

Astraodoric Acids A–D: New Lanostane Triterpenes from Edible Mushroom *Astraeus odoratus* and Their Anti-*Mycobacterium tuberculosis* H₃₇Ra and Cytotoxic Activity

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Supporting Information

ABSTRACT: Tuberculosis (TB) is one of the chronic infectious diseases caused by *Mycobacterium tuberculosis* that causes about 2–3 million deaths per year. Isoniazid and rifampicin are examples of first line drugs used for TB treatment; however, they are potentially hepatotoxic. More effective and safer drugs are urgently needed, especially from natural products. Basidiomycete mushrooms are known as important sources of pharmaceutically active metabolites including an anti-TB agent. In this work, the chemical constituents of the edible mushroom *Astraeus odoratus* were isolated and investigated for antibacterial activity against *M. tuberculosis* H₃₇Ra. The cytotoxic activity against cancerous cell lines was also evaluated. Four new lanostane triterpenes, astraodoric acids A–D, and new 5-hydroxyhypaphorine have been isolated together with four known compounds. The structures were elucidated by NMR spectroscopic methods, HR-ESI-MS results, and X-ray crystallographic analysis. Astraodoric acids A and B exhibited moderate antibacterial (MICs of 50 and 25 µg/mL) and cytotoxic activities (IC₅₀ values of 34.69 and 18.57 µg/mL against KB and 19.99 and 48.35 µg/mL against NCI-H187), respectively. The results of this study show that *A. odoratus* could be a significant natural source for safer antitubercular and anticancer agents.

KEYWORDS: *Astraeus odoratus*, lanostane triterpene, astraodoric acids A–D, hypaphorine, antituberculosis, cytotoxic activity

INTRODUCTION

Tuberculosis (TB) is a condition caused by an infection of *Mycobacterium tuberculosis*. One third of the world's population is latently infected, and it is responsible for the death of at least 2–3 million per year.^{1,2} The treatment of TB requires the long-term usage of multidrugs, that is, at least two of first-line antibiotics, for example, isoniazid, rifampicin, pyrazinamide, and ethambutol, to prevent the risk of drug resistance. Recent studies^{3,4} have shown that this could lead to drug-induced hepatotoxicity, which would be more severe in patients with hepatitis or HIV. The emergence of multidrug-resistant strains has also raised concerns for the difficulty of treating TB in the future.⁵ Therefore, the need for new antitubercular agents is urgent, especially those from natural products, to overcome the obstacle of side effects. Medicinal mushrooms⁶ have been long exploited throughout Asia. Mushrooms such as *Gonoderma*, *Lentinus*, *Tramete*, and *Argaritus* spp. have played an important role in medicinal remedies, producing a variety of biological activities such as antimicrobial, anticancer, antidiabetes, and hepatoprotective activities.^{6–8} There are approximately 7000 unidentified species⁷ of mushrooms that have never been investigated for their pharmaceutically active metabolites, and very little is known so far for those that have been identified. Therefore, basidiomycete-edible mushrooms are crucial sources of biological metabolites that have yet to be discovered. Our

work is a part of the search for bioactive compounds including antitubercular agents from the edible mushrooms of *Astraeus* spp. in Thailand.

*Astraeus*⁹ belonging to Astraeaceae family (Sclerodermatineae suborder, Boletales order, Gasteromycetes class, and Basidiomycota phylum) can be found in many areas of the world. The most well-known distinctive feature of *Astraeus* spp. is the star-shaped split of the exoperidium that occurs when it reaches maturity. This is why it is also known as the false earthstar mushroom. There are currently five known species including *Astraeus hygrometricus*, which is found throughout the world; *Astraeus pteridis*, which is found only in North America and the Canary Islands; and *Astraeus asiaticus* (similar to *Astraeus thailandicus*), *Astraeus odoratus*, and *Astraeus koreanus* (also known as *Astraeus hygrometricus* var. *koreanus*), which are mainly found in Asia.¹⁰ The chemical constituents and biological activities of *Astraeus* spp. were mostly studied in *A. hygrometricus* and *A. pteridis*. *A. hygrometricus*^{11,12} has been used as a hemostatic in Chinese folk medicine, and its constituents exhibited versatile biological activities such as free radical

Received: June 5, 2012

Revised: September 9, 2012

Accepted: September 9, 2012

Published: September 10, 2012



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