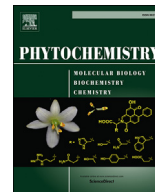




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journal homepage: www.elsevier.com/locate/phytochemBiologically active xanthenes from *Codonopsis ovata*[☆]

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ABSTRACT

Five new xanthenes, named coxanthenes A–E (**1**–**5**), together with 21 known secondary metabolites (**6**–**26**) that include seven xanthenes, five flavonoids, two steroids and seven triterpenoids were isolated from the chemically unexplored whole plant *Codonopsis ovata*. The structures of new metabolites were elucidated by HRMS, interpretation of NMR spectra and other spectroscopic techniques. The absolute configuration of the stereogenic centre of coxanthone B (**2**) was determined by electronic circular dichroism (ECD) spectroscopy. This is the first report of xanthenes from the genus *Codonopsis*. All isolated metabolites were evaluated for cytotoxic activity by SRB assay against six human cancer cell lines A549 (lung), PC-3 (prostate), HCT-116 (colon), MCF-7 (breast), SF-295 (CNS), and MDAMB-435 (melanoma). Among the new compounds, coxanthone B (**2**) exhibited significant inhibitory activity against SF-295 and MDAMB-435 with IC₅₀ values of 7.0 and 15.0 μM, respectively. Coxanthone A (**1**) displayed cytotoxicity against A549 cell line at IC₅₀ value of 22.5 μM. Cytotoxic activity of 1-hydroxy-3,5-dimethoxyxanthone (**7**), swertiperenine (**9**) and 1,7,8-trihydroxy-3-methoxyxanthone (**10**) are reported here first time that exhibited the IC₅₀ values of 3.0, 5.0 and 21.0 μM against A549, MDAMB-435, and A549 cell lines, respectively. Kaempferol (**13**) showed most potent cytotoxic activity with an IC₅₀ values in the 1.0–2.3 μM range against all tested cancer cell lines.

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1. Introduction

The genus *Codonopsis* (family Campanulaceae) comprises 42 species which are perennial herbs, endemic to East Asia. Several species of this genus are used in Indian, Chinese, Vietnamese, Korean traditional and folk medicine to treat appetite loss, diarrhoea, dyspepsia, vomiting, lung ailments, rheumatism and menstrual disturbances for hundreds of years (Ishida et al., 2008; Zhao et al., 2012). In addition to their medicinal applications, roots of several species from this genus are also used in food therapy recipes (Chao et al., 2015). The genus *Codonopsis* is known to produce structurally diverse secondary metabolites from different chemical classes including alkaloids, flavonoids, isoflavonoids, steroids, triterpenoids, saponins, and polyacetylenic compounds (Ishida et al.,

2008; Dar et al., 2014; Yuda et al., 1990). Some of these compounds have been demonstrated to exhibit a wide range of biological activities, particularly cytotoxic and anti-inflammatory activities (Zhang et al., 2014; Van et al., 2009; Liu et al., 2011).

Codonopsis ovata Benth., locally known as “Ludut”, is an important medicinal plant native to Asia, typically found at an altitude of 3000–4200 m in the Western Himalayan region (Dar et al., 2014). The roots and leaves of this plant are used for the treatment of wounds, poultice for bruises, ulcers, and skin disinfectants by the Indian System of Medicine (ISM) (Varma and Tandon, 1989; Chopra et al., 1986). The alcoholic extract of this plant is reported to possess significant oxytocic and antifertility properties (Varma and Tandon, 1989). Recently, we reported quantitative analysis of eight secondary metabolites and their antioxidant profile by HPTLC (Dar et al., 2014). The traditional folklore applications of *C. ovata* and our preliminary work prompted us to perform a thorough chemical investigation of the whole plant. Therefore, systematic studies of the chemical constituents of the whole *C. ovata* plant and their cytotoxic activity against six

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