Chemistry and Pharmacological Action of Caffeoylquinic Acid Derivatives and Pharmaceutical Utilization of Chwinamul (Korean Mountainous Vegetable)

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Chwinamul is a mountainous vegetable that refers to several species belonging to the family Compositae. Chwinamul has been used as a side dish or a medicinal herb to treat hypercholesterolemia, diabetes, common cold, atherosclerosis, and cardiovascular disease. Caffeoylquinic acids (CQs) are present in high levels in chwinamul, though caffeoyltartaric acids (CTs) are often occurred in the vegetables of Compositae. Here I review the chemical and pharmaceutical aspects of CQs and CTs. In particular, $^{13}$C-NMR data and CQ stereochemistry are discussed. CQ derivatives have antioxidative, peroxynitrite-scavenging, hepatoprotective, antiviral, antiobese, and antidiabetic activities.

Key words: Chwinamul, Compositae, Mountainous vegetable, Caffeoylquinic acid, Caffeoyltartaric acid, $^{13}$C-NMR

INTRODUCTION

Chwinamul refers to a mountainous vegetable belonging to Compositae: e.g., Aster yomena (buzikkaen-gee), Solidago virga var. gigantea (ulleungmiyokchwi), Solidago virga-aurora var. asiatica (miyokchwi), Astrisitae acerifolia (danpoongchwi), Caicalla firma (byungpoongchwi), Aster scaber (chamchwi), Saussurea grandifolia (seolchwi), Aster spatulifolius (haeguk), Aster oharai (wanghaeguk), Aster tataricus (gaemichwi), Aster koreensis (bulgaemichwi), Ligularia fischeri var. spiciformis (numchwi), Ligularia fischi (gomchwi), Ligularia stenocephala (gondalbi), and Synurus exelcocus (keunsurichwi) (Kim, 1996). Chwinamul occupies about 13% of all land cultivated for mountainous vegetables in Korea, particularly, Compositae. Chwinamul is used as a flavoring and has hepatoprotective, anti-cholesterolemic, antiviral (scarlet fever and common cold), antiabetic and antiatherosclerosis. Other Compositae herbs include the dandelion of Taraxacum officinale in Western countries (Schütz et al., 2006) and Taraxaci Herba of Taraxacum platycarpum of Eastern countries (Kim, 2006), but these are different from chwinamul.

Chwinamul contains high levels of caffeoylquinic acids (CQs) as analyzed by HPLC (Nugroho et al., 2009). Particularly, the CQ levels in this plant decrease with plant age. CQ has a number of pharmacological actions, many consistent with the medicinal use of mountainous vegetables. CQs are difficult to isolate and identify because of their density in plants. Therefore, $^{13}$C-NMR data of common CQs and caffeoyltartaric acids (CTs) are presented. Pharmacological actions of quinic acid derivatives and other natural products such as flavonoids, coumarins, sesquiterpenoids, triterpenoids, and steroids are summarized.

CQs are the main constituents of chwinamul

CQs contain quinic acid as the parent moiety, and phenylpropanoids such as caffeic acid, coumaric acid, or ferulic acid as the substitutted moiety. Bonding of phosphoenol pyruvic acid and erythrose 4-phosphate produces phenylpropanoids via the shikimic acid pathway (Kim et al., 2003). Counter-clockwise numbering is recommended by IUPAC and used throughout this review, but clockwise numbering can also be used (Fig. 1).
CQs may be biosynthesized from the shikimic acid pathway because quinic acid is the reductant of 5-dehydroquinic acid or a compound produced by hydration of shikimic acid. Chemical processes such as isomerization, substitution and other chemical modification produce diverse CQ derivatives. Quinic acid is the primary parent moiety, with its stereoisomers, epi-quinic acid (Kim and Lee, 2005) and muco-quinic acid (Kwon et al., 2000) possible, though less common. Tartaric acids instead of quinic acid also esterify the hydroxyls of phenylpropanoids to produce CTs (Cheminat et al., 1988). CQs can be classified into four groups, monocaffeoylquinic acids (MQs), dicaffeoylquinic acids (DQs), tricaffeoylquinic acids (tri-CQs), and tetracaffeoylquinic acids (tetra-CQs).

CQs can be qualitatively and quantitatively measured using standard CQs in HPLC analysis in chwinamul: A. yomena, S. virga var. gigantea, S. virga aurea var. asiatica, A. acerifolia, C. firma, A. scaber, S. grandifolia, L. fischi var. spiciformis (numchwi), L. fischi (gomchwi), and L. stenocephala (gondalbi). These CQs may mediate the pharmacological actions of chwinamul, since they contain total 20 to 39% of the chemical constituents (Nugroho et al., 2009, 2010; Park et al., 2009).

**Potential biosynthetic pathway and stereochemistry of CQs**

Phenylpropanoids are biosynthesized via the shikimic acid pathway. CQs may also use this biosynthetic pathway, since the three members of this pathway, 3-dehydroquinic acid, 3-dehydroshikimic acid, and shikimic acid, are changed by simple chemical steps (Fig. 2). The first step for caffeoylation becomes an esterification to 5β-OH because almost all the CQs have a caffeic acid moiety at 5β-OH. The chlorogenic acid (5-CQ) of the most common CQ further esterifies caffeic acids to other hydroxyls of quinic acid to produce DQs, tri-CQs and even tetra-CQs.

**Fig. 1.** More and less used numbering of quinic acid (1α, 3α, 4α, 5β-tetrahydroxyxyclohexane-1-carboxylic acid)

**Fig. 2.** Possible biosynthesis of caffeoylquinic acids (CA, caffeic acid)