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Review Article

Asparagus (Asparagus officinalis L.) and pennyroyal (Mentha pulegium L.), impressive advantages with wondrous health-beneficial phytochemicals

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Abstract

Asparagus (Asparagus officinalis L.), belonging to the Asparagaceae family and has substantial medicinal properties. The name for asparagus comes from the Greek meaning sprout or shoot. This review aims to summarize the most important traditional and modern health benefits and pharmaceutical advantages of asparagus. This manuscript included randomized control experiments, review articles, observational and analytical studies, which have been surveyed in Google Scholar, Scopus, Research Gate and PubMed. We screened the articles first by reviewing titles and abstracts and subsequently reading the whole manuscript of those publications deemed suitable. The searches focused on publication from 1980 to January 2022. The most notable volatile organic compounds responsible for the smell are methanethiol, dimethyl sulfide, dimethyl disulfide, dimethyl sulfoxide and dimethyl sulfone. The most important health benefits of asparagus are antitumor, hepatoprotective, antioxidant, hypocholesterolemic, neuroprotective, immunoprotective, antimutagenic and hypoglycemic activities. The major pennyroyal (Mentha pulegium L.) essential oils are pulegone, menthone, isomenthone, piperitone, mentol, neo-menthol and 3-Octanol. The major health benefits of pennyroyal are antiseptic, depurative, digestive, anti-rheumatic, anti-arthritic, antimicrobial, antibacterial, stomachic, astringent, emmenagogue, decongestant and insecticide. Due to its pharmacological activities, asparagus is a high potential medicinal herb and the suggestion is to increases by doing research in both safety and efficacy. Natural herbal medicines which are also non-synthetic drug, super-fruit and functional foods is recommended and medicinal plants could be considered as organic super-fruit in all over the world. The phytochemical and pharmacological characteristics of asparagus show that asparagus is one of the most important medicinal plants in both traditional and modern pharmaceutical sciences. Pennyroyal has notable promising health benefits, and its phytochemical and pharmacological benefits indicate its important to be utilized in modern medicinal studies. This review also suggests more evidences for other researchers to use asparagus and pennyroyal as the ancient efficacious natural drugs.

Keywords: antioxidant activity; asparagus; natural products; pharmaceutical benefits

Introduction

Application of medicinal herbs and plants date back to the origin of human civilization (Marmitt and Shahrajabian, 2021; Shahrajabian *et al.*, 2021a,b; Sun *et al.*, 2021a,b,c). Medicinal plants and foods may provide phytotherapy a new dimension and enable their applications to prevent and treat many diseases (Shahrajabian *et al.*, 2020a,b,c,d), with the advantages of reducing chemical and synthetic drugs (Sun *et al.*, 2019a,b,c,d). The fruit and food we consume has significant and specific impacts and they classify as either cooling or warming (Shahrajabian *et al.*, 2019a,b,c,d). Asparagus (*Asparagus officinalis* L.), belonging to *Allium* of the *Liliaceae* family, is the famous perennial highly nutrition vegetable among more than 200 species of asparagus because of its unique flavor, presence of many phytochemical, physiological functions and texture (Kato-Noguchi *et al.*, 2017; Chitrakar *et al.*, 2019; Dong *et al.*, 2019). The current searching was done by the keywords in main indexing systems including PubMed/MEDLINE, Scopus, and Institute for Scientific Information Web of Science as well as the search engine of Google Scholar. The keywords were asparagus, natural products, pharmaceutical benefits, antioxidants, and dimethyl sulfide. This mini-review aims to survey the most notable pharmaceutical and health benefits of asparagus and pennyroyal.

Asparagus

The word asparagus originates from the Greek language meaning sprout or shoot. Asparagus has a high respiration rate and short shelf-life (Lwin et al., 2020), and its main bioactive compound is phenolics (Noperi-Mosqueda et al., 2020). While the green form is most common, the white form is appreciated by its consumers because of its structure and flavour profile (Siccama et al., 2021). The production of asparagus comprised 9.1 million tons globally in 2018. The appearance of the spear such as size, shape and color are very important, when it comes to commercial grading standards (Siomos, 2018; Anastasiadi et al., 2020). China is one of the largest planting country of asparagus, and Caoxian is the most famous asparagus township in China, which is famous for producing both high quality and yield of asparagus (Zhang et al., 2020). Asparagus yield increase has relationship with the root biomass linear increase (Drost, 2018). Its leaves and pericarp are rich in flavonoids (Hamdi et al., 2017). It was discovered that covering the crowns with sandy loam produced significantly higher spear number, spear yield and better spearhead quality than covering with a heavier soil such as silt loam, and the increase in spear yield was due to a significant boost in spear number; moreover, spear-head quality decreased with soil depth (Liao et al., 1999). The most important asparagus pathogens which can decrease the quality and quantity of spears are Fusarium oxysporum and Fusarium proliferatum (Waskiewicz et al., 2013; Surono and Narisawa, 2018). Strategies designed to manage inoculums, host and environment of different species of *Fusarium* can ameliorate the adverse effect of *Fusarium* crown and root rot (Elmer, 2015).

Chemical constituents of asparagus

Asparagus contains various valuable bioactive compounds such as amino acids, flavonoids, fructan and saponins, and the most abundant flavonoids in asparagus is rutin (queretin-3-rhamnosyl glucoside) (Park et al., 2016). Fan et al. (2015) reported that five important antioxidant compounds of asparagus were ferulic acid, kaempferol, quercetin, rutin and isorhamnetin. Asparagusic acid (1,2-dithiolane-4-carboxylic acid) is unique to asparagus, and it is responsible for the odorous urine excreted after eating asparagus (Mitchell and Waring 2014). Asparagus stem has a C/N ratio of 20.5 and could be utilized as the sole feedstock for methane production (Chen et al., 2014). Asparagus can be considered as target crop for Se biofortification for spears production with enhanced Se content and antioxidant properties (Conversa et al., 2019). Li et al. (2016) isolated two new acetylenic compounds, namely asparoffins A and B, and also nyasol and 3"-methoxynyasol from stems of asparagus. It accumulates inulin and inulin neoseries-type fructans in root, which are synthesized

by three fructosyltransferases-sucrose: sucrose 1-fructosyltransderase (1-SST, EC 2.4.1.99), fructan:fructan 1-fructosyltransderase (1-FFT, EC 2.4.1.100), and fructan:fructan 6^G-fructosyltransferase (6G-FFT, EC 2.4.1.243) (Ueno *et al.*, 2020). Asparagus is root contains steroidal aponins, sarsasapogenin, shatavarin I-IV, galactogogue, quercetin and ruitn, its shoot contains thiophene, thiazole, aldehyde, ketone vanillin, asparagusic acid, and methyl/ethyl esters, its leaves contain diosgenin and quercetin-3-glucuronide, its flowers contain quercetin, rutin (2.5% dry basis), and hyperoside, and other important compounds are vitamins (A, B, C, E), inorganic compounds (Mg, P, Ca, Fe and folic acid), essential oils, amino acids (asparagines, arginine, tyrosine), secondary metabolites (flavonoids, kaempferol, resin, and tannins) (Guan *et al.*, 2015; Iqbal *et al.*, 2017).

Medicinal benefits and usages of asparagus

Asparagus is cited in Ayurveda as a nervine tonic, famous in the ancient Greek, Persian and Chinese traditional medicine, and possess neuroprotective, anti-diabetic, antioxidant, adaptogenic, nootropic activity as well as preventing oxidative neuronal damage (El-Ishaq et al., 2019; Rajasekhar et al., 2019; Vadivelan et al., 2019; Majumdar et al., 2021). Asparagus extract improved human umbilical vein endothelial cells (HUVECs) proliferation inhibited by trimethylamine N-oxide (TMAO), as TMAO repressed the proliferation of HUVECs (Wu et al., 2019). Nishimura et al. (2013) reported that the bottom-stem intake meaningfully decreased both left cardio-ankle vascular index score and the total cholesterol level (T-CHO), and it may have possibility that asparagus cladophylls and bottom-stems significantly improve hyperglycemia, hypertension and dyslipidemia. Poormoosavi et al. (2018) reported that Asparagus officinalis extract is a potential protective agent against oxidative stress, kidney and liver damage. The most important pharmacological benefits of Asparagus officinalis are shown in Table 1.

Pennyroyal (Mentha pulegium L.)

Medicinal plants and herbs have become the focus of intense researches through identification and determination of their health benefits with considering their various chemical components (Shahrajabian and Sun, 2022; Shahrajabian *et al.*, 2022a,b). A growing interest in utilization of natural products with bioactive properties from plant origin, instead of synthetic chemicals have been reported (Shahrajabian *et al.*, 2021; Shahrajabian *et al.*, 2022b; Sun *et al.*, 2021d). The genus *Mentha* is an important member of the Labiatae family, which consists eighteen species and eleven hybrids, and they have been used in traditional medicine of different countries for many years (Benabdallah *et al.*, 2016). Plants from the genus *Mentha* are aromatic, carminative and stimulant (Johnson *et al.*, 2011). Pennyroyal (*Mentha pulegium* L.) is a chief source of essential oils and phenolics which are used in food, insecticide medicine, and cosmetic applications (Gordon and Khojasteh, 2015). The yield of essential oil, based on the dry weight for *Mentha pulegium* changes from 1.90% to 6.20% (Benlarbi *et al.*, 2014; Cherrat *et al.*, 2014). The goal of this mini-review article is survey on pharmaceutical benefits of pennyroyal with considering its chemical constituents.

Chemical constituents

The study of the essential oils obtained from 10 wild *Mentha pulegium* L. populations distributed all over Greece has indicated that the content of pulegone changes considerably, ranging from <0.1-90.7% of tin total oil (Kokkini *et al.*, 2002). Yasa*et al.* (2012) reported that the chief components of headspace analysis of *Mentha pulegium* L. on DB5 column were isomenthone (52.6%), pulegone (29.5%), and menthol (3.6%) in Turkey. Nickavar and Jabbareh (2018) also found that pulegone and menthone were the important active constituents.

Table 1. The most important pharmacological activities of Asparagus officinalis

Medicinal properties	important pharmacological activities of Asparagus offici Key points	Reference
Antiapoptosis	Asparagus extract alleviated acrolein-induced mitochondrial apoptosis through upregulating NEAT1 and Bmal1/Clock in VSMCs.	Chen et al. (2020)
	Asparagus extract reversed the rhythm disorders of circadian clock induced by acrolein in vascular smooth muscle cells.	Chen et al. (2020)
Anticancer activity	Asparagus is an appropriate aspirant for future breast cancer chemotherapeutic drug, due to its selective cytotoxicity on cancer and non-cancerous cells.	Mfengwana <i>et al</i> . (2019)
Antidiabetic activity	The long-term administration of asparagus has antidiabetic impacts on non-obese type 2 diabetic rats because its application may enhance insulin secretion and the modulation of pancreatic β-cell function.	Hafizur <i>et al.</i> (2012)
Antifungal activity	Asparagus extract inhibited growth of <i>Fusarium</i> oxysporum pathogenic to horticultural crops.	Rosado-Alvarez et al. (2014)
Antimicrobial activity	Ethyl acetate extract was superior in inhibition of Gram-positive bacterial strains, while dry shoot and root methanol extracts, fresh shoot and callus ethyl acetate extracts were the most inhibiting of Gramnegative bacteria strains.	Desoukey et al. (2020)
	The film produced by 0.01 g/mL asparagus cellulose solution showed a swelling ratio of 125.4% and excellent antimicrobial activity against <i>Escherchia coli</i> and <i>Staphylococcus aureus</i> using the disk agar diffusion method.	Jin <i>et al.</i> (2021)
Antioxidant activity	Asparagus showed antioxidant and antityrosinase activity which was enhanced by hydrothermal treatment.	Fuentes-Alventosa <i>et al.</i> (2013) Zhang <i>et al.</i> (2018) Yu and Fan (2021)
	Rutin was not found in New Zealand <i>A. officinalis</i> roots (AR) and caffeic acid was found to be the dominant phenolic in AR extracts.	Symes <i>et al.</i> (2018)
Anti-tumor activity	Asparinin A isolated from asparagus showed antitumor activity.	Li et al. (2017)
Anti-tyrosinase activity	It has tremendous anti-tyrosinase activity.	Yu et al. (2020)
Immunomodulatory activity	White asparagus skin polysaccharide indicated immunomodulatory activities by RAW264.7 cell lines.	Wang et al. (2020)
	WASP-40 with high degree of esterification displayed strong immunomodulatory impacts on RAW264.7 cells.	Wang et al. (2021)

In Egypt, the essential oil ingredients of the *Mentha pulegium* were isolated and the principal compounds were pulegone (43.5%), piperitone (12.2%), p-menthane-1,2,3-triol (6.5%), y-elemenene (3.6%), guaiene (cis-β) (3.0%), carvacrol acetate (2.6%), and phenyl ethyl alcohol (2.4%), and the essential oil of *Mentha pulegium* L. related to pulegone chemotype as its oil is rich in pulegone (43.5%) (El-Ghorab, 2006). The main components of the essential oil of *Mentha pulegium* L., gathered in Austria were limonene (11%), octyl-3-acetate (0.8%), octanol-3 (1%), menthone (8%), isomenthone (7%), and piperitone (70%) (Zwaving and

Smith, 1971). The essential oil of Mentha pulegium L. of Cuban origin has been investigated by a combination of GC and GC/MS, and the major constituents were neoisomenthol (20.68%), and pulegone (25.14%) (Pino et al., 1996). The main chemical ingredients reported from one study in former Yugoslavia were menthone (30.9%), pulegone (14.1%), neomenthal (13.8%), and caryophyllene oxide (9.0%) (Chalchatet al., 2000), while in Bulgaria, the yields of oil obtained by water and steam distillation were 1.54% and 1.48%, respectively, and the main components were pulegone (42.9-45.4%), piperitenone (21.7-23.1%), and isomenthone (11.3-12.8%) (Stoyanova et al., 2005). In Tunisia, thirty-four components including 78.4% of the total extract were identified, and pulegone (41.8%), followed by isomenthone (11.3%) and carvone (6.2%) were the main compounds (Mkaddem et al., 2007). In one experiment in Greece, the quantitative constituents of the different oils altered markedly with most variable compounds being pulegone (ranging from <0.1-90.7% of the total oil), piperitone, menthone (0.2-53.4%), isomenthone (0.1-45.1%), piperitenone (<0.1-39.8%) and isopiperitenone (Kokkiniet al., 2004). On the island of Zakynthos, pulegone was the principal constituent of all of the oil followed by piperitenone, isomenthone, and piperitone (Cook et al., 2007). In Iran, the most important compounds were pulegone (2.5-51.7%), menthone (0.2-25.3%), limonene (0.0-35.4%), 1,8-cineol (0.0-33.4%), piperitenone oxide (0.2-55.2%), and trans-piperitone epoxide (0.0-28.5%) (Mollaeiet al., 2020). Essential oils acquired by hydrodistillation from leaves of Mentha pulegium L., from Uruguay analyzed by GC-FID and GC-MS revealed that its major components were pulegone, isomenthone and menthone (Lorenzo et al., 2002). Aerial parts dried in the shade is the best optimal method to get the maximum yield of essential oil, while drying in oven at 50 °C is suggested to increase the antioxidant potency of their essential oil for food and pharmaceutical applications (Ahmed et al., 2018). Environmental factors have significant impact on the essential oil content and its antioxidant activity (Mollaei et al., 2020). Phytochemical components of Mentha pulegium essential oil were methylglyoxal (1.497%), Furan, 2,5-diethyltetrahydro Bicyclo [3.1.0] hexane, 4-methyl-1-(1-methylethyl)-, didehydroderiv (1.402%), β-pinene (0.350%), (+)camphene (1.921%), 4-methyl-5-decanol (0.669%), (E)-p-mentha-2-en-1-ol (12.157%), L-α-pinene (0.083%), γ-terpinen (0.072), Cyclohexene, 5-methyl-3-(1-methylethenyl)-,trans-(-)- (0.453%), 3-methylene-1,5,5trimethylcyclohexene (0.149%), 3-octanol, acetate (0.248%), 3,3'-dimenthol (18.859%), Isopulegone (2.971%), Terpineol (1.215%), cis-pulegone oxide (45.676%), (+)-isopiperitenone (0.229%), 1-cyclohexene-1-methanol,α,2,6,6-tetramethyl- (0.859%), Nona-3,5-dien-2-ol (0.226%), 4H-1,3,2-dioxaborin, 6-ethenyl-2ethyl-4-methyl-4-(2-methylpropyl)- (3.618%), 2,5-dimethylhydroquinone (2.045%), \(\beta\)-elemen (0.218%), Cinerolone (0.106%), Caryophyllene (2.481%), (Z)-β-farnesene (0.298%), α-caryophyllene (0.308%), Germacrene D (1.021%), γ-elemene (0.295%), and Caryophyllene oxide (0.169%) (Dehghani et al., 2018).

Traditional and modern pharmaceutical properties

Pennyroyal oil, the aromatic mint-like oil utilized as a fragrance and flavoring factor and as a herbal medicine (Gordon et al., 1982). It has been used since ancient times, from Greek, Roman and Medieval cultures for its numerous medicinal properties, such as emmenagogue, abortifacient impacts, skin itching and gastrointestinal ailments (Gordon and Khojasteh, 2015; Nickavar and Jabbareh, 2018). In the Iranian traditional medicine, Mentha pulegium L. leaves are used for the treatment of functional dyspepsia (Khoncheet al., 2017). Mentha pulegium L. essential oil has been considered as an active antimicrobial and antioxidant agent (Candan and Tarhan, 2012; Cherrat et al., 2014), and it has also showed the strongest radical scavenging activity (Fatihaet al., 2015), as well as a bioactive alternative for food hygiene and a natural substitute for harmful synthesized chemicals (Abdelliet al., 2016). Mentha pulegium hot water extract had the maximum antioxidant activity and phenol content, and its essential oil exhibited antibacterial activity against some bacterial strains (Teixeira et al., 2012; Ekramiet al., 2019). The oil indicated an excellent anticholinesterase activity and significant antioxidant activity (Yakoubiet al., 2021). Natural oil extracted from Mentha pulegium

was considered as corrosion inhibitor of steel in molar hydrochloric using weight loss measurements and electrochemical polarization (Bouyanzer *et al.*, 2006; Khadraoui *et al.*, 2016). Pennyroyal essential oil is an effectual biocide against a wide range of pests (Domingues and Santos, 2019). Dietary supplementation of pennyroyal ameliorated feed conversion ration and lactic acid bacteria count as well as lessened *Escherichia coli* count of the jejunum in broilers (Erhan *et al.*, 2012). Its essential oils can be considered as a potential grain protectant and a botanical substitute fumigant and could be utilized in the management of various life stages of *Callosobruchus maculatus* (Loni and Panahi, 2015).

Table 2. The most important health benefits of pennyroyal

Health benefits	Key point	
	Mentha pulegium contains anthelmintic characteristics and could be a potent	
Anthelmintic properties	source of novel compounds for management of helminth parasites as well as its	
	associated oxidative damage.	
Antibacterial activity	Its essential oil exhibited bactericidal activity which shows an alternative choice	
	to treat methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) infections.	
Anticancer activity	An advantageous impact of pennyroyal phenolic extract on the amelioration of	
	Inflammatory Bowel Disease severity and on the impairment of processes	
	applicable for progression into Colorectal cancer is reported.	
Antidiabetic activity	Anticholinergic and antidiabetic of <i>Mentha pulegium</i> was found.	
Antifungal activity	Algerian and Tunisian <i>Mentha pulegium</i> showed notable antifungal activity.	
	Its essential oil indicated antifungal effects against Crypotococcus neoformans and	
	the Dermatophytes trichophyton rubrum.	
	The antimicrobial activity of Mentha pulegium oil was concentration-dependent	
Antimicrobial activity	on Bacillus subtilis, staphylococcus aureus, Escherichia coli, Salmonella typhi,	
	Pseudomonas aeroginosa, Aspergilus niger and Candida albicans.	
	Algerian Mentha pulegium essential oil exhibited appropriate activity against	
	four Gram-positive and Gram-negative bacteria: Staphylococcus aureus, Bacillus	
	subtilis, Pseudomonas aeruginosa, and Escherichia coli.	
Antioxidant activity	It showed antioxidant activity and it can be used to prevent oxidation in	
Antioxidant activity	different food products.	
	Its essential oil has antioxidant activity, and can be applied in protecting tissue	
	from oxidative stress.	
Insecticide activity	Its essential oil and kaolin had high capability in controlling different stages of	
	Callosobruchus maculatus.	
	Its ethanolic extract can be utilized as a secure and safe acaricide on <i>Tetranychus</i>	
	urticae Koch.	
	Significant pest repellent activity was indicated with <i>Mentha pulegium</i> where	
	the repellency impact reached 60% after 1 and 24h of exposure against	
	Tribolium castaneum at dose of 0.078 μL/cm ² .	
	Its essential oil can be an alternative for a better management of Aphis spiraecola	
	Patch and the cotton aphid <i>Aphis gossypii</i> Glover.	
Wound healing activity	Mentha pulegium essential oil-loaded into nanostructures lipid carriers might	
would itealing activity	accelerate the infected wound healing process.	
	Mentha pulegium essential oil-loaded into nanostructures lipid carriers may	
	boost fibroblast migration-re-epithelialization and collagen biosynthesis and	
	decrease in wound size.	
	Its aerial parts can be employed in the treatment of wounds.	

The oil of *Mentha pulegium* L. has an influential antimicrobial activity and the Iranian *Mentha pulegium* L. oil related to piperitone/piperitenone type (Mahboubi and Haghi, 2008). *Mentha pulegium* essential oil nanoliposome exhibited enhancing fumigant toxicity against *Tribolium castaneum* compared to the crude essential oil (Faraji *et al.*, 2020). Its essential oil may be used as potential natural preservative agents for food products due to its antimicrobial activity (Ait-Ouazzou *et al.*, 2012; Salarbashi *et al.*, 2014).

The aqueous extract of *Mentha pulegium* (L.) is efficacious reducing constituents for green synthesis of zinc oxide nanoparticles (ZnO NPs) with notable antimicrobial potential (Shahriyari Rad *et al.*, 2019). Its essential oil not only can boost organoleptic properties of cheese but also can decrease and postpone the growth of *Listeria monocytogenes* in this product (Sadeghi *et al.*, 2016). *Mentha pulegium* hydroalcoholic extract leaves may ameliorate anxiety in rats by dose-dependent manner (VeisiHampa and Sofiabadi, 2019). The use of 0.5% of *Mentha pulegium* L. in the diets of broilers has positive effects on their performance and carcass traits (Nobakht *et al.*, 2011). Goodarzi and Nanekarani (2014) reported that application of 2% of pennyroyal medicinal plant in the diets of broilers has positive impacts on their performance and carcass traits. Pennyroyal oil has indicated a dominant fumigant impact against *Sitophilus oryzae* (L.) adults, and this effect is affected by the tested doses and exposure periods (Zekri *et al.*, 2013). The notable pharmaceutical benefits of pennyroyal are showed in Table 2.

Conclusions

Traditional herbal medicines have been recognized as an important source of curative remedy, as their chemical components are used to promote health and prevent diseases. Asparagus officinalis has been traditionally consumed as a medicinal plant for many years, especially in Asian countries. The most notable volatile organic compounds responsible for the smell are methanethiol, dimethyl sulfide, dimethyl disulfide, dimethyl sulfoxide and dimethyl sulfone. The most important health benefits of asparagus are antitumor, hepatoprotective, antioxidant, hypocholesterolemic, neuroprotective, immunoprotective, antimutagenic and hypoglycemic activities. Asparagus is full of proteins, minerals, vitamins, a good source of dietary fiber and also it is known as fat-free food. Nutrition therapy according to the traditional Asian medicine is effective at treating common diseases. Pennyroyal is a Mediterranean aromatic plant, usually used in gastronomy as a spice that recently sparkled the interest of the food industry. Its essential oil exhibited antibacterial activity against several bacterial strains. Its major component was pulegone, menthone, piperitenone, piperitone, isomenthone, limonene, and octaan-3-ol. The most important pharmaceutical benefits of pennyroyal is anti-hepatic effect, antibacterial effect, antifungal effect, antioxidant effect, acaricidal effect, hepatotoxicity effect, relaxant effects, spasmolytic effects, antimicrobial effect, antimyometrium effect, anti-steel corrosion effect and wound healing activities. According to pharmacological and phytochemical advantages, pennyroyal shows its importance as a medicinal plant in both modern medicinal science and traditional medicine.

Authors' Contributions

Both authors read and approved the final manuscript.

Ethical approval (for researches involving animals or humans)

Not applicable.

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Conflict of Interests

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

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