidating the mechanisms of action of the isolated compounds; analysing the effects of different processing methods on these herbs; evaluating their toxic effects if any; and exploring their potentials of developing herbal and pharmaceutical products. Notwithstanding, the prospects of studies on additional biological and pharmacological properties of these two ulam herbs are equally promising.

6. References

1. Reihani SFS, Azhar ME. Antioxidant activity and total phenolic content in aqueous extracts of selected traditional Malay salads (ulam). Int Food Res J. 2012; 19:1439–44.
2. Bunawan H, Baharum SN, Bunawan SN, Amin NM, Noor NM. *Cosmos caudatus* Kunth: A traditional medicinal herb. Global J Pharmacol. 2014; 8:420–6.
3. Cheng SH, Barakatun-Nisak MY, Anthony J, Ismail A. Potential medicinal benefits of *Cosmos caudatus* (ulam raja): a scoping review. J Res Med Sci. 2015; 20:1000–6.
4. Sasmitamihardja D. *Oenanthe javanica* (Blume) DC. In: Siemonsma JS, Piluek K, editors. Plant resources of South-East Asia No. 8: Vegetables. Leiden: Backhuys Publisher; 1993. p. 220–2.
5. Kim JY, Kim KH, Lee YJ, Lee SH, Park JC, Nam DH. *Oenanthe javanica* extract accelerates ethanol metabolism in ethanol-treated animals. BMB Rep. 2009; 42:482–5.
6. Park JC, Yu YB, Lee JH. Isolation of steroids and flavonoids from the herb of *Oenanthe javanica* DC. Korean J Pharmacogn. 1993; 24:244–6.
7. Fujita T, Kadoya Y, Aota H, Nakayama M. A new phenylpropanoid glucoside and other constituents of *Oenanthe javanica*. Biosci Biotechnol Biochem. 1995; 59:526–8.
8. Park JC, Young HS, Yu YB, Lee JH. Isorhamnetin sulphate from the leaves and stems of *Oenanthe javanica* in Korea. Planta Med. 1995; 61:377–8.
9. Cho HW, Lee SH, Nam DH, Kim JY, Lim SK, Lee JS, et al. Antioxidant activity and phytochemical study on the aerial parts of *Oenanthe javanica.* Korean J Pharmacogn. 2008; 39:142–5.
10. Ma CJ, Lee KY, Jeong EJ, Kim SH, Park J, Choi YH, et al. Persicarin from water dropwort (*Oenanthe javanica*) protects primary cultured rat cortical cells from glutamate-induced neurotoxicity. Phytother Res. 2010; 24:913–8.
11. Hwang SJ, Park SJ, Kim JD. Component analysis and antioxidant activity of *Oenanthe javanica* extracts. Korean J Food Sci Technol. 2013; 45:227–34.
12. Ogita T, Manaois RV, Wakagi M, Oki T, Ishikawa YT, Watanabe J. Identification and evaluation of antioxidants in Japanese parsley. Int J Food Sci Nutr. 2016; 67:431–40.
13. Pattiram PD, Lasekan O, Tan CP, Zaidul ISM. Identification of the aroma-active constituents of the essential oils of water dropwort (*Oenanthe javanica*) and kacip fatimah (*Labisia pumila*). Int Food Res J. 2011; 18:1021–6.
14. Seo WH, Baek HHJ. Identification of characteristic aroma active compounds from water dropwort (*Oenanthe javanica* DC). Agric Food Chem. 2005; 53:6766–70.
15. Chan EWC, Tan YP, Chin SC, Gan LY, Kang KX, Fong CH, et al. Antioxidant properties of selected fresh and processed herbs and vegetables. Free Radical Antioxid. 2014; 14:39–46.
16. Fatimah AMZ, Norazian MH, Rashidi O. Identification of carotenoid composition in selected 'ulam' or traditional vegetables in Malaysia. Int Food Res J. 2012; 19:527–30.
17. Kongkachuichai R, Charoensiri R, Yakoh K, Kringkasemsee A, Insung P. Nutrients value and antioxidant content of indigenous vegetables from Southern Thailand. Food Chem. 2015; 173:838–46.
18. Hwang CR, Hwang IG, Kim HY, Kang TS, Kim YB, Joo SS, et al. Antioxidant component and activity of dropwort (*Oenanthe javanica*) ethanol extracts. J Korean Soc Food Sci Nutr. 2011; 40:316–20.
19. Tae HJ, Park JH, Cho JH, Kim IH, Ahn JH, Lee JC, et al. *Oenanthe javanica* extract increases immunoreactivities of antioxidant enzymes in the rat kidney. Chin Med J. 2014; 127:3758–63.
20. Tan YP. Antioxidant, antityrosinase, antibacterial and anti-quorum sensing activities of selected ulam herbs in Malaysia [MSc thesis]. Malaysia: UCSI University; 2013. p. 141.
21. Wahab NAA, Zain MSM, Kader J, Radzi SM, Noor, HM. Study of selected on anti-quorum sensing potential local ulam in Malaysia. World J Pharm Pharm Sci. 2014; 3:203–11.
22. Kwon EJ, Kim MM. Effect of *Oenanthe javanica* ethanolic extracts on antioxidant activity and melanogenesis in melanoma cells. J Life Sci. 2013; 23:1428–35.
23. Tan YP, Chan EWC. Antioxidant, antityrosinase and antibacterial properties of fresh and processed leaves of *Anacardium occidentale* and *Piper betle*. Food Biosci. 2014; 6:17–23.
24. Chiang SH, Chen YS, Hung MS, Lee SM, Lin CC. The enhancement effect of *Salvia miltiorrhiza* on melanin production of B16F10 melanoma cells. J Med Plant Res. 2012; 6:4338–42.
25. Yang XB, Huang ZM, Cao WB, Zheng M, Chen HY, Zhang JG. Antidiabetic effect of *Oenanthe javanica* flavone. Acta Pharmacol Sin. 2000; 21:239–42.
26. Yoshida J, Seino H, Ito Y, Nakano T, Satoh T, Ogane Y, et al. Inhibition of glycogen synthase kinase-3β by falcarindiol

isolated from Japanese parsley (*Oenanthe javanica*). J Agric Food Chem. 2013; 61:7515–21.

27. Ji G, Yao X, Zang Z, Huang Z. Antiarrhythmic effect of *Oenanthe javanica* (Bl.) DC injection. J Chin Mater Med. 1990; 5:429–31.
28. Kim TH, Ku KS, Bae JS. Anti-inflammatory activities of isorhamnetin-3-*O*-galactoside against HMGB1-induced inflammatory responses in both HUVECs and CLP-induced septic mice. J Cell Biochem. 2013; 114:336–45.
29. Kim TH, Ku SK, Bae JS. Persicarin is anti-inflammatory mediator against HMGB1-induced inflammatory responses in HUVECs and in CLP-induced sepsis mice. J Cell Physiol. 2013; 228:696–703.
30. Lee JM, Kim NJ, Cho DH, Chung MY, Hwang KT, Kim HJ, et al. Ethanol extract of *Oenanthe javanica* modulates inflammatory response by inhibiting NF-κB mediated cyclooxygenase-2 expression in RAW 264.7 macrophage. Food Sci Biotechnol. 2006; 15:303–7.
31. Yang JH, Kim SC, Shin BY, Jin SH, Jo MJ, Jegal KH, et al. *O*-methylated flavonol isorhamnetin prevents acute inflammation through blocking of NF-κB activation. Food Chem Toxicol. 2013; 59:362–72.
32. Park JH, Cho JH, Kim IH, Ahn JH, Lee JC, Chen BH, et al. *Oenanthe javanica* extract protects against experimentally induced ischemic neuronal damage via its antioxidant effects. Chin Med J. 2015; 128:2932–7.
33. Chen BH, Park JH, Cho JH, Kim IH, Shin BN, Ahn JH, et al. Ethanol extract of *Oenanthe javanica* increases cell proliferation and neuroblast differentiation in the adolescent rat dentate gyrus. Neural Regen Res. 2015; 10:271–6.
34. Park JC, Choi JW. Effects of methanol extract of *Oenanthe javanica* on the hepatic alcohol metabolizing enzyme system and its bioactive component. Phytother Res. 1997; 11:260–2.
35. Cho HW, Kim MH, Hwang KY, Min BW, Park JC, Kim JH. Effects of *Oenanthe javanica* extracts on mercury accumulation in organs of the mouse. J Toxicol Publ Health. 1999; 15:1–8.
36. Ku SK, Kim TH, Bae JS. Anticoagulant activities of persicarin and isorhamnetin. Vasc Pharmacol. 2013; 58:272–9.
37. Ku SK, Kim TH, Lee S, Kim SM, Bae JS. Antithrombotic and profibrinolytic activities of isorhamnetin-3-*O*-galactoside and hyperoside. Food Chem Toxicol. 2013; 53:197–204.
38. Lee SI, Park YS, Cho SY. Protective effect of *Oenanthe javanica* on the carbon tetrachloride-induced hepatotoxicity in mice. J Korean Soc Food Sci Nutr. 1993; 22:392–7.
39. Park JC, Yu YB, Lee JH, Hattori M, Lee CK, Choi JW. Protective effect of *Oenanthe javanica* on the hepatic lipid peroxidation in bromobenzene-treated rats and its bioactive component. Planta Med. 1996; 62:488–90.
40. Park JC, Kim JY, Lee YJ, Lee JS, Kim BG, Lee SH, et al. Protective effect of *Oenanthe javanica* extract on acetaminophen-induced hepatotoxicity in rats. Yakhak Hoeji. 2008; 54:316–21.
41. Lee CH, Park JH, Cho JH, Kim IH, Ahn JH, Lee JC, et al. Effect of *Oenanthe javanica* extract on antioxidant enzyme in the rat liver. Chin Med J. 2015; 128:1649–54.
42. Ai G, Huang ZM, Liu QC, Han YQ, Chen X. The protective effect of total phenolics from *Oenanthe javanica* on acute liver failure induced by D-galactosamine. J Ethnopharmacol. 2016; 186:53–60.
43. Yang SA, Jung YS, Lee SJ, Park SC, Kim MJ, Lee EJ, et al. Hepatoprotective effects of fermented field water-dropwort (*Oenanthe javanica*) extract and its major constituents. Food Chem Toxicol. 2014; 67:154–60.
44. Sun ZX, Liu S, Zhao AQ, Su RQ. Protective effect of chlorogenic acid against carbon tetrachloride-induced acute liver damage in rats. Chin Herbal Med. 2014; 6:36–41.
45. Choi H, You Y, Hwang K, Lee J, Chun J, Chung JW, et al. Isolation and identification of compound from dropwort (*Oenanthe javanica*) with protective potential against oxidative stress in HepG2 cells. Food Sci Biotechnol. 2011; 20:1743–6.
46. Dong GZ, Lee JH, Ki SH, Yang JH, Cho IJ, Kang SH, et al. AMPK activation by isorhamnetin protects hepatocytes against oxidative stress and mitochondrial dysfunction. Eur J Pharmacol. 2014; 740:634–40.
47. Lee MK, Yang H, Ha NR, Sung SH, Kim YC. Isorhamnetin from *Oenanthe javanica* attenuates fibrosis in rat hepatic stellate cells via inhibition of ERK signaling pathway. Nat Prod Sci. 2008; 14:81–5.
48. Lee JY, Kim MY, Shin SH, Shin YO, Lee AR, Park CH, et al. Persicarin isolated from the *Oenanthe javanica* attenuates diabetes induced liver injury through the hyperglycemia upregulated NADPH oxidase activation. Integr Med Res. 2015; 4:75.
49. Han YQ, Huang ZM, Yang XB, Liu HZ, Wu GX. *In vivo* and *in vitro* anti-hepatitis B virus activity of total phenolics from *Oenanthe javanica*. J Ethnopharmacol. 2008; 118:148–53.

50. Wang WN, Yang XB, Liu HZ, Huang ZM, Wu GX. Effect of *Oenanthe javanica* flavone on human and duck hepatitis B virus infection. Acta Pharmacol Sin. 2005; 26:587–92.
51. Qi F, Wang Z, Cai P, Zhao L, Gao J, Kokudo N, et al. Traditional Chinese medicine and related active compounds: a review of their role on hepatitis B virus infection. Drug Discov Ther. 2013; 7:212–24.
52. Qiu LP, Chen KP. Anti-HBV agents derived from botanical origin. Fitoterapia. 2013; 84:140–57.
53. Won BY, Shin KY, Ha HJ, Chang KA, Yun YS, Kim YR, et al. Effect of dropwort (*Oenanthe javanica*) extracts on memory improvement in Alzheimer's disease animal model, Tg2576 mice. Korean J Food Sci Technol. 2015; 47:779–84.
54. Won BY, Shin KY, Ha HJ, Wee JH, Yun YS, Kim YR, et al. Inhibitory effects of dropwort (*Oenanthe javanica*) extracts on memory impairment and oxidative stress and the qualitative analysis of isorhamnetin in the extracts. J Korean Soc Food Sci Nutr. 2016; 45:1–11.
55. An ST, Choi YD, inventors; An ST, assignee. Production of tonic beverage composition. Korean patent 20020062806. 2004 Apr 4.
56. Jung GU, inventor; Daegun Food Co Ltd, assignee. Manufacturing method of alcohol detoxification beverage. Korean patent KR20030006670. 2004 Aug 11.
57. Lee IP, inventor; Lee IP, assignee. Minari extract for preventing the induction and metastasis of cancer by carcinogens contained in cigarette smoke, fermented foods or alcoholic drinks. United States patent US7273625. 2007 Sep 25.
58. Kim ES, Kim HJ, Lee GY, Lee JY, Sung SH, Yoon JS, inventors; Elcom Science Co Ltd, assignee. Composition for improving brain function and cognitive function of human. Korean patent KR20020042740. 2004 Jan 31.
59. Suh YH, Shin KY, Won BY, Lee HJ, Lee HG, Hee JK, et al., inventors; Braintropia Co Ltd, assignee. Composition containing *Oenanthe javanica* extract as an active ingredient for preventing or treating learning disabilities or memory disorders, and method for preparing same. World Intellectual Property Organization patent WO2011KR06591. 2012 Mar 15.
60. Suh YH, Shin KY, Won BY, Lee HJ, Lee HG, Jung KH, et al., inventors; Braintropia Co Ltd, assignee. Composition for treatment or prevention of learning or memory malfunctions comprising minari extract as an effective component and preparation method thereof. Korean patent KR20110090839. 2012 Mar 16.
61. Bodeker G. Health and beauty from the rainforest: Malaysian traditions of Ramuan. Kuala Lumpur: Didier Millet; 2009. p. 256.
62. Amna OF, Nooraain H, Noriham A, Azizah AH, Husna RN. Acute and oral subacute toxicity study of ethanolic extract of *Cosmos caudatus* leaf in Sprague Dawley rats. Int J Biosci Biochem Bioinfor. 2013; 3:301–5.
63. Rahman AHMM. An ethnobotanical investigation on Asteraceae family at Rajshahi, Bangladesh. J Busin Admin Manag Sci Res. 2013; 2:133–41.
64. Shui G, Leong LP, Wong SP. Rapid screening and characterisation of antioxidants of *Cosmos caudatus* using liquid chromatography coupled with mass spectrometry. J Chromatogr B. 2005; 827:127–38.
65. Mediani A, Abas F, Khatib A, Tan CP. *Cosmos caudatus* as a potential source of polyphenolic compounds: optimisation of oven drying conditions and characterisation of its functional properties. Molecules. 2013; 18:10452–64.
66. Abas F, Shaari K, Lajis NH, Israf DA, Kalsom YU. Antioxidative and radical scavenging properties of the constituents isolated from *Cosmos caudatus* Kunth. Nat Prod Sci. 2003; 9:245–8.
67. Andarwulan N, Batari R, Sandrasari DA, Bolling B, Wijaya H. Flavonoid content and antioxidant activity of vegetables from Indonesia. Food Chem. 2010; 121:1231–5.
68. Andarwulan N, Kurniasih D, Apriady RA, Rahmat H, Rotoc AV, Bolling BW. Polyphenols, carotenoids, and ascorbic acid in underutilized medicinal vegetables. J Funct Food. 2012; 4:339–47.
69. Lee TK, Vairappan CS. Antioxidant, antibacterial and cytotoxic activities of essential oils and ethanol extracts of selected South East Asian herbs. J Med Plant Res. 2011; 5:5284–90.
70. Dian-Nashiela F, Noriham A, Noorain H, Azizah AH. Antioxidant activity of herbal tea prepared from *Cosmos caudatus* leaves at different maturity stages. Int Food Res J. 2015; 22:1189–94.
71. Cheng SH, Khoo HE, Ismail A, Abdul-Hamid A, Barakatun-Nisak MY. Influence of extraction solvents on *Cosmos caudatus* leaf antioxidant properties. Iranian J Sci Technol. 2016; 40:51–8.
72. Rasdi NHM, Samah OA, Sule A, Ahmed QU. Antimicrobial studies of *Cosmos caudatus* Kunth. (Compositae). J Med Plant Res. 2010; 4:669–73.
73. Salehan NM, Meon S, Ismail IS. Antifungal activity of *Cosmos caudatus* extracts against seven economically

important plant pathogens. Int J Agric Biol. 2013; 15:864–70.

74. Ajaykumar TV, Anandarajagopal K, Sunilson AJ, Arshad A, Jainaf RAM, Venkateshan N. Anti-inflammatory activity of *Cosmos caudatus*. Int J Univ Pharm Bio Sci. 2012; 1:40–8.
75. Amalia L, Sukrasno AK, Fidrianny I, Inggriani R. Antihypertensive potency of wild cosmos (*Cosmos caudatus* Kunth, Asteraceae) leaf extract. J Pharmacol Toxicol. 2012; 7:359–68.
76. Radman HM, Yusof K, Saad QM, Ngah WZW, Abdullah A. The effect of ulam raja (*Cosmos caudatus*) on drug-metabolizing enzymes, lipid peroxidation and antioxidant status in mice liver. Int J Pharm Tech Res. 2014; 6:1213–25.
77. Abdullah A, Dhaliwal KK, Roslan NNF, Lee CH, Kalaiselvam M, Radman HM, et al. The effects of *Cosmos caudatus* (ulam raja) on detoxifying enzymes in extra-hepatic organs in mice. J Appl Pharm Sci. 2015; 5:82–8.
78. Loh SP, Hadira O. *In vitro* inhibitory potential of selected Malaysian plants against key enzymes involved in hyperglycemia and hypertension. Malay J Nutr. 2011; 17:77–86.
79. Mun'im A, Azizahwati K, Andriani A, Mahmudah KF, Mashita M. Screening of inhibitory activity of some Indonesian medicinal plants. Int J Med Aromat Plant. 2013; 3:144–50.
80. Javadi N, Abas F, Hamid A, Simoh S, Shaari K, Ismail IS. GC-MS-based metabolite profiling of *Cosmos caudatus* leaves possessing alpha-glucosidase inhibitory activity. J Food Sci. 2014; 79:1130–6.
81. Mohamed N, Khee SGS, Shuid AN, Muhammad N, Suhaimi F, Othman F, et al. The effects of *Cosmos caudatus* on structural bone histomorphometry in ovariectomized rats. Evid-based Complement Altern Med. 2012; 817814:6.
82. Mohamed N, Sahhugi Z, Ramli ESM, Muhammad N. The effects of *Cosmos caudatus* (ulam raja) on dynamic and cellular bone histomorphometry in ovariectomized rats. BMC Res Notes. 2013; 6:239.
83. Mohamed N, Yin CM, Shuid AN, Muhammad N, Babji AS, Soelaiman IN. The effects of *Cosmos caudatus* (ulam raja) supplementation on bone biochemical parameters in ovariectomized rats. Pak J Pharm Sci. 2013; 26:1027–31.
84. Godspower PR, Mohamed N, Shuid AN. *Cosmos caudatus* enhances fracture healing in ovariectomised rats: a preliminary biomechanical evaluation. Int J Appl Res Nat Prod. 2015; 8:12–9.
85. Perumal V, Hamid AA, Ismail A, Shaari K, Abas F, Ismail IS, et al. Effect of *Cosmos caudatus* Kunth leaves on the lipid profile of a hyperlipidemia-induced animal model. J Food Chem Nutr. 2014; 2:43–51.
86. Norazlina M, Ehsan SZ, Noor Adilah K, Lee CP, Farhana E, Derick P, et al. Acute toxicity study of *Cosmos caudatus* on biochemical parameters in male rats. Sains Malaysiana. 2013; 42:1247–51.
87. Cheng SH, Ismail A, Anthony J, Ng OC, Hamid AA, Yusof BN. Effect of *Cosmos caudatus* (ulam raja) supplementation in patients with type 2 diabetes: study protocol for a randomized controlled trial. BMC Complement Altern Med. 2016; 16:84.
88. Cheng SH, Ismail A, Anthony J, Ng OC, Hamid AA, Barakatun-Nisak MY. Eight weeks of *Cosmos caudatus* (ulam raja) supplementation improves glycemic status in patients with type 2 diabetes: a randomized controlled trial. Evid-based Complement Altern Med. 2015; 405615:7.