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Research article

Comparative discriminant analysis of *Mesua ferrea* L. and its adulterants

Mubareke Kuerban [a,b], Fangyuan Ma [a], Lianlian Shan [a], Yali Wang [a], Gang Zhou [a,*]

[a] *Key Laboratory of Ethnic Medicine and Traditional Chines, Xinjiang Uygur Autonomous Region Institute for Drug Control, Urumqi, 830054, China*
[b] *Turpan City Institute of Drug Control, Turpan, 83800, China*

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ABSTRACT

The Uygur medicinal material *Mesua ferrea* L. has different plant sources in the market. The flower bud of *Mammea siamensis* T. Anders, which originated from Myanmar and Thailand, is actually used in the dosage room of Uygur hospitals and pharmaceutical enterprises in Xinjiang Region. On the contrary, flowers of *Mesua ferrea* L. are less frequently used. In this study, the taxonomic characteristics, liquid chromatography-mass spectrometry (LC/MS) and liquid chromatography (HPLC) were used to compare the similarities and differences between the two species. The results showed that the flowers of the two plants were significantly different in morphology, but the similarity of chemical components was high. At the same time, the study also found that *Mesua ferrea* L. and *Mammea siamensis* T. Anders contain a large amount of vitexin and isovitexin, which can be used for qualitative and quantitative research. This study provides a reference for the identification, development and utilization of *Mesua ferrea* L medicinal materials and the revision of quality standards.

1. Introduction

Mesua ferrea Linn. is a perennial evergreen tree in the family Clusiaceae, mainly distributed in Yunnan and Guangxi of China, along with India, Sri Lanka, Thailand, Malaysia and other countries [1]. Its various parts are utilized individually or collectively for treating diverse ailments. For instance, its flowers and leaves exhibit substantial medicinal value and properties. One of its important applications is in its flowers, a mixture of its flowers with butter and sugar is very useful in the treatment of bleeding piles and burns on the feet. Moreover, leaves and flowers are also antidotes to snakebites and scorpion stings [2]. In Ayurveda, it is the main ingredient of Naga-kesharayaga, used to treat bacillary dysentery and Naga-keshara yaga. In unani medicine, it is an important ingredient of Jawarish Shehryaran (a liver tonic) and Hab Pachuluna (an appetizer). It also has anticonvulsant effects. Seizures can be cured by this plant [3]. *Mesua ferrea* Linn. in Uighur medicine refers to the dried flower buds of *Mesua ferrea* L., which is a commonly used medicinal material in Uighur medicine. Its Uighur name is "Nalmisik". It is used to treat diseases caused by dampness-cold or phlegm-dampness, such as cold deficiency of heart, depression, neurasthenia, cold body and impotence, and dampness-cold stomach deficiency [4]. The main chemical constituents of *Mesua ferrea* L. flowers include coumarins, flavonoids, triterpenoids, and mangiferic acids [5]. Modern pharmacological studies have shown that it has antibacterial [6], anti-inflammatory [7], anticholinesterase [8], antioxidant [9], anti-platelet aggregation [10] etc (see Table 1).

* Corresponding author.
E-mail addresses: 111711mm@Sina.com (M. Kuerban), mafangyuan900731@163.com (F. Ma), chen18208822026@163.com (L. Shan), wangyali225@126.com (Y. Wang), zhougang740414@126.com (G. Zhou).

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The quality standard for *Mesua ferrea* L. medicinal materials is listed in the "Compilation Standards of Uygur Medicine and Uygur Medicine Decoction Pieces in Traditional Chinese Medicine" in Xinjiang Uygur Autonomous Region (2020 version) [11]. It's utilized for neurasthenia, frigid physique, impotence, dampness-cold stomach weakness, diarrhea, assorted moist sores, bleeding piles, etc. The main source is the dried flower buds of *Mesua ferrea* L., part of the Clusiaceae family, aligning closely with the original depiction of Mesua ferrea L. in 'China Flora', 'Compendium of Chinese Medical Supplies', and 'Indian Unani Pharmacopoeia' 2007 version [12,13]. their physical depictions don't match. They are categorized as follows: the product is spherical, 0.5–0.7 cm in diameter, with a sharp tip at the beginning, about 1 mm in length, 0.5–2.5 cm in pedicel length, cap-shaped pedicel tail, most residues, calyx surface light brown to brownish red, visible fine longitudinal texture, 4 petals, reddish brown, obovate wedge-shaped, imbricate arrangement, 2 outside slightly larger than 2 inside, most stamens, filamentous, yellow brown, ovary conical, 2 chambers, stigma shield-shaped, unisexual flowers with or without stamens, light body, crisp, light aroma, light taste, slightly bitter. It is a typical character of Ochrocarpus plants, which is a standard setting error. According to the inquiry of China Digital Herbarium (CVH), the characteristics of medicinal materials are similar to the buds of *Mammea yunnanensis* (H. L. Li) Kosterm, but *Mammea yunnanensis* has 6 petals, while the actual medicinal materials are only 4 petals. In the ' The Unani Pharmacopeoia of India', two species are under the genus *Ochrocarpus*, namely *Ochrocarpos longifolius* T. Anderson. and *Mammea siamensis* T. Anders. It is described as follows.

Ochrocarpos longifolius T. Anderson: leaves are long elliptic to round or obtuse, pedicels clustered, petals sharp. Young branches terete, smallest 4 segments. Leaves 6 to 8, 2 to 2 inches, thick leathery, dark green, whorled, midveins stout and protuberant, veins few and inconspicuous, very slender, joined by numerous small reticulate veins, giving very beautiful lacunae to the dry leaves, petiole short, stout, 1/4 in. Flowers are 2/3 inches in diameter. Buds globose, pedicels 1 inch, thin. Calyx 2-split, reflexed during flowering, petals 4, thin, white. Stamens many, style conical, stigma flat. The fruit measures 1 inch and is obliquely ovoid with a hard pointed style at the apex., 1 seed (Cultivated flowers are mostly hermaphrodites).

Mammea siamensis T. Anders: leaf linear oblong or obtuse oblong, flowers solitary or 2 connate, petals rounded at the top. It grows in the dry mountainous areas of Bogu and Arakan, Myanmar, and is very similar to the long-leaf lattice vein tree. The flowers are aromatic, rarely clustered, and the petals are obtuse. The fruit measures 1/4 inch and is ovate, smaller, and more pointed with a smooth surface. By comparison, it was found that the actual medicinal material of *Mesua ferrea* L used in Xinjiang market for a long time was the flower bud of *Mammea siamensis* T. Anders [14].

In view of the fact that this variety has become the mainstream variety of medicinal materials in Xinjiang in the past 10 years, the related research articles on chemical composition and pharmacological efficacy are based on this variety. If the chemical composition of the two plants is similar, after finding out the source and resources of the variety, it can be included in the source of the medicinal materials of *Mesua ferrea* L. together. Therefore, this paper discusses the possibility of establishing the quality standard of the two plants at the same time from the comparison of pharmacognosy characteristics and the similarity of chemical components.

2. Results and discussion

2.1. Trait identification

2.1.1. The trait characteristics of flowers of Mesua ferrea L

The trait Characteristics of flowers of *Mesua ferrea* L. (Fig. 1) are as follows: the blooms are bisexual, measuring around 5–8.5 cm across; the flower stalk is 3–5 mm long; there are 4 sepals, with the outer 2 slightly larger than the inner 2, nearly circular, concave, thick and leathery, wrinkled, with a membranous edge, and sometimes covered with white hairs. The petals are white, forming an inverted ovate-wedge shape, measuring approximately 3–3.5 cm long. The flowers are adorned with numerous stamens attached individually. Each stamen possesses an elongated oval anther that is golden yellow and approximately 1.5 mm long. The filaments of the stamens are thread-like, measuring approximately 1.5–2 cm long. The ovary is conical, standing approximately 1.5 cm tall, and bearing a style measuring 1–1.5 cm long. The stigma that is shield-shaped.

Table 1
A comparison table of the main characteristics of the flowers of *Mesua ferrea* L., *Mammea siamensis* T. Anders and *Ochrocarpos longifolius* Benth. & Hook. f. ex T. Anderson.

Feature	Mesua ferrea L.	Mammea siamensis T.Anders	*Ochrocarpos longifolius* Benth. & Hook. f. ex T. Anderson
flower	Flowers bisexual, 5–8.5 cm in diameter	Flowers are miscellaneous, mostly male flowers (pistil degeneration), less bisexual flowers.	The flowers are miscellaneous, mostly bisexual, 2 /3 inch in diameter (about 1.7 cm).
pedicel	The pedicel is 3–5 mm long, thick and short.	Pedicel thin, long, solitary or secondary, rarely clustered.	Pedicel 1 inch long (about 2.5 cm), slender, long. Pedicel clustered
calyx	4 pieces, 2 large and 2 small, thick leather	2 pieces, hemispherical.	2 pieces, hemispherical, paper characteristics, with longitudinal stripes.
corolla	4 pieces, white, petals nearly round	4 pieces, white, obtuse round petals	4 pieces, white, petals sharp
staman	majority, separation of stamen	Majority, connation of stamens	Majority, connation of stamens
pistil	The style is 1–1.5 cm long and the stigma is shield-shaped.	Style conical, stigma flat.	Style conical, stigma flat.

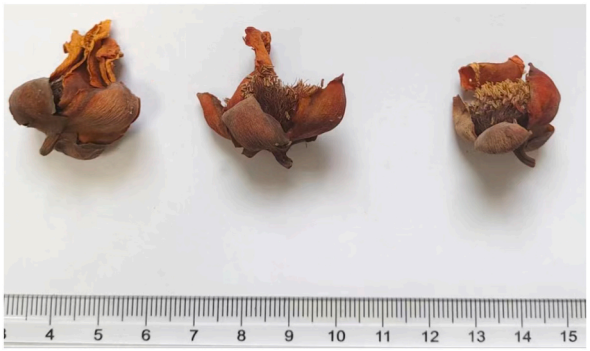

Fig. 1. This is figure of *Mesua ferrea* L. flowers.

2.1.2. The trait characteristics of flowers of Mammea siamensis T.Anders

The Characteristics of flowers of *Mammea siamensis* T.Anders (Fig. 2) are as follows: diverse in appearance, measuring0.3–0.8 cm in diameter; pedicel is 2–4 cm in long, often pedicellate at the base, sepals are in pairs, closed, occasionally dehiscent, suborbicular, leathery, with parallel longitudinal ribs, petals are in groups of 4, 0.2–0.5 cm long, may be white or yellow; stamens are numerous, united and arranged in a round, anthers are oblong, golden yellow, aapproximately 0.5 mm in length; stigma is peltate, with 3 lobes, frequently reduced and disappearing.

2.1.3. Comparison of characteristics of Mesua ferrea L., Mammea siamensis T.Anders, and Ochrocarpos longifolius Benth. & Hook. f. ex T. Anderson

According to the ' Flora of China ', ' Flora of India 'and some references [15,16], the characteristics of the actual samples, the flowers of *Mesua ferrea* L., *Mammea siamensis* T. Anders and *Ochrocarpos longifolius* Benth. & Hook. f. ex T. Anderson were compared. The results are summarized in Tabie 1.

2.2. Microscopic identification

The result of microscopic identification is shown in Fig. 3 (Supplementary Figs. 1–5). The pollen microscopic features of two plant flowers include vascular tissues (spiral, reticulate, and ladder-like), pollen grains (double-layered structure, with three germinal apertures), thin-walled cells, cork cells, and corolla epidermal cells. The main differences lie in that the *Mesua ferrea* L. powder contains numerous non-glandular hairs, and the corolla epidermal cells have obvious bead-like thickenings, while the corolla thin-walled cells of *Mammea siamensis* T. Anders plants contain large amounts of calcium oxalate clusters. From the powder situation, there is no essential difference. Fig. 1. This is a figure. Schemes follow the same formatting.

2.3. TLC identification

After TLC separation, the chromatograms of *Mesua ferrea* L. and *Mammea siamensis* T. -Anders samples were obtained as shown in Fig. 4 (Supplementary Fig. 1). It can be seen that under the given chromatographic conditions, the TLC profiles of *Mesua ferrea* L. and *Mammea siamensis* T. -Anders are well separated with clear spots, and there are significant differences in their main chromatographic spots. In addition, in the chromatogram of the test product, spots of the same color are shown in the same position as the chromatogram of the control product.

Fig. 2. This is figure of flowers of *Mammea siamensis* T. Anders.

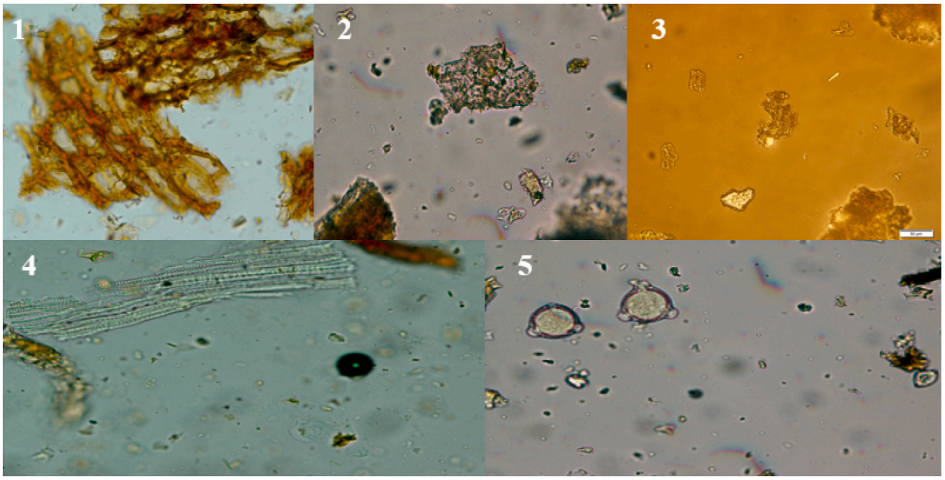

Fig. 3. Microscopic characteristic diagram of *Mesua ferrea* L. medicinal powder. 1: Corolla parenchyma cells, 2: Calyx epidermal cells, 3: Calcium oxalate crystals, 4: Catheter, 5: Pollen grains.

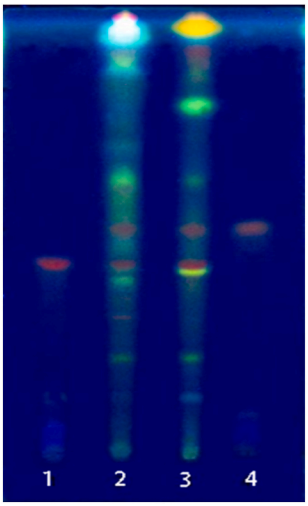

Fig. 4. TLC of *Mesua ferrea* L. and *Mammea siamensis* T. Anders. In the figure, 1 stands for vitexin, 2 stands for *Mammea siamensis* T. Anders, 3 stands for *Mesua ferrea* L, and 4 stands for isovitexin.

2.4. LC analysis

In this experiment, 10 μL of each of the reference and the sample solutions was accurately taken and injected into the liquid chromatograph for detection at 337 nm. The results of liquid phase analysis are shown in Fig. 5. . In the graph, A represents the chromatogram of isovitexin reference material, B represents the chromatogram of vitexin reference material, and C represents the chromatogram of six batches of samples. The retention time of the 1st and 2nd chromatographic peaks of the test solution was consistent with the retention time of the chromatographic peaks of vitexin and isovitexin reference solutions. There are eight obvious visible chromatographic peaks in the liquid chromatogram of the medicinal herb Irdisiae Rhizoma, among which vitexin and isovitexin were selected as quality control indicators with retention times of 15.056min (Peak 1) and 15.981 min (Peak 2), respectively. The asymmetry of peak 1 (isovitexin) was 1.20, the theoretical plate number was 614269, and the resolution between vitexin was 3.53, indicating that the liquid chromatography analysis conditions were ideal. It can be used for the study of fingerprint identification and content determination of two plant flowers, which is of practical significance for improving the quality standard of Uygur medicinal materials.

2.5. UPLC-TOF/MS analysis

The results of HPLS-MS analysis of *Mesua ferrea* L. and *Mammea siamensis* T. Anders were shown in Fig. 6 to Fig. 11. Among them,

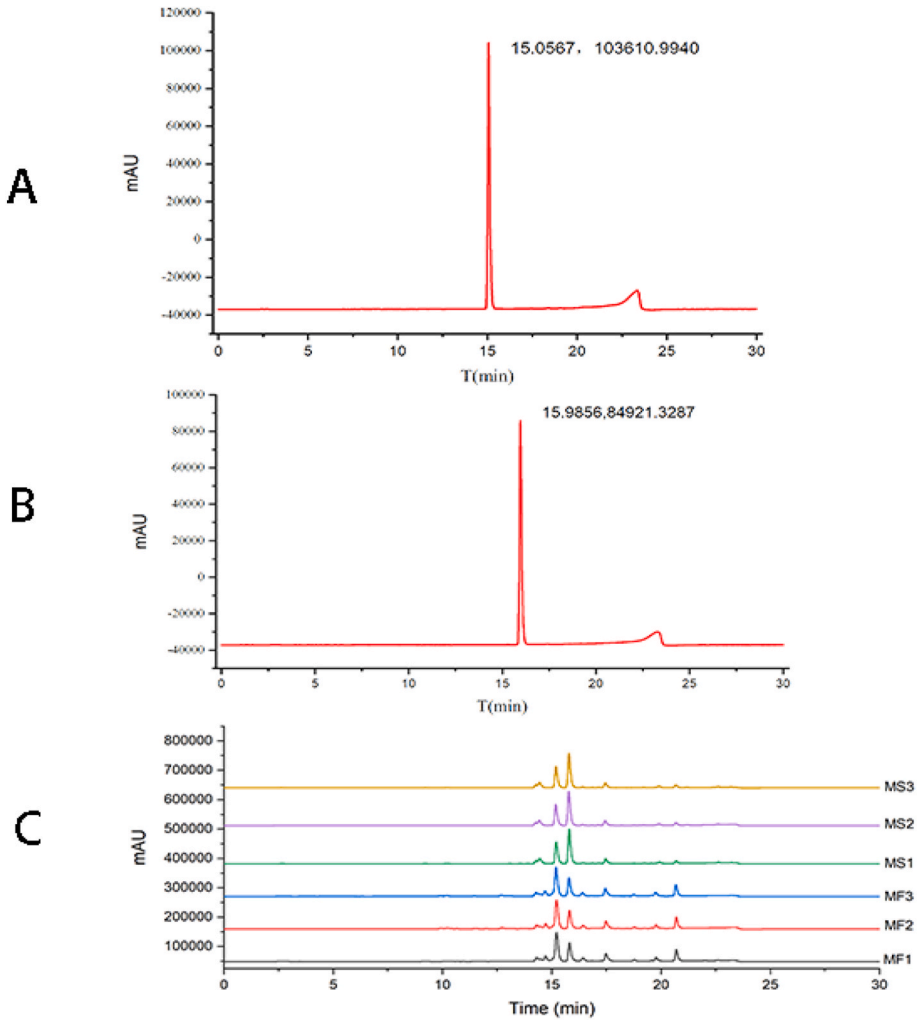

Fig. 5. A is isovitexin, B is vitexin, C is the stacked HPLC spectra of *Mesua ferrea* L and *Mammea siamensis* T. Anders, MF1, MF2, and MF3 represent three therapeutics of *Mesua ferrea* L, similarly MS1, MS2, and MS3 signify three additional therapeutics of *Mammea siamensis* T. Anders.

Figs. 6 and 7 are chromatograms and TIC diagrams, and Fig. 8, Fig. 9, Fig. 10, Fig. 11 are secondary mass spectra. From the chromatogram of the two medicinal materials, we can see that no residual substance peaks after 8 min, indicating that the elution is clean. A total of 4 maximum chromatographic peaks were detected, which were 5.65, 5.68, 7.02, 7.72, and denoted by 1, 2, 3, and 4, respectively. Among them, the Peak 1 corresponds to a substance with a quasi-molecular ion peak (M+1) at *m/z* 433.13, and the fragmented ions observed are at *m/z* 158.01, 209.07, 313.08, and 415.12, the Peak 2 corresponds to a substance with a quasi-molecular ion peak at *m/z* 433.14, and the fragmented ions observed are at *m/z* 158.01, 209.06, 313.08, and 415.12, the Peak 3 corresponds to a substance with a quasi-molecular ion peak at *m/z* 303.06. and the fragmented ions observed are at *m/z* 158.01, 182.99, 209.07, and 229.15, the Peak 4 corresponds to a substance with a quasi-molecular ion peak at *m/z* 541.14, and the fragmented ions observed are at *m/z* 163.04, 209.07, 219.19, and 237.20. The quasi-molecular ion peak of the substance corresponding to the No.1 chromatographic peak and the No.2 chromatographic peak is the same, and the ion fragment peak is also very similar. It should be an isomer or approximate homologue. Based on literature, it is determined to be vitexin and isovitexin [17], with a molecular weight of 432.28. Vitexin is mainly used for the treatment of cardiovascular diseases, and it is also a component of anti-cancer and anti-tumor. It has good antioxidant activity in vitro. Isovitexin is an anti-tumor compound, vitexin and isovitexin also have very good hypotensive, lipid-lowering and heat-dispelling effects [18]. Vitexin and isovitexin are important functional components in *Mesua ferrea* L. and *Mammea siamensis* T. Anders. Peak 3 is quercetin, a common component of plant flowers, which is not representative. Peak 4 is a biflavonoid of *Mesua ferrea* L., and there is no relevant reference substance for sale. Finally, we selected vitexin and isovitexin as index of measurement for *Mesua ferrea* L. The TIC diagram showed that under this extraction condition, there were a total of 174 (see Fig. 9).

Fig. 5. Liquid chroatograms of *Mesua ferrea* L, *Mammea siamensis* T. Anders and reference substance. Among them,A is isovitexin, B is vitexin, C is *Mesua ferrea* L and D is *Mammea siamensis* T. Anders.

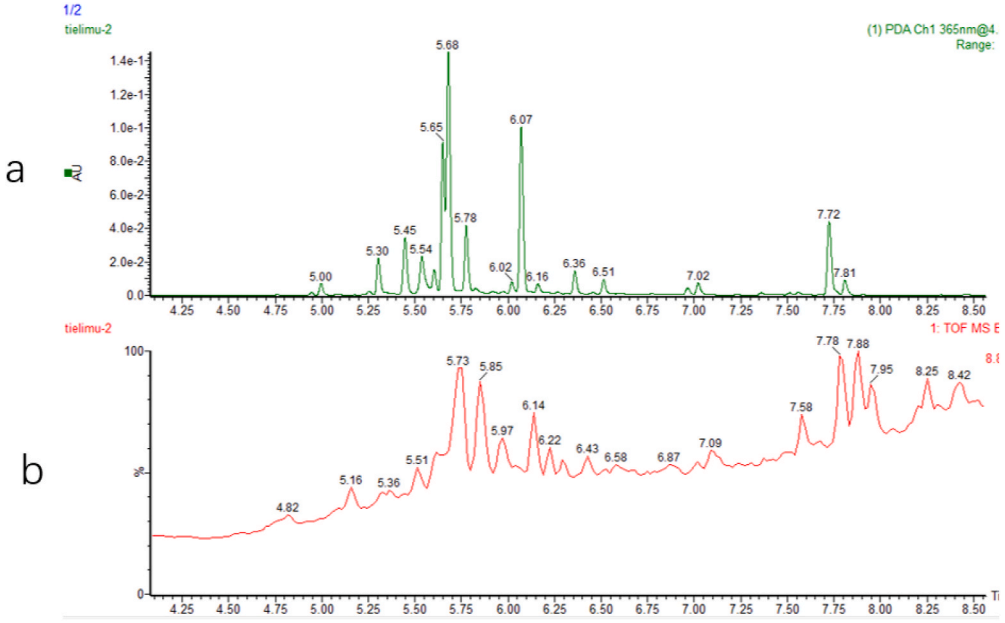

Fig. 6. Chromatogram (a) and TIC diagram (b) of *Mesua ferrea* L.

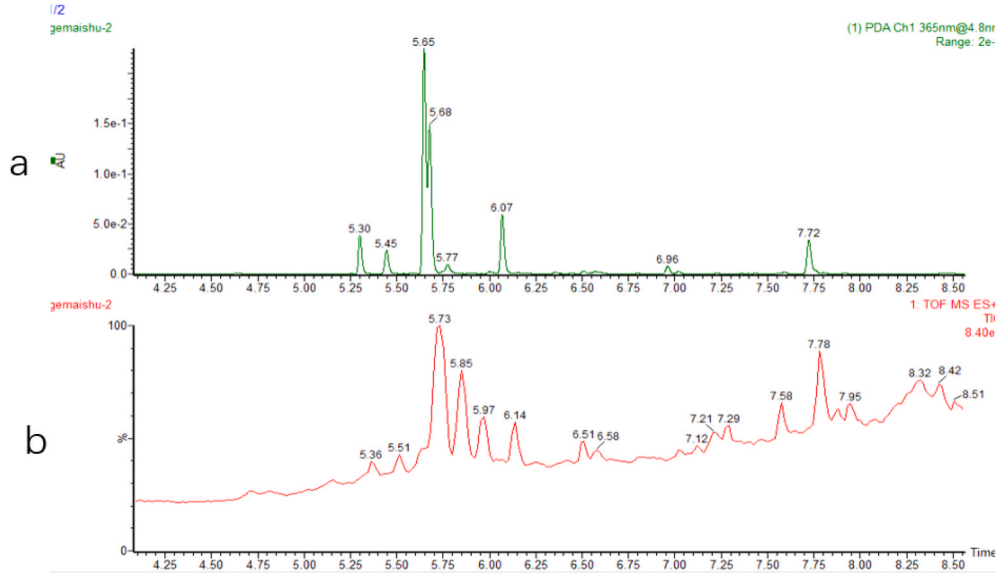

Fig. 7. Chromatogram (a) and TIC diagram (b) of *Mammea siamensis* T. Anders.

3. Materials and methods

3.1. Reagents and materials

Vitexin (lot number 110747–202011, purity about 98.8%, assayed) and isovitexin (lot number 110747–202011, purity about 98.8%, assayed) were purchased from the National Institute of Food and Drug Control (Beijing, PR China). Methanol, acetonitrile and Formic acid are chromatographically pure, and all were purchased from Merck (Darmstadt, Germany). Glacial acetic acid of chromatographically pure was purchased from from McLean. (Shanghai, China). Sodium dihydrogen phosphate and chloral hydrate were analytically pure. Sodium dihydrogen phosphate was purchased from Tianjin Fuchen Chemical Reagent Factory (Tianjin, China) and chloral hydrate was purchased from Shandong Haizhou Biological Engineering Co., LTD (Shandong, China). the water used is ultrapure water, which was obtained from a Milli-Q (Millipore) water purification system.

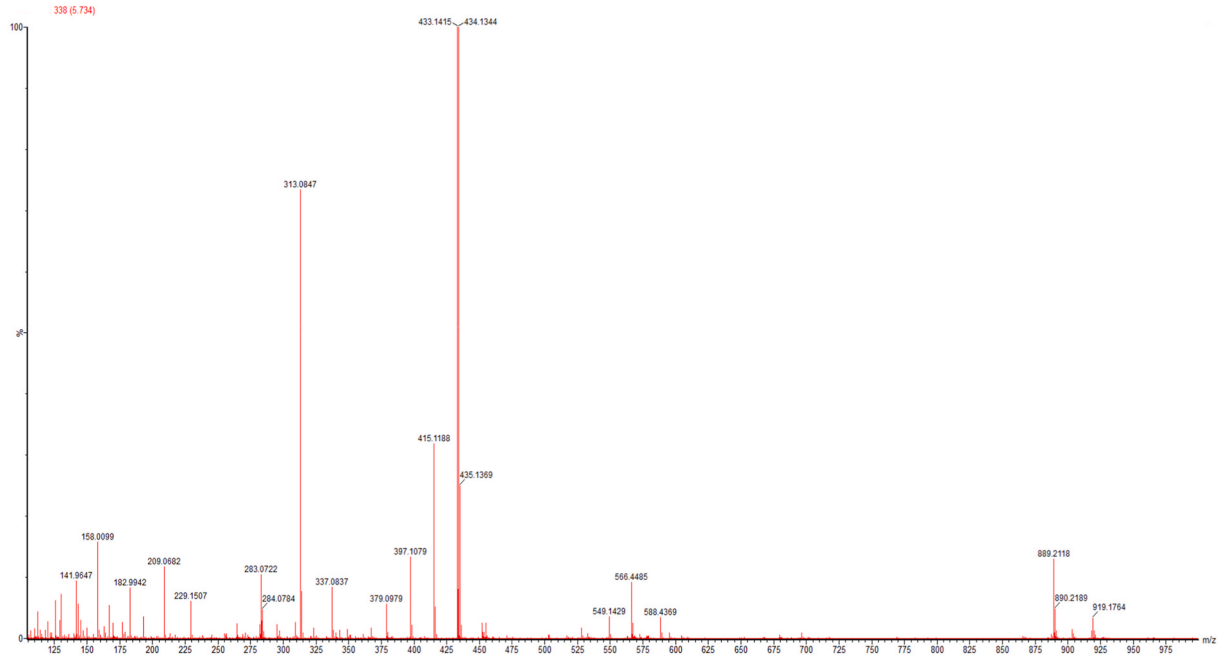

Fig. 8. The MS graph of Peak 1.

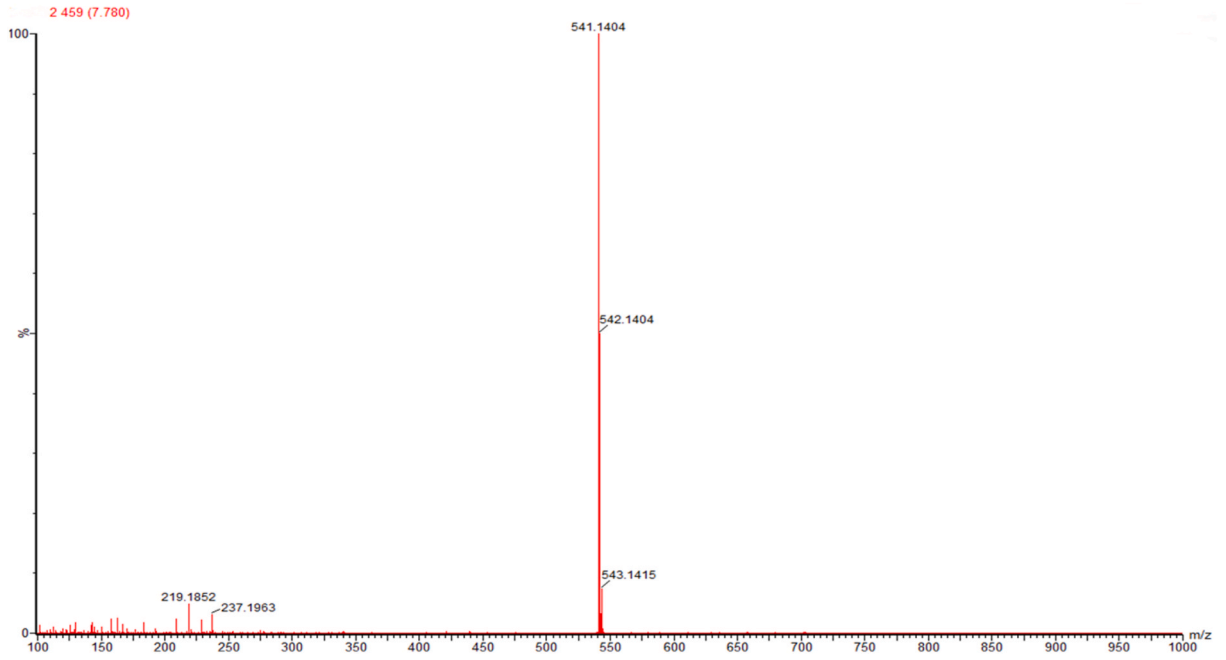

Fig. 9. The MS graph of Peak2.

Three batches of *Mesua ferrea* L. herbal medicine and three batches of *Mammea siamensis* T. Anders from a certain plant of the Genus Grewia were collected from the market, and all were identified by Mr. Pang Kejian, Master of Pharmacognosy, Distinguished researcher of the Key Laboratory of Xinjiang Botanical Resources Utilization of Ministry of Education, Shihezi University. He mainly devoted himself to the research on the origin, standards and resources of ethnic medicine.

Fig. 10. The MS graph of Peak3.

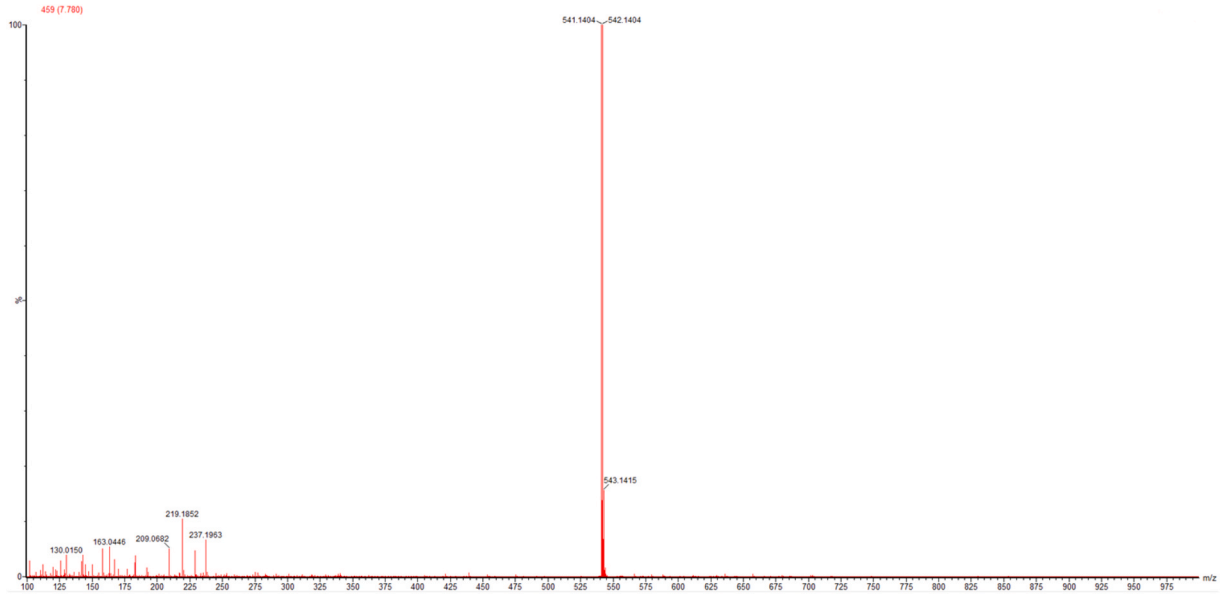

Fig. 11. The MS graph of Peak4.

3.2. Trait identification

Soak the flowers of ironwood and Pink Shower tree in water for 30 min, remove and dry them, take a dissecting needle, and then dissect the pedicel, calyx, corolla, stamen, and pistil in order.

3.3. Microscopic identification

According to the Liu et al.'s method [19], After grinding and crushing the samples of *Mesua ferrea* L and *Mammea siamensis* T. Anders, an appropriate amount of medicinal powder was taken and placed on a glass slide. Two drops of chloral hydrate were added to the herbal powder, then uniformly heated on an alcohol lamp to make it transparent. The slide was mounted and examined under a microscope.

3.4. TLC identification

The powder of the two medicinal materials was 1g, respectively, placed in a triangular flask, each with methanol 20 mL, ultrasonic extraction (50 KHZ, 500 W) for 30 min, filtered, the filtrate was evaporated, and the residue was dissolved with methanol 1 mL as the test solution. 10.68 mg Vitexin and 10.60 mg isovitexin were taken and placed in 10 mL volumetric bottles with methanol, respectively, as control solution. Each 10 μL of the four solutions was drawn and spotted on the same silica gel G thin layer plate, and expanded with ethyl acetate-methanol-water (25: 5: 3), removed, dried, and examined under an ultraviolet lamp at 365 nm. In the chromatogram of the test product, the same color spots are shown in the same position as the control product.

3.5. LC analysis

3.5.1. The condition of chromatographic

The Thermo Ulitim ate-3000 PLC system was also used for LC analysis (UV detector, Chameleon 7.0 chromatographic workstation). The Liquid Chromatography (LC) analysis was carried out using a Shim-pack GIST-C18 column (4.6 mm × 250 mm, 5 μm) with a mobile phase consisting of methanol (A) and 0.1% formic acid solution (B). The gradient elution program was performed as follows: 15% A for 0–3 min, 25–50% A for 3–10 min, 50–80% A for 10–20 min, and 15% A for 21–30 min, at a flow rate of 1.0 mL/min and a column temperature of 35 °C. Detection was conducted at a wavelength of 337 nm and the injection volume was set at 10 μL.

3.5.2. The preparation of the sample solution

Weigh 0.5 g of *Mesua ferrea* L. powder and *Mammea siamensis* T.Anders powder, and mix them with 100 mL of 80% methanol. The mixture was then heated and treated with an ultrasonic treatment instrument (power of 250 Watts, frequency of 35 kHz) for 10 min to help the sample fully dissolve. Then, the filtrate was collected and filtered through the filter paper, and the test solution was finally obtained.

3.5.3. The preparation of reference solution

Take appropriate amounts of Vitexin and isovitexin reference substances, accurately weigh them, and dissolve them in 80% methanol solution to prepare solutions that contain 0.104 mg/mL and 0.109 mg/mL, respectively.

3.6. UPLC-TOF/MS analysis

3.6.1. Chromatographic and mass spectrometry conditions for UPLC-TOF/MS analysis

The chemical constituents were profiled and identified by using an Waters G2-Q-TOF LC-MS equipment (Milford, China). The chromatographic column used is ACQUITY BEH C18 (2.1mm × 100 mm, 1.7 μm). Acetonitrile is used as mobile phase A, and 0.1% formic acid solution is used as mobile phase B. The column temperature was 35 °C, the detection wavelength was 365 nm, gradient elution: 10% B (0–3 min), 10%–60% B (3–8 min), 60% B (8–12min), 60%–10% (12–12.5 min), 10% B (12.5–17.5 min), the flow rate was 0.3 mL/min. The MS parameters were set as follows: the ion source is electrospray ionization (ESI) source, the ionization method is atmospheric pressure ionization, the positive ion detection mode, the positive ion resolution mode, the voltage is 3.00 kV, the ion source temperature is 120 °C, and the solvent gas is 600 L/h.

3.7. The preparation of the sample solution

The powder of *Mesua ferrea* L. flower and *Mammea siamensis* T.Anders flower bud were respectively taken from 0.5 g, added with 20 mL methanol, ultrasonic treatment (power 250 W, frequency 35 KHZ) for 10 min, filtered, and used as the test stock solution. Take 1 mL of stock solution, put it in 100 mL volumetric flask, add methanol to scale, shake, filter, take 10 μL of filtrate, inject sample.

4. Discussion

Research results have shown that there is currently a situation of mixed use of *Mesua ferrea* L. medicinal materials. In scrutinizing the practice in Xinjiang region over the past decade, the flower buds of *Mammea siamensis* T. Anders are mainly used, and the flowers of *Mesua ferrea* L. are supplemented. Both of the two medicinal materials come from the Clusiaceae plants with similar chemical compositions, and are used as the medicinal materials of *Mesua ferrea* L. in Xinjiang. It may be considered to include them together as the source of *Mesua ferrea* L. herbal medicine on condition that the original plant source and resources are clarified. It is not appropriate to blindly negate the previous research results, which may have more practical significance for the quality control of medicinal materials of *Mesua ferrea* L.

A considerable proportion of Uyghur medicinal materials come from abroad, which make it difficult to identify origin and investigate resources. In addition, there is a general concept of ' substitutes ' in ancient literature books, that is, in the absence of authentic medicinal materials, other medicinal materials can be used to replace them. However, some of these substitutes have no relationship with the authentic medicinal herbs in terms of botanical classification and chemical composition, contradicting the research on herbal medicine. Adequate attention should be paid to this issue. In the development and research of medicinal materials from foreign countries, we should pay attention to basic research, and should have the identification results of the original materials and the relevant materials of resource survey or artificial planting resources. Our original work focused on studying the chemical

constituents between the plants of *Mesua ferrea* L. and *Mesua Linn.*, and built technical reserves for the improvement of the quality standards of ethnic medicines in Xinjiang. However, we found that the quality standards of *Mesua ferrea* L. in Xinjiang local medicinal materials were incorrect, and the actual use of medicinal materials was different from those recorded in books. Moreover, the plants of Ochrocarpus Thou., such as *Mammea yunnanensis* (H. L. Li) Kosterm., *Ochrocarpos longifolius* T. Anderson, and *Mammea siamensis* T. Anders, were not clearly distinguished, and even used the flowers of the Ehretia plants of Boraginaceae to impersonate (The corolla base of this genus is connate, cylindric, often aggregating into a conical cyme.). Therefore, this paper describes the origin and traits of plants from different sources in the actual use of *Mesua ferrea* L. medicinal materials, and translates some foreign literature to verify our original identification results.

5. Conclusion

For the first time, we discovered that the two are mixed, which in the long run has a very significant impact on the development of *Mesua ferrea* L. First of all, in order to better control and research the quality of *Mesua ferrea* L., it is urgent to further extract and study the differences between the active ingredients of the two, and formulate more accurate corresponding standards for medicinal materials. Secondly, only through more research and the development of clear standards can the current situation of mixed use be improved, and we are also conducting relevant research to provide technology and guidance for guiding the correct use of *Mesua ferrea* L., rational use of drugs, and preparation research. Thirdly, it draws the public's attention to and studies medication usage in this regard, and provides research ideas and reference significance for improving the current situation of confusion in the basic source of ethnic medicine. Finally, modern analysis technology and data processing technology are used to cultivate a more accurate identification and quality management system of ironwood. Only on the basis of systematic basic research and the establishment of an effective quality control system can we further guide the scientific development of the traditional Chinese medicine industry.

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Data availability statement

Not applicable.

CRediT authorship contribution statement

Mubareke Kuerban: Writing – original draft, Data curation, Conceptualization. **Fangyuan Ma:** Writing – review & editing, Methodology, Data curation. **Lianlian Shan:** Software, Investigation. **Yali Wang:** Writing – review & editing, Formal analysis. **Gang Zhou:** Writing – review & editing, Project administration, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Zhou gang reports equipment, drugs, or supplies was provided by Xinjiang Uygur Autonomous Region Drug Inspection Institute. Zhou gang reports a relationship with Xinjiang Uygur Autonomous Region Drug Inspection Institute that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

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