BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Articulo Original / Original Article

Comparative analysis of flavonoid content of six *Cecropia* species using LC-HRESI-MS

[Análisis comparativo del contenido de flavonoides de seis especies de *Cecropia* utilizando LC-HRESI-MS]

Yancho Zarev[1], Anzhelika Dakovska[1], Preslav Enchev[1], Andrés Rivera-Mondragón[2] & Iliana Ionkova[1]

[1]Department of Pharmacognosy, Faculty of Pharmacy, Medical University of Sofia, 2 Dunav str., 1000 Sofia, Bulgaria.
[2]Centro de Investigaciones Farmacognósticas de la Flora Panameña (CIFLORPAN), Departamento de Química Medicinal y Farmacognosia, Facultad de Farmacia, Universidad de Panamá, Panama City, Panama

Reviewed by:
Ricardo Diego de Albuquerque
Universidad Nacional de Trujillo
Peru

Juana Chavez
Universidad Norbert Wiener
Peru

Correspondence:
Yancho ZAREV
yzarev@pharmfac.mu-sofia.bg

Section Phytochemistry

Received: 4 August 2024
Accepted: 1 December 2024
Accepted corrected: 19 December 2024
Published: 30 May 2025

Citation:
Zarev Y, Dakovska A, Enchev P, Rivera-Mondragón A, Ionkova I
Comparative analysis of flavonoid content of six *Cecropia* species using LC-HRESI-MS
Bol Latinoam Caribe Plant Med Aromat
24 (3): 453 - 478 (2025)
https://doi.org/10.37360/blacpma.25.24.3.33

Abstract: The genus *Cecropia*, comprising approximately 61 species, is primarily distributed in Brazil and Latin America. These species are renowned in traditional medicine for treating various ailments, including diabetes, high blood pressure, and respiratory disease. Despite their ethnopharmacological importance, complete phytochemical data are lacking for many *Cecropia* species. This study aims to fill this gap by conducting a comparative phytochemical analysis of six *Cecropia* species, *C. insignis*, *C. longipes*, *C. obtusifolia*, *C. peltata*, *C. hispidissima* and *C. heterochroma*, collected in Panama. Seven flavonoids and one phenolic acid were identified by LC-HRESI-MS. Rutin, quercetin-3-O-β-D-glucoside and apigenin-7-O-β-D-glucoside are the major compounds in the evaluated *Cecropia* species. *C. obtusifolia* and *C. hispidissima* showed the most diverse flavonoid profiles. These results enhance our understanding of phytochemical diversity within the genus, provide the basis for developing herbal remedies using *Cecropia* species, and lay the groundwork for more in-depth phytochemical and pharmacological studies.

Keywords: *Cecropia* species; Phytochemical analysis; Flavonoids; LC-HRESI-MS análisis; Comparative analysis

Resumen: El género *Cecropia*, que comprende aproximadamente 61 especies, se distribuye principalmente en Brasil y América Latina. Estas especies son reconocidas en la medicina tradicional por su uso en el tratamiento de diversas dolencias, incluyendo diabetes, hipertensión y enfermedades respiratorias. A pesar de su importancia etnofarmacológica, faltan datos fitoquímicos completos para muchas especies de *Cecropia*. Este estudio tiene como objetivo llenar este vacío mediante la realización de un análisis fitoquímico comparativo de seis especies de *Cecropia*: *C. insignis*, *C. longipes*, *C. obtusifolia*, *C. peltata*, *C. hispidissima* y *C. heterochroma*, recolectadas en Panamá. Se identificaron siete flavonoides y un ácido fenólico mediante LC-HRESI-MS. La rutina, el quercetina-3-O-β-D-glucósido y el apigenina-7-O-β-D-glucósido son los compuestos principales en las especies de *Cecropia* evaluadas. *C. obtusifolia* y *C. hispidissima* mostraron los perfiles de flavonoides más diversos. Estos resultados mejoran nuestra comprensión de la diversidad fitoquímica dentro del género, proporcionan una base para el desarrollo de remedios herbales utilizando especies de *Cecropia* y sientan las bases para estudios fitoquímicos y farmacológicos más profundos.

Palabras clave: Especies de *Cecropia*; Análisis fitoquímico; Flavonoides; Análisis LC-HRESI-MS; Análisis comparativo.

INTRODUCTION

The genus *Cecropia* includes about 61 species mainly found in Brazil and Latin America. These fast-growing trees from the Urticaceae family are commonly used in traditional medicine to treat conditions such as cough, asthma, bronchitis, high blood pressure, inflammation, and heart disease, and also as diuretics. Typically growing in rainforests and moist habitats, *Cecropia* trees are known for their palmate leaves and hollow stems. They contain a range of phytochemicals, including alkaloids, flavonoids, tannins, saponins, and terpenes, which offer various pharmacological benefits such as anti-inflammatory, antioxidant, and antitumor effects (Enchev *et al*., 2024). Originally classified under the Moraceae family in the 1970s, the genus Cecropia was later included in a newly proposed family, Cecropiaceae, a change that was accepted by many researchers. However, recent taxonomic studies using morphological and phylogenetic approaches have proposed reclassifying the genus *Cecropia* into the family Urticaceae (Costa *et al*., 2011). *C. obtusifolia* is a 20 m tall tree growing as secondary vegetation in tropical rainforests. It is a fast-growing tree from tropical America, and in ethnopharmacological reports, the plant is traditionally used as an infusion mainly of dried leaves by the Mexican population against type II diabetes. Traditionally, the leaves, bark and root of the plant are boiled in water and the resulting infusion is drunk throughout the day (Rivera-Mondragón *et al*., 2021). In an *in vivo* experiment with streptozotocin induced diabetes in rats, aqueous and butanol extract of *C. obtusifolia* leaves demonstrated antidiabetic activity. The main components present in both extracts were phenolic derivatives, isoorientin and chlorogenic acid. Since these compounds exhibit significant hypoglycemic activity, it can be assumed that they contribute to the hypoglycemic effect that *C. obtusifolia* possesses (Andrade-Cetto & Wiedenfeld, 2001). Aqueous extracts of *C. obtusifolia* demonstrate significant hypoglycemic effects without adverse side effects, suggesting their potential for development into a phytomedicine, though their mechanism does not involve stimulating insulin secretion (Revilla-Monsalve *et al*., 2007). In an identical experiment, *C. peltata* was also described as having antidiabetic activity. The possible mechanism of action involves the reduction of hepatic glucose output through to the inhibition of glucose-6-phosphatase by chlorogenic acid, which likely triggers gluconeogenesis and glycogenolysis simultaneously (Andrade-Cetto & Heinrich, 2005). Another study suggests that *C. obtusifolia* and *C. peltata* improve glycemic control by inhibiting hepatic glucose production, supporting their traditional use in managing type 2 diabetes through the inhibition of glucose-6-phosphatase activity (Andrade-Cetto & Vázquez, 2010). *C. obtusifolia* is also used in traditional medicine as an anti-inflammatory medicine. The neurodepressant effects of the aqueous extract of *C. obtusifolia* leaves were also investigated in various experimental models to unify data from ethnomedical sources. Regarding the analgesic activity, a study conducted using a hot plate test found that the extract showed no activity; however, had a significant effect when pain was induced by chemical stimuli. This suggests the presence of an analgesic effect of the extract on the peripheral nervous system. The extract also shows local and systemic anti-inflammatory effects. This may explain the widespread use of *C. obtusifolia* in rheumatic and renal inflammations (Pérez-Guerrero *et al*., 2001). Methanol extracts of *C. lyratiloba* and a flavonoid-rich fraction induce dose-dependent aortic vasodilation. However, the main flavonoids identified in the extract, isoorientin, orientin and isovitexin, did not exhibit this activity when tested individually (Ramos Almeida *et al*., 2006). *C. pachystachya* and *C. hololeuca* are other species of *Cecropia* genus common in Brazil, widely used to treat respiratory diseases. Phytochemical studies show that their leaves are rich in phenolic compounds, mainly *C*-glycosidated flavonoids. Orientin and isorientin have been reported in both species, while vitexin and isovitexin have been described only in *C. pachystachya*. In addition, both are rich in chlorogenic acid and have procyanidins. In some cases, syrups and teas are made from mixtures of leaves from different species, which can affect the efficacy and safety of this natural remedy. This is a prerequisite for studying the chemical profile of the leaves of these species. Thus, Da Silva Mathias and Rodrigues De Oliveira (2019), identified thirty-seven compounds, including flavonoids, phenolic acids, flavan-3-ols, condensed tannins (procyanidins) and iridoids, by UV analysis and tandem mass spectrometry (MS/MS). Chlorogenic acid, orientin and isoorientin were observed as major constituents in both extracts. Another chemical analysis of a flavonoid fraction from *C. pachystachya* leaves

revealed a presence of *C*-glycosyl flavonoids, particularly derivatives of luteolin and apigenin. The fraction rich in *C*-glycoside flavonoids demonstrated antidepressant effects that could be related to the antioxidant properties of flavonoids (Ortmann *et al*., 2017). *C. pachystachya* also has hypoglycemic and antioxidant effects, which confirms the traditional use of the plant for the treatment of diabetes. This action is probably due to chlorogenic acid and *C*-glycosides. A glucose tolerance test was performed, which showed that in diabetic rats, the extract produced a significant hypoglycemic effect, with a reduction in blood sugar of up to 68% after 12 hours. The administration of the extract in rats with alloxan-induced diabetes caused a significant reduction in blood sugar levels more pronounced after 90 minutes (reduction by up to 60%) (Aragão *et al*., 2010). *C. insignis* and *C. hispidissima* have been poorly studied in high-quality scientific literature concerning their phytochemical composition and pharmacological properties, likely due to their limited geographical distribution. Despite this, *C. insignis* has been traditionally used as a diuretic and for treating hypertension, asthma, bronchitis, and inflammation. Conversely, the traditional medicinal use of *C. hispidissima* remains largely undocumented (Rivera-Mondragón *et al*., 2019).

In this study, six *Cecropia* species (Urticaceae), commonly used in traditional medicine to treat conditions such as diabetes, hypertension, and lung diseases, were selected. Although some species have been studied, there is a lack of comprehensive phytochemical profiles of these medicinal plants. A comparative phytochemical analysis among these species could elucidate the compounds responsible for their reported pharmacological effects.

MATERIAL AND METHODS

Plant material

The plant material used in the present study are leaves of six species of the genus *Cecropia*: *C. insignis*, *C. longipes*, *C. obtusifolia*, *C. peltata*, *C. hispidissima*, *C. heterochromata*, collected in different regions of the Republic of Panama in 2021 (Table No. 1). The taxonomical classification was carried out by the botanist Orlando O. Ortiz and deposited at the Herbarium of the University of Panama.

Table No. 1
Sex *Cecropia* species collected from Panama

ID	Species	Author	Province (Collection Site)	Coordinates	Date
1	*C. obtusifolia*	Bertol.	Panamá (Cerro Azul)	9°13′03″N, 79°22′38″W	07/08/2021
2	*C. peltata*	L.	Panamá (Camino de Cruces)	9°00′40″N, 79°35′44″W	07/08/2021
3	*C. insignis*	Liebm.	Panamá (Cerro Azul)	9°13′03″N, 79°22′38″W	06/11/2021
4	*C. longipes*	Pittier	Panamá Oeste (Arraiján)	8°55′59″N, 79°44′20″W	06/11/2021
5	*C. hispidissima*	Cuatrec.	Panamá (Cerro Azul)	9°13′03″N, 79°22′38″W	07/08/2021
6	*C. heterochroma*	C. C. Berg and P. Franco	Veraguas (Escudo de Veraguas)	9°05′53″N, 81°33′16″W	27/10/2021

General experimental procedures

Mass spectral data were obtained by LC-HRESI-MS analysis using Q Exactive Plus mass spectrometer coupled to a Dionex UltiMate 3000 LC system (Thermo Fischer Scientific, Germering, Germany). Sample recording was performed under both positive and negative ionization. Full MS scan duration was performed from 0,87 to 29,28 min, at resolution 70,000; AGC target 3e6, max. IT 100 ms, scan range 150 to 1500 *m/z*. The MS/MS scan was set to resolution 17,500 and AGC target 1e5, maximum IT 50 ms, scan range 200 to 2000 *m/z*, isolation window 2,0 *m/z* and step (N)CE 10, 30, 60 The following parameters were used: dry gas flow (N_2 8,0 L/min, capillary temperature 320°C, source temperature 320°C, sheath gas flow - 36 AU, auxiliary flow - 11 AU, source voltage – 3,5 kV and capillary voltage – 320 V. Data acquisition and processing were performed using Thermo Xcalibur 2.2 software (Thermo Fischer Scientific Inc., Waltham, MA,

USA).Optimum separation was performed on a Zorbax SB-C18 inverted column phase (150 mm x 2.1 mm internal diameter; 3,5 µm particle size) (Agilent Technologies, Waldbronn, Germany) under gradient elution conditions using a binary mobile phase composed of 0.1% formic acid (A) and acetonitrile with 0.1% formic acid (B) The following gradient program was used: 0 min, 5% B; 10 min, 18% B; 15 min, 30% B; 25 min, 50%; 28 min, 95% B; 30 min, 95%. The mobile phase flow rate was 0,3 mL/min, and the column temperature was set at 40.0°C. The injection volume is 2,5 µl.

Extraction and purification

All solvents of use are at least analytical grade delivered from Fisher Chemicals (Loughborough, UK). Water for assays was collected from a dispenser via a Milli-Q system from Millipore (Bedford, MA, USA) and filtered through a 0,22 µM membrane filter.

The dried leaves were extracted with 70% MeOH (1:15 w/v) for 30 min under heating (60°C), and the extraction was repeated three times. The obtained extract is lyophilized and stored in a dry and dark place. Purification of the total extract is performed by column chromatography (CC) at atmospheric pressure against Diaion® HP-20 sorbent (Supelco, Japan). For this purpose, 1.0 g of the total leaf extracts of the six *Cecropia* species were applied to Diaion and eluted with increasing percentages of MeOH/H_2O (v/v) mixture, respectively: 30% MeOH, 50% MeOH and 90% MeOH. The resulting fractions are concentrated by a rotary vacuum evaporator.

Sample and standards preparation for LC-MS analysis

Each of the fractions was dissolved in MeOH (100%) and by subsequent dilutions was reached concentration of the samples for analysis between 50-150 µg/mL. Standards of syringic acid (≥ 95%, HPLC, Sigma-Aldrich, China), trans-ferulic acid (≥ 99%, HPLC, Sigma-Aldrich, China), caffeic acid (≥ 98%, HPLC, Sigma-Aldrich, China), rutin (97%, Acros Organics, Belgium), quercetin (≥ 95%, Cayman Chemical Company, USA), p-coumaric acid (≥ 98%, HPLC, Sigma-Aldrich, China), apigenin (≥ 98%, Cayman Chemical Company, USA), kaempferol (≥ 97%, HPLC, Sigma-Aldrich, China), quercetin-3-*O*-*β*-D-glucoside (≥ 90%, HPLC, Sigma-Aldrich, China), myricetin (95%, Acros Organics, Belgium), luteolin (91,7%, HWI pharma services GmbH, Germany), apigenin-7-*O*-*β*-D-glucoside (93,47%, HWI pharma services GmbH, Germany) and rhamnetin (≥ 99%, HPLC, EXTRASYNTHESE, France) were used. The selected standards are phenolic derivatives, main components contained in the research species, according to literature search. To prepare the standard solutions, an accurate amount of each standard between 1.0 and 15.0 mg is dissolved in 50% MeOH. The appropriate dilutions were prepared in 50% MeOH right before the analysis. The calibration models were built based on seven concentration levels, with varying concentrations for the different standards, with two injections for each level (Table No. 2). The regression line, determination coefficient and equation were calculated.

RESULTS AND DISCUSSION

Identification of phenolic derivatives in extracts from six cecropia species

After LC-HRESI-MS analysis, eight out of fourteen investigated standards (flavonoids and phenolic acids) were detected in extracts of *C. insignis*, *C. longipes*, *C. obtusifolia*, *C. peltata*, *C. hispidissima* and *C. heterochromata*. By comparing the retention time and the observed spectrum with that of the standard of the corresponding compound, it can be concluded that the observed metabolite is identical to the standard. In LC-HRESI-MS analysis of fractions from *C. insignis*, *C. peltata*, *C. hispidissima* and *C. heterochroma* a deprotonated molecular ion $[M-H]^-$ with *m/z* 179,0342, with molecular formula $C_9H_7O_4$ and retention time R*t* 6,70 min was observed. Due to the similarity of the observed spectrum with that of the standard and identical retention time, we can identify the metabolite as caffeic acid (Figure No. S1). During LC-HRESI-MS analysis of fractions from *C. insignis*, *C. hispidissima*, *C. heterochroma* a deprotonated molecular ion $[M-H]^-$ with *m/z* 609,1472, wituh molecular formula $C_{27}H_{29}O_{16}$ and retention time Rt 11,49 min was observed. Due to the similarity of the observed spectrum with that of the standard and identical retention time, we can identify the metabolite as rutin (Figure No. S2). The LC-HRESI-MS analysis of *C. longipes* fractions revealed deprotonated molecular ions $[M-H]^-$ with *m/z* 301,0356 ($C_{15}H_9O_7$, Rt 15.88 min) and *m/z* 285,0408 ($C_{15}H_9O_6$, Rt 15.97 min). The close alignment of the observed spectra with those of the standards, coupled

with identical retention times, enabled us to confidently identify these metabolites as quercetin and kaempferol, respectively (Figures No. S3 & No. S4). Within the fractions of *C. insignis*, *C. longipes*, *C. obtusifolia*, *C. peltata* and *C. hispidissima* were observed also some glycoside. The close match of the spectra between the observed deprotonated molecular ions $[M-H]^-$ with *m/z* 463,0891 ($C_{21}H_{19}O_{12}$, Rt 11,85 min) and *m/z* 431,0988 ($C_{21}H_{19}O_{10}$, Rt 13,25 min) and those of the standards, along with the identical retention times, allowed us to confidently identify these metabolites as quercetin-3-*O*-*β*-D-glucoside and apigenin-7-*O*-*β*-D-glucoside, respectively (Figures No. S5 & No. S6). Additionally, the analysis of the same fractions detected a deprotonated molecular ion $[M-H]^-$ with *m/z* 447,0938 ($C_{21}H_{19}O_{11}$, Rt 10,18 min), which, based on its spectrum and retention time, was identified as orientin (Figure No. S7). Only in the fractions from *C. insignis* was observed a deprotonated molecular ion $[M-H]^-$ with *m/z* 285,04071, with molecular formula $C_{15}H_9O_6$ and retention time Rt 18,07 min, which due to the similarity with the spectrum of the standard and identical retention time is identify as luteolin (Figure No. S8).

Calibration models

The calibration models for all standards were assessed by examining the regression line, the corresponding equation, and the determination coefficient. The calibration curves for those standards were linear across the different concentration levels (0,01-2,04 µg/mL). Each curve demonstrated excellent linearity, with correlation coefficients greater than 0,99 (as shown in Table No. 2 and Figure No. S9-22).

Table No. 2
Determination coefficient, regression equations, linear range and retention time of all standards

	Determination coefficient r^2	Linear range (µg/mL)	Regression equations	Number of levels	R*t* (min)
Syringic acid	0,9911	0,02-1,18	y = 6E+06x - 252482	7	7,36
Trans-Ferulic acid	0,9970	0,02-1,11	y = 6E+07x - 886946	7	10,57
Caffeic acid	0,9999	0,02-0,82	y = 4E+08x - 2E+06	7	6,70
Rutin	0,9994	0,02-1,02	y = 9E+07x - 1E+06	7	11,49
Quercetin	0,9964	0,02-0,81	y = 4E+08x - 2E+07	7	15,88
p-Coumaric acid	0,9997	0,02-1,20	y = 2E+08x - 298998	7	9,24
Apigenin	0,9984	0,02-0,98	y = 2E+08x - 4E+06	7	17,87
Kaempferol	0,9977	0,04-2,04	y = 4E+08x - 824127	7	15,97
Quercetin-3-*O*-*β*-D-glucoside	0,9977	0,03-1,73	y = 5E+08x - 824127	7	11,85
Myricetin	0,9861	0,03-1,52	y = 3E+08x - 3E+07	7	13,57
Luteolin	0,9997	0,02-0,94	y = 1E+09x - 2E+07	7	18,07
Apigenin-7-*O*-*β*-D-glucoside	0,9996	0,03-1,40	y = 2E+08x + 975911	7	13,25
Rhamnetin	0,9947	0,01-0,42	y = 2E+09x - 2E+07	7	20,26
Orientin	0,9947	0,01-0,67	y = 2E+09x - 2E+07	7	10,18

Quantification of phenolic derivatives in extracts from six Cecropia species

The amounts of identified compounds were calculated based on the area of the peaks in the respective extracts and the built calibration models (Table No. 3 & Figure No. 1).

CONCLUSION

The identification of phenolic derivatives in extracts from six *Cecropia* species, *C. insignis*, *C. longipes*,

C. obtusifolia, *C. peltata*, *C. hispidissima*, and *C. heterochroma*, was achieved through LC-HRESI-MS analysis. Out of the fourteen standards investigated, seven flavonoids and one phenolic acid were successfully detected, among which rutin, quercetin-3-*O*-*β*-D-glucoside, and apigenin-7-*O*-*β*-D-glucoside as the primary flavonoids in six *Cecropia* species, with notable concentrations in *C. hispidissima*, *C. obtusifolia*, and *C. longipes*. Rutin, which content significantly exceeded all other flavonoids and particularly abundant in *C. hispidissima*, is well-documented for its anti-inflammatory and antioxidant activities, properties that align with traditional uses of *Cecropia* for inflammatory and metabolic disorders, as described in existing literature (Andrade-Cetto & Wiedenfeld, 2001; Rivera-Mondragón *et al*., 2021). The use of *Cecropia* species, especially *C. obtusifolia*, in managing diabetes is supported by our results which describe quercetin-3-*O*-*β*-D-glucoside as another dominant flavonoid, known to modulate glucose metabolism and exhibit hypoglycemic effects, supporting (Andrade-Cetto & Heinrich, 2005). The other significant component in *C. longipes* and *C. peltata*, apigenin-7-*O*-*β*-D-glucoside, contributes to anti-anxiety and anti-inflammatory effects, as seen in other plant-based studies, aligning with *Cecropia*'s use in respiratory and mood disorders. These findings contribute to a better understanding of the phenolic content in *Cecropia* species and their potential biological significance targeting oxidative stress, inflammation, and glucose regulation. Furthermore, this research could guide the selection of *Cecropia* species for more targeted and detailed phytochemical investigations.

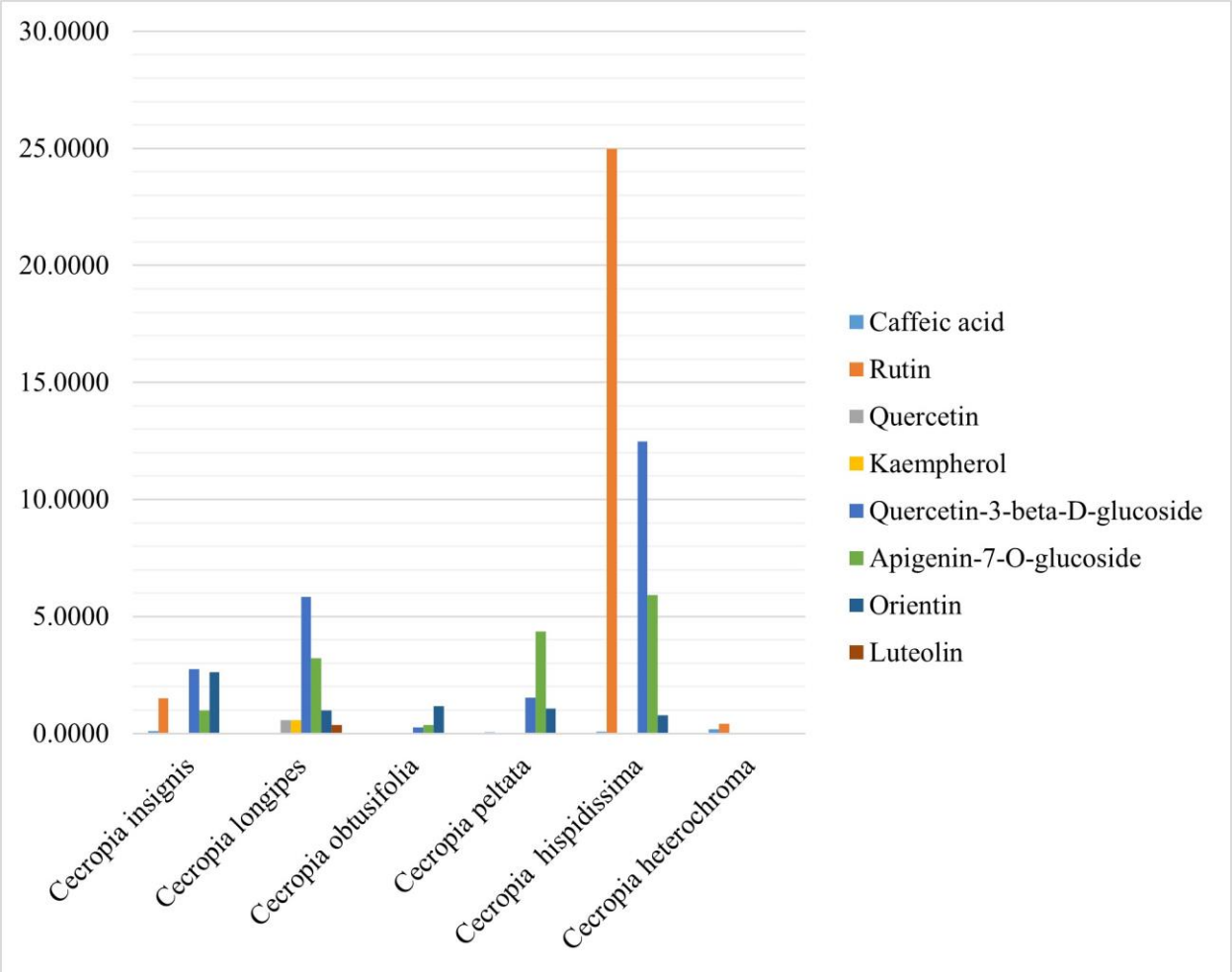

Figure No. 1
Identified phenolic derivatives in six *Cecropia* species

Table No. 3
Amounts of phenolic derivatives (µg/mg) in extracts from six *Cecropia* species

Standard	*C. insignis*	*C. longipes*	*C. obtusifolia*	*C. peltata*	*C. hispidissima*	*C. heterochroma*
Caffeic acid	0,0994	0,0000	0,0000	0,0595	0,0751	0,1756
Rutin	1,4965	0,0000	0,0000	0,0000	24,9794	0,4175
Quercetin	0,0000	0,5752	0,0000	0,0000	0,0000	0,0000
Kaempferol	0,0000	0,5822	0,0000	0,0000	0,0000	0,0000
Quercetin-3-*β*-D-glucoside	2,7489	5,8430	0,2491	1,5372	12,4762	0,0000
Apigenin-7-*O*-glucoside	0,9839	3,2180	0,3664	4,3578	5,9200	0,0000
Orientin	2,6207	0,9741	1,1747	1,0742	0,7896	0,0000
Luteolin	0,0000	0,3722	0,0000	0,0000	0,0000	0,0000

CONFLICT OF INTEREST
No potential conflict of interest.

FINANCIAL SUPPORT
This study is financed by The Council of Medicinal Science at the Medical University of Sofia, contract № D-202/03.08.2023 is acknowledged.

ACKNOWLEDGEMENTS
Thanks, are also due to the incentive program of the National Investigation System (SNI) of the Republic of Panama for supporting A. Rivera-Mondragón.

REFERENCES

Andrade-Cetto A, Heinrich M. 2005. Mexican plants with hypoglycaemic effect used in the treatment of diabetes. **J Ethnopharmacol** 99: 325 - 348. **https://doi.org/10.1016/j.jep.2005.04.019**

Andrade-Cetto A, Vázquez RC. 2010. Gluconeogenesis inhibition and phytochemical composition of two *Cecropia* species. **J Ethnopharmacol** 130: 93 - 97. **https://doi.org/10.1016/j.jep.2010.04.016**

Andrade-Cetto A, Wiedenfeld H. 2001. Hypoglycemic effect of *Cecropia obtusifolia* on streptozotocin diabetic rats. **J Ethnopharmacol** 78: 145 - 149. **https://doi.org/10.1016/S0378-8741(01)00335-X**

Aragão DMO, Guarize L, Lanini J, da Costa JC, Garcia RMG, Scio E. 2010. Hypoglycemic effects of *Cecropia pachystachya* in normal and alloxan-induced diabetic rats. **J Ethnopharmacol** 128: 629 - 633. **https://doi.org/10.1016/j.jep.2010.01.008**

Costa GM, Schenkel EP, Reginatto FH. 2011. Chemical and pharmacological aspects of the genus *Cecropia*. **Nat Prod Commun** 6: 1934578X1100600. **https://doi.org/10.1177/1934578X1100600637**

Da Silva Mathias M, Rodrigues De Oliveira R 2019. Differentiation of the phenolic chemical profiles of *Cecropia pachystachya* and *Cecropia hololeuca*. **Phytochem Anal** 30: 73 - 82. **https://doi.org/10.1002/pca.2791**

Enchev P, Zarev Y, Dakovska A, Rivera-Mondragón A, Kozuharova E, Ionkova I. 2024. Terpenes from *Cecropia* species and their pharmacological potential. **Pharmaceuticals** 17: 399. **https://doi.org/10.3390/ph17030399**

Ortmann CF, Abelaira HM, Réus GZ, Ignácio ZM, Chaves VC, Santos TC, Carvalho P, Carlessi AS, Bruchchen L, Danielski LG, Cardoso SG, Campos AM, Petronilho F, Rebelo J, Morais MOS, Vuolo F, Dal-Pizzol F, Streck EL, Quevedo J, Reginatto FH. 2017. LC/QTOF profile and preliminary stability studies of an enriched flavonoid fraction of *Cecropia pachystachya* Trécul leaves with potential antidepressant-like activity. **Biomed Chromatography** 31: e3982. **https://doi.org/10.1002/bmc.3982**

Pérez-Guerrero C, Herrera MD, Ortiz R, Alvarez de Sotomayor M, Fernández MA. 2001. A pharmacological study of *Cecropia obtusifolia* Bertol aqueous extract. **J Ethnopharmacol** 76: 279 - 284. **https://doi.org/10.1016/S0378-8741(01)00253-7**

Ramos Almeida R, Montani Raimundo J, Rodrigues Oliveira R, Coelho Kaplan MA, Rocah Gattass C, Takashi Sudo R, Zapata-Sudo G. 2006. Activity of *Cecropia lyratiloba* extract on contractility of cardiac and

smooth muscles in Wistar rats. **Clin Exp Pharm Physiol** 33: 109 - 113. **https://doi.org/10.1111/j.1440-1681.2006.04332.x**

Revilla-Monsalve MC, Andrade-Cetto A, Palomino-Garibay MA, Wiedenfeld H, Islas-Andrade S. 2007. Hypoglycemic effect of *Cecropia obtusifolia* Bertol aqueous extracts on type 2 diabetic patients. **J Ethnopharmacol** 111: 636 - 640. **https://doi.org/10.1016/j.jep.2007.01.014**

Rivera-Mondragón A, Bijttebier S, Tuenter E, Custers D, Ortíz OO, Pieters L, Caballero-George C, Apers S, Foubert K. 2019. Phytochemical characterization and comparative studies of four *Cecropia* species collected in Panama using multivariate data analysis. **Sci Rep** 9: 1763. **https://doi.org/10.1038/s41598-018-38334-4**

Rivera-Mondragón A, Ortíz OO, Gupta MP, Caballero-George C. 2021. Pharmacogenetic evaluation of ten species of medicinal importance of *Cecropia*: Current knowledge and therapeutic perspectives. **Planta Med** 87: 764 - 779. **https://doi.org/10.1055/a-1495-9785**

SUPPLEMENTARY MATERIAL

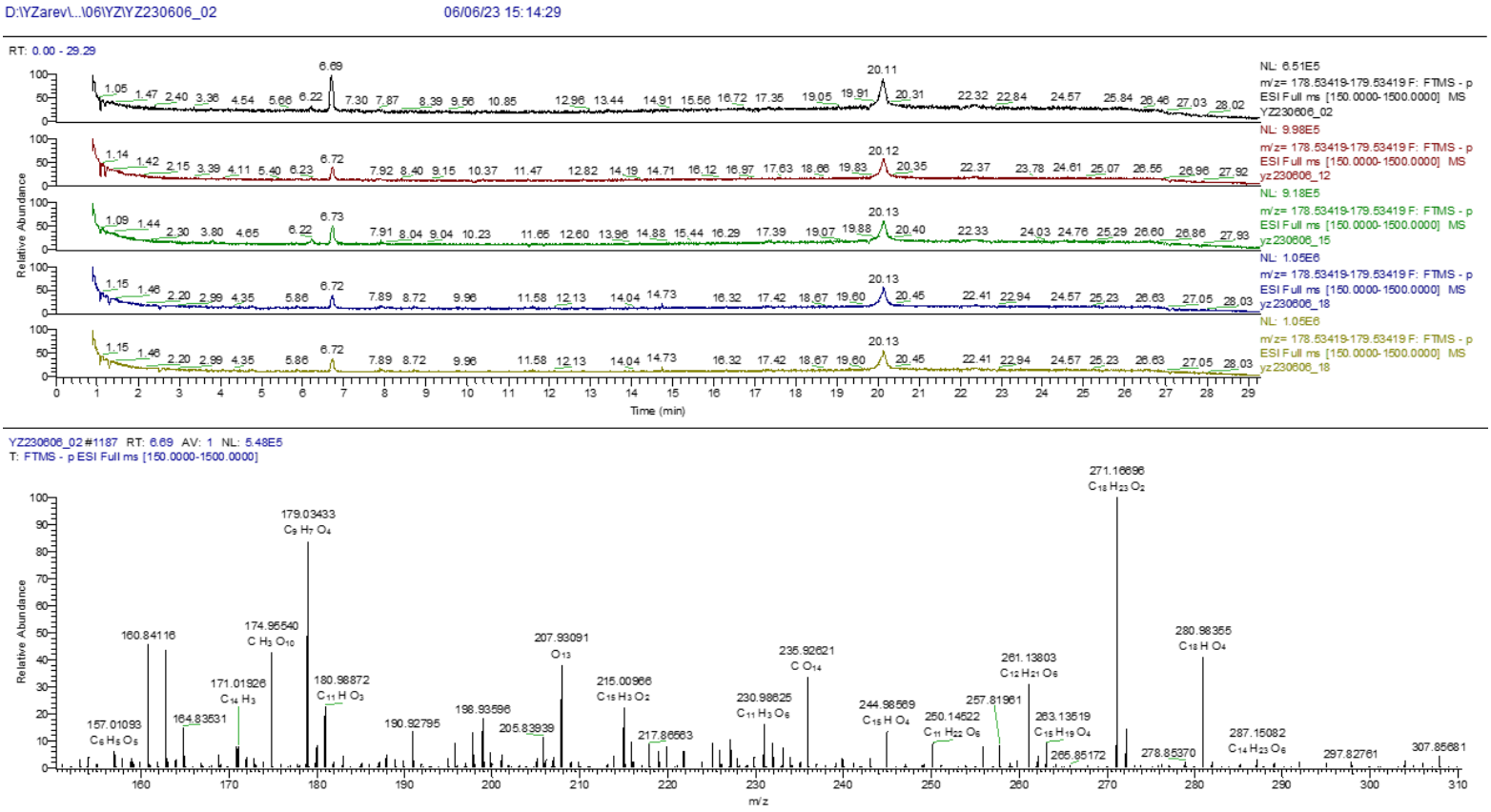

Figure No. S1
LC/MS spectra of caffeic acid in extracts from *C. insignis, C. peltata, C. hispidissima, C. heterochroma*

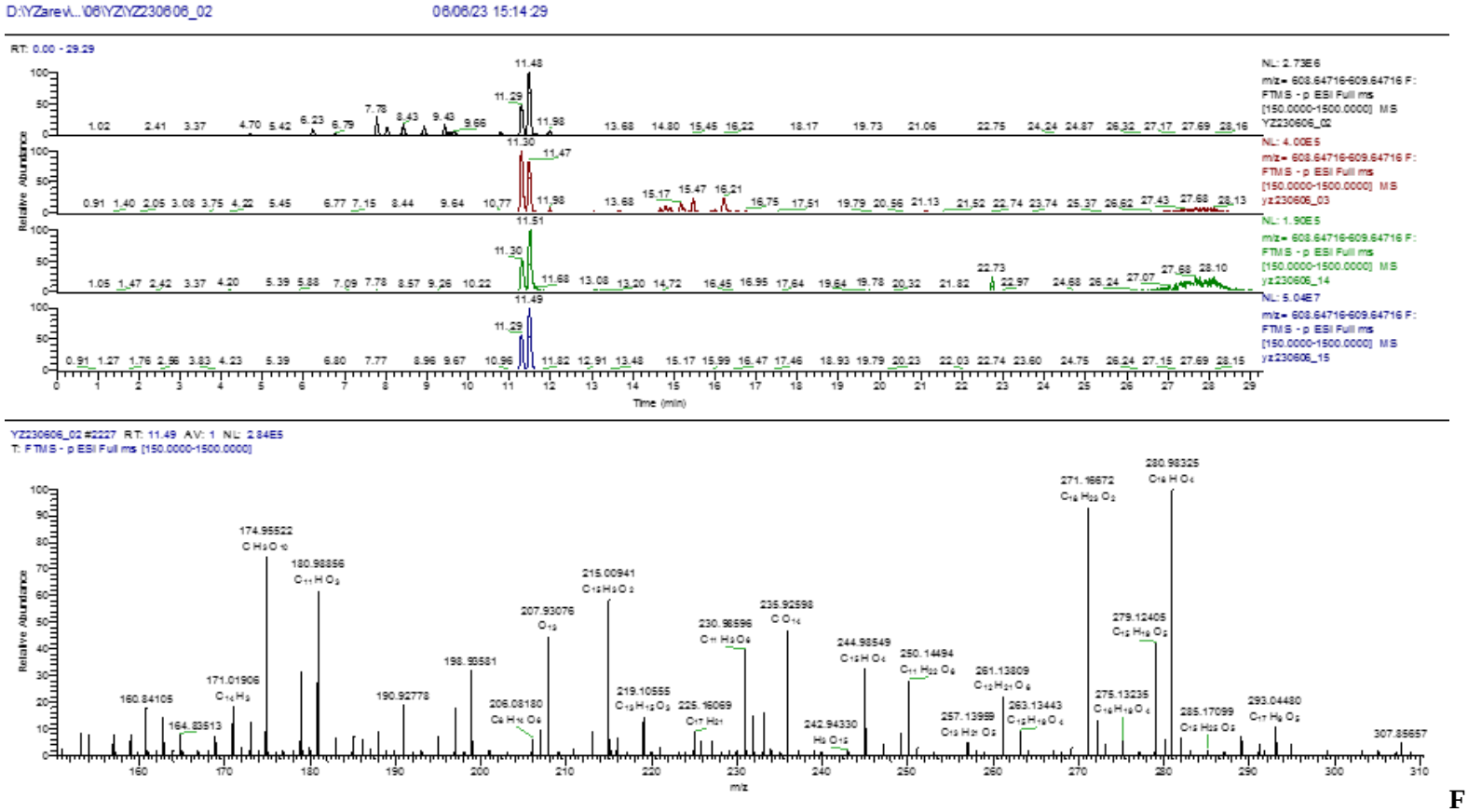

Figure No. S2
LC/MS spectra of rutin in extracts from *C. insignis, C. hispidissima, C. heterochroma*

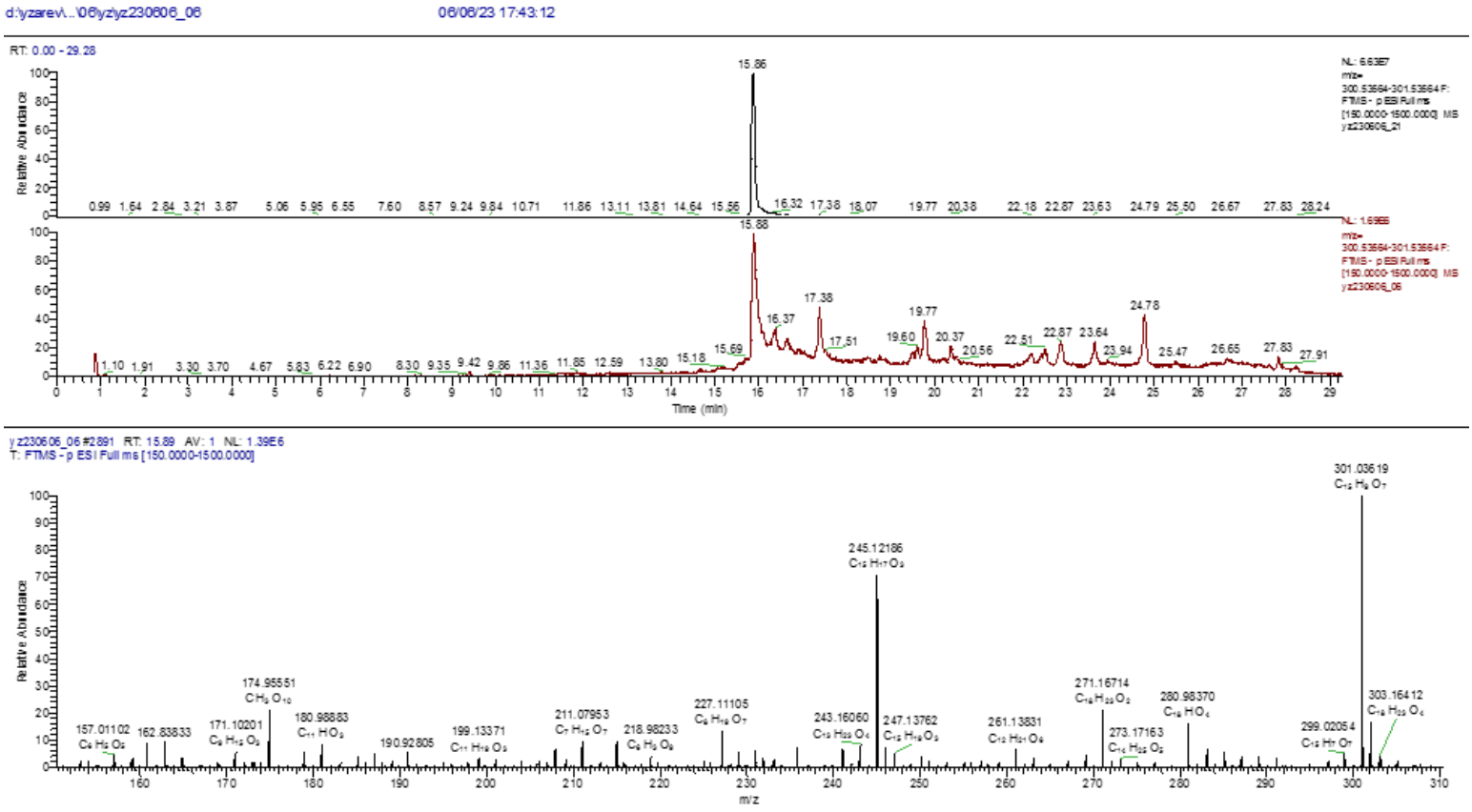

Figure No. S3
LC/MS spectra of quercetin in extract from *C. longipes*.

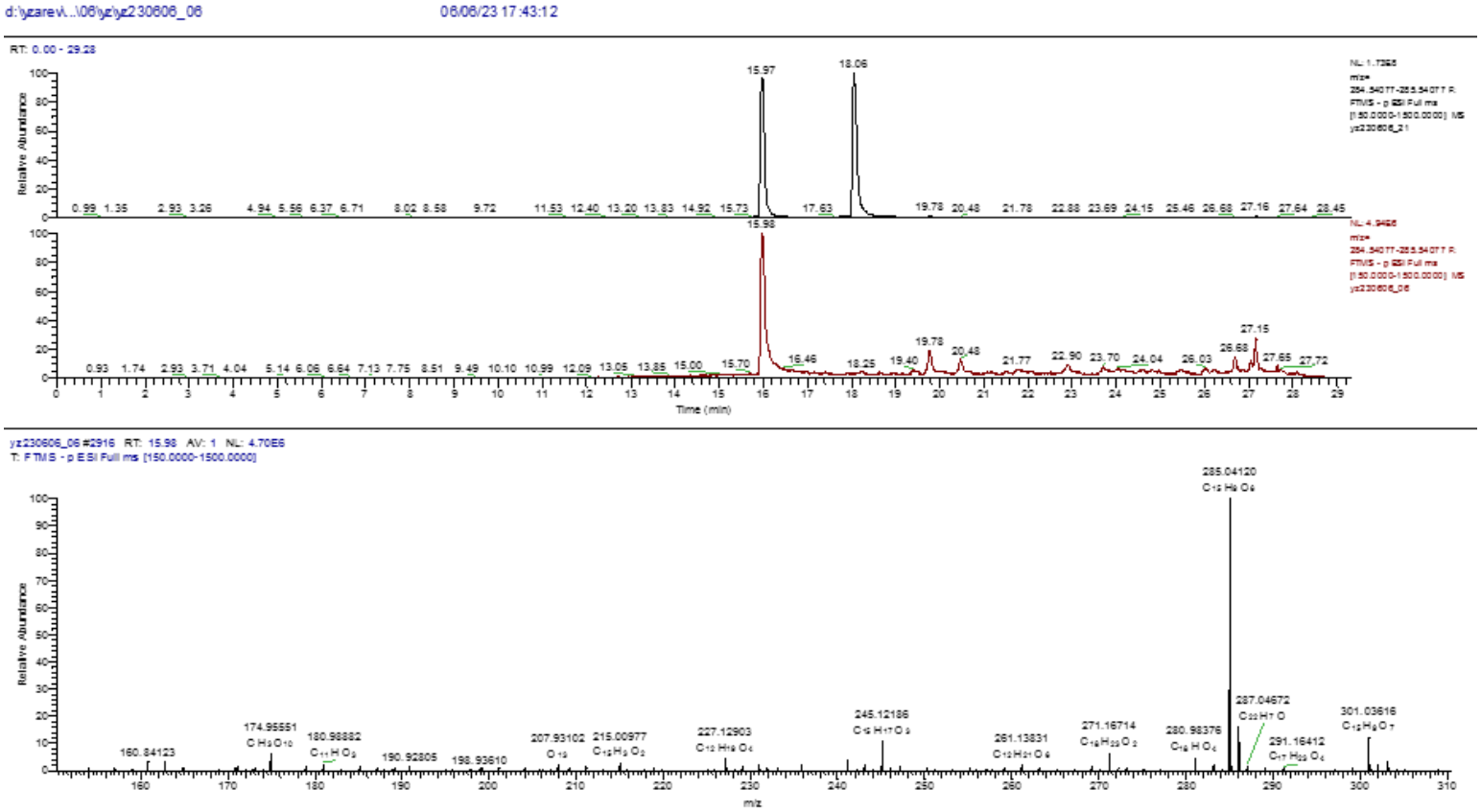

Figure No. S4
LC/MS spectra of kaempferol in extract from *C. longipes*

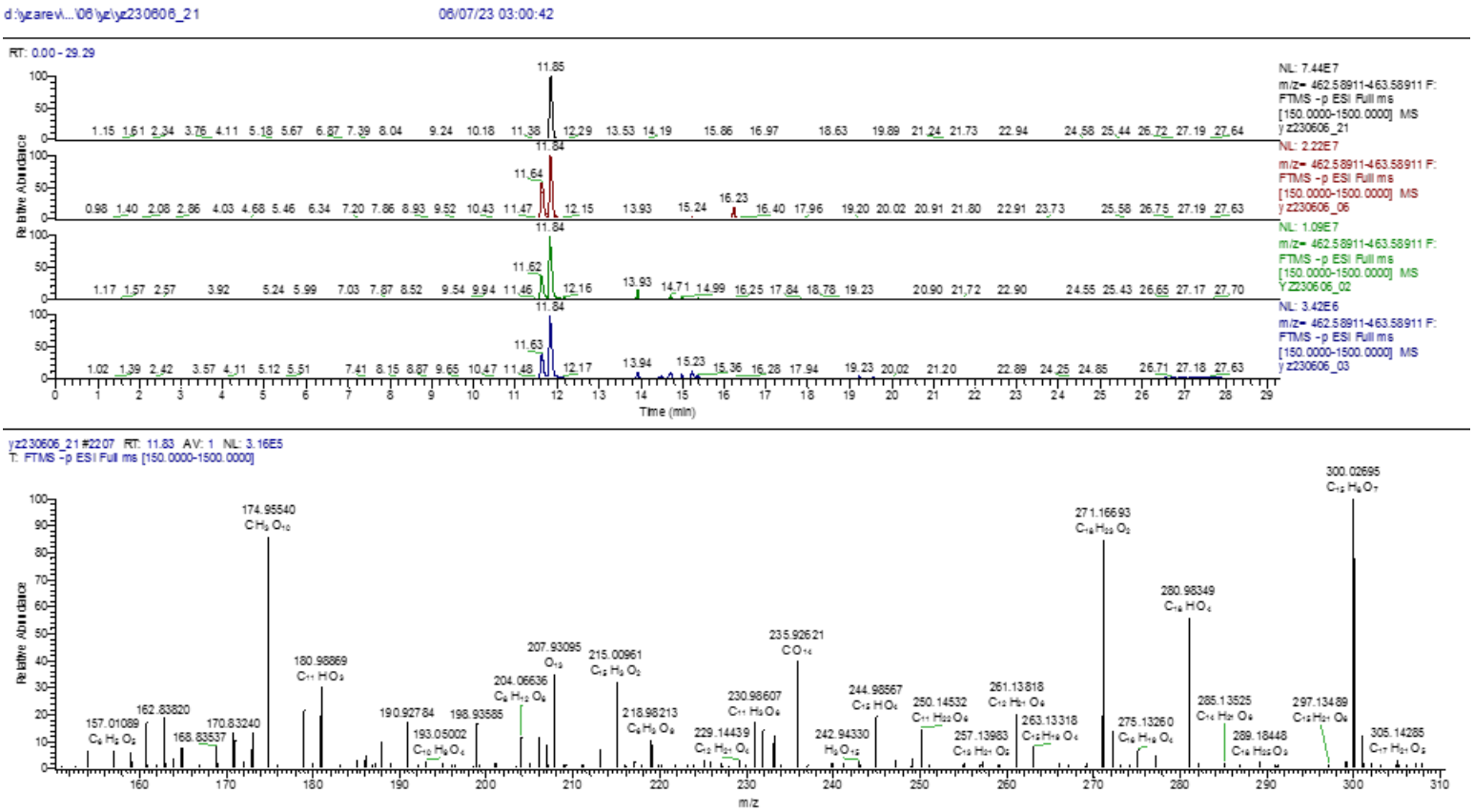

Figure No. S5.1
LC/MS spectra of quercetin-3-*O*-*β*-D-glucoside in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*

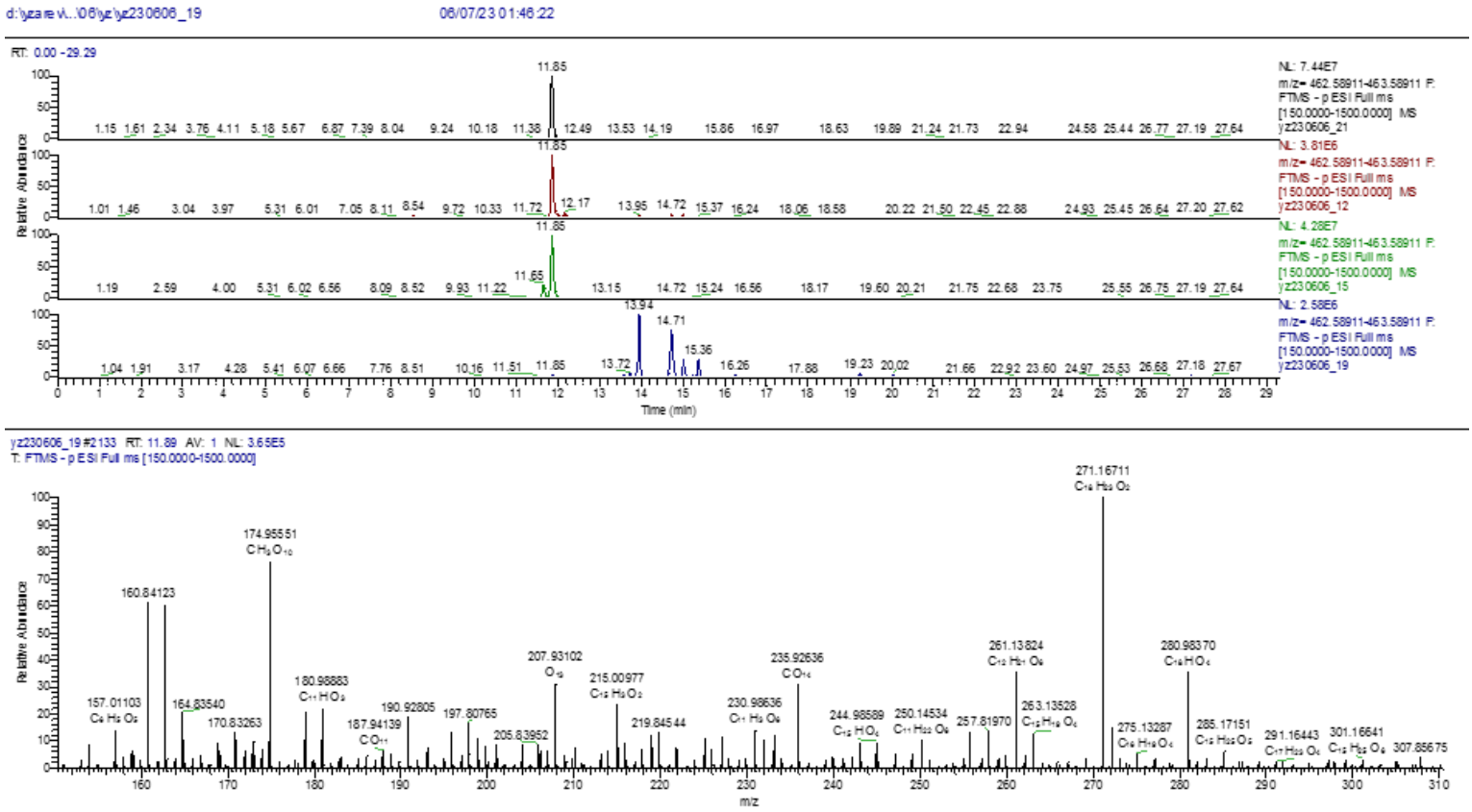

Figure No. 5.2
LC/MS spectra of quercetin-3-*O*-*β*-D-glucoside in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*

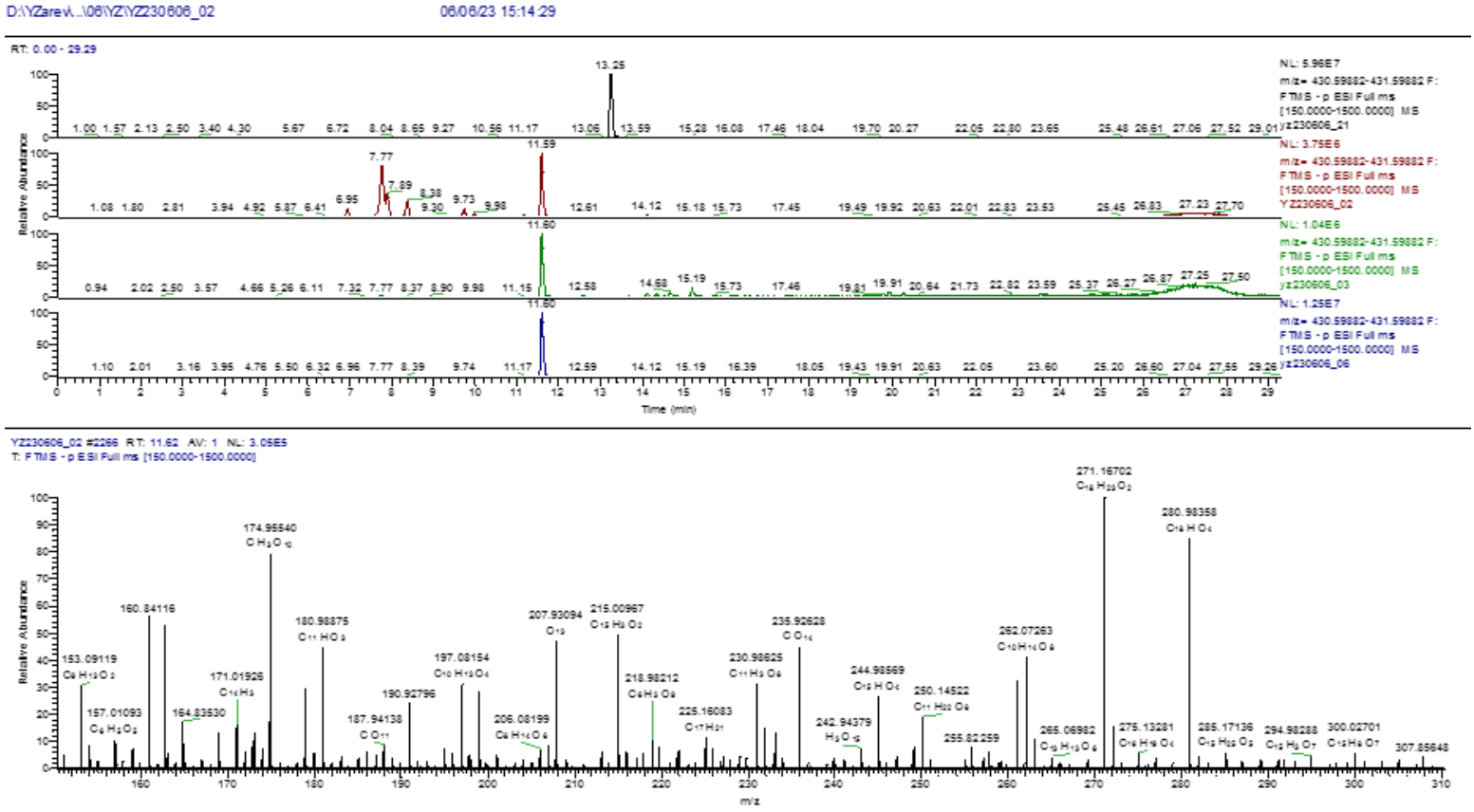

Figure No. 6.1
LC/MS spectra of apigenin-7-*O*-*β*-D-glucoside in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*

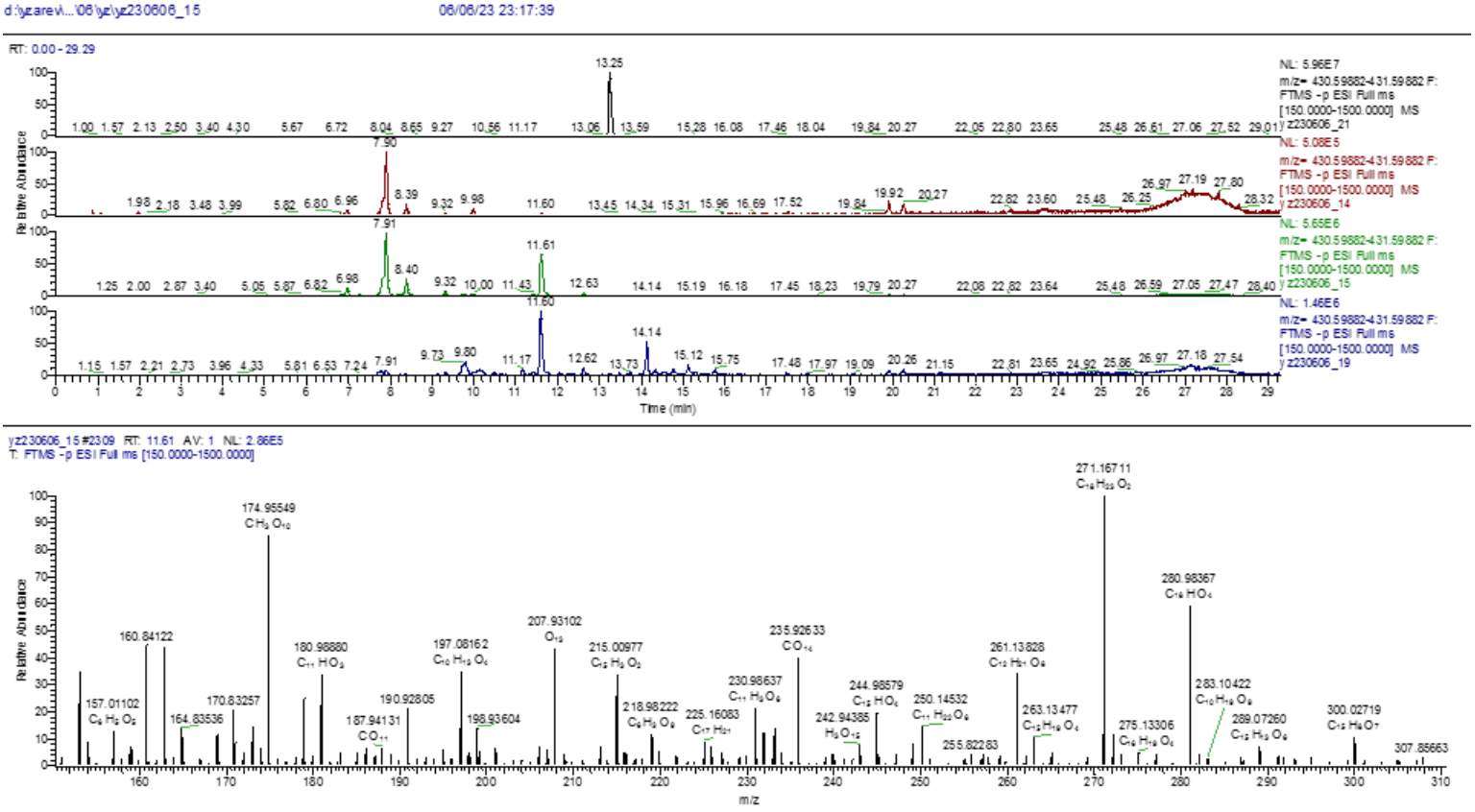

Figure No. 6.2
LC/MS spectra of apigenin-7-*O*-*β*-D-glucoside in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*.

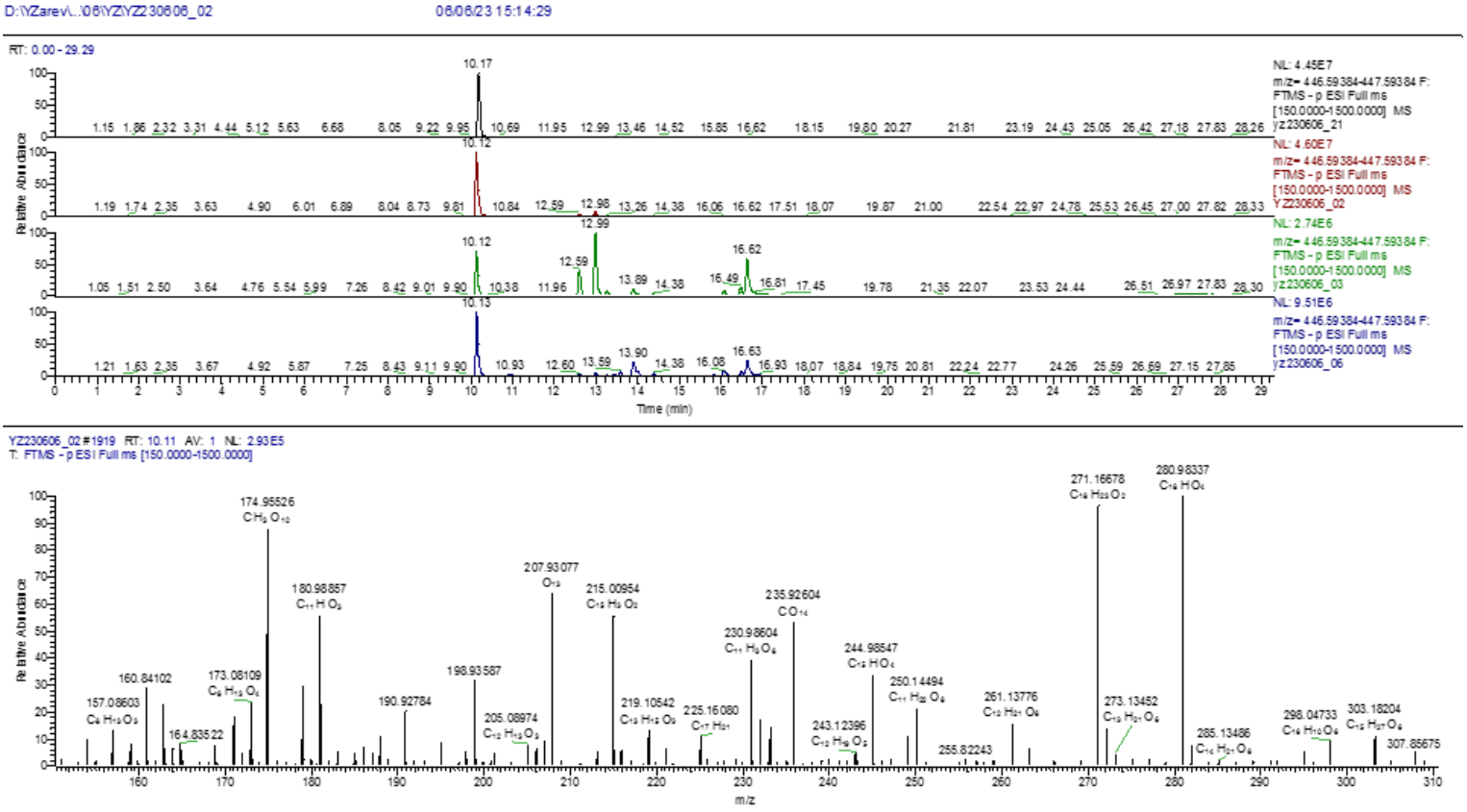

Figure No. S7.1

LC/MS spectra of orientin in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*.

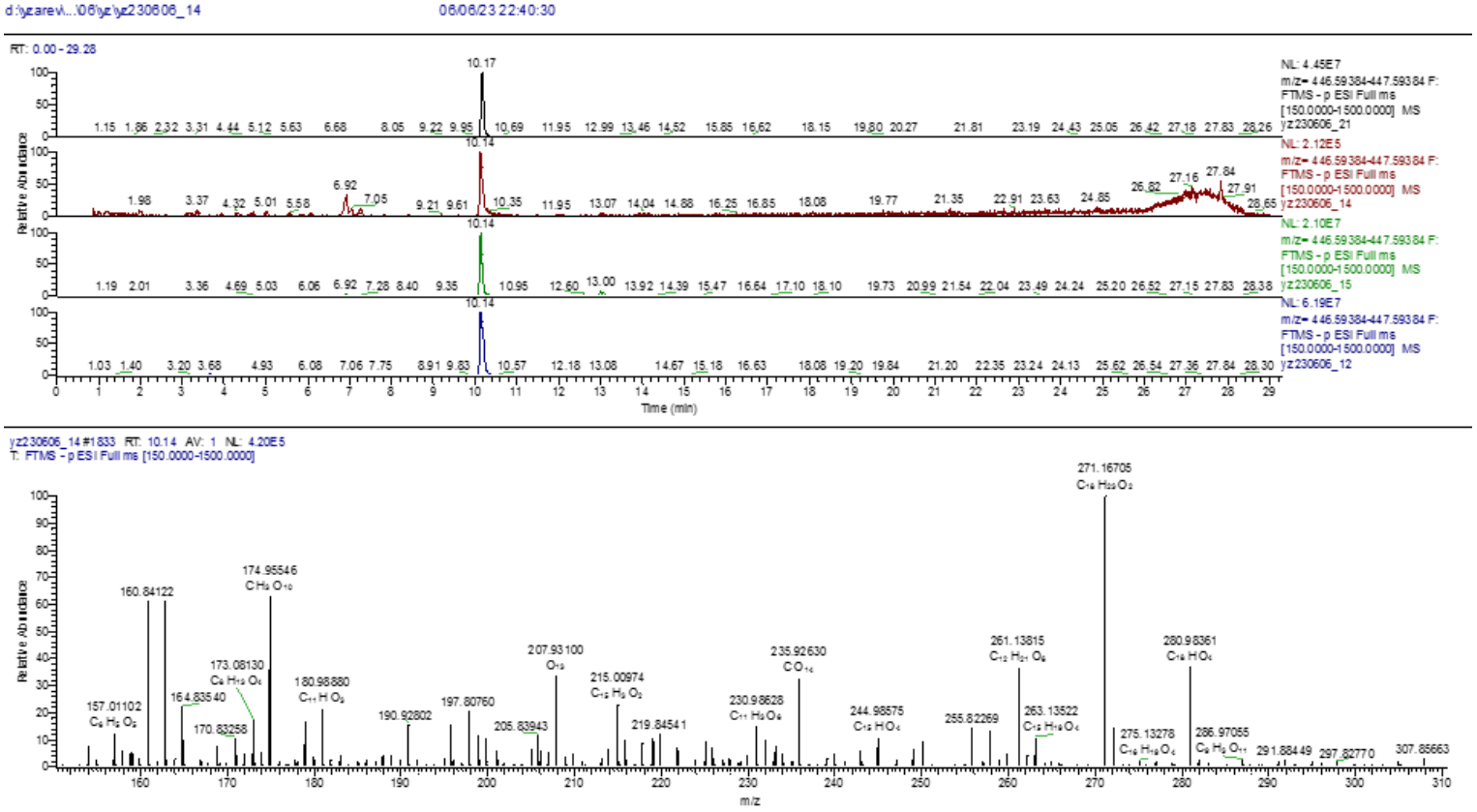

Figure No. 7.2
LC/MS spectra of orientin in extracts from *C. insignis, C. longipes, C. obtusifolia, C. peltata, C. hispidissima*

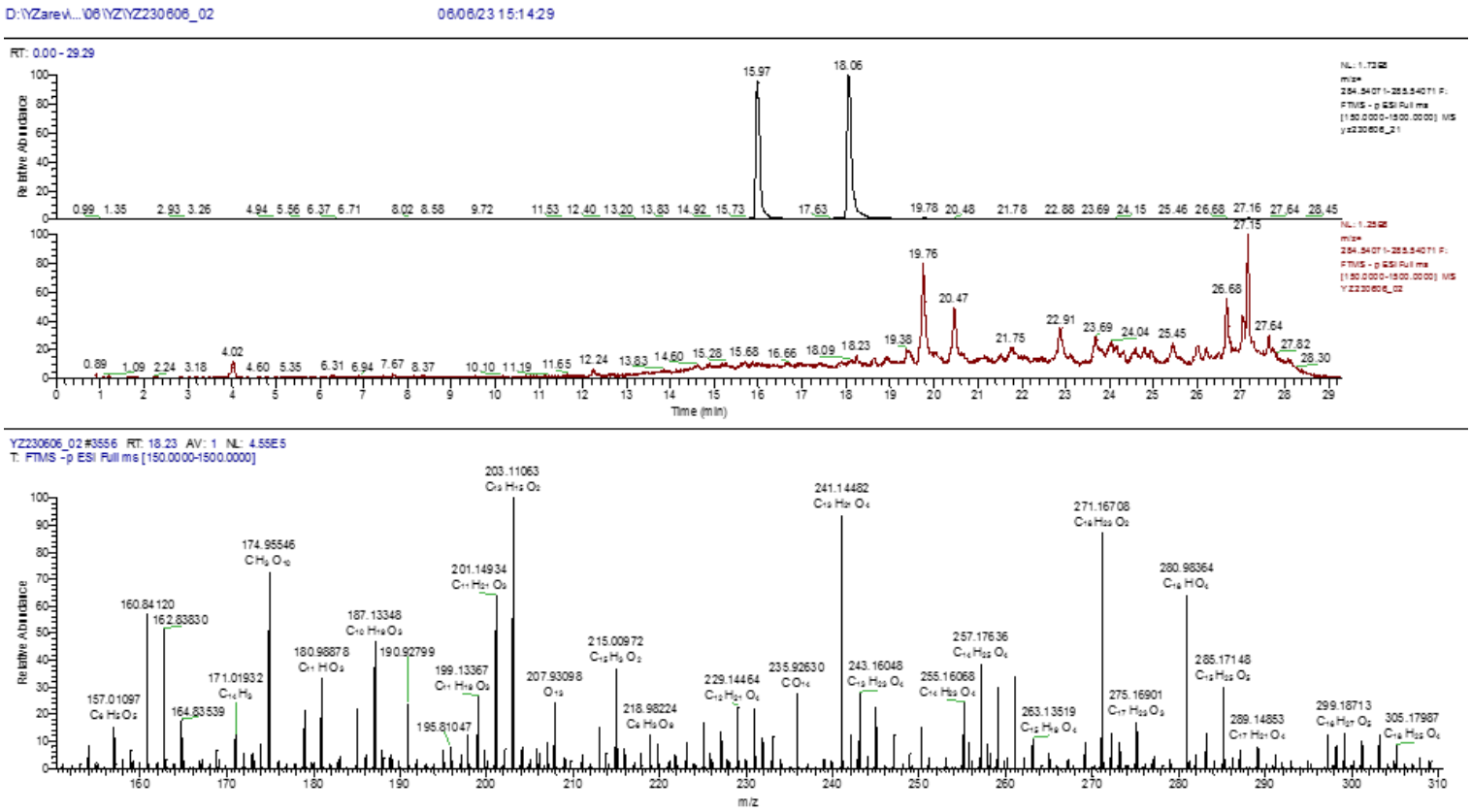

Figure No. S8
LC/MS spectra of luteolin in extract from *C. longipes*.

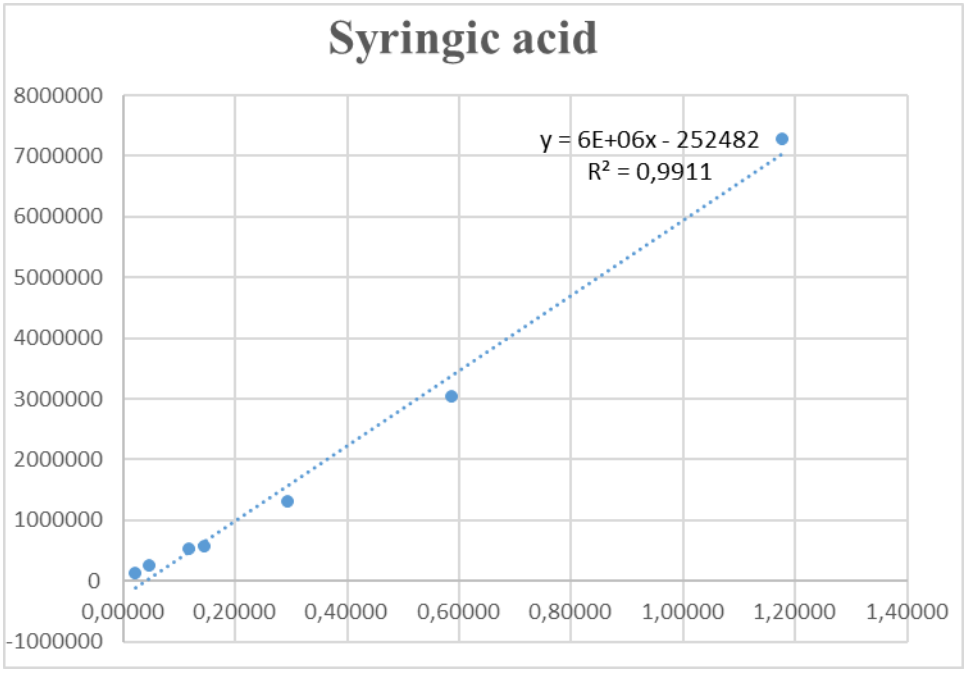

Figure No. S9
Calibration curve of syringic acid

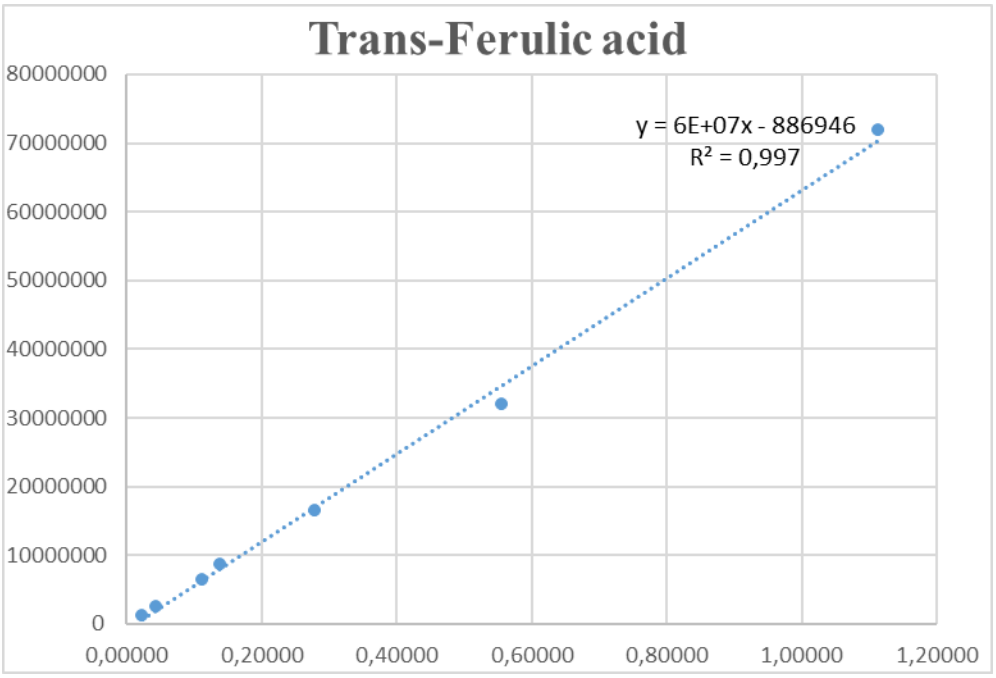

Figure No. S10
Calibration curve of trans-ferulic acid

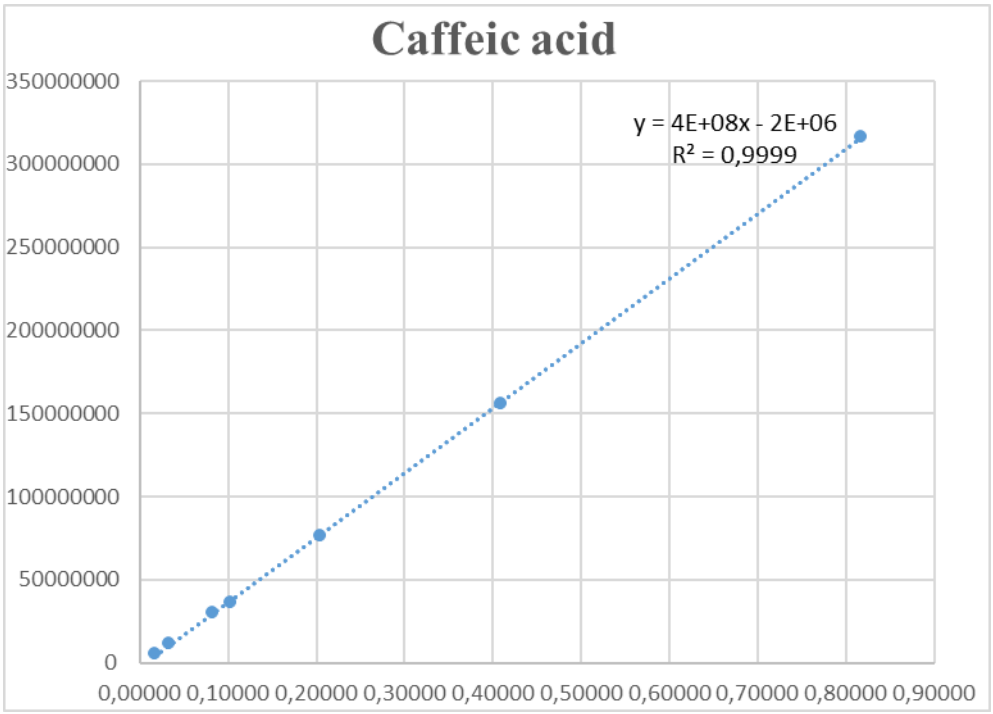

Figure No. S11
Calibration curve of caffeic acid

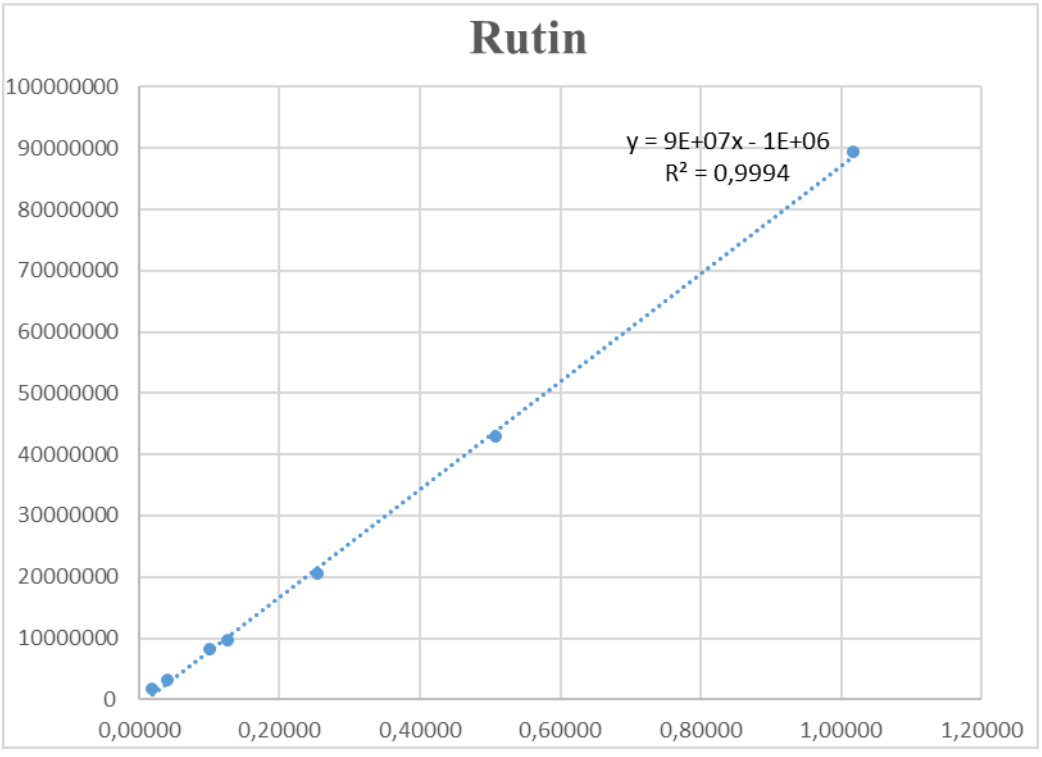

Figure No. S12
Calibration curve of routine

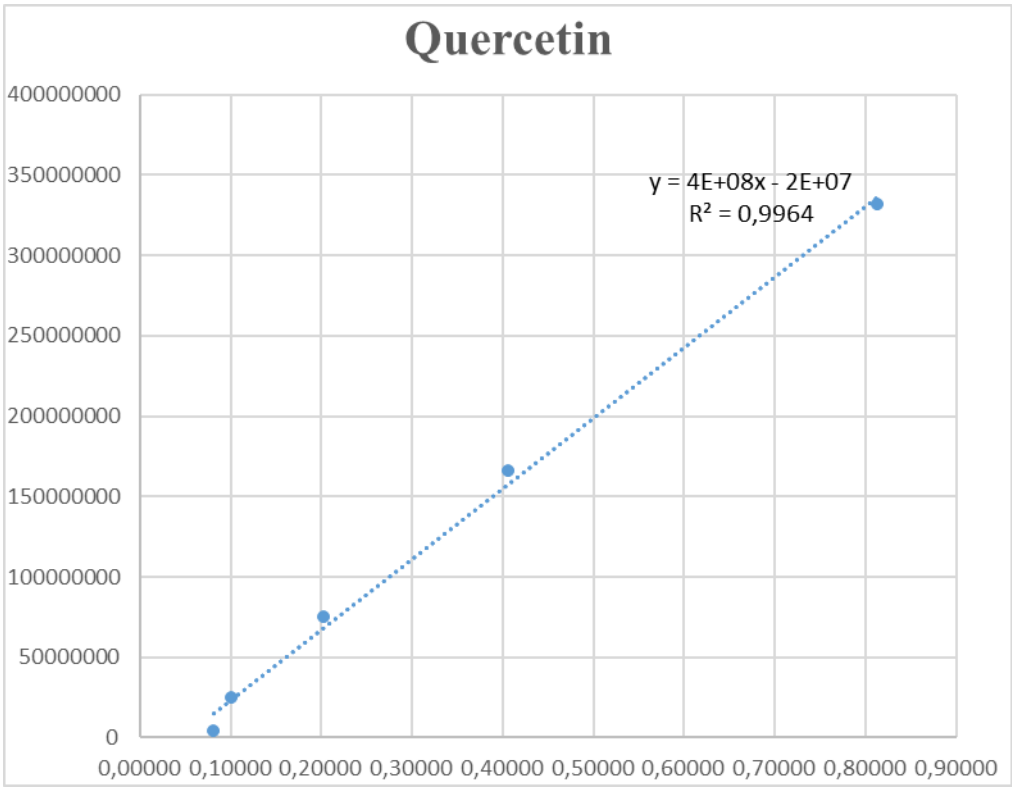

Figure No. S13
Quercetin calibration curve

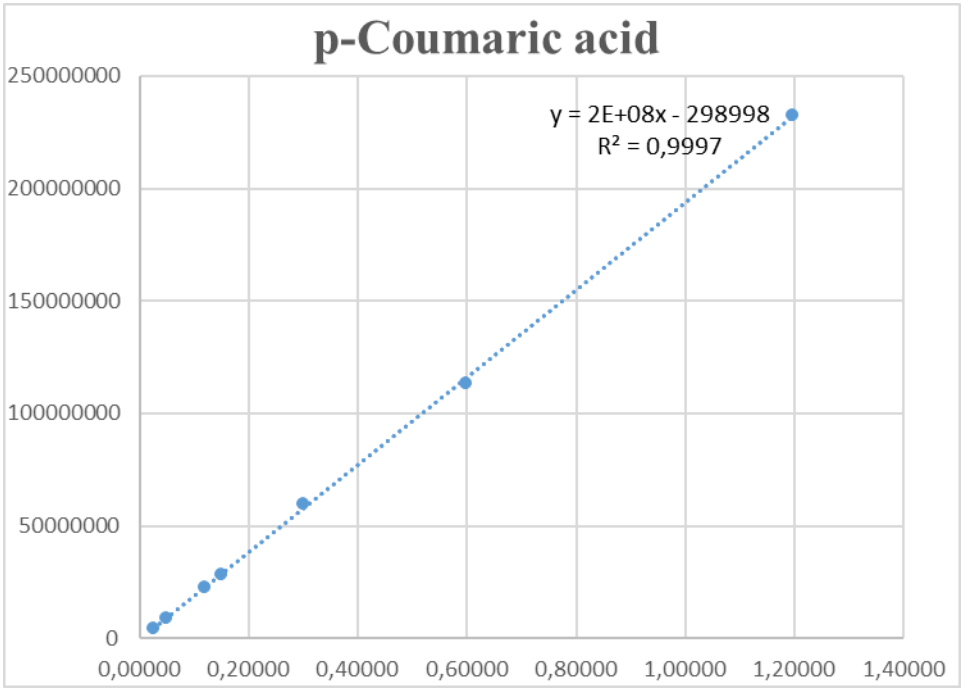

Figure No. S14
Calibration curve of para-coumaric acid

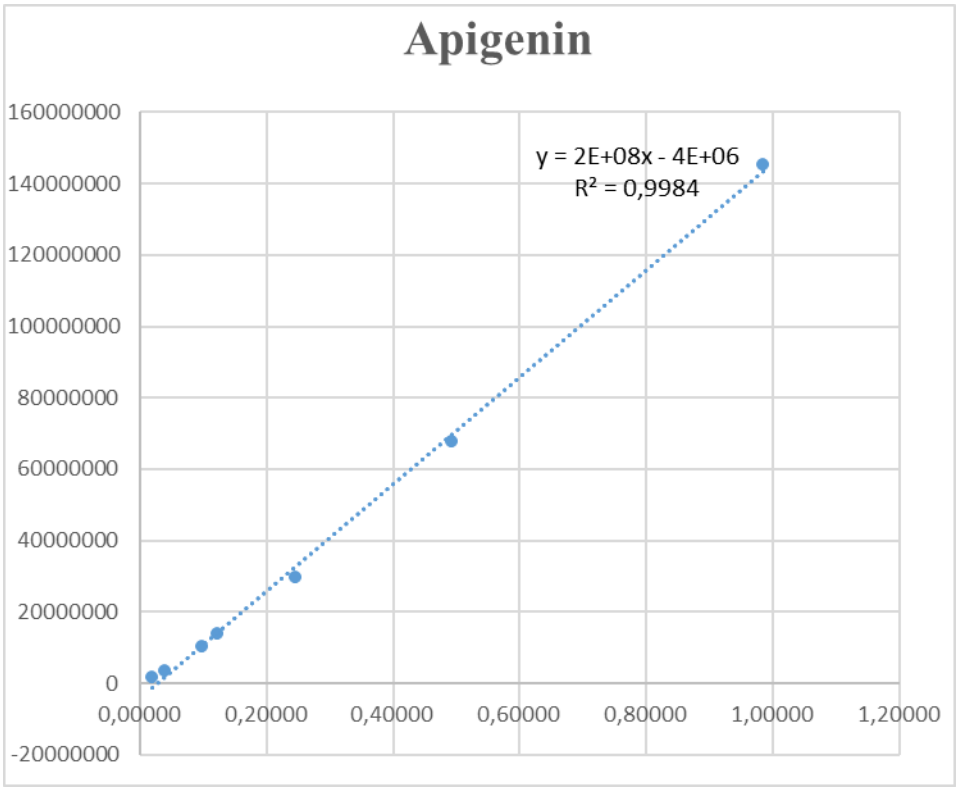

Figure No. S15
Apigenin calibration curve

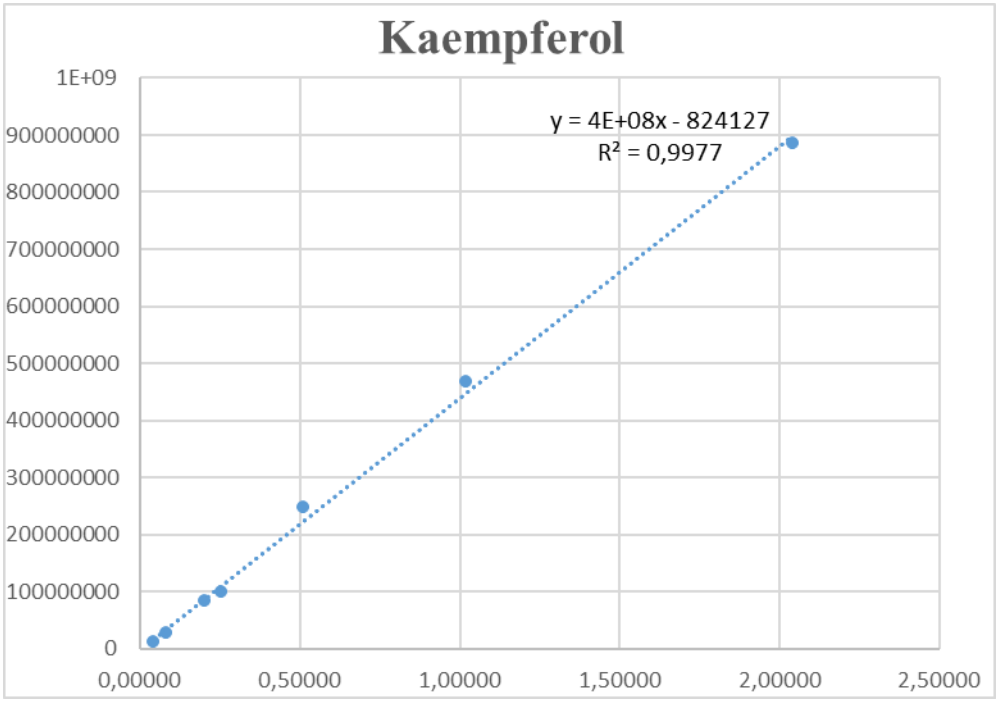

Figure No. S16
Kaempferol calibration curve

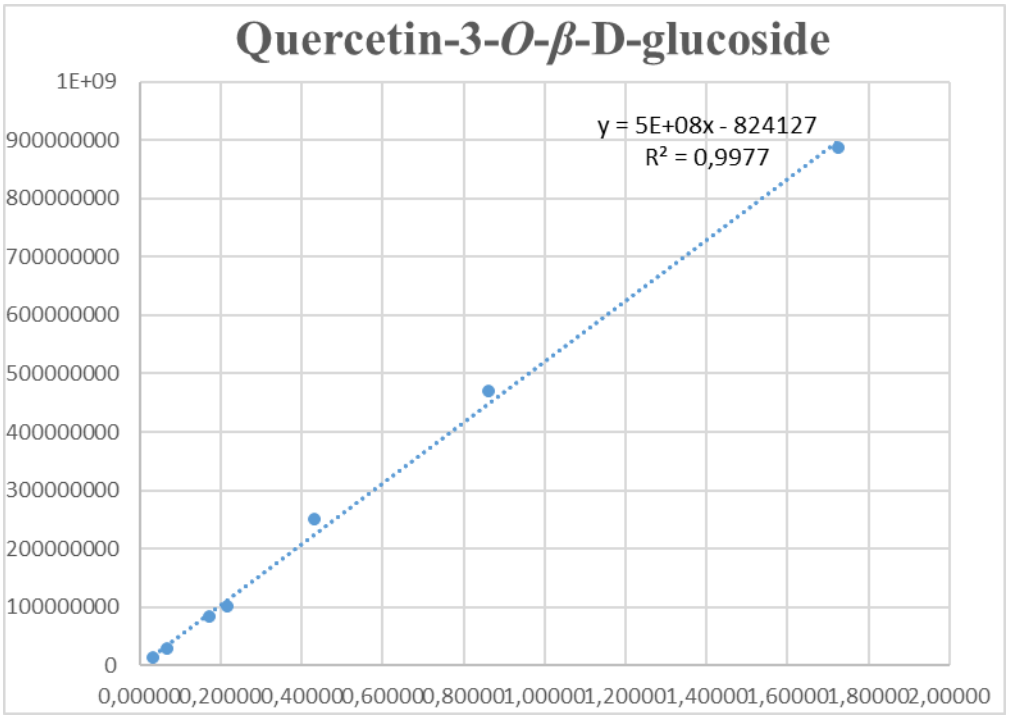

Figure No. S17
Calibration curve of quercetin-3-*O*-*β*-D-glucoside

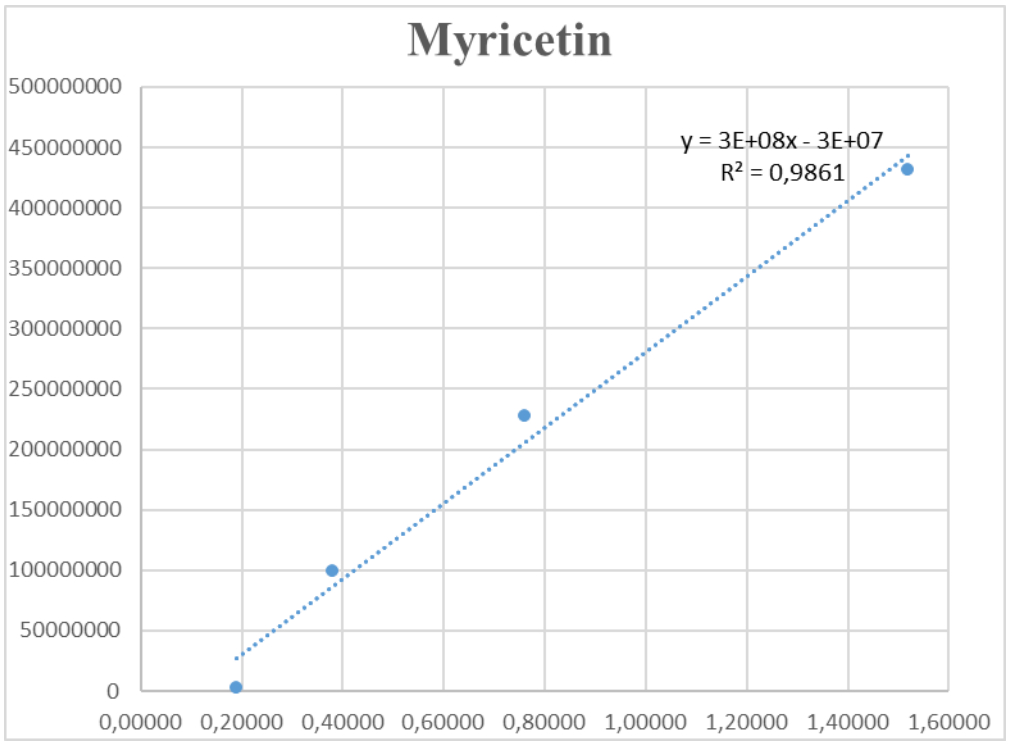

Figure No. S18
Calibration curve of myricetin

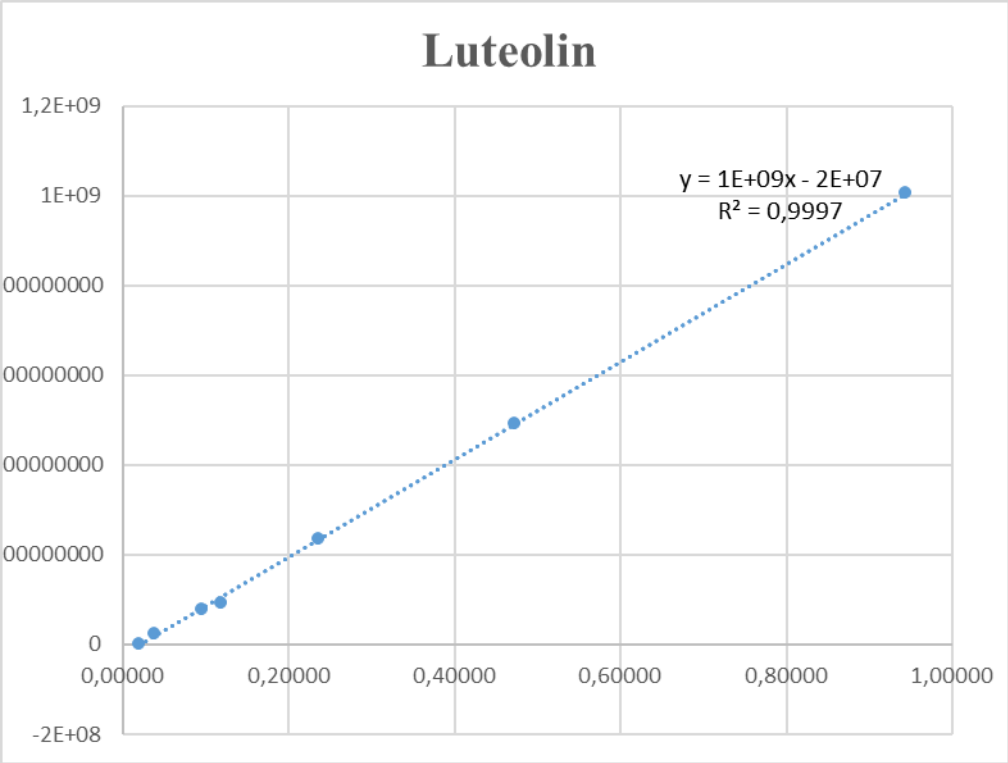

Figure No. S19
Luteolin calibration curve

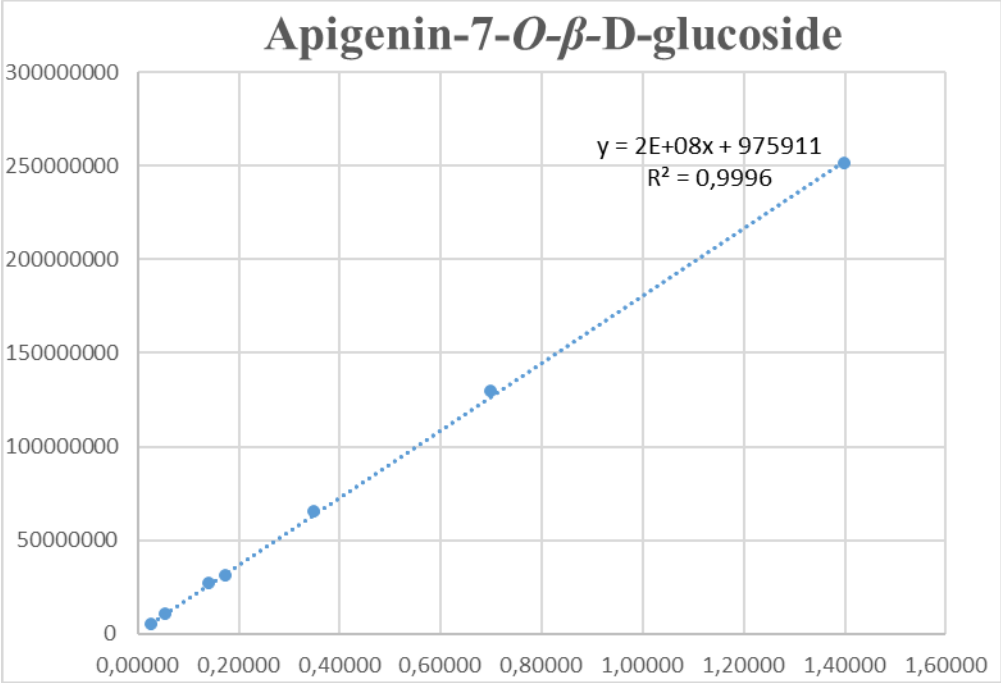

Figure No. S20
Calibration curve of apigenin-7-*O*-*β*-D-glucoside

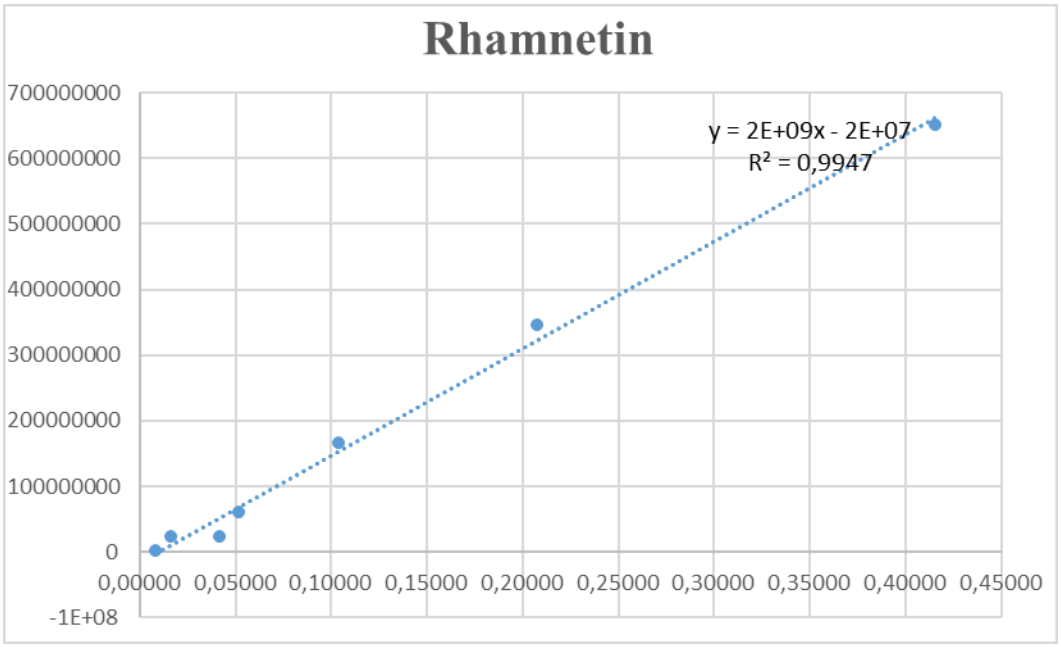

Figure No. S21
Rhamnetin calibration curve

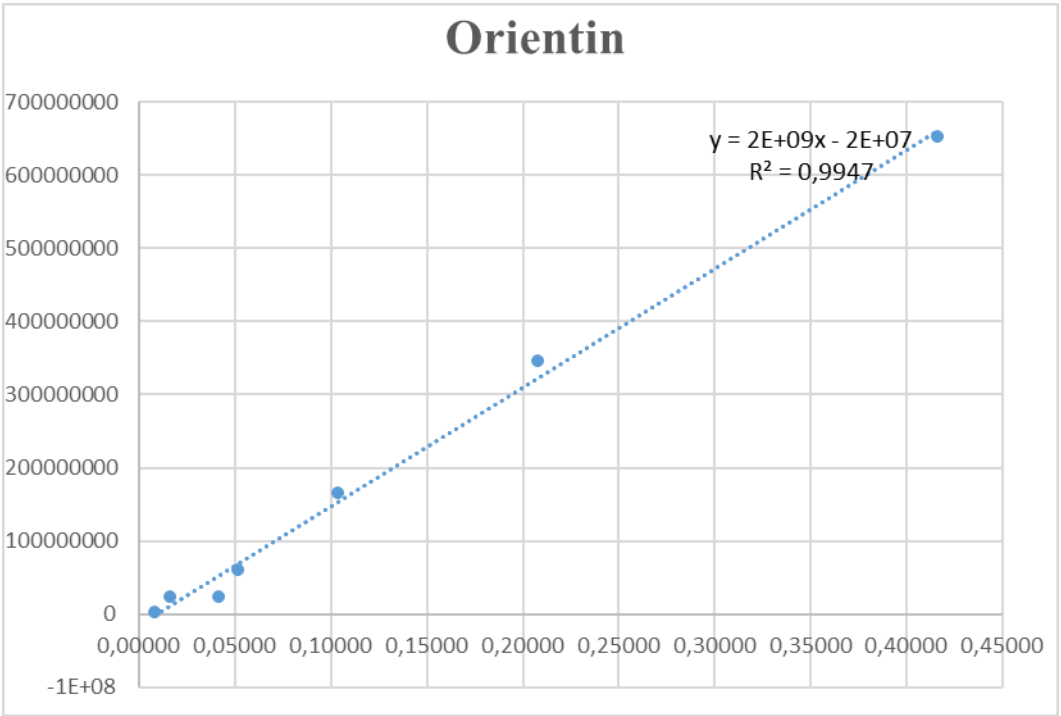

Figure No. S22
Orientation calibration curve