Evaluation of Hypolipidemic and Antioxidant Effects in Phenol-rich Fraction of *Crataegus pinnatifida* Fruit in Hyperlipidemia Rats and Identification of Chemical Composition by Ultra-performance Liquid Chromatography Coupled with Quadropole Time-of-flight Mass Spectrometry

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Submitted: 12-09-2016  Revised: 03-11-2016  Published: 13-11-2017

**ABSTRACT**

**Background:** Hawthorn (*Crataegus pinnatifida*) fruit has enjoyed a great popularity as a pleasant-tasting food associated with hypolipidemic and antioxidant effects. **Objective:** Our aim was to screen the effective fraction of hawthorn fruit in the treatment of hyperlipidemia rats. **Materials and Methods:** In this study, ethanol extract of hawthorn fruit (Fr.1) and four fractionated extracts (Fr.2, Fr.3, Fr.4, and Fr.5) were compared to total phenol content evaluated using Folin–Ciocalteu method, and hypolipidemic and antioxidant effects were assessed in hyperlipidemic rats. **Results:** Total phenol content of Fr.4 was higher than other fractions by at least 2 fold. Furthermore, this fraction possessed the strongest hypolipidemic and antioxidant effects in hyperlipidemic rats. On this basis, 15 phenolic compounds and four organic acids in Fr.4 were positively or tentatively identified using ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. In addition, 5-O-caffeoyl quinic acid butyl ester was first reported in hawthorn fruit. **Conclusion:** Phenol-rich fraction in hawthorn fruit exhibited satisfactory hypolipidemic and antioxidant effects, and this could be exploited for further promotion of functional foods. **Key words:** Antioxidant effect, *Crataegus pinnatifida* fruit, hypolipidemic effect, phenolic compounds, ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry

**SUMMARY**

- Phenol-rich fraction in hawthorn fruit possesses most potent hypolipidemic and antioxidant effects in hyperlipidemia rats.

**INTRODUCTION**

Hawthorn (*Crataegus pinnatifida*), from Rosaceae family, is a deciduous tree mainly distributed and cultivated in temperate areas, including China, Korea, and Russia.¹ The eatable and medicinal history of hawthorn fruit in China could be dated back to about 300 AD.² It has been used as a traditional medicine for the treatment of dyspepsia, cardiovascular disease, and hyperlipidemia.³ Recent reports have disclosed hypolipidemic and antioxidant effects of the traditional medicine.⁴ Besides, our previous investigation had indicated that these effects of hawthorn fruit were probably caused by the existence of phenols.⁵ Dietary phenols appear to possess antioxidant property, which scavenges reactive oxygen and nitrogen species, thereby potentially contributing against the pathogenesis of cardiovascular disease.⁶ Phenols in hawthorn fruit are responsible for free radical quenching activity and considered to be the best antilipoperoxidants.⁷ Hawthorn fruit is abundant in phenolic compounds, including isoquercetin, hyperoside, protocatechuic acid, and chlorogenic acid,⁸ which usually have hypolipidemic and antioxidant effects.⁹ For the above reasons, we hypothesized that phenol-rich fraction in hawthorn fruit probably has hypolipidemic and antioxidant effects in hyperlipidemic rats.

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**Cite this article as:** Shao F, Gu L, Chen H, Liu R, Huang H, Chen L, et al. Evaluation of hypolipidemic and antioxidant effects in phenol-rich fraction of *Crataegus pinnatifida* fruit in hyperlipidemia rats and identification of chemical composition by ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. Phcog Mag 2017;13:725-31.
Although previous investigation has shown that high-performance liquid chromatography (HPLC)-electrospray ionization (ESI) mass spectrometry (MS) has been used in the characterization of 42 phenolic compounds in 80% ethanol extract of hawthorn fruit,[11,12] it is still unknown information concerning bioactive fraction and its compounds in hyperlipidemic and antioxidant effects. At present, ultra performance liquid chromatography coupled with quadrupole time-of-flight MS (UPLC-Q-TOF-MS/MS) demonstrated to be a more powerful tool for analyzing natural products, mainly because of its high resolution as well as accuracy in weight measurements.13 It helps us to get more information concerning phenolic compounds and others in bioactive fraction of hawthorn fruit.

Hence, this study was designed to determine total phenol content of ethanol extract and four fractionated extracts by the Folin–Ciocalteu method to evaluate hypolipidemic and antioxidant effects in hyperlipidemic rats and to identify phenolic compounds and others in bioactivity fraction by UPLC-Q-TOF-MS/MS.

MATERIALS AND METHODS

Materials and chemicals

Hawthorn (C. pinnatifida Bge. var. major N. E. Br) fruit was collected from Pingyi County (Shandong Province, China) and authenticated by Professor Kezhong Deng in School of Pharmacy, Jiaxi University of Traditional Chinese Medicine. A voucher specimen (No. 20121123) has been deposited in the Key Laboratory of Modern Preparation of TCM, Ministry of Education, Jiaxi University of Traditional Chinese Medicine.

Total cholesterol (TC) assay kit (Lot No. ZG3001), triglyceride (TG) assay kit (Lot No. ZG3001), low-density lipoprotein-cholesterol (LDL-C) assay kit (Lot No. ZG9003), and high-density lipoprotein-cholesterol (HDL-C) assay kit (Lot No. ZG3001) were offered by Sigma Co, Japan. Glutathione peroxidase (GSH-Px) assay kit (Lot No. 20130831), suxoracide dismutase (SOD) kit (Lot No. 20130831), malondialdehyde (MDA) assay kit (Lot No. 20130831), catalase (CAT) assay kit (Lot No. 20130903), nitric oxide (NO) assay kit (Lot No. 20130827), and NO synthase (NOS) assay kit (Lot No. 20130903) were obtained from Nanjing Jiancheng Bio-Engineering Company, China. No. 3 bile salt (Lot No. 20130531-00) was purchased from Hangzhou Hongbo Biological Engineering Co., Ltd, China. Propylthiouracil (Lot No. 20130523) and cholesterol were obtained from Wuhan Sheng Tianyu Biological Technology Co., Ltd, China. Lard was purchased from Henan Zhumadian Dingsheng Food Co, Ltd, Zhumadian, China.

Hyperoside (99%), quercetin (99%), vitamin (98%), and isovitexin (98%) were purchased from Must Bio-technology Co., Ltd. Chengdu, China.

Acetonitrile and formic acid for UPLC were obtained from Dikma Biotechnology Co., Ltd., Zhumadian Dingsheng Food Co., Ltd, Zhumadian, China.

Serum lipids and antioxidant enzyme activities

Serum lipid levels (TC, TG, LDL-C, and HDL-C) were measured by an automatic biochemical analyzer (Serial No. CHEMIX-180, Sysmex, Japan). The antioxidant enzyme activities (SOD, CAT, and GSH-Px) and the levels of MDA, NO, and NOS in serum and liver were, respectively, determined using commercial analysis kits by Microplate Reade (Serial No. SpectraMax 190, Molecular Devices, USA).

Ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry analysis

A Shimadzu UPLC system combined with an AB SCIEX triple TOF™ 5600+ mass spectrometer system equipped with a DuosprayTM source was used to acquire mass spectra of bioactivity fraction. The separations were performed on a 2.1 mm × 100 mm ACUIITY UPLC HSS T3 column (1.8 μm, USA) at 30°C, and the UV absorbance was monitored at 270 nm. The solvent system composed of acetonitrile (A) and 0.1% formic acid in water (B) using an optimized gradient program as follows: 0–5.0 min, 5%–5% of A; 5.0–65.0 min, 5%–34% of A.

Optimum parameters of MS in negative ESI modes were set as follows: ion spray voltage, −4500 V; collision energy, −40 V; and declustering potential, −100 V. The nebulizing gas (Gas 1) was 50 psi, heater gas (Gas 2) was 35 psi. The analysis was performed in the range of m/z 50–1000. The mass spectra were acquired in the range of m/z 100–1000.
2) was 60 psi, and the curtain gas was 30 psi. Mass scan was over the m/z 100–1600, and turbo spray temperature was 600°C. Data were analyzed by Peak View Software™ 1.2 (AB SCIEX, Canada).

Statistical analysis
Values were presented as mean ± standard deviation. A paired t-test was employed to evaluate statistical significance between the two groups with SPSS software (version 22 for Windows, Chicago, IL, USA). Differences are considered to be statistically significant when P < 0.05.

RESULTS AND DISCUSSION

Determination of total phenol content
Phenolic compounds are considered the most critical bioactive compounds in *C. pinnatifida* BUNGE.[9] These chemical constituents possess potential health effects, such as lowering blood lipids and attenuating oxidative stress.[6,13] In this study, according to acidity and polarity principle, their ethanol extract (Fr.1) was fractioned into four fractionated extracts (Fr.2, Fr.3, Fr.4, and Fr.5) [Figure 1]. Compared with four others, Fr.4 was rich in phenols by possessing more than 2 times of total phenol content, as shown in Table 1. Hence, Fr.4 was probably attributed to the hypolipidemic and antioxidant activities with its abundant phenols.

Evaluation of hypolipidemic effect
TC, TG, LDL-C, and HDL-C are regarded as the key evaluation indexes of hyperlipidemic model. Serum lipid profiles can be attenuated by ethanol extract of hawthorn fruit.[14] In this study, compared to normal rats, TC, TG, and LDL-C levels in serum were markedly raised (P < 0.01) by administrating rats with a high-fat emulsion for 4 weeks, as shown in Figure 2. However, there was no significant difference between control group and model group for HDL-C that might be associated with the compensatory mechanism of rats themselves.[6,15] On the basis of established model, we estimated hypolipidemic capacity of ethanol extract (Fr.1) and four fractionated extracts (Fr.2, Fr.3, Fr.4, and Fr.5) in hyperlipidemic rats. As a result, compared with the model, Fr.4 is the only one that at all doses lowered the TC, TG, and LDL-C contents significantly in hyperlipidemic rats (P < 0.05). Simultaneously, Fr.4 at medium and high doses and Fr.1 at medium dose elevated the level of HDL-C, but no significant difference was observed (P > 0.05), consistent with several previously published reports.[16-18] It is noteworthy that compared with other fractions, Fr.4 at low dose decreased the levels of TC, TG, and LDL-C more obviously in hyperlipidemic rats (P < 0.05), as shown in Figure 2. Therefore, Fr.4 showed more significant ameliorative action than others in the serum lipid levels of hyperlipidemic rats.

Determination of antioxidant effect
Oxidative stress is a causative factor, which links hyperlipidemia with the pathogenesis of atherosclerosis,[19] and is induced by reactive oxygen species, for example, superoxide anions (•OOH) and hydroxyl radicals (•OH).[20] The activities of GSH-Px, SOD, and CAT directly reflect the ability of scavenging...
In addition, MDA, the end product of lipid peroxidation, is caused by free radical chain reaction. In this study, after 4 weeks of treatment, compared to control group, decreased activities of SOD, CAT, and GSH-Px and increased content of MDA in serum and liver were observed in hyperlipidemic rats, respectively, as shown in Figures 3 and 4. Phenolic compounds reduce the risk of hyperlipidemia and oxidative injury through increasing antioxidant enzyme activity and reducing free radical formation. In the similar report, seven phenolic compounds, namely, hyperoside, isoquercitrin, epicatechin, quercetin, rutin, chlorogenic acid, and protocatechuic acid in hawthorn fruit are extremely effective in protecting LDL from oxidation. As there is phenol-rich fraction in hawthorn fruit, Fr.4 at high dose is the most remarkable one to increase the lowered SOD, CAT, and GSH-Px activities (P < 0.01) and to decrease the elevated MDA level (P < 0.01) in serum.

Figure 3: Effects of *Crataegus pinnatifida* fruit on malondialdehyde, nitric oxide content, and the activities of catalase, superoxide dismutase, glutathione peroxidase, and nitric oxide synthase of serum in rats fed on high-fat emulsion or normal diet. The low-, medium-, and high-doses were equivalent to about 75, 150, and 300 mg/kg body weight, respectively. Values are shown as mean ± standard deviation (n = 8). *P* < 0.05 and **P** < 0.01 compared with the control group. *P* < 0.05 and **P** < 0.01 compared with the model group.

Figure 4: Effects of *Crataegus pinnatifida* fruit on malondialdehyde content and the activities of superoxide dismutase, catalase, and glutathione peroxidase of liver in rats fed on normal diet or high-fat emulsion diet. The low-, medium-, and high-doses were equivalent to about 75, 150, and 300 mg/kg body weight, respectively. Values are shown as mean ± standard deviation (n = 8). *P* < 0.05 and **P** < 0.01 compared with the control group. *P* < 0.05 and **P** < 0.01 compared with the model group.
and liver of hyperlipidemic rats. Furthermore, antioxidant capacity of Fr. 4 at medium dose was approximately equivalent or stronger than that of other groups at high dose in serum of hyperlipidemic rats, as shown in Figure 3. A similar situation also existed for the SOD, CAT, and GSH-Px analyses in liver of hyperlipidemic rats, as shown in Figure 4.

NO, which is produced by endothelial NOS, is the principal factor that inhibits vessel platelet aggregation and dilate vessels so as to prevent vascular atheros and thrombus formation. Isolated artery experiments have revealed that phenolic compounds could cause NO-mediated endothelium-dependent relaxations and increase the endothelial formation of NO. In this study, the NOS and NO levels of Fr. 4 were higher than those of other administration groups at corresponding dose in serum of hyperlipidemic rats, as shown in Figure 3. These results indicated that phenol-rich fraction in hawthorn fruit exhibited more significant antioxidant capacity than others in hyperlipidemic rats.

Identification of compounds in Fr. 4

Based on the above results, compound identification of Fr. 4 was carried out by UPLC-Q-TOF-MS/MS. The negative ionization mode was more sensitive under the conditions, and was therefore selected for further use. As a result, 15 phenolic compounds (including six phenolic acids and nine flavonoids) and four organic acids have been identified or tentatively identified according to their retention times and fragment ions, as shown in Figure 5 and Table 2.

Phenolic acids

Six phenolic acids, such as protocatechuic acid (5), Chlorogenic acid isomers (6, 7), vanillic acid (8), and ferulic acid (18), 5-O-caffeoyl quinic acid butyl ester (19) were tentatively identified. Phenolic acids have strong in vitro and in vivo antioxidant activities associated with their ability to scavenge free radicals, break radical chain reactions, and chelate metals.

Chlorogenic acid has attracted continuous attention among phenolic acids with its alleged biological effects. Classically, chlorogenic acids are a family of esters formed between certain cinnamic acids and quinic acid. Peaks 6 and 7 were tentatively characterized as chlorogenic acid isomers for which they displayed the similar parent molecule ion at m/z 353.0878 and 353.0889. They presented the similar fragmentation pattern at m/z 191.0565 and 191.0560, corresponding to [quinic acid–H]− ion. The deprotonated caffeic acid fragment at m/z 179.0348 was also found at compound 7, revealing that the quinic acid was substituted at 3-position with the hydroxyl group, while compound 6 was not 3-OH replacement for the absence of m/z 179 fragmentation. Peak 19 showed a pseudomolecular ion at m/z 409.1528. Its MS/MS spectra gave m/z 191.0561 [quinic acid–H]−, 179.0560 [caffeic acid–H]−, 167.0350, 153.0198, and 133.0133 ions, as shown in Figure 5 and Table 2.

Table 2: Mass data of compounds detected in Fr. 4 of Crataegus pinnatifida fruit

| n  | Compound                     | Formula                     | Ion mode | t_R (min) | Calculated m/z | Experimental m/z | Product ion m/z | Error (ppm) |
|----|------------------------------|-----------------------------|----------|-----------|----------------|------------------|-----------------|-------------|
| 1  | Quinic acid                  | C_8H_8O_5                     | [M−H]−   | 1.62      | 191.0561       | 191.0559         | 191.0564, 127.0410, 111.0095, 93.0358 | −1          |
| 2  | Malic acid                   | C_6H_12O_6                    | [M−H]−   | 1.80      | 133.0143       | 133.0152         | 133.0133, 115.0035 | 7.2          |
| 3  | Citric acid                  | C_6H_8O_7                     | [M−H]−   | 2.28      | 191.0197       | 191.0204         | 111.0096        | 3.7          |
| 4  | Succinic acid                | C_4H_6O_4                     | [M−H]−   | 2.67      | 117.0193       | 117.0203         | 116.9290, 99.9265, 83.9314 | 8.6          |
| 5  | Protocatechuic acid          | C_7H_6O_3                     | [M−H]−   | 7.56      | 153.0193       | 153.0198         | 109.0340        | 3.1          |
| 6  | Chlorogenic acid isomers     | C_8H_8O_4                     | [M−H]−   | 16.58     | 353.0878       | 353.0894         | 191.0565        | 4.5          |
| 7  | Chlorogenic acid isomers     | C_8H_8O_4                     | [M−H]−   | 18.19     | 353.0878       | 353.0889         | 353.0892, 191.0560, 179.0348, 173.0452, 135.0453 | 3.1          |
| 8  | Vanillic acid                | C_9H_8O_4                     | [M−H]−   | 23.35     | 167.0350       | 167.0357         | 167.0361, 152.0116, 109.0260, 108.0229, 91.0205 | 4.3          |
| 9  | Violanthin                   | C_9H_8O_4                     | [M−H]−   | 29.45     | 577.1563       | 577.1607         | 577.1621, 487.1267, 457.1192, 367.0836, 337.0729 | 7.6          |
| 10 | Rutin                        | C_21H_18O_9                   | [M−H]−   | 30.15     | 609.1461       | 609.1516         | 609.1522, 301.0374, 300.0296, 271.0264 | 9           |
| 11 | Schaltoside                  | C_9H_8O_4                     | [M−H]−   | 31.16     | 593.1512       | 593.1570         | 593.1580, 473.1101, 413.0911, 311.0593, 293.0460 | 9.9          |
| 12 | Vitexin                      | C_21H_18O_9                   | [M−H]−   | 31.93     | 431.0984       | 431.1006         | 431.1025, 341.0696, 311.0578, 283.0626 | 5.2          |
| 13 | Vitexin rhamnoside           | C_21H_18O_9                   | [M−H]−   | 32.09     | 577.1563       | 577.1615         | 577.1635, 457.1189, 413.0915, 311.0579, 293.0475 | 9           |
| 14 | Isovitexin                   | C_21H_18O_9                   | [M−H]−   | 32.73     | 431.0984       | 431.1008         | 431.1026, 341.0673, 311.0585, 283.0627 | 5.7          |
| 15 | Hyperoside                   | C_9H_8O_4                     | [M−H]−   | 32.95     | 463.0955       | 463.0923         | 463.0911, 301.0367, 300.0285, 271.0260, 255.0313 | −6.9         |
| 16 | Isoquercitrin                | C_12H_10O_4                   | [M−H]−   | 33.81     | 463.0955       | 463.0923         | 463.0970, 301.0361, 300.0280, 271.0254, 255.0307 | −7.3         |
| 17 | Astragalin                   | C_12H_10O_4                   | [M−H]−   | 36.31     | 447.0933       | 447.0957         | 447.0964, 285.0412, 284.0399, 255.0306, 227.0353 | 5.3          |
| 18 | Ferulic acid                 | C_12H_10O_4                   | [M−H]−   | 37.15     | 193.0506       | 193.0513         | 193.500, 178.0267, 161.0244, 133.0298 | 3.2          |
| 19 | 5-O-caffeoyl quinic acid butyl ester | C_21H_18O_9 | [M−H]−   | 50.50     | 409.1528       | 409.1540         | 409.1528, 191.0561, 179.0560, 161.0244, 133.0454 | 0.8          |
161.0244 [caffeic acid–H₂O]⁻, and 135.0456 [caffeic acid–CO₂–H]⁻. It has previously reported that 5-O-cafeoyl quinic acid gave the ion at m/z 191 in its MS/MS fragmentation, while 3-O- and 4-O-cafeoyl quinic acids showed different behaviors at m/z 163 and 173, respectively.[30] Accordingly, peak 19 was deduced as 5-O-cafeoyl quinic acid butyl ester, which was first reported in hawthorn fruit. The detailed fragmentation pathway of peak 19 is shown in Figure 6.

Peak 5 was characterized as protocatechuic acid with the [M−H]⁻ at m/z 153.0198. Furthermore, MS/MS data showed a fragment at m/z 109.0303 (loss of CO₂).[31]

Peaks 8 and 18 were assigned as vanillic acid and ferulic acid, respectively. The loss of a CH₄ moiety from deprotonated ion of peak 8 ([M−H]⁻ at m/z 167.0350) and peak 18 ([M−H]⁻ at m/z 193.0513) resulted in the MS² ion at m/z 152.0116 and 178.0267, respectively. Peak 8 also showed fragment ions at 108.0229 ([M−H–CH₂–CO₂]⁻), 91.0205 ([M−H–CH₂–CO₂–OH]⁻). Peak 18 showed fragment ions at 161.0244 ([M−H–CH₂–OH]⁻), 133.0298 ([M−H–CH₂–OH–CO₂]⁻) as well.

**Flavonoids**

As a large group of plant phenol secondary metabolites, flavonoids act through scavenging free radicals, promoting anti-oxidase or inhibiting oxidative enzymes while regulating the blood flow and keeping the heart healthy. Nine compounds were unambiguously identified as flavonoid glycosides.

Peaks 15, 16, and 10 all originated from quercetin, they all displayed a characteristic fragment ion at m/z 300, representing the quercetin ion moiety. In this case, the ion at m/z 300, proposed as diagnostic ion for quercetin glycoside, is higher than ion at m/z 301, and could be due to formation of the quinone anion, obtained after hemolytic cleavage of the O-glycosidic bond.[32] Peaks 15 and 16 that shared [M−H]⁻ at m/z 463 were deduced as hyperoside and isoquercitrin, respectively, based on spectra and comparison with standards.[32] Peak 10 had a [M−H]⁻ at m/z 609.1516 and characterized as rutin, with a chief MS/MS pattern at m/z 300.0296 (loss of rutinoside).

Peaks 12 and 14 gave the deprotonated ions at m/z 431, and MS² characteristic fragments at m/z 341 [M−H–90]⁻ ([M−H–C₆H₄O₃]⁻), at m/z 311 [M−H–120]⁻ ([M−H–C₆H₄O₃]⁻), which were consistent with the characteristic ions of a C-glycosidic flavonoid.[33] Accordingly, peaks 12 and 14 were deduced to be vitexin and isovitexin, respectively, in accordance with the MS and MS² data of reference compounds.

Peaks 13 and 9 showed negative ion modes at m/z 577 and were characterized as vitexin rhamnoside and violanthin, respectively, for their fragmentation patterns differed. In the MS² spectrum of peak 13, an ion at m/z 413.0915 was noted to lose its terminal rhamnose unit, followed by loss of a C₆H₄O₃ group to give a fragment at m/z 293.0475. Peak 9 displayed characteristic ions at m/z 487.1267 [M−H–90]⁻, 457.1192 [M−H–120]⁻, 367.0836 [M−H–120–90]⁻, and 337.0729 [M−H–120–120]⁻ of a C-glycosidic flavonoid with two glycosyls, which were in accordance with the fragmentation pathway of violanthin.

Peak 11, with deprotonated ion at m/z 593.1580, was tentatively identified as schaftoside, which is a C-glycosidic flavonoid with MS/MS fragments at m/z 473.1101 [M−H–120]⁻, 413.0911 [M−H–120–120]⁻, 311.0593 [M−H–120–120–120]⁻, and 293.0460 [M−H–120–120]⁻.

Peak 17 gave a higher signal at m/z 447 ([M−H]⁻) which was characterized as astraigin. The fragment pattern gave a main fragment ion at m/z 285 (kaempferol aglycone moiety) for the neutral loss of the glucose unit. A higher signal at m/z 284 was also observed, which accorded with previously reported rule that [kaempferol–H]⁻ ion is sometimes higher than kaempferol ion in 3-OH position-substituted glycosidic flavonols.[33,34]

**Organic acids**

Peaks 1, 2, 3, and 4 were assigned as organic acids. Peak 1 showed a typical fragmentation behavior at m/z 191.0564, m/z 127.0410 ([M−H–CO₂–H₂O]⁻), m/z 111.0095 ([M−H–CO₂–2H₂O]⁻), and m/z 93.0358 ([M−H–CO₂–3H₂O]⁻), corresponding to quinic acid. Peak 2, characterized as malic acid, showed a negative molecular ion at m/z 133.0133, with MS/MS pattern at m/z 115.0035 for the loss of water. Peak 3 had a deprotonated ion at m/z 191.0204 and was deduced as citric acid because the characteristic fragment of citric acid appeared at m/z 111.0096 ([M−H–CO₂–2H₂O]⁻). The [M−H]⁻ fragment of peak 3 was different from peak 1 for the number variance after the decimal point. Peak 4, with a [M−H]⁻ at m/z 117.0203, was identified as succinic acid and its fragments at m/z 99.9265, corresponding to elimination of water, and m/z 83.9314 corresponding to loss of another water.

**CONCLUSION**

In our study, compared with other fractions, phenolic-rich fraction in hawthorn fruit exhibited more significant ameliorative action in lipid profile levels and higher antioxidant contribution in hyperlipidemic rats. Moreover, 15 phenolic compounds and 4 organic acids in this fraction were identified based on MS data and MS/MS fragmentation pattern by UPLC-Q-TOF-MS/MS. Given these findings, we suggested that polyphenolic compounds of hawthorn fruit probably play the key role
in hypolipidemic and antioxidant effects, and phenolic-rich fraction in hawthorn fruit would be used in the further development of functional food.

Acknowledgement
Our special thanks are due to Ms. Huiming Hu for proofreading on the manuscript.

Financial support and sponsorship
This project was supported by grants from the National Natural Science Foundation of China (No. 81260638), the Nature Science Foundation of Jiangxi Province, China (No. 20161BAB205220 and No. 20132BAB205083), the Health and Family Planning Commission of Jiangxi province, China (No. 2013A152 and No. 2014A041), the Innovation Project for Postgraduate Research Fund of Jiangxi province, China (No. YC2016-B079), and the Innovation Project for Doctoral Research Fund of Jiangxi University of Traditional Chinese Medicine, China (No. JZYC16B02).

Conflicts of interest
There are no conflicts of interest.

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