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

Yuan-Yuan Cui [a], Cheng-Xiong Yang [b,*], Xue-Dong Yang [a,*], Xiu-Ping Yan [b]

[a] School of Pharmaceutical Science and Technology, Tianjin University, Tianjin, 300072, China
[b] College of Chemistry, Research Center for Analytical Science, Tianjin Key Laboratory of Molecular Recognition and Biosensing, State Key Laboratory of Medicinal Chemical Biology, Nankai University, Tianjin, 300071, China

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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 μg 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-

* Corresponding authors.
E-mail addresses: cxyang@nankai.edu.cn (C.-X. Yang), yangxd@tju.edu.cn (X.-D. Yang).

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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

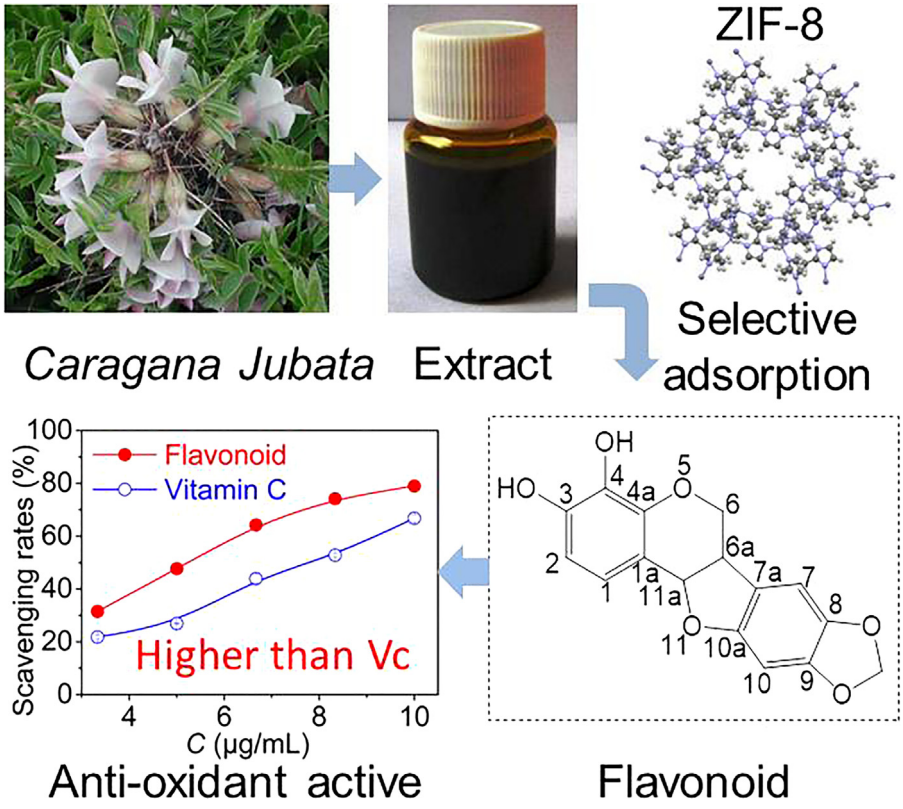

Fig. 1. Schematic illustration for selective extraction of Flavonoid from *Caragana Jubata* using ZIF-8 as the sorbent.

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purchased from Concord Technology Co., Ltd. (Tianjin, China). $FeSO_4{\cdot}7H_2O$, $Na_2HPO_4{\cdot}12H_2O$ and $NaH_2PO_4{\cdot}2H_2O$ were purchased from Yuan Li Chemical Co., Ltd. (Tianjin, China). Vitamin C was purchased from Aladdin Chemistry Co., Ltd. (Shanghai, China). 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and butylated hydroxy toluene (BHT) were acquired from Sigma Chemical Co., Ltd. (Beijing, China).

2.2. Instrumentation

The X-ray diffraction spectrometry (XRD) patterns were recorded on a D/max-2500 diffractometer (Rigaku, Japan) using Cu-Ka radiation (λ = 1.5418 Å). The thermal gravimetric analysis (TGA) was performed on a PTC-10A thermal gravimetric analyzer (Rigaku, Japan) from room temperature to 800 °C at a ramp rate of 10 °C min^{-1}. The scanning electron microscopy (SEM) images were recorded on JSM-6390LV scanning electron microscope (Rigaku, Japan) at 20 kV. The N_2 adsorption experiments were performed on an ASAP 2010 micropore physisorption analyzer (Micromeritics, Nor-cross, GA, USA) using N_2 at 77 K. The single crystal X-ray diffraction was conducted on XtaLAB P200 (Rigaku, Japan). X-ray photoelectron spectroscopy (XPS) measurements were performed on an Axis Ultra DLD (Kratos Analytical Ltd. Britain). High performance liquid chromatography (HPLC) experiments were performed on a Chuangxin Tongheng LC3000 instrument (Beijing, China) equipped with a P3000 gradient pump, a UV3000 UV–vis detector, aCXTH-3000 chromatography workstation, and a Cosmosil $5C_{18}$-MS-II (4.6 × 250 mm, 5 μm) column. Liquid chromatography-mass spectrometry (LC–MS) experiments were studied on an Agilent-Bruker instrument (1290 UHPLC/microTOF-Q II). Nuclear magnetic resonance spectroscopy (NMR) data were acquired on a Bruker AV-400 spectrometer.

2.3. Synthesis of ZIF-8

The ZIF-8 was synthesized according to Park et al. [27]. Typically, 239 mg of $Zn(NO_3)_2{\cdot}6H_2O$, 60 mg of 2-methylimidazole and 18 mL of DMF were mixed in a 30 mL Teflon-lined bomb. The Teflon-lined bomb was capped and stayed in a 140 °C oven for 24 h. After cooling down to the room temperature, the colorless ZIF-8 was collected and washed with DMF and methanol for three times, and then evacuated in vacuum at room temperature for 12 h.

2.4. Preparation of DCM extract of Caragana Jubata

The heartwood of the rhizomes of *Caragana Jubata* was collected from Tibet of China. The air-dried heartwood was smashed and then extracted with 95% ethanol at room temperature. The ethanol extract was suspended in water and partitioned successively with petroleum ether, DCM, ethyl acetate, and *n*-butanol. The DCM extract was selected as the model matrix for extraction.

2.5. Antioxidant activity analysis [37,38]

Scavenging activity against DPPH free radical. Briefly, proper amount of compound 1, compound 2, Vitamin C and DCM extract were dissolved with ethanol to form the sample solution with the initial concentration of 0.1–0.3 mg mL^{-1}. A 2.9 mL dose of DPPH (120 μM) in ethanol was then added into 0.1 mL of each sample solution. The mixtures were shaken and incubated in dark at 37 °C for 30 min. The final concentration of the tested four samples was in the range of 3.3–10.0 μg mL^{-1}. The absorbance of the mixture solution was measured at 517 nm. Ethanol was used as the control. The Vitamin C was used as the positive control. The whole tests were performed in triplicate. DPPH radical scavenging activity was calculated by the following equation: DPPH radical scavenging activity (%) = $(1 - A_{sample}/A_{blank}) \times 100\%$.

Assay of ferric reducing/antioxidant power. One hundred microliter of compound 1, compound 2, Vitamin C and DCM extract with different initial concentration (0.3–0.7 mg mL^{-1}) were mixed with 2.0 mL of TCA (10%, w/v). After centrifuging for 10 min, 1.0 mL of each supernatant was mixed with 3 mL $FeCl_3$ (1.7 mM), and then determined at 700 nm. The final concentration of the tested four samples was in the range of 1.6–3.6 μg mL^{-1}. Ethanol was used as the control. The Vitamin C was used as positive control. All tests were carried out for three times.

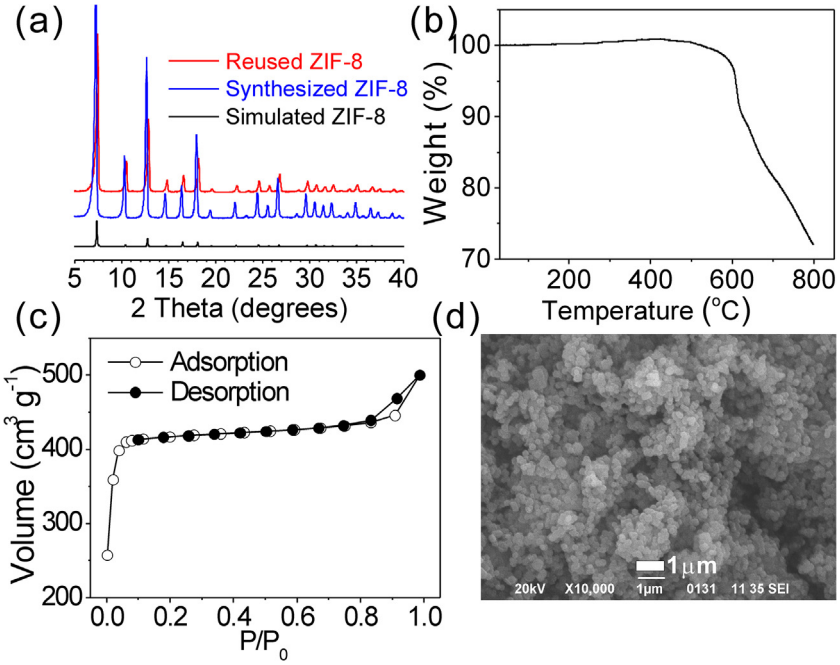

Fig. 2. (a) XRD patterns of the synthesized, reused and simulated ZIF-8; (b) TGA curve of the synthesized ZIF-8; (c) N_2 adsorption-desorption curves of the synthesized ZIF-8; (d) SEM image of the synthesized ZIF-8.

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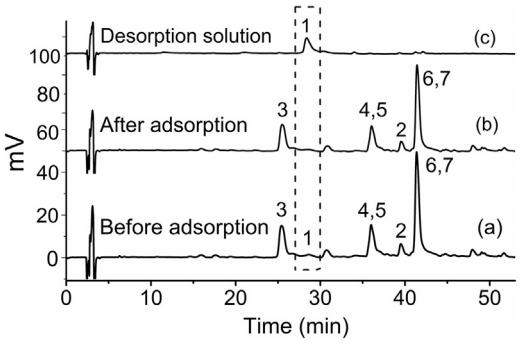

Fig. 3. HPLC chromatograms of the DCM extract of *Caragana Jubata* before (a) and after (b) adsorption with ZIF-8, and the desorption solution of ZIF-8 after adsorption (c).

Inhibitory effect on lipid peroxidation induced by Fe^{2+}/ascorbate. The rats livers were cut into small pieces, washed rapidly and homogenized in physiological saline at 4 °C. The reaction mixtures consist of 0.1 mL of sample solution with different initial concentration (0.2–1.8 mg mL^{-1}), 0.25 mL of 0.01 mM Vitamin C, 0.25 mL of 0.01 mM $FeSO_4$, 0.9 mL of PBS (0.05 M, pH 7.4), 0.5 mL of tissue homogenate and 0.5 mL physiological saline. The above reaction solution was incubated at 37 °C for 30 min. And then 1.0 mL of TCA (20%, w/v) and 1.0 mL of TBA (0.67%, w/v) were added into the above mixture solution and placed the tubes into a boiling water bath for 15 min, followed by ice bath. After centrifugation at 3800 rpm for 15 min, the absorbance of the supernatant was determined with UV at 532 nm. The final concentration of the tested four samples was in the range of 0.005–0.045 mg mL^{-1}. All the assays were conducted in triplicate. BHT was used as positive control. The percent inhibition of lipid peroxidation of samples was calculated by the following formula: Inhibition (%) = $(1 - A_{sample}/A_{blank}) \times 100\%$.

3. Results and discussion

3.1. Characterization of ZIF-8

The obtained ZIF-8 was characterized with XRD, TGA, SEM and N_2 adsorption-desorption experiments (Fig. 2). The XRD pattern of the prepared ZIF-8 was in good agreement with the simulated one, suggesting the successful synthesis of ZIF-8. The reused ZIF-8 also gave the same XRD pattern with the synthesized one, showing the good stability of ZIF-8 during the adsorption and desorption (Fig. 2a). The TGA curve reveals the synthesized ZIF-8 is stable up to 500 °C (Fig. 2b). N_2 adsorption-desorption experiments show the synthesized ZIF-8 has a Brunauer-Emmett-Teller (BET) surface area of 1652 m^2 g^{-1} (Fig. 2c). The SEM image shows the synthesized ZIF-8 has a particle size of about 200 nm (Fig. 2d).

3.2. Selective extraction of compound 1

HPLC separation of DCM extract under an optimized gradient mobile phase was first evaluated. The results reveal the complex nature of medicinal plants extract (Fig. 3a). The DCM extract (1 mg mL^{-1}, 1 mg DCM extract dissolved in 1 mL DCM) was extracted with ZIF-8 at a dose of 1 mg mL^{-1} (1 mg ZIF-8/1 mL DCM extract). The residual solution after extraction is still complex (Fig. 3b). However, the peak height of compound 1 was decreased after adsorption with ZIF-8 (Fig. 3b). The ZIF-8 after adsorption was then eluted with methanol. After adsorption/desorption experiments, the trace component compound 1 was selectively extracted with ZIF-8 and became the main proportion in the eluent (Fig. 3c). In contrast, the other main constituents before adsorption turned into the trace parts in the eluent (Fig. 3c). The peak areas of compound 1 in the DCM extract before adsorption and desorption solution were 78265 and 4516912 mV min, respectively, giving an enrichment factor of 57.7. The recoveries of ZIF-8 for compound 1 at three spiked levels (50, 100, and 150 mg mL^{-1}) in DCM extract were 62.1%, 66.4% and 75.4% with the RSDs of 1.6%, 1.1% and 2.9%, respectively (Table S1). The poor recoveries of ZIF-8 for compound 1 likely resulted from the complex matrix of *Caragana Jubata* DCM extract. The compound 1 also gave good linearity (R^2 = 0.999) in the concentration range of 5–1000 mg L^{-1} (Fig. S28). These results revealed the good selectivity of ZIF-8 for compound 1 and the ability of ZIF-8 to selective extract of compound 1 out from the complex DCM extract matrix.

The adsorption time, desorption solution, desorption time, and desorption circles were also studied (Fig. S1). The adsorption equilibrium of compound 1 on ZIF-8 can be achieved within 1.5 h. Methanol gave the best desorption efficiency among the studied desorption solution. The desorption equilibrium of compound 1 on ZIF-8 can be achieved within 30 min ultrasonication. In addition, one desorption circle is sufficient to desorb the adsorbed compound 1 from ZIF-8 (Fig. S1).

3.3. Adsorption mechanism study

To elucidate the adsorption mechanism of ZIF-8 for compound 1, the structure of the selective adsorbed compound 1 was characterized with high-resolution mass spectrometry (HR MS), ^{1}H and ^{13}C NMR (Fig. 4a, S2-S4). The results reveal the compound 1 is a flavonoid named 3,4-dihydroxy-8,9-methylenedioxypterocarpan [39], which is the first time isolated from *Caragana Jubata*. To confirm whether the adsorption of compound 1 was happened in or out of the ZIF-8 pore, the single crystal x-ray diffraction (SXRD) experiments before and after adsorption were studied (Fig. S5). The results demonstrated that the ZIF-8 has a hexagonal window with the free opening of 3.35 Å, which is comparable to the data reported in the literature [27]. However, the molecular dimension of compound 1 is about 5.5 Å × 12.8 Å (Fig. S6), which is much larger than that of the ZIF-8 pore window. The SXRD data after adsorption also reveal the compound 1 did not enter into the ZIF-8 pore. These results indicated that the selectivity of ZIF-8 for compound 1 resulted from the surface adsorption rather than the intra-pore adsorption.

To further reveal the adsorption mechanism of ZIF-8 for compound 1, other six poor selective adsorbed compounds 2–7 on ZIF-8 were also prepared via the semi-preparative chromatography and characterized with HR MS, ^{1}H and ^{13}C NMR (Fig. 4, Figs. S7-S20). Among all of these compounds, compound 1 and compound 2 have the same pterocarpan nucleus structure (Fig. 4), however, quite different selectivity on ZIF-8. The only difference between these two compounds is the C_4—OH group on the benzene ring (Fig. 4). The results suggest that the *o*-dihydroxy may lead to the good selectivity of ZIF-8 for compound 1.

To elucidate this hypothesis, the adsorption experiments of ZIF-8 for phenol and catechol were performed (Fig. 5). ZIF-8 gave much larger adsorption capacities for catechol with *o*-dihydroxy than those of phenol without *o*-dihydroxy at the concentration of 200 and 500 mg L^{-1}, respectively. These results reveal the *o*-phenolic hydroxyl played significant roles on the selective adsorption of compound 1 on ZIF-8 in our study. The same *ortho*-position selectivity on ZIF-8 and other MOFs was also reported in other papers [40–42].

The X-ray photoelectron spectroscopy (XPS) experiments were further applied to elucidate the adsorption mechanism (Fig. 6). There were no obvious changes of the bonding energies for Zn 2p1/2 and 2p3/2 peaks of ZIF-8 before and after adsorption of compound 1, suggesting the Zn metal center in ZIF-8 should not be the binding sites for compound 1. However, the N1 s peaks at 397.20 eV and

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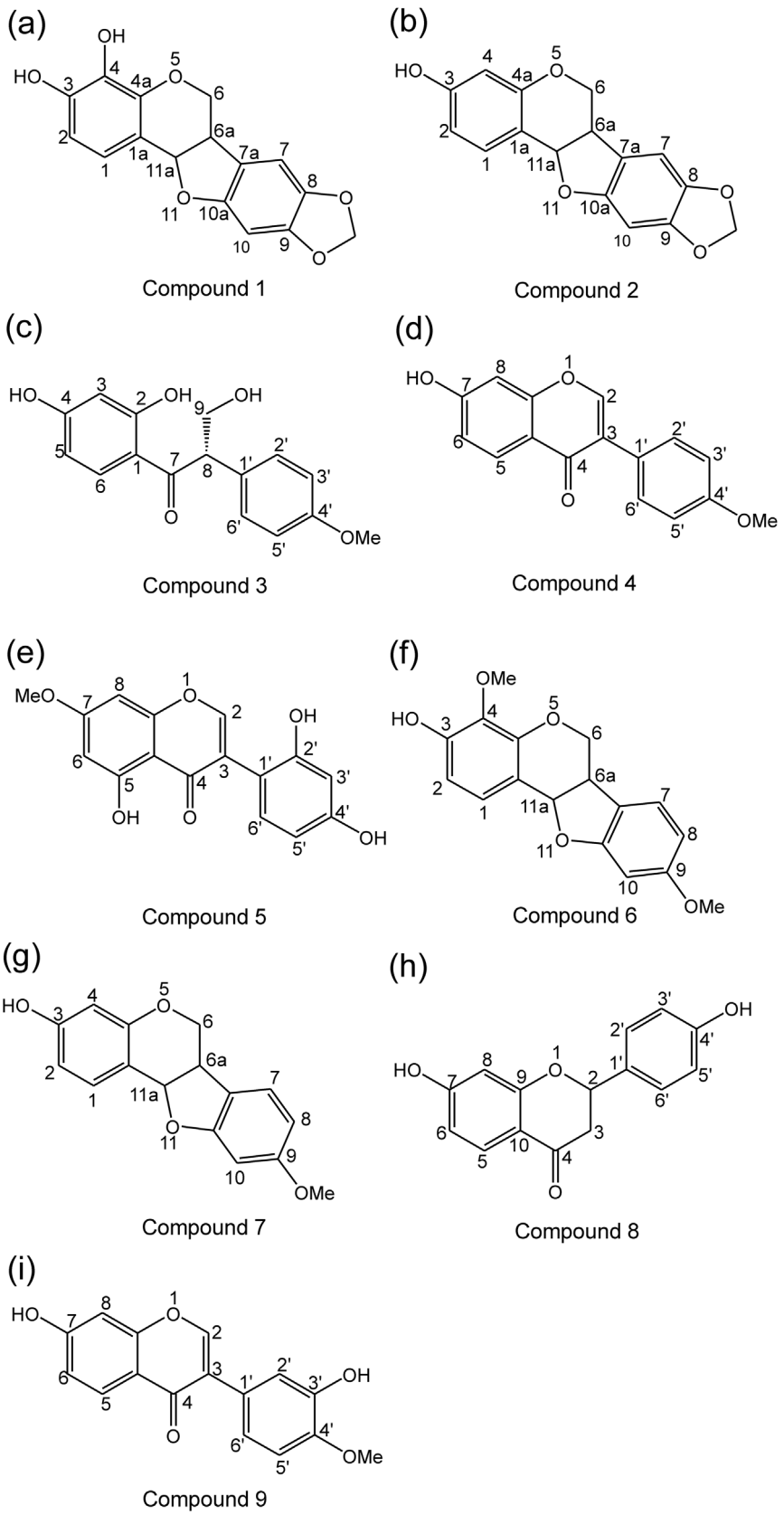

Fig. 4. The structures of compounds 1–9.

398.59 eV for ZIF-8 were shifted to 397.07 eV and 396.81 eV after adsorption of compound 1, revealing the N sites on ZIF-8 played significant roles for adsorption of compound 1. Therefore, we speculate that the N···H···O hydrogen bond interactions between the two N atoms on ZIF-8 and two −OH on compound 1 result in the good selectivity of ZIF-8 for compound 1.

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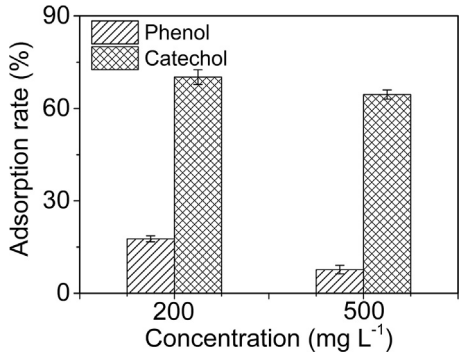

Fig. 5. The adsorption rate (adsorbed amount versus initial amount%) of ZIF-8 for phenol and catechol at the concentration of 200 and 500 mg L^{-1}.

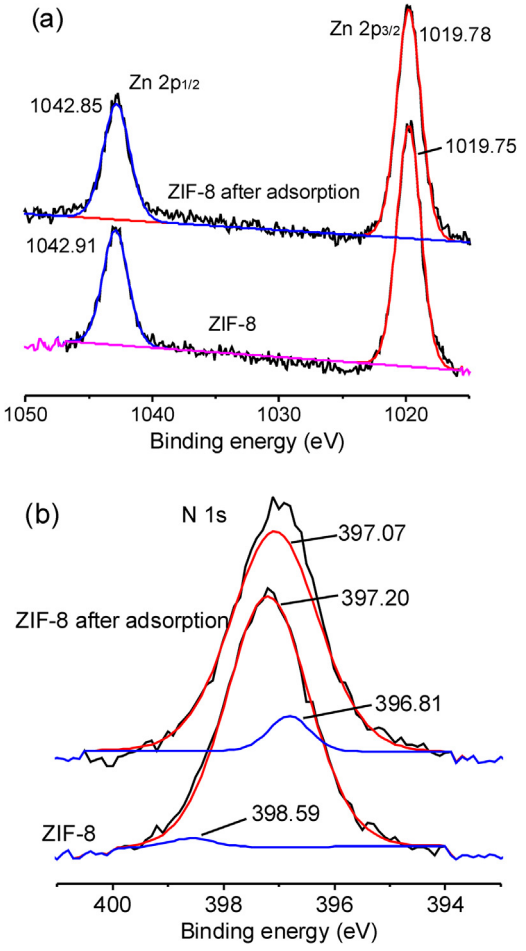

Fig. 6. XPS spectra of (a) Zn and (b) N for ZIF-8 before and after adsorption of compound 1.

3.4. Anti-oxidant activity evaluation

Previous papers have reported that *Caragana* species plants possessed good anti-oxidant activity to treat anti-aging and some degenerative diseases including Parkinson's disease, cancer and heart disease [31,43]. In addition, the red heartwoods of the stems and roots of *Caragana Jubata* were the main medicinal parts in traditional Tibetan medicine to cure many diseases [30–32]. Therefore, the antioxidant activity of compound 1 was studied under three typical antioxidant models (Fig. 7) [37,38]. Scavenging activity against DPPH free radical results (Fig. 7a) revealed compound 1 gave the best ability of scavenging DPPH radicals among the

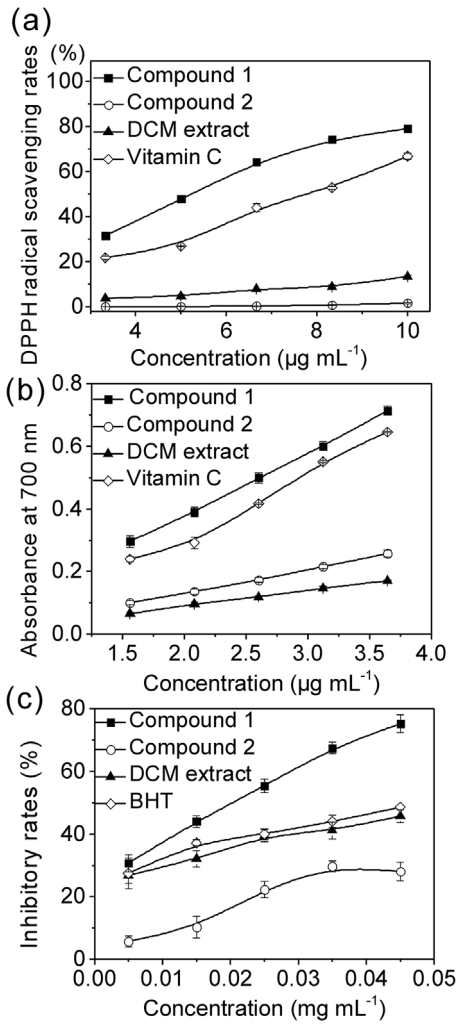

Fig. 7. Antioxidant activities of the samples. (a) Scavenging activity against DPPH free radical; (b) Ferric reducing/antioxidant power activity; (c) Inhibitory effect on lipid peroxidation induced by Fe^{2+}/ascorbate. Error bars show the standard deviations for triplicate measurements.

tested four samples. The scavenging rates of compound 1, compound 2, the positive control Vitamin C and DCM extract were found to be 79.03%, 1.66%, 66.80% and 13.43% at the concentration of 10 μg mL^{-1}, respectively. In addition, the half inhibition concentration (IC_{50}) of compound 1 is 5.438 ± 0.068 μg mL^{-1}, which is much lower than those of compound 2 (190.973 ± 0.152 μg mL^{-1}) and the DCM extract (34.756 ± 0.089 μg mL^{-1}), and even lower than the positive control Vitamin C (7.724 ± 0.104 μg mL^{-1}) (Table 1).

In the ferric reducing/antioxidant power assay (Fig. 7b), the antioxidant power of the tested four samples increased with the growing concentration and displayed a good linear ($R^2 > 0.998$) in the studied concentration range. The absorbances at 700 nm of compound 1, compound 2, the positive control Vitamin C and DCM extract at the concentration of 3.6 μg mL^{-1} were 0.71, 0.26, 0.65, 0.17, respectively. The reducing power decreased in the order of compound 1 > Vitamin C > compound 2 > DCM extract, showing the compound 1 had the best antioxidant power in the tested samples and was superior to the positive control Vitamin C.

Inhibitory effect on lipid peroxidation induced by Fe^{2+}/ascorbate (Fig. 7c) implied that compound 1 had a remarkable inhibition activity among the studied samples. The inhibition rates of compound 1, compound 2, the positive control BHT and DCM extract were found to be 75.30%, 28.00%, 48.57% and 45.71% at the concentration of 0.045 mg mL^{-1}, respectively. The IC_{50} values of all

Table 1
The IC_{50} values of the tested samples and positive control on antioxidant models.

Samples	IC_{50} ($\mu g\,mL^{-1}$)	
	DPPH radical scavenging activities	Inhibitory effects on lipid peroxidation
Compound 1	5.438 ± 0.068	20.970 ± 0.083
Compound 2	190.973 ± 0.152	67.130 ± 0.099
DCM extract	34.756 ± 0.089	52.200 ± 0.089
Positive control[a]	7.724 ± 0.104	45.590 ± 0.052

[a] Positive controls of DPPH radical scavenging activities and inhibitory effects on lipid peroxidation are Vitamin C and BHT, respectively.

samples were list in Table 1. Generally, the results of three antioxidant models were consistent well with each other and revealed that compound 1 had the best antioxidant activity and the lowest IC_{50} values.

3.5. Extraction of trace components on other MOFs

The above results show the feasibility of ZIF-8 to selective extract a highly antioxidant component out from the DCM extract of *Caragana Jubata*. To further confirm the prospect of this method, extraction of *Caragana Jubata* DCM extract on other MOFs such as MIL-101(Cr), MIL-100(Fe), NH_2-MIL-53 and ZIF-7 were studied (Fig. S27).

ZIF-7 also gave good selectivity for compound 1 from the DCM extract of *Caragana Jubata*. ZIF-7 has smaller pore window size (2.9 Å) and pore size (4.3 Å) than the critical diameter of compound 1 and ZIF-8, suggesting the surface adsorption dominant the selectivity of compound 1 on ZIF-7. In addition, these two ZIFs have the same zinc metal centers and similar imidazolate ligands (2-methylimidazole for ZIF-8, benzimidazole for ZIF-7), further confirming the significant roles of N···H···O hydrogen bond interactions between the two N atoms on imidazolate ligands for ZIFs and two −OH on compound 1 during the adsorption.

The MIL series MOFs (MIL-101(Cr), MIL-100(Fe), NH_2-MIL-53) gave poor selectivity to the compounds with pterocarpan nucleus structures such as compounds 1, 2, 6 and 7, but good affinity for isoflavones and flavanones including compounds 3, 4, 5, 8 and 9 (Fig. S27). For examples, the MIL-100(Fe) and MIL-101(Cr) with large pentagonal and hexagonal windows and 3D pores both gave good extraction performance for compounds 3, 8 and 9 from the complex DCM extract. In addition, compounds 8 and 9 were the first time obtained from *Caragana Jubata* (Fig. 4, Figs. S21-26). However, NH_2-MIL-53 with 1D rhombic-shaped tunnels shows obvious selectivity for three isoflavones 4, 5 and 9. These results suggest the hydrogen bond interaction and steric effect of the MILs should play significant roles in the selective extraction of trace flavones from complex *Caragana Jubata* DCM extract on these MILs (Fig. S27).

3.6. Comparison with other sorbents for selective extraction of flavonoids

The proposed method was then compared with the other reported sorbents for selective extraction of flavonoids (Table S2). The ZIF-8 gave comparable precisions and lower recovery than other reported sorbents for the extraction of flavonoids. The low recovery of ZIF-8 for compound 1 likely resulted from the complex matrix of *Caragana Jubata* DCM extract. However, all the reported methods were carried out by using the known standard targets such as quercetin, apigenin, kaempferol, mycricetin et al. Our method was performed on much more complex medicinal plant samples and on unknown flavonoids (unknown at least before identification) in the medicinal plant. Therefore, our results still revealed the potential of MOFs in selective extraction of medicinal compositions or active components out from complex medicinal plant samples.

4. Conclusions

In conclusion, we have reported the feasibility of ZIF-8 to selectively extract of the trace components out from the complex medicinal plants extract. The obtained compound 1 revealed a highly anti-oxidant activity than positive control Vitamin C and BHT. Such method makes us possible to rapidly and simply enrich trace components from complex matrices which can be hardly achieved on the separation procedures using traditional sorbents. In addition, such methods can be expanded to other MOFs for selective extraction of trace compounds from medicinal plants. The novelty of this work should be concluded as the following three points. (1) Presented the first example of MOFs in selective extraction of medicinal compositions or active components from complex medicinal plants. (2) Expended MOFs as novel sorbents in medicinal plants extraction and separation. (3) Revealed the feasibility of MOFs for directly selective extraction of trace active compounds out from medicinal plants. The current work may open a new way of MOFs in selective extraction of pharmacological active components from medicinal plants. The follow-up works should pay more attentions to the post-modification of MOFs in extraction and separation of pharmacological active components from medicinal plants.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.chroma.2018.02.046.

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