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Zeolitic imidazolate framework-8 for selective extraction of a highly active anti-oxidant flavonoid from *Caragana Jubata*

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ABSTRACT

The medicinal compositions or active components in medicinal plants are the major sources to find new drugs or lead compounds. Exploring novel sorbents with good selectivity for extraction and separation of medicinal compositions or active components from complex medicinal plants are interesting and challenging. Metal-organic frameworks (MOFs) show great potential in adsorption and extraction recently. Herein, we report our primary attempt of zeolitic imidazolate framework-8 (ZIF-8) as a model MOF for selective extraction of a flavonoid named 3,4-dihydroxy-8,9-methylenedioxypterocarpan (compound 1) from a traditional medicinal plant *Caragana Jubata*. The enrichment factor of ZIF-8 for compound 1 is 57.7. The recoveries of compound 1 at three spiked levels (50, 100, 150 $mg\,L^{-1}$) in *Caragana Jubata* dichloromethane extract are 62.1%, 66.4%, and 75.4%, respectively, with the relative standard deviations of less than 2.9%. The compound 1 also gave good linearity (R^2 of 0.999) in the concentration range of 5–1000 $mg\,L^{-1}$. The obtained compound 1 gave highly antioxidant activity (DPPH radical scavenging rate of 79.03%, inhibitory rate on lipid peroxidation of 75.30%, which were higher than the positive controls Vitamin C and BHT) and low IC_{50} values (5.438 ± 0.068, 20.970 ± 0.083 $\mu g\,mL^{-1}$ for DPPH radical scavenging activities and inhibitory effects on lipid peroxidation, respectively). These results demonstrated the feasibility of MOFs in selective extraction of medicinal compositions or active components from complex medicinal plants. The current work may open a new way of MOFs in selective extraction of pharmacological active components from medicinal plants.

1. Introduction

Medicinal plants are the major sources of human beings to obtain drugs to prevent and cure diseases [1–6]. The medicinal compositions or active components in medicinal plants are also the efficient ways to find new drugs or lead compounds. For example, taxol, the famous anti-cancer drug for ovarian, uterine, lung, esophageal and prostate cancers, was isolated from the bark of *Pacific Yew* [7–9]. Artemisinin, another star antimalarial, was extracted from the bark of *Artemisia annua Linn* [10,11]. However, extraction and separation of these medicinal compositions or active components from medicinal plants are quite challenging and time-consuming due to the complex nature of medicinal plants. Until now, many traditional porous materials including silica-gel, activated carbon, and alumina have been applied for the extraction and separation of medicinal compositions or active components from medicinal plants [12–14]. Exploring novel sorbents with good selectivity and large capacities for extraction and separation of medicinal compositions or active components from medicinal plants are interesting and challenging not only for the development of materials science but also for the discovery of new drugs or lead compounds.

Metal-organic frameworks (MOFs) are an emerging class of multifunctional porous hybrid materials assembled by metal ions or cluster nods and organic ligands [15–17]. Rely on their large surface area, good thermal stability, tunable pore topology and structures, MOFs have become the most promising candidates in gas storage [18], catalysis [19], sensing [20], chromatography [21] and separation [22]. The semi-organic frameworks, rigid pore size, activated open metal sites, and large adsorption capacities make MOFs potential in selective adsorption and extraction of diverse targets such as sulfur-containing compounds, peptides, aromatic contaminants, metal ions and dyes from diverse matrices from simple to com-

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plex [23–26]. Considering the good prospects of MOFs in extraction and adsorption and the significant roles of medicinal compositions or active components in complex medicinal plants, application of MOFs in selective extraction and separation of medicinal compositions or active components from complex medicinal plants should be a promising topic, however, has not been reported so far. The aim of this work is to study the feasibility of MOFs in selective extraction and separation of medicinal compositions or active components from complex medicinal plants and to expend novel sorbents in medicinal plants extraction and separation.

Herein, we report our primary attempt of zeolitic imidazolate framework-8 (ZIF-8) as a model MOF for selective extraction of a highly active anti-oxidant flavonoid from a traditional medicinal plant *Caragana Jubata*. ZIF-8 is one of the star MOFs constructed from zinc ions and 2-methylimidazole. The large surface area, good thermal and solvent stability make it good candidate in adsorption and extraction [27–29]. *Caragana Jubata* is one of the medicinal plants in *Leguminosae*, distributed in Gansu province and Qinghai-Tibet plateau of China. "*Zuo Mu Xing*", the red heartwoods of the stems and roots of *Caragana Jubata*, was the main medicinal parts in traditional Tibetan medicine to cure Alpine polyemia, blood-heat and hypertension, *etc*. The modern pharmacological activities of this species mainly contained anti-hypertensive, anti-oxidant, anti-viral, anti-inflammatory, anti-tumor and inhibition of platelet aggregation [30–32]. Therefore, to precisely elucidate the pharmacological activities of medicinal compositions or active components in *Caragana Jubata*, a selective extraction and separation strategy should be studied.

Flavonoids are the typical components in *Leguminosae*, featuring many significant pharmacological activities such as anti-inflammatory, antioxidant, antithrombotic, antiviral and so on [33–36]. Selective extraction of flavonoids from the complex medicinal plants has received great concerns recently. For example, Wu and co-workers established a two-phase liquid–liquid extraction and following conical counter-current chromatography separation strategy for selective extraction and isolation of flavonoids from *Dysosma versipellis* (Hance) [33]. Wang et al. demonstrated the feasibility of subcritical ethanol extraction of flavonoids from *Moringa oleifera* leaf [34]. Li et al. and Kubo et al. reported the progress of hybrid molecularly imprinted polymers for rapid purification of flavonoids from medicinal plants [35,36]. Development of novel sorbents for flavonoids extraction and separation in complex medicinal plants still gains great interests.

In this work, ZIF-8 was used as the adsorbent for selective extraction of a flavonoid named 3,4-dihydroxy-8,9-methylenedioxypterocarpan (compound 1) from the complex dichloromethane (DCM) extract of *Caragana Jubata* (Fig. 1). Such method was also expended for other MOFs such as MIL-100(Fe), MIL-101(Cr), NH_2-MIL-53 and ZIF-7 for selective extraction of trace compounds from *Caragana Jubata*. These results demonstrated the feasibility of MOFs in selective extraction of medicinal compositions or active components from complex medicinal plants.

2. Experimental

2.1. Chemicals and reagents

All chemicals and reagents were at least of analytical grade. Ultrapure water (18.2 MΩ cm) was obtained from a WaterPro Water Purification System (Tianjin On-well Scientific Co., Ltd. Tianjin, China). Zinc nitrate hexahydrate (99%), 2-methylimidazole (98%) (Aladdin Chemistry Co., Ltd. Shanghai, China), *N,N*-dimethylformamide (DMF) were used to prepare ZIF-8. Trichloroacetic acid (TCA, 20%, w/v), potassium ferricyanide ($K_3[Fe(CN)_6]$), and ethanol were purchased from Guangfu Fine Chemicals (Tianjin, China). Methanol, petroleum ether, *n*-butanol, acetonitrile, dichloromethane (DCM), and ethyl acetate were

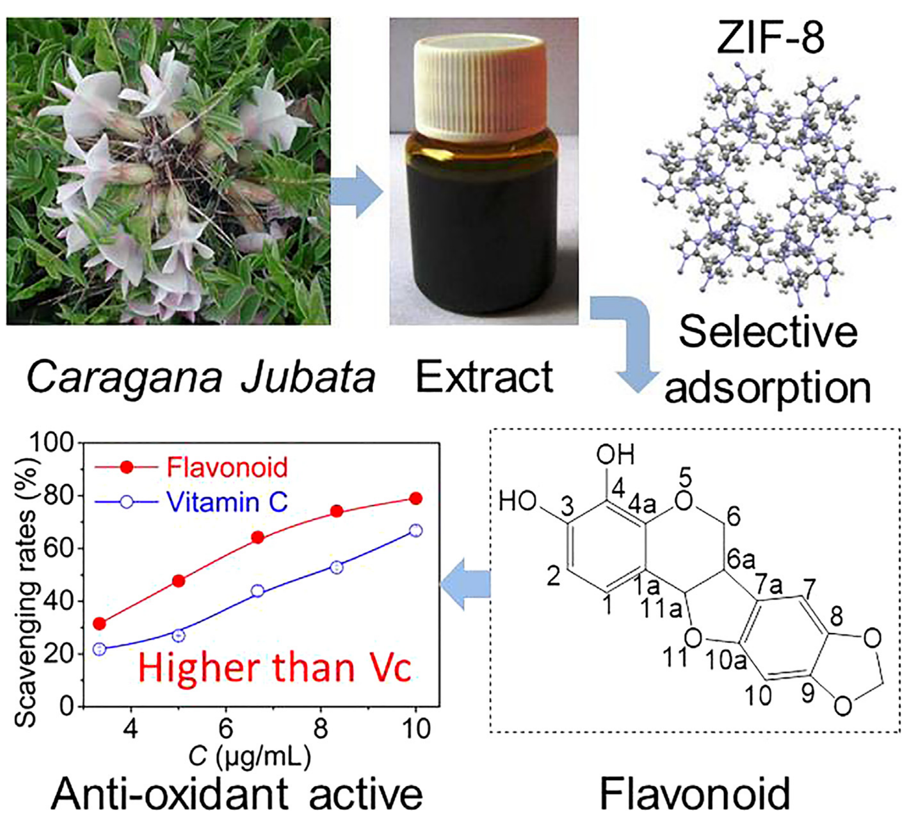

Fig. 1. Schematic illustration for selective extraction of Flavonoid from *Caragana Jubata* using ZIF-8 as the sorbent.