Mini review

Some characteristics and functional properties of Chunma (*Gastrodia elata*) as a food supplement: a short review

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**Abstract**

Gastrodin elata blume (Tianma in Chinese, Chunma in Korean) is a perennial parasitic herbaceous plant native to Korea, Japan and China (Chae et al., 2008). The plant has recently received very good attention, especially in Korea, due to its excellent health-promoting properties. This plant is reported to have excellent antioxidant, anticancer and anti-inflammatory properties. This paper briefly reviews some characteristics and functional properties of Chunma.

**Introduction**

*Gastrodin elata* blume (Tianma in Chinese, Chunma in Korean) is a perennial parasitic herbaceous plant native to Korea, Japan and China (Chae et al., 2008). It belongs to the family Orchidaceae and grows symbiotically with *Armillaria mella* (Kim et al., 2005). The dry tuber has been traditionally described in the treatment of headache, migraine, dizziness, epilepsy, rheumatism, neuralgia, paralysis and other neuralgic and nervous disorders in eastern Asian medicine for more than 2000 years (Tang and Eisenbrand, 1992; Hsieh et al., 2001; Bensky et al., 2004; Chae et al., 2008; Xue et al., 2013). Sedation, anti-convulsion and anti-epilepsy activities have been associated with the herb (Lin et al., 2008).

Analysis of *G. elata* has identified several constituents present in the plant (Kim et al., 2005). Most of the constituents are phenolic compounds such as phenolic glycosides, sulphurous phenolic compounds and organic acids, sugars, B-sitosterol, sterols, cholesterol, p-hydroxy benzyl alcohol, p-hydroxybenzaldehyde and vanillin (Zhou et al., 1979; Taguchi et al., 1981; Noda et al., 1995; Wu et al., 1996; Hsieh et al., 1997; Hayashi et al., 2002; Liu et al., 2002). Among the compounds, three phenolic glycosides were identified from *G. elata*: gastrodin, parishin and parishin B (Chae et al., 2008).

In an attempt to validate its long pharmaceutical use in traditional Chinese medicine, several reports study the activity of *G. elata* extracts, decoctions and isolated compounds. The biological activities of *G. elata* extracts using different solvents are well documented. The aqueous extract of *G. elata* improved memory loss in mice and cured vasoneural headache (Hsieh et al., 1997), improved performance deficit in senescent mice (Hsieh et al., 1997) and has been reported to have scavenging activities (Liu and Mori, 1993; Hsieh et al., 1997). Decreased dopamine was observed in rat brains administered with *G. elata* (Hsieh et al., 1997). Meanwhile, the methanol extract of *G. elata* improved scopolamine – induced deficit in rats (Wu et al., 1996), and prevented PC 12 cell apoptosis (Huang et al., 2004). The ethanolic extract...
of *G. elata* fermented with *Lactobacillus brevis* increased sleep when administered in mice (Lee *et al*., 2013). The mixture works by inhibiting the receptor antagonist to the benzodiazepine receptor of the mice orifice (Lee *et al*., 2013). The ethyl ether fraction reduced neuronal death in neuroblastoma cells (Kim *et al*., 2003), while the ether fraction attenuates decrease in GABA and glutamate content (Ha *et al*., 2000) and exhibits anti-convulsant effects (Huh *et al*., 1995). *G. elata* also reportedly inhibited glutamate-induced apoptosis in neuron cells (Lee *et al*., 1999), reduces lipid peroxide levels (Li and Mori, 1993) and protects against brain injury induced by transient ischemia (Yu *et al*., 2005). A decoction of *G. elata* and Uncaria exerts interesting pharmacological activity on neurodegenerative diseases (Chik *et al*., 2013). This paper briefly reviews some characteristics and functional properties of Chunma.

**Gastrodin**

Gastrodin (p-hydroxymethylphenyl-b-D-glucopyranoside) is the major active compound found in *G. elata*, constituting almost 0.3%-1.97% of *G. elata* (Li *et al*., 2001; Chae *et al*., 2008). The molecular formula of gastrodin is \( C_{13}H_{18}O_7 \), with a molecular weight of 286.28 (Lin *et al*., 2008). It was first described by Baek *et al.* (1999) as the compound responsible for anticonvulsive effect in *G. elata* and has since been reported as the most active constituent in *g. elata* (Zhao *et al*., 1999). Gastrodin is listed as an index component in Chinese Pharmacopoeia (Yang *et al*., 2001; Ong *et al*., 2007; Chae *et al*., 2008) and was approved for safe use by the Korean Food and Drug Administration in 2000.

**Neuroprotective**

**Anti-inflammatory and anti-oxidant**

The molecular structure of gastrodin and HBA containing at least one aromatic ring with one or more hydroxyl groups attached reflect their capability to interact with radicals to eliminate them (Chik *et al*., 2013). Several studies report the strong antioxidant activity of gastrodin. Evidence shows that neurodegenerative diseases such as Parkinson’s disease, stroke, brain trauma etc. are facilitated by oxidative stress, inflammation and apoptosis of neuron cells. Oxidative stress is the result of the inability of cells to effectively eliminate ROS generated in the cells, which promote membrane lipid peroxidation and DNA fragmentation, resulting in cell death (Beckman and Crowe, 1993; Simonian and Coyle, 1996; Choi *et al*., 1998; Zhang *et al*., 2002). Gastrodin effectively acts on these mechanisms through its anti-oxidant and anti-inflammatory properties.

Gastrodin has been reported to increase the expression of antioxidant proteins, attenuate inflammatory response and decrease lipid peroxidation in the brain (Yang *et al*., 2009; Kumar *et al*., 2013; Peng *et al*., 2015; Li and Zhang, 2015). Furthermore, gastrodin’s antioxidant activity decreases the expression level of neurotoxic proinflammatory mediators in microglial cells which are responsible for general neuronal injury, or more chronic neurodegenerative brain disorders such as Parkinson’s disease and Alzheimer’s disease (Dai *et al*., 2011; Zong *et al*., 2011; Zhao *et al*., 2012; Li *et al*., 2012; Yang *et al*., 2013; Kumar *et al*., 2013; Wang *et al*., 2014; Jiang *et al*., 2014). Gastrodin has been described as a well-known natural calcium channel blocker (Li and Ma, 2014); high calcium influx through calcium channels is a trigger leading to cell death (Zeng *et al*., 2006; Liu *et al*., 2009).

**Analgesic**

Gastrodin has been reported as an effective analgesic, relieving trigeminal neuralgia, migraine and vascular headache (Zhu *et al*., 2006). It inhibits the acid-sensing ion channels which are responsible for mediating pain (Qiu *et al*., 2014). Additionally, gastrodin attenuates mechanical allodynia and thermal hyperalgesia mediated by reversing the potassium currents, regulating neuron hyper excitability responsible for painful diabetic neuropathy (Sun *et al*., 2012).

**Cardioprotective**

Traditional uses of *G. elata* indicate its usefulness in treating cardiovascular conditions such as hypertension (Wang *et al*., 2007; Zhang *et al*., 2008). Scientific reports of the cardiovascular-protective effects of gastrodin have been reported. Shu *et al.* (2011) describe the mechanism of cardiovascular protection of gastrodin. Gastrodin prevented cardiac hypertrophy mediated by ERK ½ signalling and GATA-4 activation (Shu *et al*., 2011). They further report that gastrodin protects against fibrosis (Sun *et al*., 2011).

**Anticancer immunomodulatory**

Gastrodin upregulates the anti-cancer immune response and represses tumor growth in a study by Shu *et al.* (2012). In this study comparing the anti-hepatocellular carcinoma activity of gastrodin, vanillin and parishin in vivo, only gastrodin showed significant anticancer activity (Shu *et al*., 2012). The results of this study suggest that gastrodin was more effective and less toxic compared to standard
treatment using cisplatin in the repression of hepatic ascetic tumor cell growth in mice (Shu et al., 2012).

**Extraction of gastrodin**

Traditionally, gastrodin was obtained via extraction of *G. elata* rhizomes and flowers. Soxhlet extraction methods using methanol and pressurized liquid extraction have been reported with good extraction efficiencies (Ong et al., 2007). Besides classic solvent methods, greener and safer methods have been described. Kim et al. (2005) describe an extraction method using enzymes to facilitate high yield of extraction while minimizing solvent use. However, traditional extraction from *G. elata* is becoming less attractive because not only is it time-consuming, but also costly, with low yields (0.1%). Moreover, wild *G. elata* is fast depleting due to the excessive collection (Bai et al., 2016). Therefore, synthesis of gastrodin has been explored by researchers and industries.

**Chemical synthesis of gastrodin**

Zhou et al. (1980) reported the first successful chemical synthesis of gastrodin (Zhou et al., 1980) followed by Jie and Guo in 1984. However, these methods depended on the heavy use of toxic materials and had low yields. Li and Ma (2014) describe an improved chemical synthesis of gastrodin using a simple, high yield, cost-effective and less toxic process. Analogues of gastrodin in the form of aryl glycosides have also been synthesized (Xue et al., 2013). Several patents describing the chemical synthesis of gastrodin have been filed (CN 104744529, BCN 103275146 A, CN 102516329 B, CN 102977161 A).

Despite the availability of methods describing the chemical synthesis of gastrodin, these procedures are unattractive for several reasons. Most chemical procedures are highly complex (Ducros et al., 2003; Peng et al., 2007), utilize high amounts of toxic and expensive solvent, and do not go past laboratory scale (Li and Ma, 2014). There is also the risk of trace reagents being present in the final product, making it unsuitable for human consumption (Ducros et al., 2003). Gastrodin is a phenolic glycoside, which is part of the glycoconjugate family, which represents one of the most difficult compounds in nature to synthesize chemically (Ducros et al., 2003). Glycosyltransferases are part of a large family of enzymes that are responsible for the synthesis of glycoconjugates in nature (Breton et al., 2005). Natural and recombinant glycosyltransferases are continuously being studied as a route for successful biosynthesis of glycoconjugates for use in drug therapies.

**Enzymatic/ microbial synthesis**

Whole-based systems using fungi and bacteria for producing natural glycosyltransferases have been reported. Hai- Feng et al. (2008) and Zhang et al. (2008) describe the biotransformation of HBA into gastrodin using *A. luteo-virens* Sacc U; a selective and highly reactive method for a similar biotransformation process was described using *Rhizopus chinensis* SAITO AS3.1165 by Zhu et al. (2010). The use of fungi *Aspergillus foetidus* ZUG1 and *Penicillium cyclopium* AS 3.4513 have also been reported (Fan et al., 2013). In their work, Zhu et al. (2010) identify the enzyme responsible for this biotransformation as gastrodin biosynthesis enzyme (GBE), a glycosyltransferase. Niu et al. (2016) described an improved gastrodin production based on the work by Zhang et al. (2008) using cell culture *Armillari luteo- virens* Sacc.. Most recently, a method for de novo biosynthesis of gastrodin in *E. coli* was described by Bai et al. (2016). The method uses glucose as the substrate and suridine sugar glycosyltransferase (UGT) to catalyse the process. The work is described to be more environmentally friendly and is easily scaled up. For the synthesis of HBA, biotransformation of gastrodin using the fungus *Mucor spinosus* strain 3.3450 has been reported (Jixun et al., 2001).

**Pharmacokinetics**

Methods for the detection and analysis of gastrodin content are essential in order to understand the pharmacokinetics of gastrodin in the body. Li et al. (2006) first described a LC-UV method for detecting gastrodin in dog plasma. This was followed by the study of Zhang et al. (2008) reporting LC-MS for the analysis of gastrodin and HBA from oral administration of *g. elata*. Due to their activity on the CNS, there is interest in analysing the presence of gastrodin and HBA in the brain and thereafter its excretion in the bile and urine. Lin et al. (2008) analysed gastrodin and HBA in blood, bile and brain using a microdialysis and LC-MS/MS method. Wang et al. (2008) then examined the distribution of gastrodin in rat brain using an improved HPLC-UV method. Most recently, Jiang et al. (2013) developed a method for simultaneous detection of gastrodin and puerarin in rat plasma via HPLC.

When administered in rats, gastrodin is rapidly taken up in the central nervous system (Wang et al., 2007). It then rapidly enters the blood-brain barrier (BBB) and is decomposed into HBA in the liver, blood and brain (Lu et al., 1985; You et al., 1994; Hsieh et al., 1997).
HBA has similar pharmacological effects to gastrodin (Wu et al., 1996). Peak concentration in the brain and bile was reached 10-20 minutes after administration of gastrodin in rats (Lin et al., 2007). Both gastrodin and HBA are able to pass through the blood-brain barrier, especially accumulating in the cerebellum the highest, where it exerts neurological effects (Lu et al., 1985, You et al., 1994, Wang et al., 2007). However, this penetration through the blood-brain barrier is poor due to the hydrophilic activity of gastrodin. This suggests that a small amount of gastrodin delivered through the BBB has significant impact on the CNS (An et al., 2003; Lin et al., 2007). Gastrodin immediately undergoes biliary excretion after 15 min, but is also excreted unchanged in the urine (Lu et al., 1985; Meljer et al., 1990; Lin et al., 2007). Jiang et al. (2013) found that when gastrodin was co-administered with puerarin, both compounds showed higher bioavailability in the body and may be promising as a combined dose.

**Hydroxybenzyl alcohol**

Hydroxybenzyl alcohol is the metabolite product of gastrodin, and has been identified beside gastrodin as a pharmacologically active component in g. elata (Yu et al., 2005).

HBA has been reported to have protective effects against brain injury caused by ischaemic stroke (Yu et al., 2005). It also inhibits DNA degradation, protects the brain after neurotoxic injury (Huh et al., 1995; Hsieh et al., 1997; Kim et al., 2003) and reduced brain lesion size (Yu et al., 2013). Besides itself exerting activity, HBA facilitates gastrodia interaction with receptors in the brain through binding with specific receptors (Guo et al., 1991). Interestingly, HBA has been mentioned in some studies as being more potent than its glycone gastrodin. In a study comparing gastrodin and HBA activity on learning and memory, Hsieh et al. (1997) report that HBA is the more potent constituent. While the mechanism for neuroprotection has not been elucidated, studies point towards the possible role of HBA as a putative antioxidant, preventing neuronal injury that mostly occurs due to oxidative stress (Yu et al., 2013). A study has also reported that g. elata reduced lipid peroxide levels and exerts free radical-scavenging activities in seizure-induced rats (Liu and Mori, 1992, 1993) which may be attributed to vanillin and HBA. HBA is preserved in the brain, where it intermediates pharmacological activity in the CNS.

**Conclusion**

Chunma (Gastrodia elata), a typical Korean plant, has been proven to contain various health-promoting agents, thus has very high potential to be developed into various end-products, including food supplement. This plant is seen to be as good as ginseng in the world market in the very near future.

**References**


Gastrodia elata Bl. on glutamate-induced apoptosis


