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Physiological Activity and Function of *Cissus quadrangularis*

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ABSTRACT

This study investigates the use and efficacy of *Cissus quadrangularis* in the treatment of various diseases. This vine is native to Bangladesh, Sri Lanka, Africa, and Southeast Asia. Depending on the region, it is also known as the *Adamant creeper, Harbhanga, Chodhari, Sannalam, Nalleru, Vajravelli,* and *Mangara vali*. It contains significant amounts of vitamins and minerals, such as vitamin C, calcium, and phosphorus, as well as various functional components, which include luteolin, β-carotene, β-sitosterol, quercetin, and isorhamnetin. Extracts of *C. quadrangularis* are reported to have bone healing, anti-obesity, free radical scavenging, antioxidant, anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, and anti-cancer activities. Therefore, extracts of *C. quadrangularis* have the potential to be applied as effective functional foods for various diseases such as osteoporosis, obesity, and cancer.

Key words: *Cissus quadrangularis*, bone health, antioxidant, anti-inflammatory, weight loss

INTRODUCTION

Cissus quadrangularis belongs to the grape family. *C. quadrangularis* is a perennial plant with square stems. It is native to India, Malaysia, Bangladesh, and Sri Lanka and mainly inhabits Africa and Southeast Asia. It is known as the *Adamant Creeper, Harbhanga, Chodhari, Sannaram, Nalleru, Vajravelli, Mangara valli,* etc., depending on the region (Anoop A *et al* 2004; Rex MC & Ravi L 2020). The *C. quadrangularis* is approximately 1.5 m high, the stem has a wide square-like shape and has a width of approximately 1.2-1.5 cm, the length of the leaf is approximately 8-10 cm, and the tip has a serrated shape. Flowers are pale white, yellow, or green and bear reddish fruits (Frank S *et al* 1995; Suresh P *et al* 2019).

C. quadrangularis is mainly composed of flavonoids such as quercetin, isorhamnetin, daidzein, and genistein, terpenoids such as friedelin, resveratrol, and piceatannol, and iridoids such as 6-0-meta-ethoxybenzozyl catapol, picroside, pallidol, phytosterols, and calcium (Sundaran J *et al* 2020). The stem of *C. quadrangularis* contains numerous amyrins, β-sitosterol, ketosetosterol, calcium oxalate, taraxeryl acetate, taraxeroliso-pentadecanoic acid, phenol, tannin, vitamin C, carotene, and phosphorus (Jainu M *et al* 2005). In addition, *C. quadrangularis* leaves are rich in ingredients such as resveratrol, piceatanon, pallidol, and parthenocissus; the fruit is rich in vitamin C and calcium, and the root contains various minerals such as potassium, calcium, zinc, iron, copper, and magnesium (Jainu M *et al* 2005; Sen MK & Dash BK 2012; Suresh P *et al* 2019).

In its native areas in Africa and Asia, *C. quadrangularis* is used in traditional medicine due to the abundance of useful ingredients in its stems, leaves, and roots. It is used to treat epilepsy, convulsions, hemorrhoids, anorexia, indigestion, and asthma (Rajpal V 2002; Shah U 2011). It has been used for a long time to treat menstrual disorders and menopause, as well as diseases related to bones (Siddiqua A & Mittapally S 2017). In particular, it has been called '*Bone Setter*' or '*Hadjod*' for a long time because of its excellent efficacy in increasing bone mass or increasing recovery rate after a fracture. Other reported properties are pain relief, wound healing, reduction in body fat, and antioxidant, anti-inflammatory, and antibacterial effects (Shirwaikar A *et al* 2003; Sarkar BK *et al* 2016). Flavonoids present in large amounts in *C. quadrangularis* have excellent antibacterial, anti-inflammatory, and anticancer effects, and terpenoids have been used as antitumor

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agents. *C. quadrangularis* plays an important role as an anti-inflammatory agent by inhibiting the production of lipoxygenase, phospholipases, and cyclooxygenase (Cushnie TPT & Lamb AJ 2011; Braca A *et al* 2012; Sirasanagandla SR *et al* 2014). In addition, *C. quadrangularis* contains a large amount of calcium and phosphorus; therefore, it is effective in preventing and improving bone-related diseases (Ramachandran S *et al* 2021).

Due to numerous reports on the efficacy of *C. quadrangularis*, it is being used as a medicinal plant. In Korea, *C. quadrangularis* extract has been recognized as a functional food that can help reduce body fat and has been commercialized in powder and tablet form and sold as various products.

Although multiple reports investigating the effect of *C. quadrangularis* have been widely published worldwide, studies localized in Korea are limited. Moreover, only few papers have systematically organized the function and efficacy of *C. quadrangularis* according to its medicinal use. Therefore, this study investigated the previous reports on the effects of *C. quadrangularis* as a medicinal plant and prepared a systematic review to organize the physiological activity and efficacy of *C. quadrangularis* by disease.

MATERIAL AND METHODS

In this study, a systematic review was conducted by dividing the study on *C. quadrangularis* into three stages. In the first stage, the definition and content of *C. quadrangularis* were planned, and a thorough review was conducted based on various available datasets. Step 2 described the content based on the research background of the selected studies. In step 3, the conclusions were inferred by objectively analyzing the contents to be emphasized in this study. The period of searching for this document and organizing the results was from December 1, 2021, to June 30, 2022, and ScienceON and PubMed were used as databases for literature search. The literature search was conducted using keywords such as *C. quadrangularis*, antioxidant, anti-inflammatory, weight loss, bone health, and related terms, and a review was prepared based on a total of 57 papers.

CONCLUSION AND DISCUSSION

1. Effects on Bone Health

C. quadrangularis has been reported to be effective in preventing and improving bone-related diseases, as it has an excellent effect on bone repair as elaborated in various studies (Table 1).

1) Osteoblast Activation Effect

Pansare TA & Chandil S (2019) reported that *C. quadrangularis* contains a significant amount of calcium and phosphorus necessary for bone formation and acts as an antagonist of the glucocorticoid hormone secreted from the adrenal cortex to facilitate smooth bone formation. The quercetin component of *Cissus* has been reported to modulate the activity of proteins involved in bone formation and thus has the potential for bone formation and resorption (Ruangsuriya J *et al* 2020). Tasadduq R *et al* (2017) reported that when MC3T3-E1 osteocytes were treated with an appropriate concentration of *C. quadrangularis*, the growth rate of MC3T3-E1 cells increased, thereby facilitating bone formation. The molecular underpinnings of this growth rate increase are yet to be explored. In a previous report, Potu BK *et al* (2009a) also reported that when mesenchymal stem cells were treated with *C. quadrangularis* extract, cell proliferation rate was improved, osteoblast differentiation was promoted, and the calcification rate was increased. The study reported that *C. quadrangularis* has the potential to be used as a natural medicinal plant that can prevent bone diseases such as osteoporosis by promoting the formation of osteoblasts. Additionally, Potu BK *et al* (2010) reported that *C. quadrangularis* feed increased the thickness of cortical bone and cancellous bone in an experimental animal model of ovariectomy-induced osteoporosis in rats.

2) Inhibitory Effect on Osteoclast Activity

In experimental studies related to ovariectomy, *C. quadrangularis* showed an excellent effect in improving osteoporosis by inhibiting osteoclast activity. Banu J *et al* (2012) reported that in a study using an ovariectomized animal model, *C. quadrangularis* flavonoids could prevent bone loss by inhibiting the production of inflammatory cytokines. Potu BK *et al* (2009b) emphasized that the detailed mechanism by which *C. quadrangularis* extract prevents bone loss requires further study. In addition, as a result of studying osteoclast activity and bone formation in experimental animals using tartrate-resistant acid phosphatase and alkaline phosphatase staining, osteoclast activity was inhibited in the experimental animal group ingesting *C. quadrangularis* extract, resulting in bone

Table 1. The effect on bone healing of *C. quadrangularis*

References	Results
Tasadduq R *et al* (2017)	The proliferation of MC3Tc-E1 cells was significantly increased at the appropriate concentrations of CQ-E.
Kanwar JR *et al* (2015)	Osteotomized rats treated with *C. quadrangularis* drastically enhanced alkaline phosphatase and cartilage tissue formation as compared to untreated, *W. somnifera* only, or the combination of both herbals.
Banu J *et al* (2012)	In the distal femoral metaphysis, femoral diaphysis, and proximal tibia, control mice had decreased cancellous and cortical bone, while CQ-fed mice showed no significant differences in the trabecular number, thickness, and connectivity density, between Sham and OVX mice, except for cortical bone mineral content in the proximal tibia.
Potu BK *et al* (2010)	CQ significantly increased the force required to break the femur (p<0.001) and significantly increased the thickness of both cortical (p<0.001) and trabecular bone (p<0.001). This action of CQ was comparable to the action of raloxifene.
Potu BK *et al* (2009b)	The petroleum-ether extract of CQ reduced bone loss, as evidenced by the weight gain in femur, and also reduced the osteoclastic activity there by facilitating bone formation when compared to the OVX group.
Potu BK *et al* (2009a)	Treatment with 100, 200 or 300 μg/mL petroleum ether extract of *C. quadrangularis* enhanced the differentiation of marrow mesenchymal stem cells into ALP-positive osteoblasts and increased extracellular matrix calcification. Treatment with 300 μg/mL petroleum ether extract of *C. quadrangularis* also enhanced the proliferation rate of the marrow mesenchymal stem cells.

loss. The amount of bone loss was reduced, and this result has been reported to play an important role in preventing ovariectomy-induced bone loss (Potu BK *et al* 2009b). In addition, Potu BK *et al* (2010) also reported that in the ovariectomy-induced bone loss model, the feeding of *C. quadrangularis* could prevent femur fractures due to external factors.

3) Chondroprotective Effect

Kanwar JR *et al* (2015) reported that *C. quadrangularis* improves bone health by protecting cartilage by inhibiting the activity of the p38 mitogen-activated protein kinase (MAPK) signaling pathway in animal models. Activation of the p38 MAPK signaling pathway promotes the production of various inflammatory cytokines that can induce inflammation and apoptosis in chondrocytes. *C. quadrangularis* can protect the cartilage by inhibiting the activation of the p38 MAPK signaling pathway, thereby inhibiting apoptosis of chondrocytes and reducing the production of pro-inflammatory cytokines that can induce cartilage destruction.

4) Other Osteoporosis Prevention Effects

Glucocorticoids bind to glucocorticoid receptors, inhibit calcium absorption in the intestine, and interfere with bone formation, leading to a decrease in bone mass. By interfering with the process of glucocorticoid binding to the glucocorticoid receptor, *C. quadrangularis* prevents a decrease in bone mass caused by glucocorticoids and induces bone formation to increase bone strength. Tasadduq R *et al* (2017) reported that *C. quadrangularis* extract increased the growth of bone cells, MC3T3-E1, and was effective in the treatment of fractures and prevention and treatment of osteoporosis. Additionally, in Ayurveda, the traditional medicine system from India, *C. quadrangularis* is known to be rich in phytoestrogens and is reported to have excellent anti-osteoporosis activity. Phytoestrogens enhance bone strength and density by promoting early bone formation and calcification. These characteristics of *C. quadrangularis* can play an important role in normal bone recovery in patients with bone diseases, such as osteoporosis or fractures (Shirwaikar A *et al* 2003).

Therefore, *C. quadrangularis* has been used as a medicinal plant for bone-related diseases for a long time, and it is worth using in the future. It is believed that *C. quadrangularis* can be effectively used in the prevention and improvement of osteoporosis.

2. Effect of *C. quadrangularis* on Reducing Body Fat and Improving Obesity

C. quadrangularis has been reported to be effective in reducing body fat and improving obesity through various studies (Table 2). In recognition of its ability to reduce body fat, it has been commercialized and sold as a powdered form of *C. quadrangularis* or *C. quadrangularis* extract worldwide. The Korean Ministry of Food and Drug Safety has also recognized *C. quadrangularis* extract as a functional food that can help reduce body fat.

1) Fat Absorption Inhibitory Effect

Excessive accumulation of body fat leads to increased blood glucose, triglyceride, and low-density lipoprotein levels, leading to problems with lipid metabolism in the body (Howard BV *et al* 2003; Rinaldi AE *et al* 2012). This leads to an increase in the oxidative damage of cellular components such as proteins, lipids, and DNA and is related to an increase in various inflammatory cytokines, such as tumor necrosis factor (TNF)- and interleukin-1 (Aggoun Y 2007; Bakris GL & Sowers JR 2008). Fat accumulation can also cause metabolic diseases such as diabetes and cardiovascular diseases (Aggoun Y 2007; Bakris GL & Sowers JR 2008). Quercetin and isorhamnetin present in *C. quadrangularis* are known to be effective in reducing body fat by inhibiting the activity of lipase secreted by the pancreas and reducing the amount of fat absorbed in the small intestine. Lee HJ *et al* (2016) reported that *C. quadrangularis* extract effectively reduced body fat by inhibiting pancreatic lipase activity and intestinal absorption in mice fed a high-fat diet.

2) High-Density Lipoprotein, Adiponectin, and Serotonin-Increasing Effect

The body-fat reducing effects of *C. quadrangularis* were verified by clinical studies conducted by dividing the group into a placebo group and *C. quadrangularis* extract-administered group. In a study conducted on patients with obesity by Nash R *et al* (2019), the participants were divided into a placebo group and *C. quadrangularis* extract-administered group to investigate the effect of *C. quadrangularis* extract on reducing body fat and improving obesity. Participants in the *C. quadrangularis* extract intake group received 300 mg of *C. quadrangularis* extract daily for 8 weeks, and after 8 weeks, it was found that body fat decreased significantly (8.9-12.8%) in the extract-administered group compared to that in the placebo group (Nash R *et al* 2019). In addition, waist circumference and blood pressure were reduced, total cholesterol and triglyceride concentrations in blood and fasting blood sugar were significantly decreased, and high-density lipoprotein cholesterol and adiponectin levels in blood were increased. Adiponectin increases the activity of AMP-activated protein kinase, which induces cellular glucose uptake. It has been reported to increase the activity of peroxisome proliferator-activated receptor-α (PPARα), which can decrease the concentration of triglycerides and increase the concentration of high-density lipoprotein cholesterol (Nash R *et al* 2019).

Table 2. The effect on reducing body fat of *C. quadrangularis*

References	Results
Nash R *et al* (2019)	The CQR-300 group had an 8.9% and 12.8% decreases in the body fat as measured by impedance and DEXA, respectively.
Lee HJ *et al* (2018)	CQR-300 decreased adipogenesis/lipogenesis-related mRNA expression levels of fatty acid binding protein (aP2), fatty acid synthase (FAS), lipoprotein lipase (LPL), stearoyl-CoA desaturase-1 (SCD-1), and acetyl-CoA carboxylase (ACC).
Oben JE *et al* (2008)	Compared to the placebo group, the two active groups showed a statistically significant difference on all six variables by week 10. The magnitude of the differences was noticeable by week 4 and continued to increase over the trial period.
Oben JE *et al* (2007)	The CQR-300 brought about significant reductions in weight, body fat, total cholesterol, LDL-cholesterol, triglycerides, and fasting blood glucose levels over the respective study periods.
Oben J *et al* (2006)	At the end of the trial period, statistically significant net reductions in weight and central obesity, as well as in fasting blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and creactive protein were observed in participants who received the formulation, regardless of diet.

Oben JE *et al* (2008) reported that, in a 10-week study of 72 overweight participants, body weight, body fat, and blood cholesterol levels were significantly reduced in the group receiving *C. quadrangularis* extract compared to that in the placebo group.

In addition, Oben JE *et al* (2007) reported that, in a group of 168 overweight or obese participants, *C. quadrangularis* extract administration led to a reduction in weight and body fat, blood triglyceride level, and cholesterol level. A decrease in fasting blood sugar and a remarkable increase in high-density lipoprotein cholesterol and serotonin concentrations have also been reported. Since the neurotransmitter serotonin can act on satiety, it has been reported that high serotonin levels can suppress appetite and prevent binge eating, thereby reducing obesity (Oben JE *et al* 2007).

3) Inhibitory Effect on Lipid Accumulation in Adipocytes

A study was also conducted to investigate the effect of *C. quadrangularis* extract on reducing body fat and improving obesity through *in vitro* experiments. In a study conducted on 3T3-L1 adipocytes, Lee HJ *et al* (2018) reported that in 3T3-L1 adipocytes treated with *C. quadrangularis* extract at various concentrations (0-200 μg/mL) without cytotoxic reactions, the accumulation of lipids in adipocytes was inhibited. In addition, the treatment of *C. quadrangularis* extract reduced the expression of lipogenesis-related genes or proteins in 3T3-L1 adipocytes, such as aP2, LPL, PPAR, C/EBPa, FAS, ACC, and SCD-1 so that the binding of fatty acids and glycerides. It has been reported that *C. quadrangularis* extract can inhibit the synthesis of triglycerides. Therefore, it is considered that *C. quadrangularis* is effective in reducing body fat and preventing obesity by inhibiting the synthesis of triglycerides in the body and improving the composition of cholesterol and lipoprotein components.

3. Antioxidant Effect

Free radicals are highly reactive and can cause several diseases by binding to intracellular proteins, lipids, and nucleic acids to alter their structure. During the process of ATP synthesis in the mitochondria, 90 to 95% of the total oxygen is consumed, and 1 to 2% of this is converted into active oxygen (Bartz RR & Piantadosi CA 2010). The process of generating and removing free radicals is regulated by metabolic processes in the body. However, when the levels of reactive oxygen species, such as peroxy radicals, superoxide radicals, and hydroxyl radicals, exceed a certain threshold, the protein, lipid, and nucleic acid structures of the cell are altered, resulting in cell death or abnormal cell proliferation and development of a tumor. Scavenging free radicals plays an important role in maintaining the health of the body, and antioxidants can prevent various diseases by eliminating free radicals in the body. Additionally, various studied have revealed the excellent antioxidant effects of *C. quadrangularis* (Table 3).

1) Peroxy Radical Inhibition

Vitamin C and β-carotene, which are present in large amounts in *C. quadrangularis*, are excellent in removing free radicals and act as powerful antioxidants (Jainu M *et al* 2005). The antioxidant effect of *C. quadrangularis* was mainly studied through *in vitro* experiments using *C. quadrangularis* extract. Vijay P & Vijayvergia R (2009) reported that *C. quadrangularis* extract could effectively scavenge peroxy radicals. Prabhavathi RM *et al* (2016) classified *C. quadrangularis* into root, stem, and leaf parts and then extracted each

Table 3. The antioxidant and anti-inflammatory effects of *C. quadrangularis*

References	Results
Dhanasekaran S (2020)	Strong antioxidant effects were recorded in EECQ and MECQ in all the cell-free models. The ethanolic extract exhibited a significant dose-dependent free radical activity in comparison with methanolic extracts.
Kuppuramalingam AP & Ramesh B (2018)	The 50% hydroethanol extract of *C. quadrangularis* L. stem possessed potent antioxidant properties.
Prabhavathi RM *et al* (2016)	The DPPH reduced with the increase in the concentration of the sample and methanolic extract of root and leaf showed least IC-50 value with 600 μg/mL. The methanolic extract of the samples proved to have a higher potential to reduce DMPD with a standard concentration of sample.

part to investigate the antioxidant effect. Active oxygen was effectively removed from all *C. quadrangularis* extracts, and in particular, the stem part of *C. quadrangularis* had excellent antioxidant effects.

2) Inhibition of Superoxide Radical and Hydroxyl Radical

Kuppuramalingam AP & Ramesh B (2018) investigated the antioxidant effect of *C. quadrangularis* stems. The *C. quadrangularis* stem extract effectively increased the superoxide and hydroxyl radical scavenging activities, establishing that the *C. quadrangularis* stem extract has antioxidant properties.

3) DPPH and ABTS Radical Scavenging Activity

Dhanasekaran S (2020) treated HL-60 cells with extract of *Cissus quadrangularis* stem. When studying the antioxidant effect, it was reported that the 2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activities were significantly increased and that superoxide radicals and hydroxyl radicals could be effectively scavenged.

Therefore, *C. quadrangularis* can effectively remove active oxygen, such as peroxy radicals, superoxide radicals, and hydroxyl radicals, to act as an antioxidant. In addition, it is considered that the *C. quadrangularis* stem containing a large amount of β-carotene has a particularly excellent antioxidant effect.

4. Other Effects of *C. quadrangularis*

In addition to improving bone health, reducing body fat, improving obesity, and antioxidant effects, various studies have reported the effects of *C. quadrangularis* (Table 4).

1) Anti-Inflammatory Effect

Flavonoids, such as luteolin and β-sitosterol, which are present in large amounts in *C. quadrangularis*, have anti-inflammatory effects (Mishra G *et al* 2010; Raj SJ & Joseph B 2011). These components can alleviate inflammation by reducing myeloperoxidase, which inhibits the influx of neutrophils into the inflamed tissue and exhibits anti-inflammatory activity against cyclooxygenase-2, which is expressed at the site of inflammation to induce an inflammatory response (Siddiqua A & Mittapally S 2017). In addition, Srisook K *et al* (2011) reported that *C. quadrangularis* extract exhibits anti-inflammatory effects by inhibiting the production of lipopolysaccharide and nitric oxide, which can induce inflammatory responses in an experiment using RAW 264.7 macrophages. Panthong A *et al* (2007) reported that *C. quadrangularis* extract can be used as an analgesic owing to its anti-inflammatory properties.

2) Antibacterial Effect

Flavonoids contained in large amounts in *C. quadrangularis* were found to exhibit antibacterial activity against pathogenic strains (Chadambara MKN *et al* 2003; Ramar K & Ayyadurai V 2015; Mummed B *et al* 2018). In particular, the stem and root parts of *C. quadrangularis* were found to exhibit strong antibacterial activity (Murthy KNC *et al* 2003). In addition, the stem and root of *C. quadrangularis* showed excellent antibacterial effects against pathogenic strains such as *Streptococcus mutans, Salmonella typhi, Streptococcus pyogenes, Escherichia coli, Proteus mirabilis, Staphylococcus aureus,* and *Pseudomonas aeruginosa* (Vanaja M *et al* 2013). Austin A *et al* (2004) reported that *the C. quadrangularis* extract is a natural antibacterial substance capable of inhi-

Table 4. Antibacterial, anti-inflammatory and anticancer effects of *C. quadrangularis*

References	Results
Suresh P *et al* (2019)	The cell viability of MG63 cells ranged between 29.65% and 73.59% at an extract concentration from 1,000 μg/mL to 7.8 μg/mL.
Mummed M *et al* (2018)	The extracts of *C. quadrangularis* had a wide spectrum of antibacterial activities against test bacterial strains while the extracts of Grewia villosa and Schinus molle did not show any inhibitory activity.
Srisook K *et al* (2011)	CQ potently inhibited lipopolysaccharide (LPS)-induced nitric oxide (NO) productionin RAW 264.7 macrophage cells in a dose-dependent manner.
Balasubramanian P *et al* (2009)	Antiviral activity of *C. quadrangularis* Linn against HSV type1 and 2 at non-cytotoxic concentration were determined.

biting the growth of *Helocobacter pylori* strains. Raj AJ *et al* (2010) reported that *C. quadrangularis* extract showed antifungal and antibacterial activities against *Mucor* sp. and *Pseudomonas aeruginosa* strains. In addition, *C. quadrangularis* extract showed higher antibacterial activity against gram-positive bacteria, such as *Staphylococcus aureus, B. subtilis, Streptococcus species,* and *B. cereus* compared to that against gram-negative bacteria (Murthy KNC *et al* 2003). According to Balasubramanian P *et al* (2009), *C. quadrangularis* extract can also exhibit antiviral properties against HSV1 and HSV2. Moreover, *C. quadrangularis* extract exhibited antiviral activity against viruses such as HSV types 1 and 2 through an *in vitro* experiment.

3) Anticancer Effect

Suresh P *et al* (2019) treated MG63 cancer cells with 7.8-1,000 μg/mL of *C. quadrangularis* extract in a study investigating the anticancer activity of *C. quadrangularis* extract. The study reported a 73.59-29.65% reduction in cell viability. In addition, when MG63 cells were treated with *C. quadrangularis* extract at a concentration of 100 μg/mL, the proliferation of MG63 cells was inhibited by approximately 50%, and the *C. quadrangularis* extract had an anticancer effect on MG63 cancer cells. Moreover, *C. quadrangularis* extract showed anticancer activity against HeLa, KB, A431, MCF7, HEp2, and HT29 cancer cells. The *C. quadrangularis* extract inhibits the growth of cancer cells in the G1 stage, by generating reactive oxygen compounds and inducing apoptosis in cancer cells (Vijayalakshmi A *et al* 2013; Kumar A *et al* 2014; Rajamaheswari K *et al* 2017).

4) Antiepileptic and Wound Healing Effects

In pilocarpine model mice of epilepsy, administration of *C. quadrangularis* water-soluble extract increased seizure latency and decreased the number and duration of seizures, suggesting that quercetin, which is contained in large amounts in *C. quadrangularis*, may have anticonvulsant and anxiolytic activities by inducing antioxidant activity and an increase in cerebral GABA to restore and maintain the balance between nerve stimulation and inhibition (Moto FCO *et al* 2018).

After topical application of *C. quadrangularis* extract-based ointment for 15 days, wound changes and healing similar to that of the positive control group were induced, and the protein content also showed similar results to that of the positive control, demonstrating the wound healing effect of *C. quadrangularis* (Marume A *et al* 2017).

C. quadrangularis alcohol extract was also reported to have anti-ulcer properties by inhibiting gastric mucosal lesions caused by aspirin administration in male albino rats (Jainu M & Devi CS 2005).

CONCLUSION

This review was composed to provide basic data for the effective use of *C. quadrangularis*. It systematically organized the various effects of *C. quadrangularis* by examining the results of previous studies on the functionality of *C. quadrangularis* used as a medicinal plant. As mentioned in the text, *C. quadrangularis* contains a large number of vitamins and minerals, including vitamin C, calcium, and phosphorus, and various functional ingredients such as luteolin, β-carotene, β-sitosterol, quercetin, and isorhamnetin. Recently, the function of *C. quadrangularis*, which is of high interest to the Korean public, is that it can be effectively used for reducing body fat and preventing osteoporosis. In particular, *C. quadrangularis* is highly likely to be used as a functional food or medicinal plant. At the present time, which is threatened by various diseases, research on *C. quadrangularis* should be continued to utilize the advantages of *C. quadrangularis*, which can be used more safely as a natural substance compared to drugs or synthetic substances. As a functional food, *C. quadrangularis* is believed to be effective in improving various diseases.

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