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Chemical constituents of the aerial parts of Algerian *Galium brunneum*: Isolation of new hydroperoxy sterol glucosyl derivatives

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ABSTRACT

The liposoluble extract of *Galium brunneum* aerial parts from North-eastern Algeria was chemically investigated. The EtOAc soluble portion contained a series of glycosyl cucurbitacins and sterols including three new glucosyl hydroperoxy sterols **1–3** among other phenolic components whereas the BuOH soluble fraction was dominated by glycosyl derivatives of flavonoids, iridoids and lignans, according to the chemistry reported in the literature for the genus *Galium*. The structure of new oxidized sterols **1–3** was determined by spectroscopic methods as well as by comparison with related known metabolites. Selected main compounds from both extracts, which revealed moderate antibacterial activities, were tested for their growth inhibitory properties against Gram-positive and Gram-negative bacteria. This is the first report of cucurbitacins in plants of genus *Galium*.

1. Introduction

The Rubiaceae family is one of the largest in the Magnoliopsida class with a cosmopolitan distribution (Robbrecht, 1988). According to recent phylogenetic molecular studies, this family is divided into three subfamilies, Rubioideae, Cinchonoideae, and Ixoroideae, including numerous tribes due to high species diversity (Bremer, 2009). The genus *Galium* consisting of about 400 herbaceous plant species represents a large genus of the subfamily Rubioideae (tribe Rubieae) that are world-wide distributed, mostly from the tropics to the temperate zones (Ehrendorfer et al., 2018, 1976; The Plant List, 2013). Many *Galium* species are used in traditional medicine to treat various pathologies such as epilepsy, hepatitis, phlebo phlogosis, kidney disorders and skin infections and as diuretic and analgesic (Jarić et al., 2007; Chinese Materia Medica, 1977; Bolivar et al., 2011; Shah et al., 2006; Kaval et al., 2014). A large number of phytochemical investigations have been conducted on several *Galium* species from different geographical areas including Algeria. These studies have reported the occurrence of iridoids, triterpenoids, anthraquinones, lignans and flavonoids displaying a variety of interesting biological (Martins and Nunez (2015); Bradic et al., 2018; Mocan et al., 2016; Chaher et al., 2016; Camero et al., 2018; Gaamoune et al., 2014).

Galium brunneum Munby is a species with a few records limited to North Africa (Algeria, Morocco and Tunisia). The plant is a perennial herb growing on calcareous rocks and is characterized by brown or reddish flowers. Inflorescences are grouped in short and axillary cymes, in the upper portion of the stems (Quezel and Santa, 1963). Neither phytochemical nor pharmacological studies have been reported in the literature to date for this plant.

In continuing our recent phytochemical investigations on Algerian plants (Bitam et al., 2008; Bouzergoune et al., 2016; Boumaraf et al., 2017; Zergainoh et al., 2018; Djebara et al., 2019), we have analyzed the content of EtOAc and BuOH soluble parts from the hydromethanolic extract of the aerial parts of *G. brunneum* collected in Ain Touta region, Batna (Algeria) in May of 2012 (Smadi, 2018). The chemical study revealed a secondary metabolite pattern characterized by flavonoids, iridoids and lignans, according to the chemistry reported in the literature for the genus *Galium*. Three unreported hydroperoxy glycosyl sterols (**1-3**, Fig. 1) were found in the EtOAc extract along with a series of known compounds (**4-14,** see Supplementary material). Among them known glycosyl triterpenoids (compounds **7**, **8**, and **10**) with cucurbitane nucleus, that was never reported to date in genus *Galium,* were identified. Previously reported compounds (**15-25,** see Supplementary material) were isolated from the BuOH extract. Due to moderate antibacterial properties exhibited by the *G. brunneum* extracts against Gram-positive and Gram-negative bacteria strains, selected main

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