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Article

Aurantoside J: a New Tetramic Acid Glycoside from *Theonella swinhoei*. Insights into the Antifungal Potential of Aurantosides

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Abstract: The chemical investigation of an Indonesian specimen of *Theonella swinhoei* afforded four aurantosides, one of which, aurantoside J (**5**), is a new compound. The structure of this metabolite, exhibiting the unprecedented *N*-α-glycosidic linkage between the pentose and the tetramate units, has been determined through detailed spectroscopic analysis. The four obtained aurantosides have been tested against five fungal strains (four *Candida* and one *Fusarium*) responsible of invasive infections in immuno-compromised patients. The non-cytotoxic aurantoside I (**4**) was the single compound to show an excellent potency against all the tested strains, thus providing valuable insights about the antifungal potential of this class of compounds and the structure-activity relationships.

Keywords: *Theonella swhinoei*; aurantosides; *N*-glycosides; antifungal activity

1. Introduction

Aurantosides and rubrosides are orange-red pigments isolated from sponges of the genera *Theonella*, *Homophymia* and *Siliquariaspongia*, all belonging to the order Lithistida [1–5]. These complex molecules include three different structural moieties: a mono- or dichlorinated long (C_{18} to C_{28}) conjugated polyene chain (terminating with an oxygenated five-membered ring in the rubroside subfamily), a tetramate ring, and an *N*-glycosidic moiety made up by one to three monosaccharide units, which are, invariably, pentose or deoxypentose sugars.

Compared to non-ribosomial cyclic and linear peptides and to polyketide macrolides, the most widely investigated secondary metabolites from sponges of the Lithistida order, aurantosides have been largely overlooked, also in terms of their biomedical potential. The reasons for this observation can be mostly found in the difficulties associated to their isolation in the pure form and to their relative instability, which is obviously related to the presence of the polyene moiety.

In the frame of our ongoing investigation of Indonesian invertebrates for bioactive secondary metabolites [6–8], we have recently analyzed a specimen of *Theonella swinhoei* (Theonellidae, Lithistida) and reported the isolation of dehydroconicasterol and of aurantoic acid (**1**) [9]. This latter compound closely resembles the polyene moiety of aurantosides G–I [4], although the biosynthetic relationship between aurantoic acid and aurantosides has not been established. Chemical analysis of the most polar fractions of the organic extract obtained from the same organism revealed that they were practically devoid of polar polypeptides or macrolides, while they contained consistent amounts of aurantosides. In this paper we describe the isolation and the structure elucidation of the three known aurantosides G–I (**2**–**4**) and of the new aurantoside J (**5**) from these fractions (see Scheme 1). In addition, we report the results of a detailed investigation of the antifungal activity of the isolated aurantosides, which revealed a strict dependency from the glycosylation pattern.

Scheme 1.