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Communication

Isatindolignanoside A, a glucosidic indole-lignan conjugate from an aqueous extract of the *Isatis indigotica* roots

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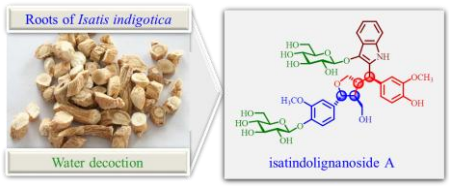
Graphical abstract



A glucosidic indole-lignan conjugate with a novel carbon skeleton, named isatindolignanoside A (**1**), was isolated from an aqueous extract of the *Isatis indigotica* roots "ban lan gen". Its structure was determined by comprehensive analysis of spectroscopic data, enzyme hydrolysis, and electronic CD calculations. Compound **1** is active against Coxsackie virus B3 and represents the first example of natural product having a structural feature of conjugation between indole and lignan, and its plausible biosynthetic pathway is postulated.

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ABSTRACT

A glucosidic indole-lignan conjugate with a novel carbon skeleton, named isatindolignanoside A (**1**), was isolated from an aqueous extract of the *Isatis indigotica* roots "ban lan gen". Its structure was elucidated by comprehensive analysis of spectroscopic data, including *J*- and NOESY correlation-based configurational analysis, circular dichroism (CD) data, enzyme hydrolysis, and theoretical ECD calculation. In a preliminary assay, compound **1** showed antiviral activity against Coxsackie virus B3. This compound is the first example of natural product having a structural feature of conjugation between indole and lignan units, and its biosynthetic pathway is postulated.

The dried roots of *Isatis indigotica* Fort. (Cruciferae), named "ban lan gen" in Chinese, is among the most popular herbal drugs for the treatment of colds, especially of the flu during influenza pandemics in China [1]. Many formulations containing extracts of "ban lan gen" or the raw material are compiled in Chinese Pharmacopoeia [2]. Agricultural cultivation of this plant not only fulfils demands of medicinal industry but also plays roles of environment protection and increasing local economy in several provinces of China. Considerable investigations on this herbal medicine indicated that "ban lan gen" extracts had antiviral, anti-endotoxic, anti-inflammatory, antipyretic, and cytotoxic activities [3-7] and contained alkaloids [8-13], lignans [14,15], flavonoids [16], and epigoitrin and related analogues [17]. However, the previous chemical studies were mainly carried out on the ethanol or methanol extracts of the drug material, which differs from a practical application by decocting with water. Therefore, an aqueous decoction of "ban lan gen" was investigated as part of a program to systematically study the chemical diversity of traditional Chinese medicines and their biological activities [18-39]. More than 100 compounds including 61 with new structures from the decoction were reported in our previous papers [39-51]. Antiviral activity against influenza virus A/Hanfang/359/95 (H3N2) or Coxsackie virus B3, protective activity against *dl*-galactosamine-induced hepatocyte (WB-F344 cell) damage, and inhibitory activity against the LPS-induced NO production in mouse peritoneal macrophage [40,41,43-45,47] were found for the isolates with varied structural types. A continuation of the study, focusing on the minor constituents, has led to characterization of an unusual glucosidic indole-lignan conjugate with a novel carbon skeleton, named isatindolignanoside A (**1**) (Fig. 1). This paper describes details of the isolation, structure elucidation, and bioassay of the new isolate.