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Analysis of caged xanthones from the resin of *Garcinia hanburyi* using ultra-performance liquid chromatography/electrospray ionization quadrupole time-of-flight tandem mass spectrometry

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ABSTRACT

On-line ultra high-performance liquid chromatography (UHPLC) coupled with electrospray quadrupole time-of-flight tandem mass spectrometry (ESI–QTOF–MS/MS/MS) has been developed for the analysis of a series of caged xanthones in the resin of *Garcinia hanburyi*. The fragmentation of protonated molecular ions for 12 known cadged xanthones was carried out using low-energy collision-induced electrospray ionization tandem mass spectrometry. It was found that Retro-Diels-Alder rearrangement occurred in the CID processes and produced the characteristic fragment ions, which are especially valuable for the identification of this class of xanthones. The fragmentation differential between some *cis*-, *trans*-isomers was uncovered. Computation methods were utilized to rationalize the observed MS behaviors. On-line UHPLC-ESI-MS/MS/MS method has proved to be rapid and efficient in that within 6 min, 15 caged scaffold xanthones, including three pairs of epimers and four pairs of isomers in gamboges, were effectively separated and identified. Among them, two known, namely isogambogenin (13) and isomorellinol (14) and one likely new caged *Garcinia* xanthones from the *Garcinia hanburyi* were tentatively characterized based on the tandem mass spectra of known ones.

1. Introduction

Gamboges, the resin of *Garcinia hanburyi* Hook. f., well-known as a natural fresh orange-yellow pigment, is used internally as a drastic purgative, an emetic and a vermifuge to treat tapeworm. The recorded use of gamboges was as a fresh yellow watercolor pigment in 8th century East Asia [1]. Evidence of yellow ink made from gamboge exists on black (khoi) paper in Thailand and a 12th century scroll depiction of The Tale of The Genji [1]. During recent centuries, gamboge was also used as a folk medicine in the treatment of chronic dermatitis, hemorrhoids, and bedsore [2]. In recent years, this

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resin has gained increasing interests due to its antitumor activities [2–7]. Efforts to identify the bioactive components of the extracts have yielded an ever growing family of natural products, the chemical structures of which featured a unique 4-oxa-tricyclo[4.3.1.$0^{3,7}$]dec-2-one scaffold built into a caged xanthone backbone [8]. Of this class, those compounds exhibiting potent antitumor activity are referred to "caged *Garcinia* xanthones". Around 100 have been reported to date, gambogic acid (GA) being the best representative, have the most potential of broad-spectrum anticancer drug candidate [9–16]. In China, the clinical trials to evaluate the efficacy and safety of GA have been carried out since the 1970s. Interest in these caged *Garcinia* xanthones has attracted many attempts to synthesize it using Claisen/Diels-Alder/Claisen rearrangement [17,18].

The continuous investigation on *G. hanburyi* in our laboratory led to a series of reports of gambogic acid derivatives with anticancer activities [5,10,19–24]. Due to the slight difference in the complicated structures of these gambogic acid derivatives, it has always been a challenge to separate and identify these analogues. Several reverse-phase high-performance liquid chromatography methods (RP-HPLC) with UV detection

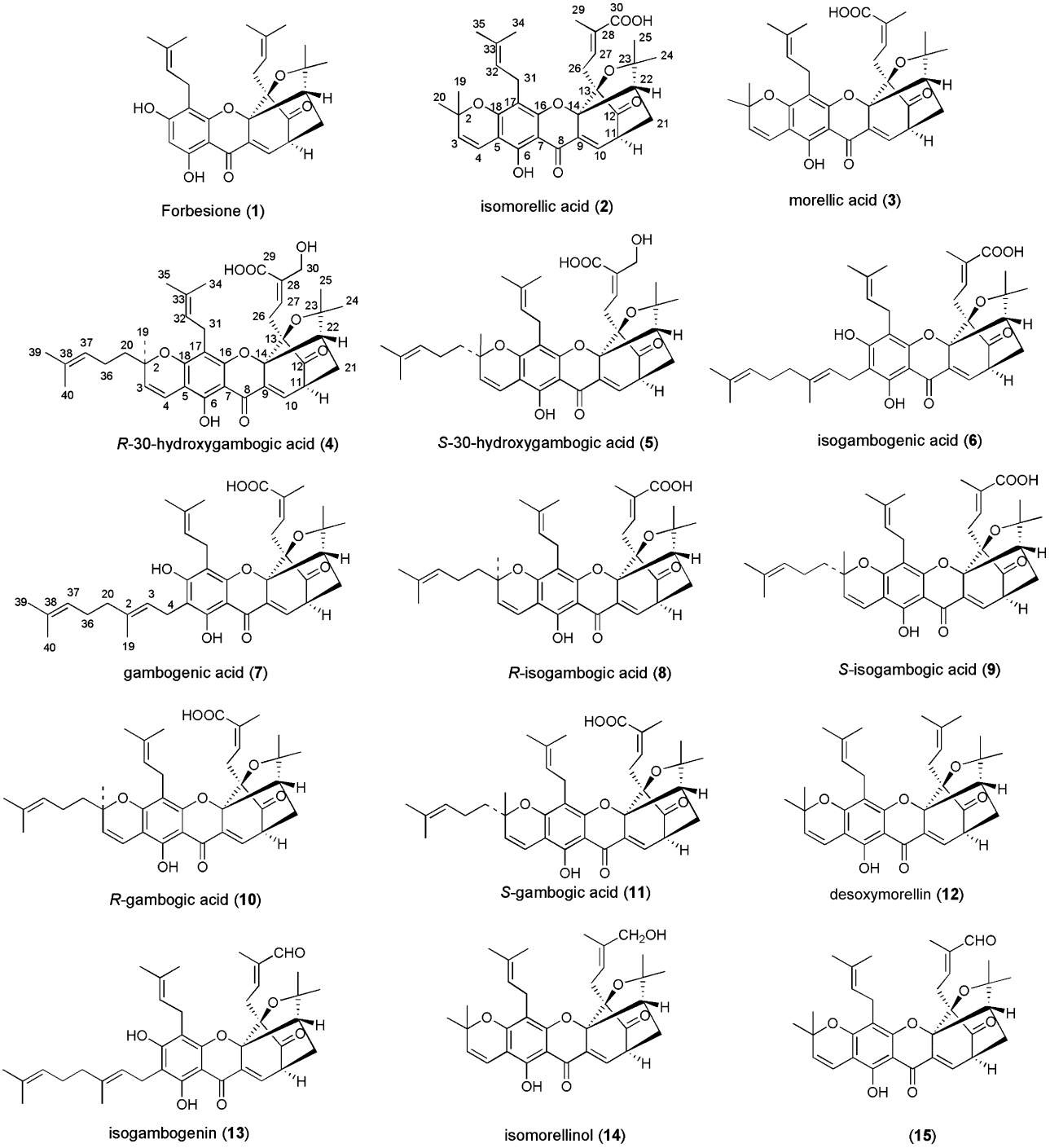

Fig. 1 – The structures of caged xanthones rom *Garcinia hanburyi*.