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Review

A review on phytochemistry and pharmacological activities of the processed lateral root of *Aconitum carmichaelii* Debeaux

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ABSTRACT

Ethnopharmacological relevance: The processed lateral root of *Aconitum carmichaelii* Debeaux (Ranunculaceae), an extensively used traditional Chinese medicine, is known as Fuzi in China (Chinese: 附子), "bushi" in Japan, "Kyeong-Po Buja" in Korea, Chinese aconite, monkshood or Chinese wolfsbane. It has been used to treat shock resulting from acute myocardial infarction, low blood pressure, coronary heart disease, chronic heart failure, *etc.*

Aim of the review: The present paper aims to provide an up-to-date review at the advancements of the investigations on the ethnopharmacology, phytochemistry, pharmacological effect and toxicity of Fuzi. Besides, the possible tendency and perspective for future research of this plant are discussed, as well.

Materials and methods: All available information on Fuzi was collected via electronic search (using Elsevier, PubMed, ACS, CNKI, Google Scholar, Baidu Scholar, and Web of Science), books and classic works about Chinese herb.

Results: 122 chemical constituents, among which C_{19}-diterpenoid alkaloids and C_{20}-diterpenoid alkaloids are the predominant groups, have been isolated and identified from Fuzi. Fuzi with its active compounds is possessed of wide-reaching biological activities, including effects on cardiovascular system, anti-inflammation and analgesic action, anti-tumor activity, effect on the immune system, hypoglycemic and hypolipidemic effects, anti-aging effect, effect of protecting kidney and effect on energy metabolism.

Conclusions: Nearly all of compounds were found from the roots of the plant, so further phytochemical studies should focus more on the other parts of the plant, such as the leaves, flowers or stems. Besides, a majority of the pharmacological studies were carried out using crude and poorly characterized extracts. Thus, more bioactive components particularly cardiotonic and analgesic compounds should be identified through bioactivity-guided isolation strategies. Moreover, investigations on how to develop Fuzi's new clinical usage on the basis of its pharmacological effects are in requirement.

Contents

Abbreviations: TCM, traditional Chinese medicine; DAs, diester-diterpenoid alkaloids; MAs, monoester-diterpenoid alkaloids; UAs, unesterified-diterpenoid alkaloids; IC_{50}, inhibitory concentration 50%; EC_{50}, effective concentration 50%; RNA, ribonucleic acid; FPS, Fuzi polysaccharides; ATP, adenosine triphosphate; GC/LC-TOF-MS, gas chromatography/liquid chromatography quadruple time-of-flight mass spectrometry

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1. Introduction

Aconitum is a large genus of the Ranunculaceae family, which consists of about 400 species distributed in the temperate regions of the north hemisphere and 211 species in China (Committee for the flora of China of Chinese Academy of Sciences, 2004). They have been of interest since ancient times because they comprise diterpene alkaloids that range from relatively nontoxic to deadly poisonous. In different parts of the world, such as China, Japan, Korea and India, they have been used medicinally and as a source of poisons throughout history. *Aconitum carmichaelii* Debeaux is a member of Aconitum, and the lateral root of *A. carmichaelii* is the unique source of one Chinese famous herb, called "Fuzi (Chinese: 附子)", officially named Radix Aconiti Lateralis Praeparata or Prepared Common Monkshood Daughter Root. It is also known as Chinese aconite, monkshood, Chinese wolfsbane, "Bushi" in Japan, and "Kyeong-Po Buja" in Korea.

Because Fuzi is extensively used as a potent herb in China but has great toxicity, it has been in the spotlight from the researchers for a long time. The present paper intends to address how it becomes a valuable herb from a lethal poison, and simultaneously to provide an up-to-date review on the advancements of the investigations on the phytochemistry and pharmacological activities of it. Besides, the possible direction and perspective for future research of this herb are discussed, as well.

2. Botany

There are 211 Aconitum species in China, of which phytochemistry, pharmacological activities and toxicities are diversified by their phylogeny (Xiao et al., 2006). *Aconitum carmichaelii* (Synonym: *Ampelopsis bodinieri* H.Lév. & Vaniot, *Aconitum carmichaelii* var. *angustius* W.T. Wang & P.K. Hsiao, *Aconitum jiulongense* W.T. Wang, *Aconitum kusnezoffii* var. *bodinieri* (H.Lév. & Vaniot) Finet & Gagnep, *Aconitum lushanense* Migo, and *Aconitum wilsonii* Stapf ex Mottet) is one of species among them, the unique source of "Fuzi". The lateral root of *A. carmichaelii* is collected from late June to early August, removed from the parent root, rootlet and soil. It is known as "Nifuzi (泥附子)", which can be processed into the some commercial varieties, such as "Yanfuzi (盐附子)", "Heishunpian (黑顺片)", "Baifupian (白附片)", all of which are called Fuzi generally (Committee for the pharmacopoeia of China, 2010). It is reported that the plant had been cultivated in Zhangming and Jiangyou in Sichuan Province, China, for nearly the past one thousand years. The ferine plant of *A. carmichaelii* has two root tubers, which will grow in number if the plant is cultivated. Particularly, different root tubers have different names and different medical effects in traditional Chinese medicine. Several historically renowned Chinese medical scientists held some personal points of view towards the name of the root tubers of the plant. For example, Hongjing Tao in the Liang Dynasty, pointed out that both Wutou (Aconiti Radix) and Fuzi are the same root tubers but Wutou is harvested in April while Fuzi is harvested in August. Shizhen Li, the author of *Compendium of Materia Medica* (《本草纲目》) in Ming Dynasty, also indicated that the initial root is Wutou, shape of which is similar to the head of crow, and that the other root attached to Wutou is Fuzi, as daughter is attached to her parent (Committee for the flora of China of Chinese Academy of Sciences, 2004).

Nowadays, the main producing areas of this two herbs are also around Jiangyou, Sichuan Province, Hubei Province and Hunan Province, China. Generally speaking, the medical products are mainly harvested from the cultivated plants, and the principal root (parent root) is named Aconiti Radix (Wutou) (Fig. 1A) while the lateral root (daughter root) is called Radix Aconiti Lateralis Praeparata (Fuzi) (Fig. 1B) (Committee for the flora of China of Chinese Academy of Sciences, 2004). Because ester alkaloids of Aconiti Radix and those of Fuzi differ in both content and composition, it is desirable to prevent mixing Aconiti Radix and Fuzi at harvest and in medical use (Kawasaki et al., 2011).

3. Ethnopharmacology

Fuzi, the processed lateral root of *A. carmichaelii*, has played an indispensable role in Chinese health care for a long time in