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Medicinal Properties of *Daucus carota* in Traditional Persian Medicine and Modern Phytotherapy

Rosita Bahrami, Ali Ghobadi , Nasim Behnoud, Elham Akhtari*

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Abstract

Daucus carota, commonly known as carrot, is a popular medicinal plant with various pharmacological activities mentioned in traditional Persian medicine (TPM) and modern phytotherapy including antioxidant, analgesic, anti-inflammatory, antimicrobial, antifungal, diuretic, lithontripic, emmenagogue, intra occular hypotensive, gastroprotective, hepatoprotective, aphrodistic, nephroprotective, antispasmodic, anticancer, antiestrogenic, cardioprotective, and wound healing activities. No serious adverse events have been recorded after ingestion of carrot except for some cases of photosensitivity. Because of its emmenagogic, abortifacient and uterus stimulation properties, it should be avoided in pregnancy. A significant interaction between carrot and lithium has also been demonstrated. Based on a pharmacokinetic study, ingestion of *Daucus carota* may increase plasma levels of vitamin C, zinc and in lactating women vitamin A, serum ferritin, and serum iron levels. The aim of this paper is to review pharmacological properties, toxicity, adverse effects and dug interaction of *Daucus carota* in TPM and modern phytotherapy.

Keywords: *Daucus Carota*, Carrot, Traditional Persian Medicine, Pharmacological Activity, Modern Phytotherapy.

Introduction

Daucus carota commonly known as wild carrot is a very commonly used nutritional and medicinal plant from the family of Umbelliferac. The names used in traditional Persian medicine (TPM) for this plant are Zardak and Gazar. The Wild Carrot is a biennial, 30 cm to 1 m high cultivated plant with a fusiform, usually red root and numerous pinnate, segmented, hairy leaves. In the second year, the plant produces a branched, angular stem with alternate jointed leaves, which terminates in the flowering umbels. *Habitat*: It is now found in its cultivated form all over the world. *Production*: Wild Carrots are the roots of *Daucus carota*. The ripe roots are harvested. *Other Names*: Carrot, Bird's Neat, Birds' Nest, Bees' Nest, Queen Anne's Lace, and Philtron.

In TPM, the entire world is made from four elements including air, fire, water, and soil, and each has its own specific quality: air is hot and moist, fire is hot and dry, water is cold and moist, and soil is cold and dry. The differences between objects are attributed to different ratios of these four elements used contained their structures. Thus, every object in the world has a specific quality based on dominant element(s) in its structure. This specific quality has been known as temperament (Sina, 2005; Aghili Khorasani, 2006). Based on this theory, *Daucus carota* is known to have a hot and moist nature (Aghili Khorasani, 2001). *Daucus carota* contains carotenoids including alpha-, beta-, gamma-, and zeta-carotene; lycopene volatile oil (very little) including p-cymene, limonene, dipenten, and geraniol; alpha- and beta- caryophyllene Polyene’s including falcarinol (carotatoxin) mono and oligosaccharides: glucose and sucrose. (Fleming, 2000)

Material and Methods

Web-based databases such as Google Scholar, Med Line, PubMed, and Elsevier were searched using the related keywords and articles published from May 2000 to February 2019 were extracted. Thereafter, the articles were assessed against the research criteria using the

Rosita Bahrami, Nasim Behnoud

School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran.
Research institute for Islamic and complementary Medicine, Iran University of Medical Sciences, Tehran, Iran.
Student Research Committee, Iran University of Medical Sciences, Tehran, Iran.

Ali Ghobadi, Elham Akhtari*
School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran.
Research institute for Islamic and complementary Medicine, Iran University of Medical Sciences, Tehran, Iran.

***Email:** eli.akhtari@gmail.com

following keywords: *Daucus carota*, Carrot, Bird's Neat, Birds' Nest, Bees' Nest, Queen Anne's Lace, Zardak, Gazar and Philtron

Findings

Pharmacologic Properties

View of TPM

Carrot eliminates obstructions of internal organs especially those in liver. It is stomach tonic and useful for stomachache, chest pain, and liver diseases. It is also diuretic and has lithontriptic property. Carrot increases sexual desire, potency, and sperm production. It is also uterus tonic. Processed carrot with vinegar is useful for diseases of spleen. This vegetable is laxative and decreases abdominal cramp. Carrot seeds are highly diuretic and emmenagogic, and elevate sexual desire especially if cooked with honey. It is also useful for dysuria and dystocia .(Tonkaboni, 2007) According to Canon of medicine, the most famous reference book of traditional Persian medicine, Daucus carota (Gazr) leaf and root are diuretic, useful for fertility, and effective against cough, pleurisy, corrosive ulcer, and dropsy. Also, Daucus carota seeds are diuretic , emmenagogic, deobstruent, and useful for intestinal pain (Sina, 2005)

Antioxidant activity

The antioxidant activity of *Daucus carota* has been demonstrated by various studies. wild carrot oil fractions have shown a unique chemical composition and significant antioxidant activities as well as hepatoprotective effects against CCl4-induced hepatotoxicity. (Bishayee, Sarkar and Chatterjee, 1995) Carrots are a major source of provitamin A, meeting 17% of the total vitamin A requirements and also rich in α- and β- carotenes. Carotenes have proven to possess antioxidant activity. Phenolic compounds as well as their antioxidant properties and distribution in carrots were investigated in a study, suggesting that phenolics could play an important role in antioxidant properties in carrots.(Zhang and Hamauzu, 2004)

Anticancer activity

Interest in the use of herbal drugs has developed widely around the world. Some studies suggest an overall herbal use level from 13% to 63% in patients who suffer from cancer .(Sparreboom et al., 2004) Several frequently used herbs have been recognized by the National Cancer Institute as agents possessing cancer-preventive properties. These herbs are members of the Allium family like garlic, the Labiatae (mint) family, the Zingiberaceae family like ginger and the Umbelliferae (carrot) family (Khodadadi, 2016).These natural products represent a rich reservoir of potential small chemical molecules exhibiting anti-proliferative and anticancer properties (Khodadadi, 2016).

The anticancer activity of carrot has been demonstrated by various studies. Antitumor activity of carrot peels has also been shown in vitro. Carrot peel extract contains the highest antitumor activity among fruits peels extracts including orange, lemon, tangerine, watermelon, kiwi, banana, and golden berry (El Zawawy, 2015). The aqueous extract of *D.carota* has been found to possess anticancer activity against human promyelocytic leukemia HL-60 cells, while the oil extract exhibited chemo-preventive effects against chemically induced skin cancer (Mroueh, El Ghaziri and Daher, 2011). The anticancer activity of the oil extract against human colon and breast cancer cell lines has also been established (Shebaby et al., 2013). A study has shown that extracts from carrots can induce apoptosis in leukemia cell lines. The findings suggest that carrots may be an excellent source of bioactive chemicals for the treatment of leukemia (Zaini, Clench and Le Maitre, 2011).

Analgesic and Anti-inflammatory activities

Volatile oil of *D. carota* seeds at 50 and 100 mg/kg resulted in 60 and 70% inhibition of carrageenan-induced rat paw edema, respectively. Writhing was also inhibited by 50 and 69% at 50 and 100 mg volatile oil/kg, respectively, indicating its analgesic activity (Porchezhian, Ansari and Ali, 2000). The anti-inflammatory effect of aqueous extracts of *Daucus carota* root in acetic acid-induced experimental colitis has been demonstrated by inhibition of releasing oxido-inflammatory mediators such as myeloperoxidase and nitric oxide (Patil, Kandhare and Bhise, 2012). An investigation has revealed the cardio-protective effects of the water extract of *D. carota root*, a nutraceutical against isoproterenol-induced myocardial infractions in rats (Muralidharan, Balamurugan and Kumar, 2008). Carrot seed has the potential to be consumed for preventing arthritic pains (Momin, De Witt and Nair, 2003). Finally, the ethanolic extract of *Daucus carota* with a dose of 100-400 mg/kg has indicated anti-inflammatory effects on formaldehyde-induced arthritis in rats (Arya, Gupta and Kaur, 2011).

CNS activity

The effects of the ethanolic extract of *Daucus carota* seeds on cognitive functions, total serum cholesterol levels, and brain cholinesterase activity has been studied in mice. DCE (200, 400 mg/kg, po) showed significant improvements in the memory scores of young and aged mice. These improvements in memory scores were observed using passive avoidance apparatus and aged mice. DCE also reversed the amnesia induced by scopolamine (0.4 mg/kg, ip) and diazepam (1 mg/kg, ip). *Daucus carota* extract (200, 400 mg/kg, po) significantly reduced the brain acetylcholinesterase activity and cholesterol levels in young and aged mice (Vasudevan and Parle, 2006). Further, the antidepressant activity of ethanol root extract of *Dacus carota* (DC) has been studied in different animal models. The antidepressant activity of DC (400 mg/kg) was comparable to that of standard drugs such as Fluoxetine (Babu et al., 2014). The seeds contain choline and can inhibit brain cholinesterase activity, and may elevate the brain acetylcholine levels via increased synthesis of acetylcholine. So, it is beneficial in cognitive dysfunctions (Gambhir et al., 1966; Gambhir et al., 1979).

Antimicrobial and Antifungal activities

Roots of the wild *Daucus carota* ssp *carota* have shown a range of mild antibacterial activities against four Gram-positive (Staphylococcus aureus, Streptomyces scabies, Bacillus subtilus, and Bacillus cereus) and two Gram-negative species (Pseudomonas aeruginosa and Escherichia coli) as well as antifungal activities against Fusarium oxysporum and Aspergillus niger (Ahmed, 2005). The flavones isolated from the methanol extract of *Daucus carota* seeds were evaluated for antibacterial effects. The results demonstrated bactericidal activity against Staphylococcus aureus and Escherichia coli, Bacillus cereus, and Citrobacter freundii (Kumarasamy, 2005). The in-vitro antimicrobial activity of essential oils of *Daucus carota* seeds has been evaluated against one Gram-positive (Staphylococcus aureus) and two Gram-negative bacteria (Escherichia coli and Salmonella typhimurium), along with a pathogenic yeast (Candida albicans). All tested essential oils exhibited antibacterial and antifungal activities against the assayed microorganisms (Rokbeni et al., 2013). The antimicrobial activity of the essential oil of *Daucus carota* subsp *carota* from Portugal was evaluated against several Gram-positive and Gram-negative bacteria, yeasts, dermatophytes, and Aspergillus strains. The results revealed a significant activity towards Gram-positive bacteria, Cryptococcus neoforman), and dermatophyte. The inhibition of germ tube formation and the effect of the oil on Candida albicans biofilms were also observed (Alves-Silva et al., 2016). The essential oil of the aerial parts of wild *Daucus carota* at the end of the flowering stage inhibited the growth of Campylobacter jejuni, Campylobacter coli, and Campylobacter lari strains, including one multidrug resistant Campylobacter jejuni (Rossi et al., 2007). The strongest antifungal activity was observed for carotol, the main sesquiterpenic compound in the carrot seed oil, which inhibited the radial growth of Alternaria alternata by 65% (Jasicka-Misiak et al., 2004).

Wound healing activity

In an animal study, topical use of a soft paraffin-based cream containing ethanolic extract of *Daucus carota* root was evaluated for possible wound healing activity of the plant. The results showed significant shrinkage of the wound area, epithelization period, and scar width without any significant skin irritation (Patil, Kandhare and Bhise, 2012).

Antispasmodic activity

A nitrogen-containing base isolated from seeds of *Daucus carota* was evaluated for possible antispasmodic activities of the plant on smooth muscles of ileum, blood vessels, uterus and trachea of different species of animals. The results indicated spasmolytic activity , but its activity was found to be about one-tenth of that of papaverine (Gambhir et al., 1979).

Effect on intraocular pressure

In a study on rabbits, topical application of *Daucus carota* seeds extract in normotensive rabbits resulted in diminished mean intraocular pressure (IOP) .In experimentally elevated IOP, topical application of the extract with a concentration of 0.6% yielded 29.39% decrease of IOP in water loaded animals which was comparable to the efficacy of Pilocarpine and 30.27% decrease of IOP in steroid pretreated rabbits, which was significantly higher than that of Pilocarpine (Agarwal et al., 2008).

Hair growth promoting activity

Animal studies were conducted using standardized *Daucus carota* extract in a gel form applied to the skin of albino rats. The results showed that petroleum ether *Daucus carota* extract promoted hair growth by inducing the anagen phase. The histomorphometric analysis data indicated that topical use of the extract in the gel form induced an earlier anagen phase and prolonged the mature anagen phase, in contrast to control and minoxidil 1% treated group. The results also showed an increase in the number and size of hair follicles of the extract treated group (Al-Snafi, 2017).

Effects on the reproductive system

The petroleum ether extract and fraction 5 (fatty acids) of carrot seeds stopped the normal estrus cycle of adult mouse and reduced the weight of ovaries significantly. The cholesterol and ascorbic acid content in ovaries were significantly elevated by the extract and fraction 5 of carrot seeds. A significant inhibition of delta 5,3-betahydroxy steroid dehydrogenase and glucose-6-phosphate dehydrogenase (the two key enzymes involved in ovarian steroidogenesis) were also recorded in mouse ovaries after 15 days of treatment (Majumder et al., 1997). The petroleum ether, alcoholic, and aqueous extracts of *Daucus carota* were evaluated for their possible anti-ovulatory activity in rabbits with copper-induced ovulation. The results indicated 40%, or less decrease in ovulation (Kapoor, Garg and Mathur, 1974). The effect of carrot seed extract on spermatogenesis, motility, and number of sperms in cauda epididyme was studied in male rats. *Daucus carota* seeds caused a significant increase in cauda epididymis sperm reserve. The extract could protect the reproductive system against gentamicin-induced toxicity and induced spermatogenesis possibly through elevating testosterone levels (Nouri et al., 2009). The alcoholic extract of *Daucus carota* seed administered at different doses ranging from 50 to 250 mg/kg bw after coitus showed a significant dose-dependent antifertility effect. The administration of the extract at a lower dose revealed anti-implantational activity, whereas higher doses caused fetal resorption. The main effect of the extract was abortifacient activity. At higher doses, the extract demonstrated an estrogenic nature, whereas lower doses showed an antiestrogenic nature. On the other hand, the extract indicated neither progestational nor antiprogestational effects (Bhatnagar, 1995).

Cardiovascular effects

Ethanolic extract of *Daucus carota* at the dose of 10–100 mg/kg caused a dose-dependent fall in systolic and diastolic arterial blood pressure in normotensive anesthetized rats (Gilani, Shaheen and Saeed, 1994). The effects of a three-week supplementation of the diet with carrot (15% dry matter) in lipid metabolism were studied in rats. A significant decline of cholesterol level in the liver was observed together with a reduction of the level of liver triglycerides. Fecal total steroid excretion increased by 30% upon feeding the carrot diet as compared to the control. The secretion of bile acids remained unchanged, while the cholesterol apparent absorption was reduced in rats fed carrot diet (Nicolle et al., 2003).

Antidiabetic activity

The effect of the methanol extract of *Daucus carota* (wild carrot) seeds (100, 200 and 300 mg/kg bw orally for 6 days) was studied on the serum levels of lipids and on the biochemical indices of kidney and liver function in streptozocin-induced diabetic (type 1) rats. Administration of the extract of *Daucus carota* seeds in diabetic rats for six days, at all doses, significantly lowered serum levels of creatinine, total cholesterol, and triglycerides. Also, oral administration of the extract significantly reduced the serum levels of low density lipoprotein (LDL) cholesterol, aspartate amino transferase, urea, and alanine aminotransferase.

Gastroprotective activity

The therapeutic potential of ethanol extract 50% of *Daucus carota* roots (EDC) was studied as antisecretory, gastroprotective, and antacid capacity using experimental rats. Assessment of EDC antisecretory and in-vivo antacid capacities was performed using a pyloric ligation-induced ulcer model. The gastroprotective effects were assessed with an absolute ethanol-induced ulcer model. The integrity of gastric mucosa was evaluated through estimating the glutathione and gastric mucus level and with histopathological examination of gastric mucosal cells. The effect of the extract on the liver was assessed by measuring serum biochemical parameters. The EDC significantly reduced gastric lesions in both models. It also significantly lowered the volume of gastric content, and the total acidity significantly dropped with the doses of 100 and 200 mg/kg of EDC. On the other hand, the mucus content and glutathione level increased significantly in the absolute alcohol-induced ulcer. The EDC also showed in-vitro antacid capacity. Histopathological studies further confirmed the effects of EDC by inhibiting congestion, edema, hemorrhage, and necrosis in gastric mucosa (Chandra, Kishore and Ghosh, 2015). In another study, the anti-peptic ulcer effects of the aqueous and methanolic extracts of *Daucus carota* umbels were investigated against ethanol-induced gastric ulcer in rats. Aqueous and methanolic extracts showed significant protection against ethanol-induced gastric ulcer with a curative ratio of 46.8 and 68.7%, at a dose of 250 mg/kg of body weight, respectively (Wehbe, Mroueh and Daher, 2009). The gastroprotective potential of the fresh juice extract of *Daucus carota* roots (200 and 400 mg/kg bw, orally) was studied in gastric ulcerations experimentally induced by pylorus ligation, aspirin, and ethanol. The *Daucus carota* extracts significantly lowered free acidity, total acidity, and ulcer index, while it increased the pH and the mucus content as compared with the control. The *Daucus carota* extract at a dose of 400 mg/kg produced 60.45, 56.80, and 43.51% ulceration inhibition when the gastric ulceration was induced by pylorus ligation, aspirin and ethanol, respectively (Khatib et al., 2010). The gastroprotective effects of 4.08 g of carrot juice administered by feeding tube was studied on the hydrochloric acid concentration in the stomach in aspirin-induced Wistar strain rats. The results of carrot juice consumption together with aspirin indicated a statistically significant reduction in HCl concentration in the stomach. The result was also significant when compared with Misoprostol (Jiin, Hidayat and Lukman, 2014).

Nephroprotective activity

The nephroprotective effects of ethanolic root extract of *Daucus carota* (200 and 400 mg/kg, po) was studied against gentamicin-induced nephrotoxicity in albino Wistar rats. Gentamicin caused elevated serum urea, BUN, uric acid, and creatinine levels, which were found to be significantly lower in groups receiving *Daucus carota* dose-dependently. The nephroprotective effects of *Daucus carota* were further confirmed by histological observations (Sodimbaku et al., 2016).

Hepatoprotective activity

The influence of carrot extract on CCl4-induced acute liver damage was studied in mice. The extracts significantly lowered the serum levels of glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, lactate dehydrogenase, alkaline phosphatase, sorbitol, and glutamate dehydrogenase elevated by CCl4-induction. The extract also decreased the elevated serum bilirubin and urea levels. The increased activities of hepatic 5'-nucleotidase, acid phosphatase, acid ribonuclease, and decreased levels of succinic dehydrogenase, glucose-6-phosphatase, and cytochrome P-450 produced by CCl4 were reversed by the extract dose-dependently (Bishayee, Sarkar and Chatterjee, 1995). The hepatoprotective effect of kaempferol (100 and 200 mg/kg bw) isolated from *Daucus carota* leaves was tested in acetaminophen-induced liver damage of albino rats. Oral treatment with kaempferol reversed all the serum and liver parameters in a dose-dependent manner (Jain et al., 2012).

Precautions and Adverse Reactions

In TPM, this herb is used cautiously in patients with hot temperament. The most important characteristics of these people include feeling hot more than normal in a hot condition, getting warm easily in a cold environment, warm fingertips under normal conditions, preferring cold drinks, not easily standing hunger, having a rather high energy, suffering from eye and head aches, sudden hot feeling under normal conditions, and having hypertension (Shahabi et al., 2008).

health risks or side effects have not been recorded following the proper administration of designated therapeutic dosages. The drug has a low potential for sensitization through skin contact. *DOSAGE Mode of Administration*: The drug is taken in a ground form or consumed as a juice or vegetable. It is found in readymade medicinal preparations (Fleming, 2000)

Because of its emmenagogic abortifacient, uterine stimulation properties, it should be avoided in pregnancy. It is also logical to avoid its usage also in kidney failure due to the irritating effects of its volatile oil. Plants in the Apiaceae (carrot, parsnip) family can act as a phototoxic agent by increasing the skin sensitivity to ultra-violet radiation (Peters, 2014). In Chinese Medicine, this herb is considered to have low toxicity with reports of adverse reactions only after ingestion of about 45 g. Symptoms may include mild headache, nausea, tinnitus, and abdominal pain. Notably, these symptoms are self-limiting (Peters, 2014). It is suggested to avoid using *Daucus carota* preparations in diabetes mellitus due to the diuretic action of the seeds and the hypoglycemic effect of the roots on mice (Brinker, 1997).

Drug Interactions

Wild carrot might have an effect like a water pill or "diuretic." Taking wild carrot might diminish the body power to eliminate lithium. This, in turn, could increase lithium levels in the body thus resulting in serious side effects. Large amounts of wild carrot might have some of the same effects as estrogen. However, wild carrot is not as strong as estrogen pills. Taking wild carrot along with estrogen pills might decrease the effects of estrogen pills. Taking wild carrot along with medications that increase sensitivity to sunlight could increase the chances of sunburn, blistering, or rashes on sun-exposed areas[1]. Based on clinical trials, consumption of carrot may increase gastrointestinal transit time (Cummings et al., 1978; Wisker et al., 1994). According to a clinical trial on 10 healthy approximately 40 year-old males, consumption of 200 g of processed and cooked carrots might significantly lower glucose and insulin/C-peptide responses (Gustafsson et al., 1994). Based on a pharmacokinetic study, ingestion of carrots may increase plasma levels of vitamin C (Agte Jahagirdar and Chiplonkar, 2006). Based on another pharmacokinetic study, ingestion of carrots may also elevate plasma levels of zinc (Agte Jahagirdar and Chiplonkar, 2006). Finally, according to a clinical study in lactating women, ingestion of grated carrots may increase serum levels of vitamin A, iron, and ferritin (Ncube et al., 2001).

Discussion and Conclusion

D. carota is a well-known medicinal plant with various pharmacological properties including antioxidant, cytotoxic, antitumor, anti-inflammatory, analgesic, antifungal, antibacterial, anti-estrogenic, emmenagogic, oculohypotensive, gastroprotective, nephroprotective, hepatoprotective, memory enhancing, uretic, lithontropic, and aphrodisiac activity.

[1] https://www.rxlist.com/wild_carrot/supplements.htm

Many of the medicinal properties claimed for this plant in TPM have been proven in modern phytotherapy such as emmenagogic, gastroprotective, uretic, nephroprotective, wound healing, lithontriptic and aphrodisiac activity.

In TPM. *D. carota* has been claimed to be useful for intestinal crampy pain. This antispasmodic effect has been demonstrated in animal studies in modern phytotherapy.

Furthermore, in TPM, *D. carota* is duretic, lithontriptic, and duretic. This nephroprotective effect of the plant has been demonstrated in animal studies and confirmed by histologic observations.

In addition, in TPM, *D. carota* has been claimed to increase sexual desire, potency, and semen production. This aphrodisiac activity of carrot leaves and seeds has been shown in various studies of modern phytotherapy. According to these studies, the extract of *D. carota* seeds can contribute to enhancing spermatogenesis as well as the number and motility of sperm in male rats.

In TPM. *D. carota* is mentioned as a gastrotonic plant. In modern phytotherapy studies, *D. carota* has shown anti-secretory, gastroprotective and acid-neutralizing capacity in experimental rats.

The hepatoprotective activity of *D. carota* is another property discussed in TPM books. The plant can contribute to eliminating obstructions leading to easier removal of waste material from the liver. Several studies have indicated hepatoprotective effects of *D.carota* in modern phytotherapic studies.

No serious toxicity or adverse events have been recorded after *D. carota* use except of some cases of allergic reactions and photosensitivity especially when consumed with drugs that cause photosensitivity.

Because of its emmenagogic, abortifacient and uterine stimulation properties, it should be avoided in pregnancy. It is logical to avoid its usage in kidney failure due to the irritating effects of its volatile oil. In TPM, *D. carota* is used cautiously in patients with hot temperament.

Owing to the duretic activity of the plant, it may interfere with plasma levels of lithium and cause severe side effects. Finally, ingestion of grated carrot may increase serum levels of vitamin A,, iron, and ferritin.

Ethics approval and consent to participate

This manuscript is a part of a PhD tesis which its study protocol was approved by the ethics committee of Iran University of Medical Sciences (code number: Ir. iums.rec1396.9321309007)

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Competing interests

The authors declare that they have no competing interests.

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