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Coriariin M, a trimeric hydrolysable tannin with dehydrodigalloyl and valoneoyl groups as linking units, and accompanying dimeric hydrolysable tannins from *Coriaria japonica*

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‡ This paper is dedicated to the late Emeritus Professor Takuo Okuda, Okayama University. He passed away on December 31, 2016.

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A B S T R A C T

Three oligomeric hydrolysable tannins, coriariins K, L, and M, which were previously undescribed, together with five known hydrolysable tannins were isolated from dried leaves of *Coriaria japonica*. Their structures were determined based on 1D and 2D NMR spectroscopy, HR-ESI-MS, and ECD spectroscopy experiments. Among the isolated compounds, coriariin M has a unique trimer structure where both dehydrodigalloyl and valoneoyl group linkages were found between the hydrolysable tannin monomers. Dimeric hydrolysable tannins coriariins K and L, having a dehydrodigalloyl group as the linking unit, were structurally related to coriariin A, the main hydrolysable tannin of this plant species. Additionally, the complexation of the eight hydrolysable tannins isolated in this study with bovine serum albumin (BSA) to form water-soluble macromolecules was analyzed using native polyacrylamide gel electrophoresis (PAGE). A comparison of the behaviors of the oligomeric hydrolysable tannins suggested the participation of the hexahydroxydiphenoyl group and the importance of the molecular sizes of the hydrolysable tannins in the formation of macromolecules.

1. Introduction

Coriaria japonica A. Gray (Coriariaceae) is a small deciduous shrub distributed in the northern part of Japan, Taiwan, and the Philippines (Satake et al., 1989; Skog, 1972). Plant species belonging to the genus *Coriaria* are known to be rich sources of tannins (Frohne and Pfänder, 2005), and the genus name “coriaria” originated from the Latin word “coriarius,” meaning tanner. *Coriaria japonica* is also known as a poisonous plant containing toxic sesquiterpene lactones such as coriamyrtin and tutin (Okuda and Yoshida, 1967). Previous reports have shown that *C. japonica* contains several hydrolysable tannins, including those with a glucose core of $^4C_1$ conformation with a dehydrodigalloyl (DHDG) or a valoneoyl group, as well as geraniin with a glucose core of $^1C_4$ conformation (Hatano et al., 1986a,b, 1992). Although numerous oligomeric hydrolysable tannins have been found from various plant species to date, those possessing a DHDG group at the anomeric carbons of their glucose cores solely with β-orientation have only been isolated from *C. japonica* (Fig. 1).

Oligomeric hydrolysable tannins have received considerable attention because of their vast structural diversity and biological activities (Yoshida et al., 2000). Among them, coriariin A (**1**) (Fig. 2), one of the representative hydrolysable tannin dimers in *C. japonica*, also displays various biological activities, including significant host-mediated antitumor activity against sarcoma-180 tumor cells (Miyamoto et al., 1987), potent inhibition of poly(ADP-ribose) glycohydrolase (Aoki et al., 1993; Maruta et al., 2007), inhibition of histamine release (Kanoh et al., 2000), and anti-herpes simplex virus activity (Fukuchi et al., 1989). Chemical synthesis of **1** as an antitumor compound has also been accomplished (Feldman and Lawlor, 2000). However, little is known about the properties or mechanisms enabling these biological activities of this compound.

On the other hand, binding with proteins is considered to be important in the various biological activities of **1** because the formation of macromolecules, as water-soluble and/or insoluble complexes bound with proteins, is a fundamental property of tannins (Haslam, 1989, 1998; Engström et al., 2016; Richard et al., 2006). However, detailed molecular mechanisms for the interactions of respective tannins, especially oligomeric hydrolysable tannins, with proteins remain incomplete due to the difficulty of

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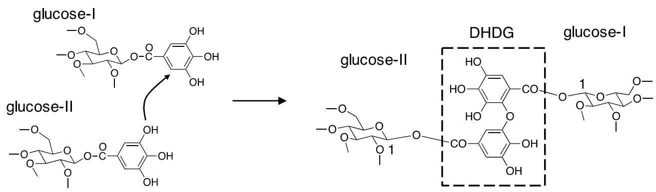

Fig. 1. Structure of the characteristic dehydrodigalloyl (DHDG) group in coriariins.

performing this type of analysis. To resolve this problem, we established methods to evaluate water-soluble tannin-protein complexes using polyacrylamide gel electrophoresis (PAGE) (Kusuda et al., 2006). However, only a few tannins or polyphenols have been examined in the PAGE analyses performed to date. Therefore, further study using tannins with different structures is required to clarify the molecular mechanisms for the formation of the tannin-protein macromolecules.

In this paper, we report the isolation of eight hydrolysable tannins, including hydrolysable tannin oligomers previously undescribed from the leaves of *C. japonica*, and their structural elucidation. The findings obtained from a comparison of the binding properties of these hydrolysable tannins with bovine serum albumin (BSA) are also presented.

2. Results and discussion

Dried leaves of *C. japonica* collected in November 2014 were homogenized in aqueous acetone, and the concentrated filtrate from the homogenate was extracted successively with chloroform, EtOAc, and *n*-BuOH. The *n*-BuOH extract was subjected to a combination of column chromatographies on Diaion HP-20, Toyopearl HW-40C, and Chromatorex ODS, followed by HPLC purification to furnish eight hydrolysable tannins, including three oligomers, named coriariins K (**6**), L (**7**), and M (**8**) (Fig. 3), which were previously undescribed.

Among them, five were previously known and identified as coriariins A (**1**) (Hatano et al., 1986a), B (**2**), (Hatano et al., 1986a), tellimagrandin II (**3**) (Feldman and Sahasrabudhe, 1999), euprostin A (**4**) (Yoshida et al., 1990), and rugosin G (**5**) (Hatano et al., 1990a)

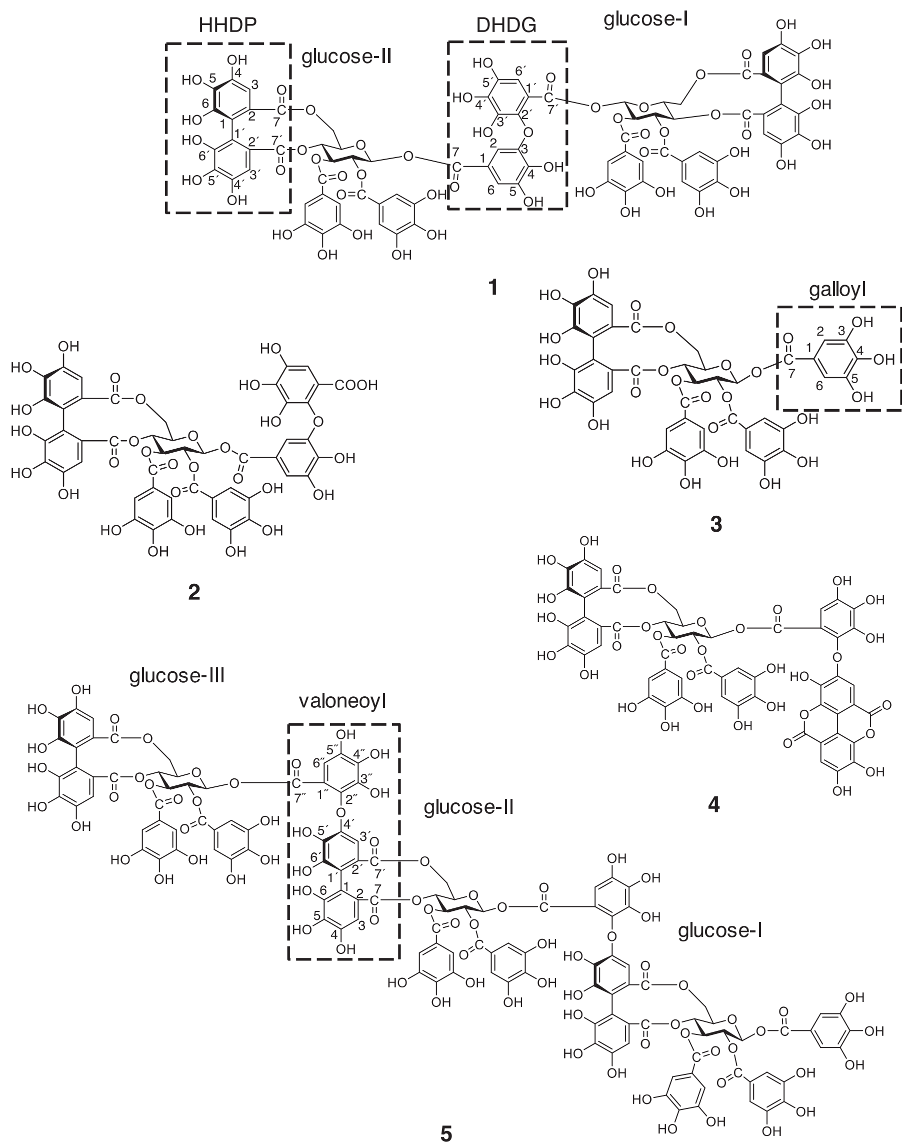

Fig. 2. Structures of known tannins isolated from *Coriaria japonica*.