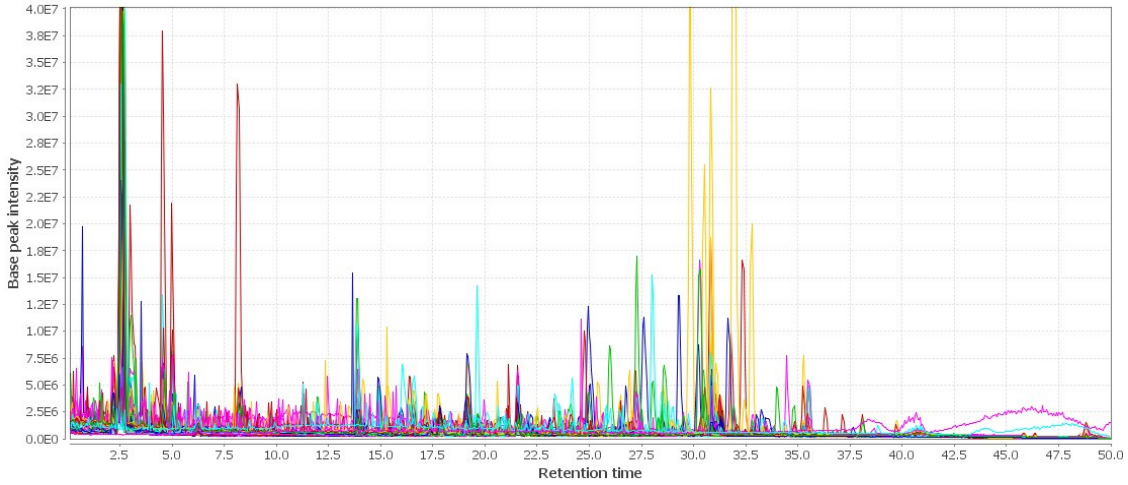
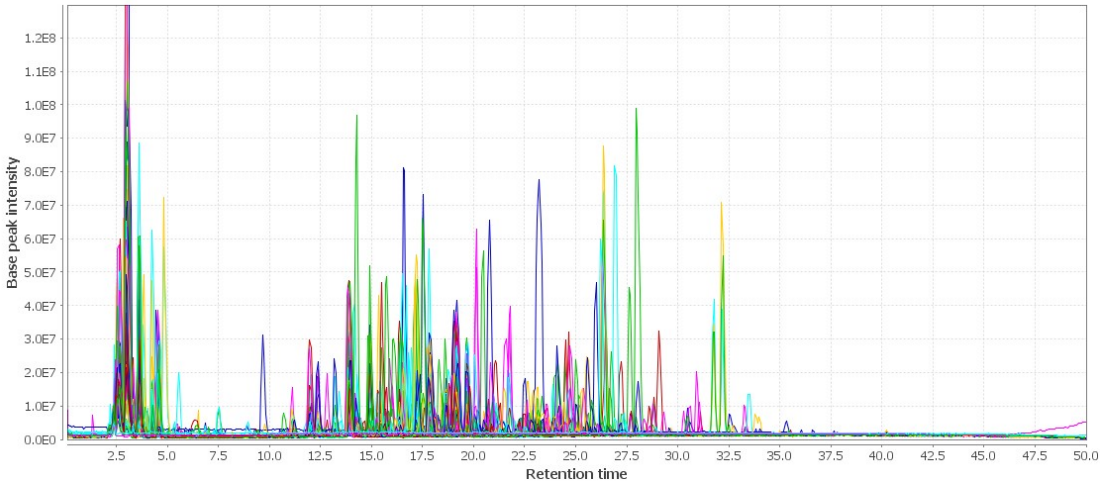
# Supplementary Material

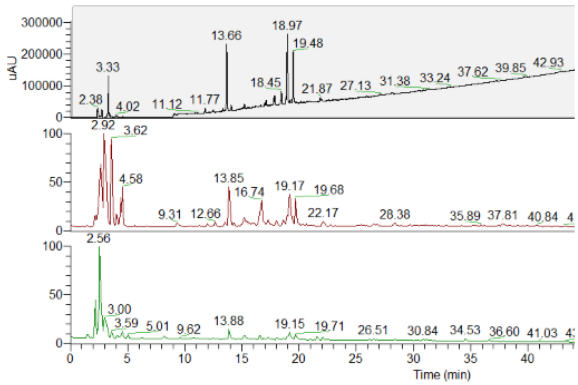



**(A)**




**(B)**

**Figure S1.** Overlap of all the HPLC-HRFTMS chromatograms visualized on the MZmine software. The chromatograms were detected in positive (**A**) and negative (**B**) modes.

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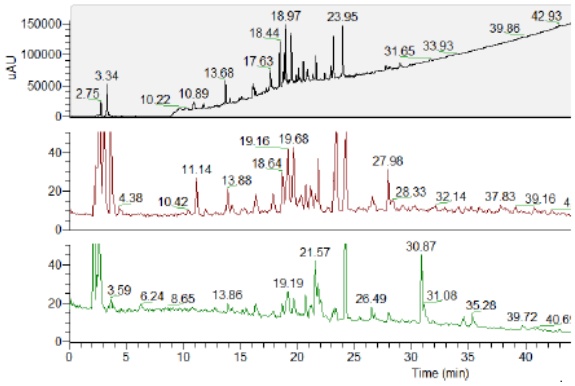


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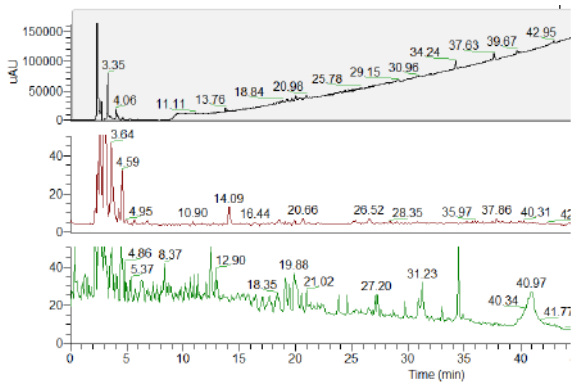
**Figure S2.** *Cont.*

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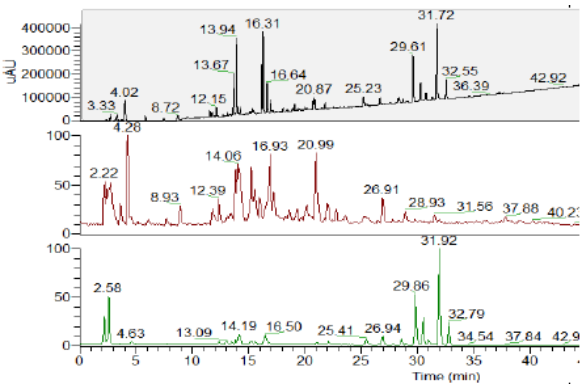


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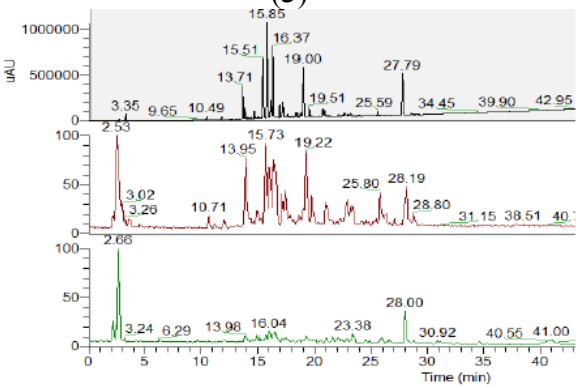


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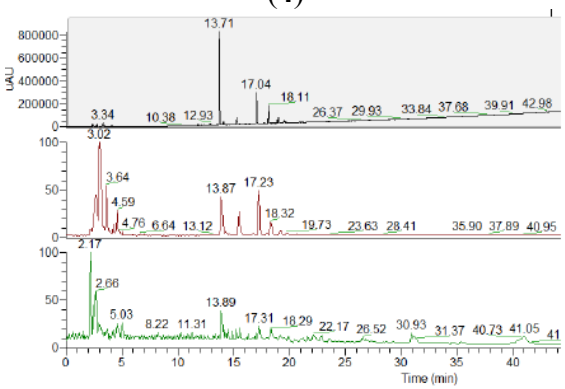


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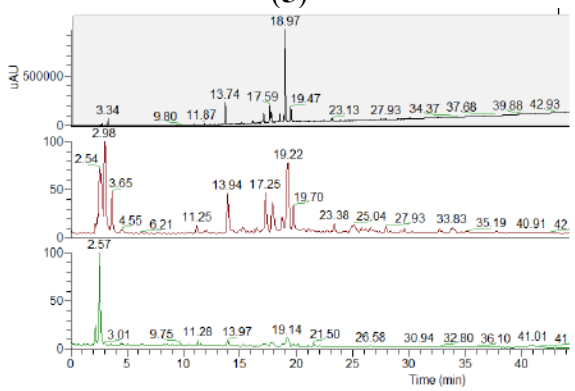


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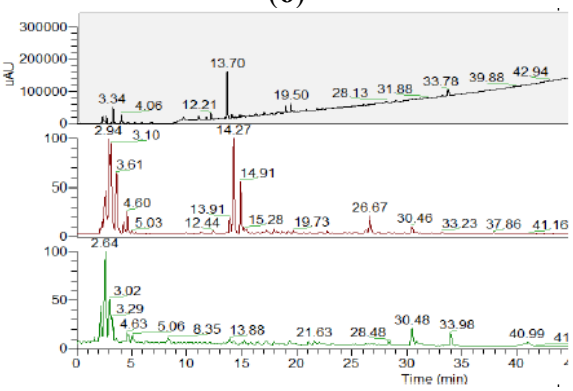


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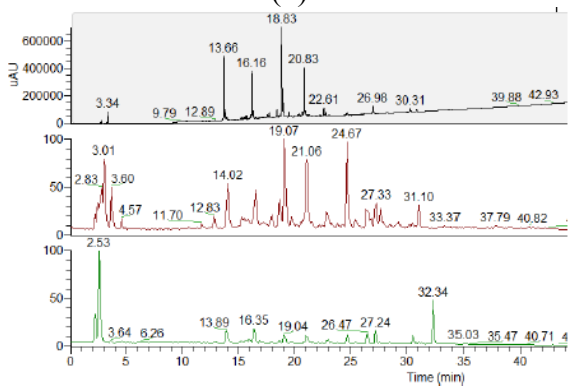


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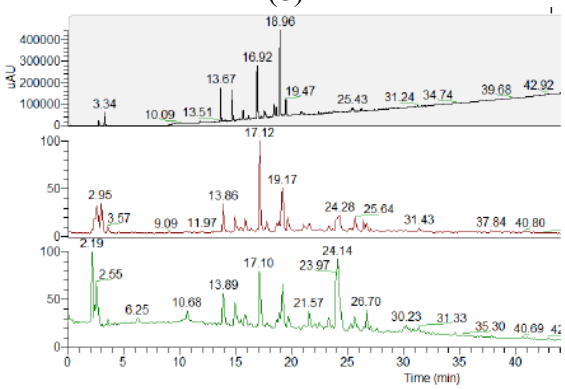


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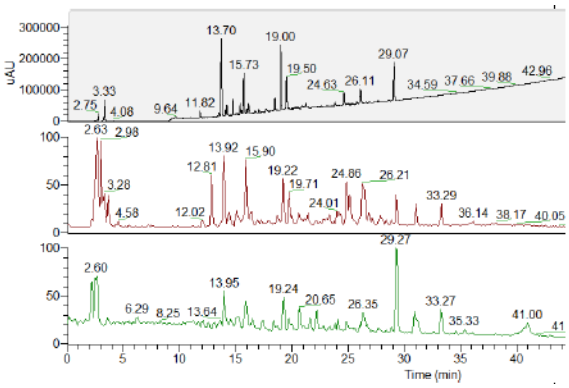


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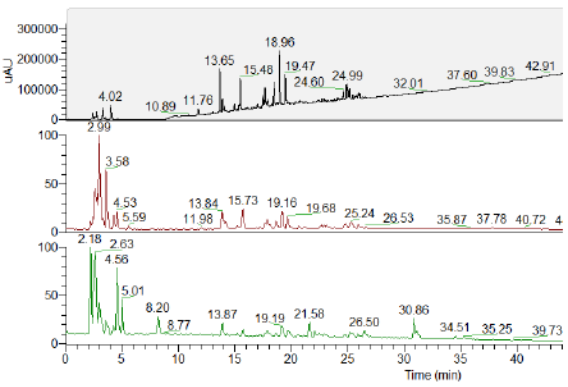


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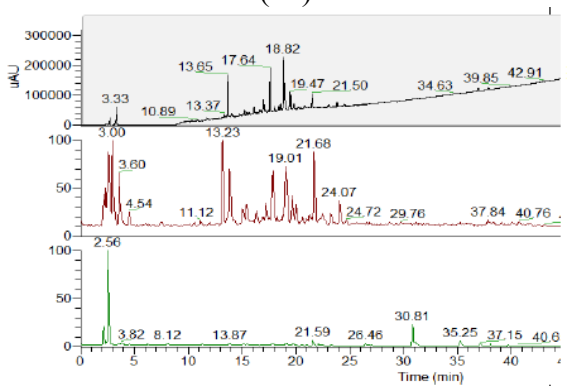


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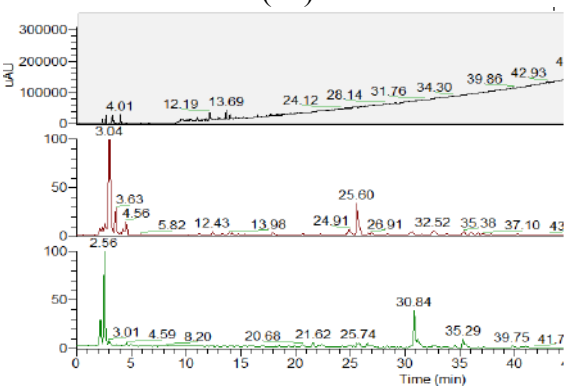


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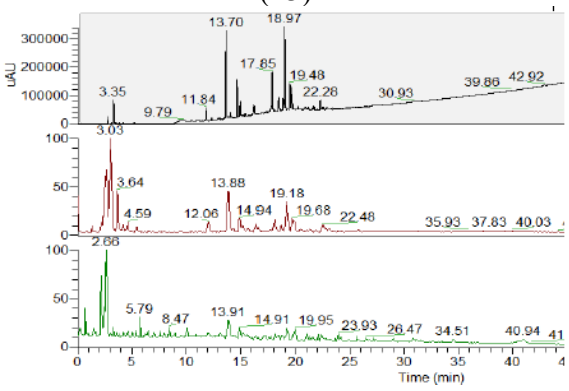


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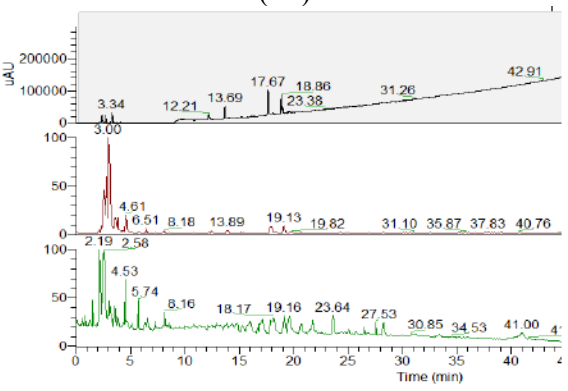


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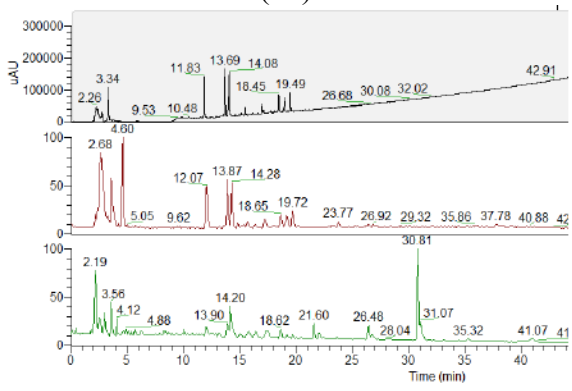


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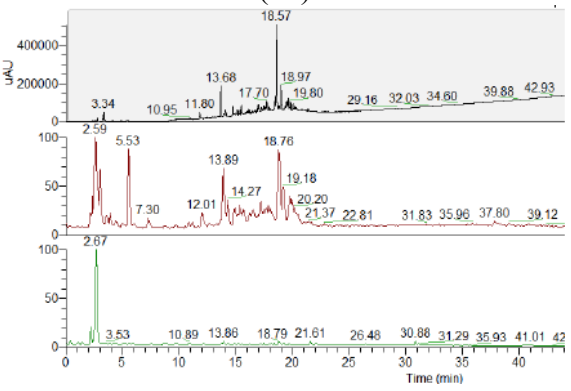


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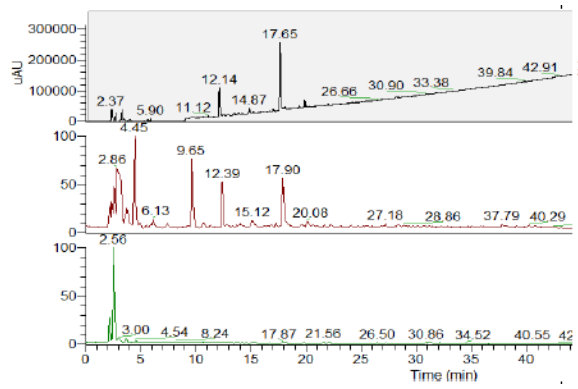


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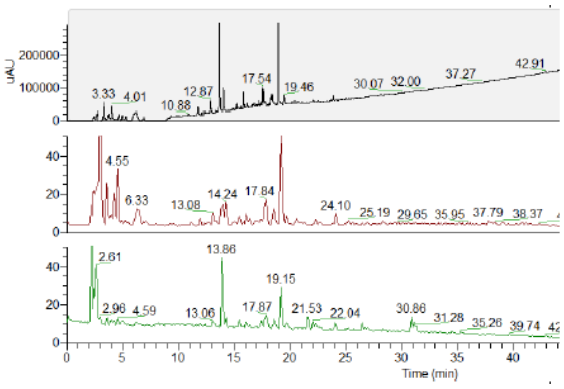


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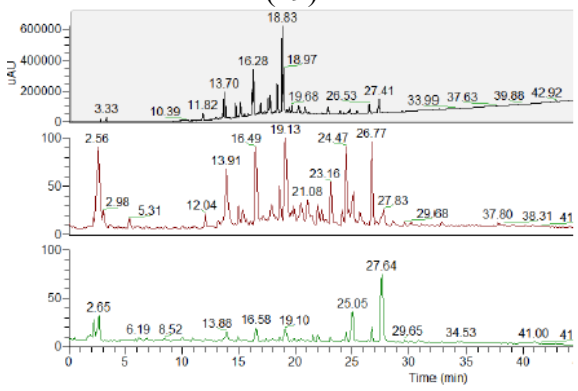


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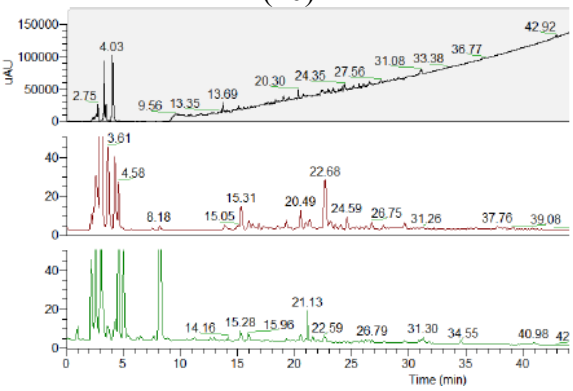


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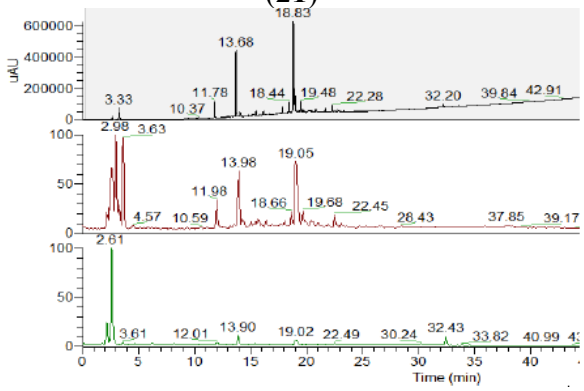


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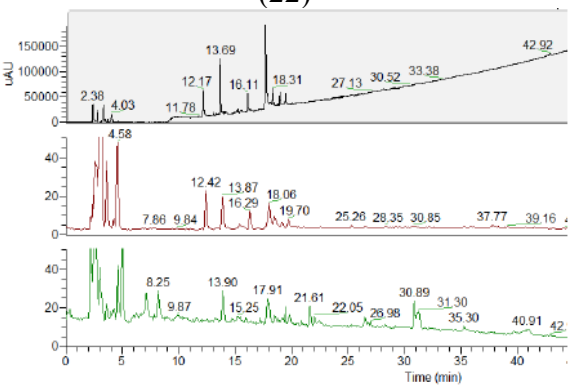


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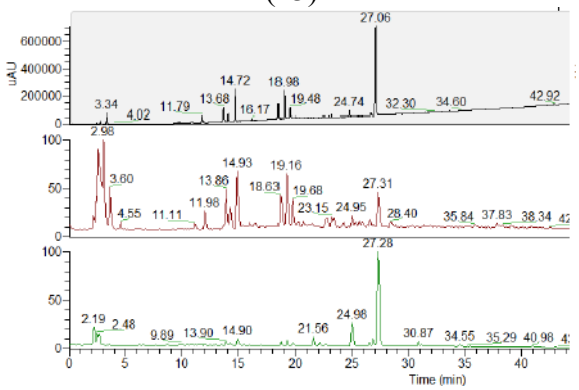


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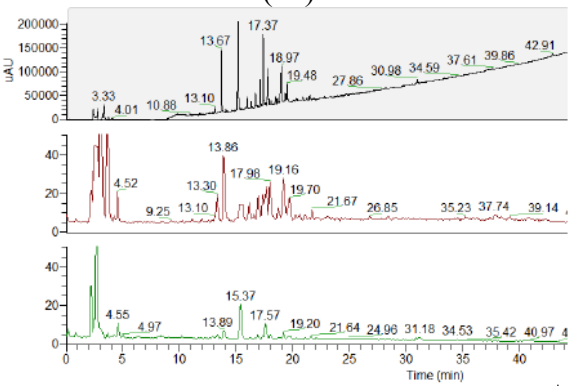


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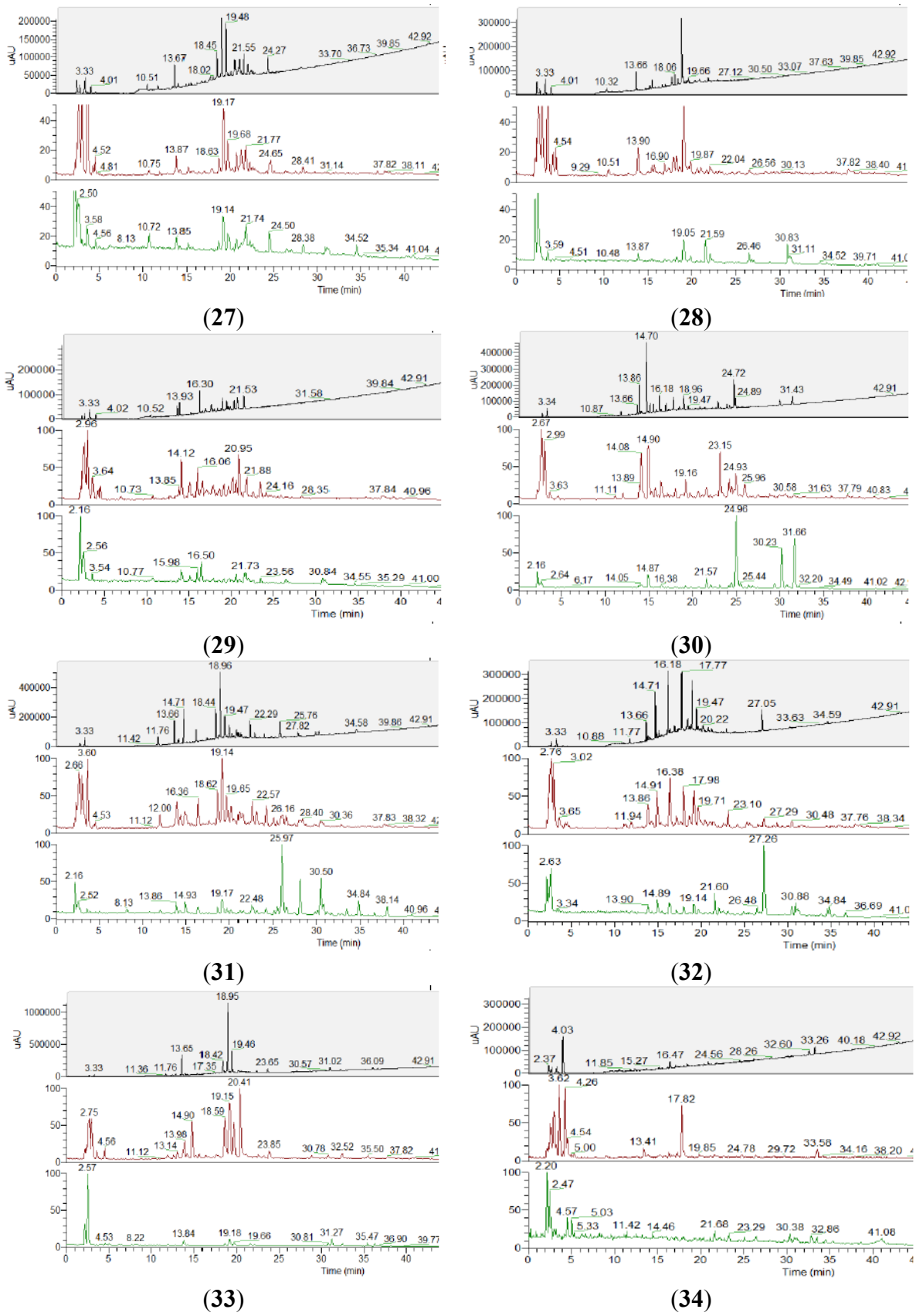


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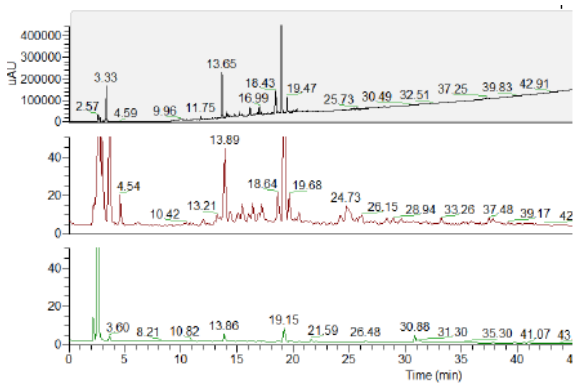


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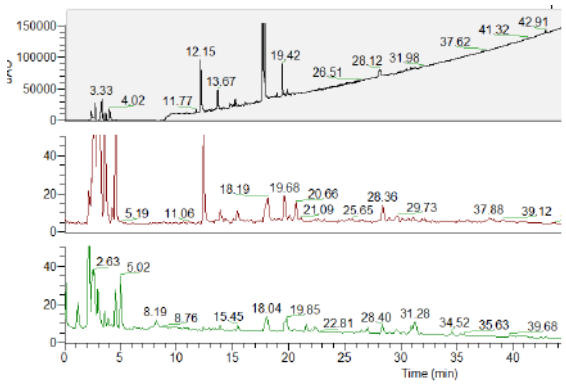


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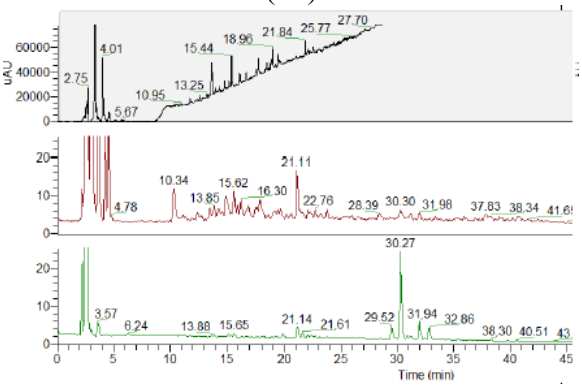


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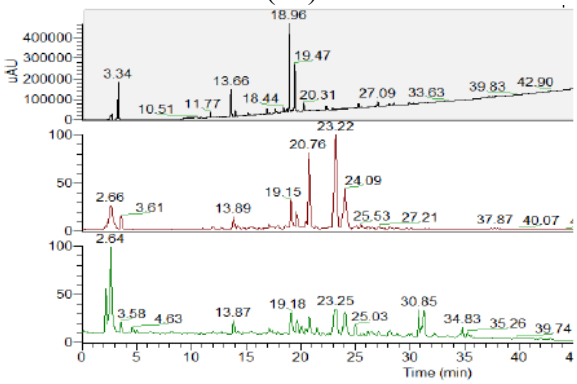


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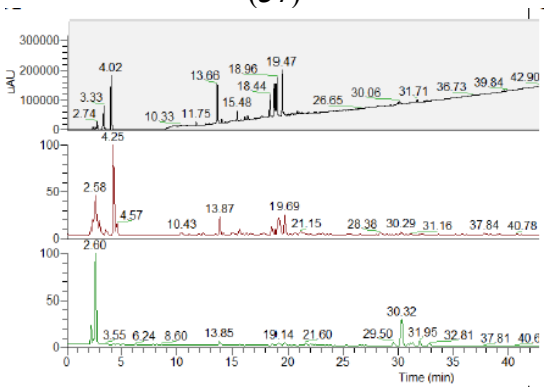


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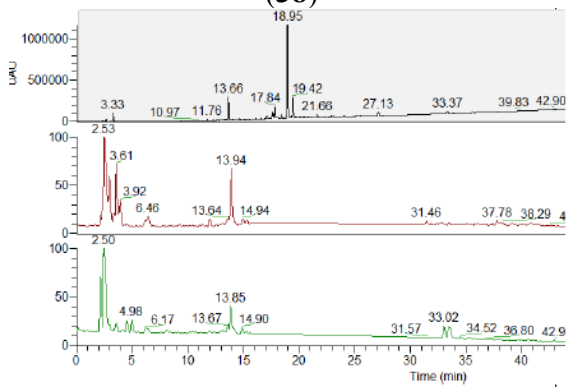


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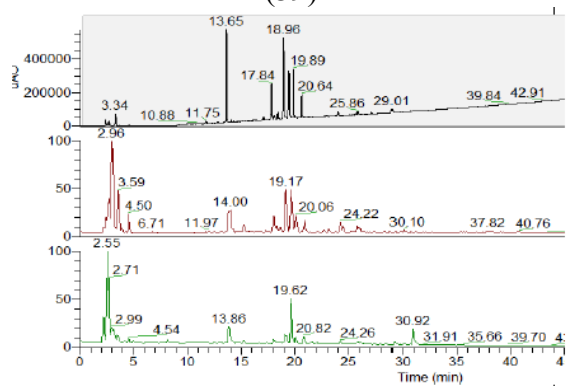


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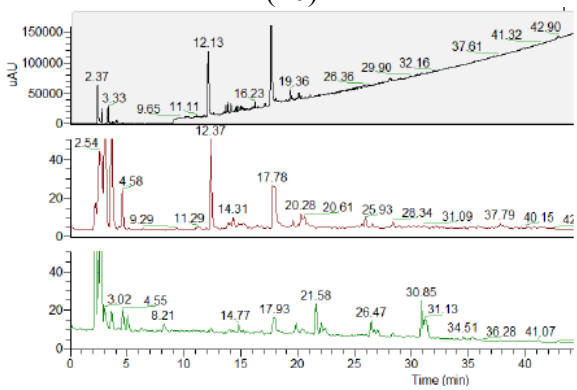
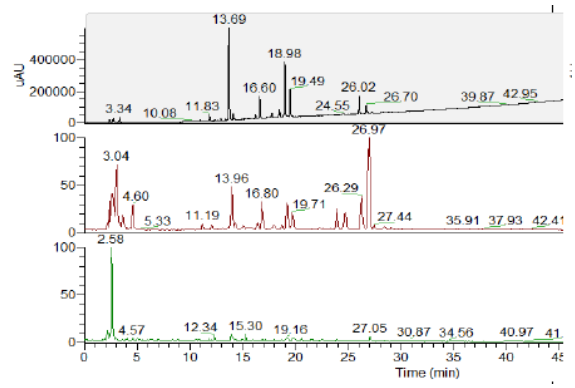



**(42)**

**Figure S2.** *Cont.*

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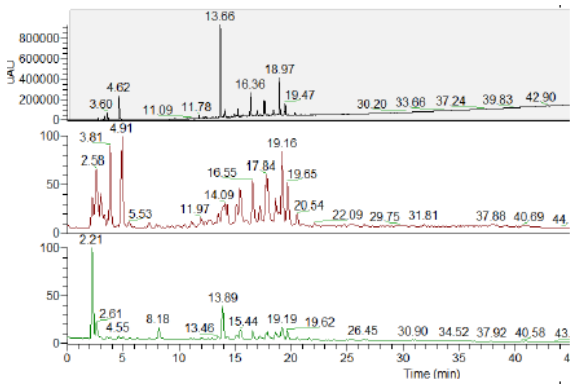


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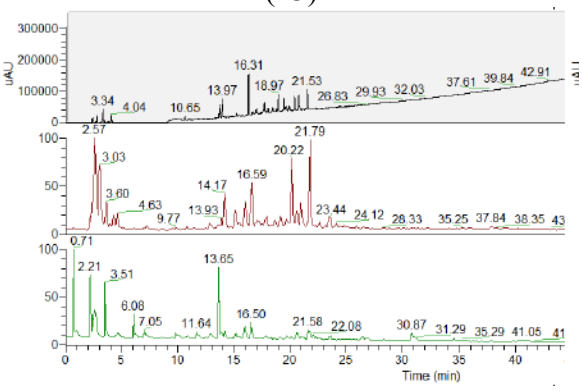


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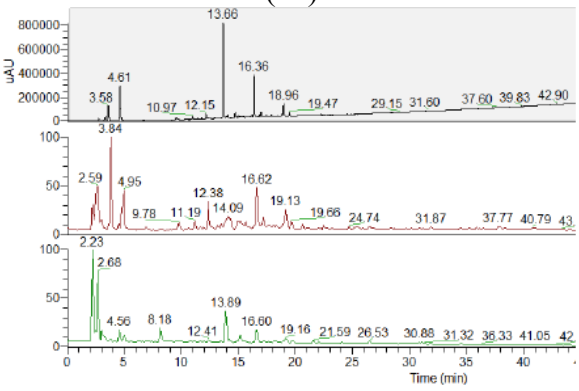


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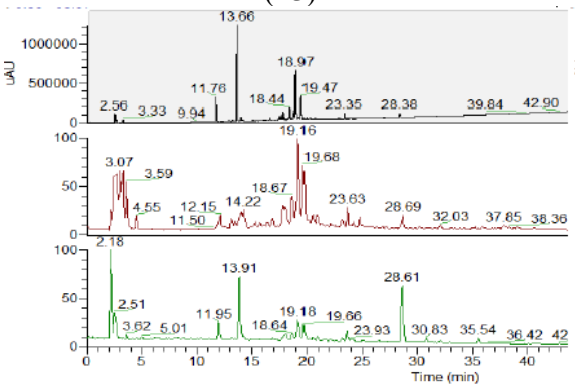


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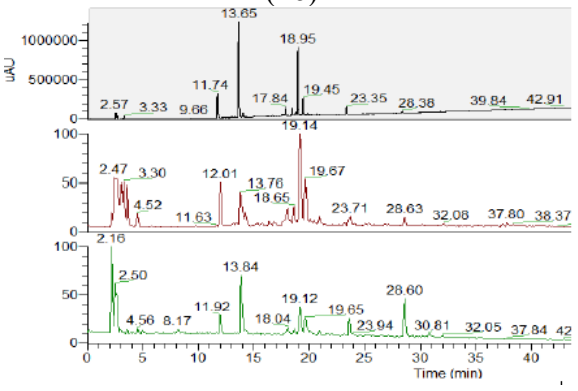


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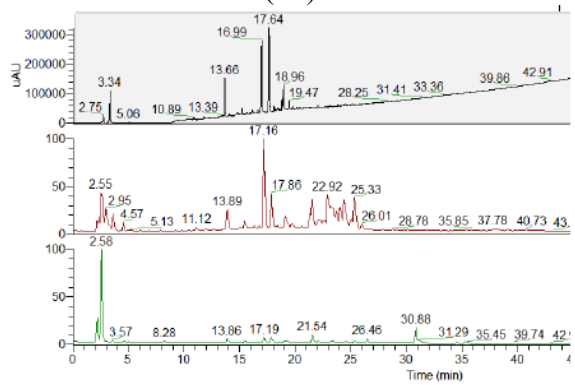


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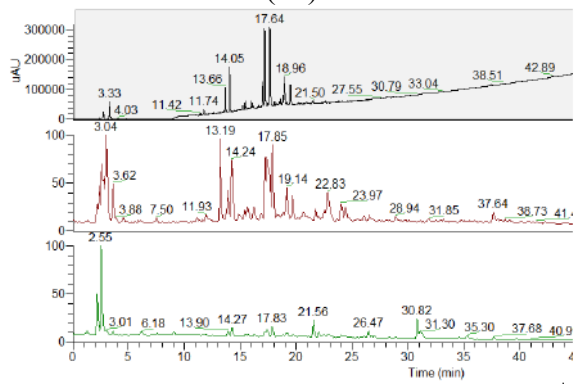



(50)

**Figure S2.** *Cont.*

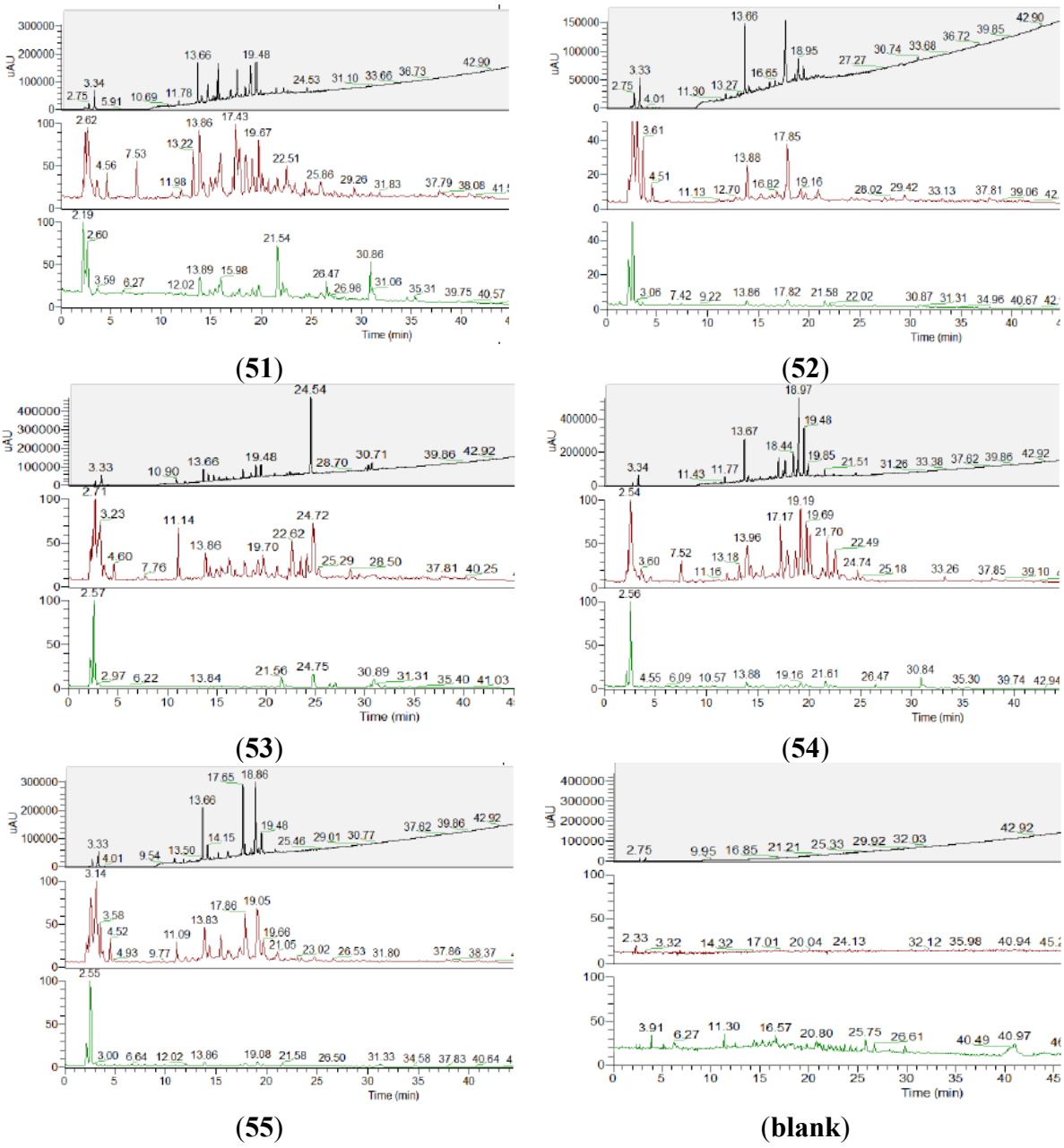
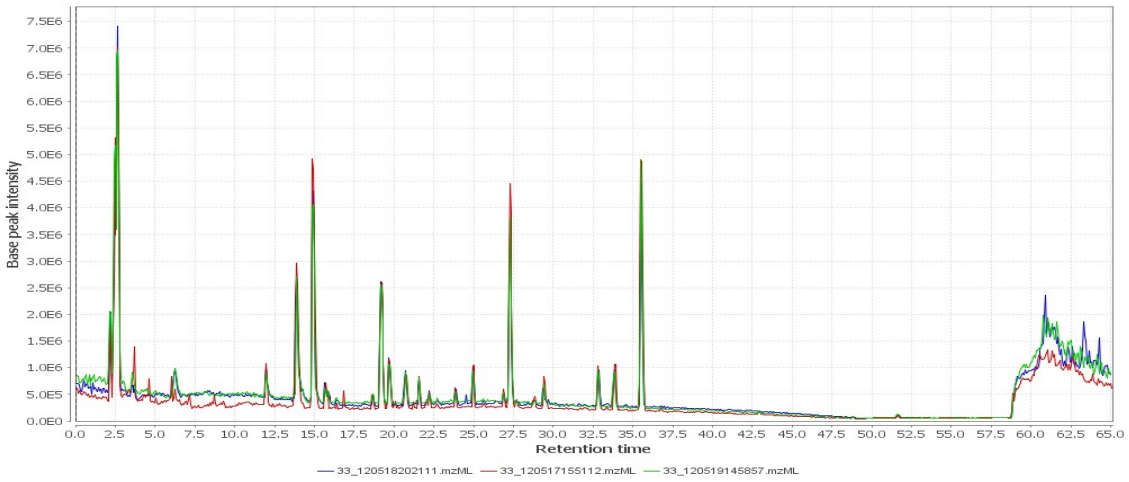
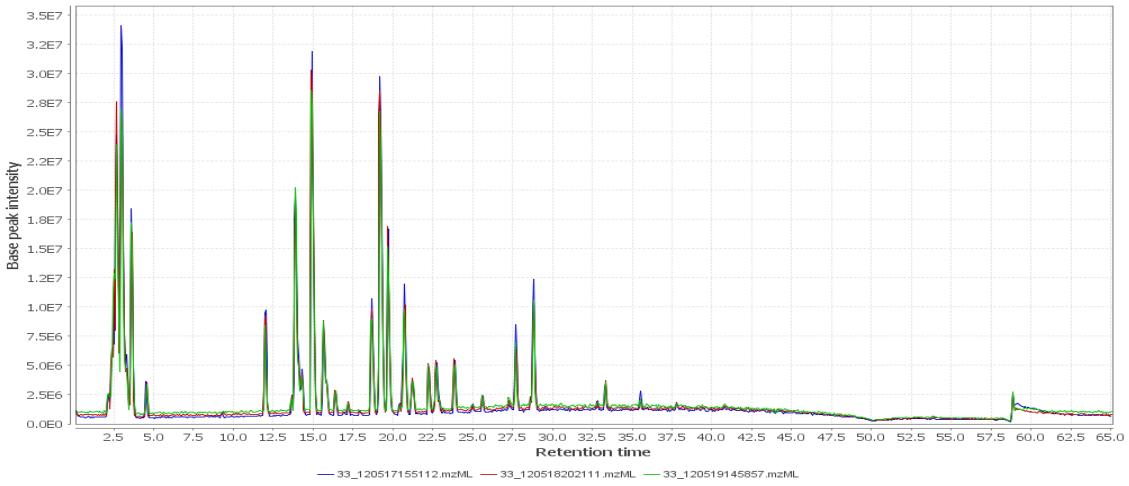



**Figure S2.** Each sample has chromatograms detected using UV (wavelength at 254 nm) (top, black line), and full lock ms in negative (middle, red line) and positive mode (bottom, green line). Each sample has chromatograms detected using UV (wavelength at 254 nm) (top, black line), and full lock ms in negative (middle, red line) and positive mode (bottom, green line). The number of the samples are above each chromatogram.

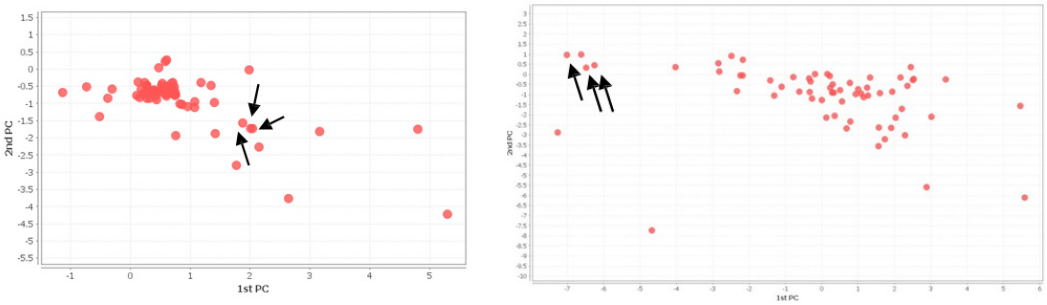



(**A**)



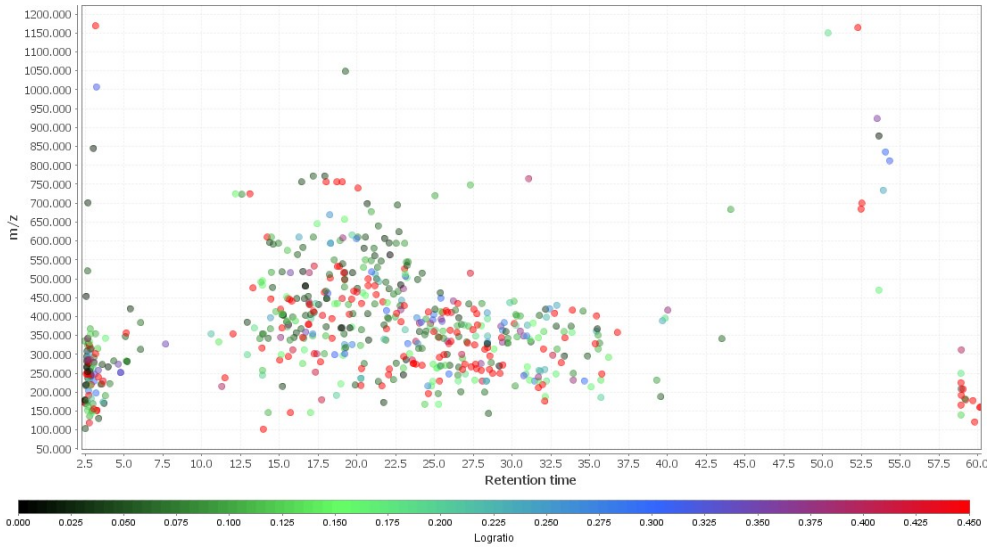

(**B**)

**Figure S3.** The same sample (#33) injected in the beginning, middle and end of the sequence of the injections, before data treatment. The overlap of the spectra shows the reproducibility of the analysis. The chromatograms were detected in the positive (**A**) and negative (**B**) mode.

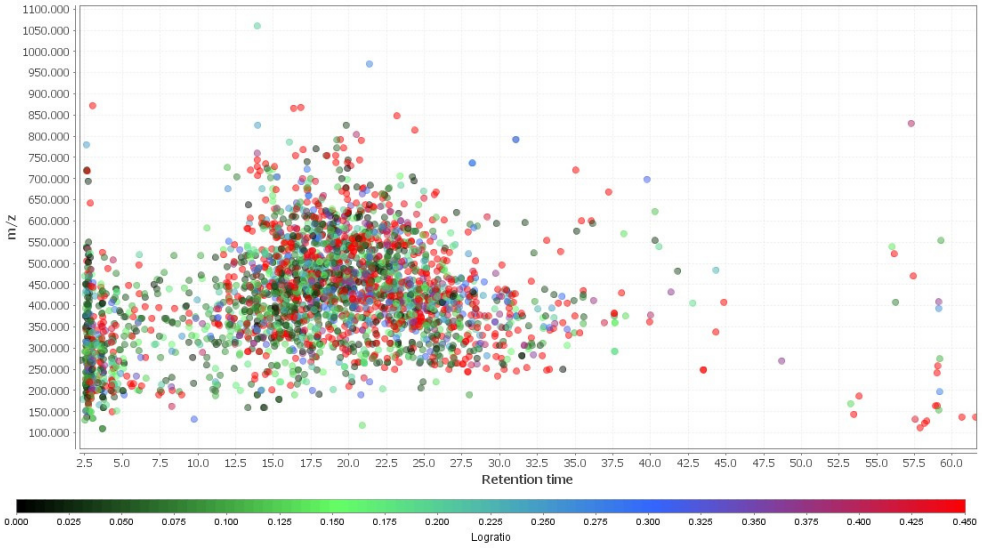



(**A**) (**B**)

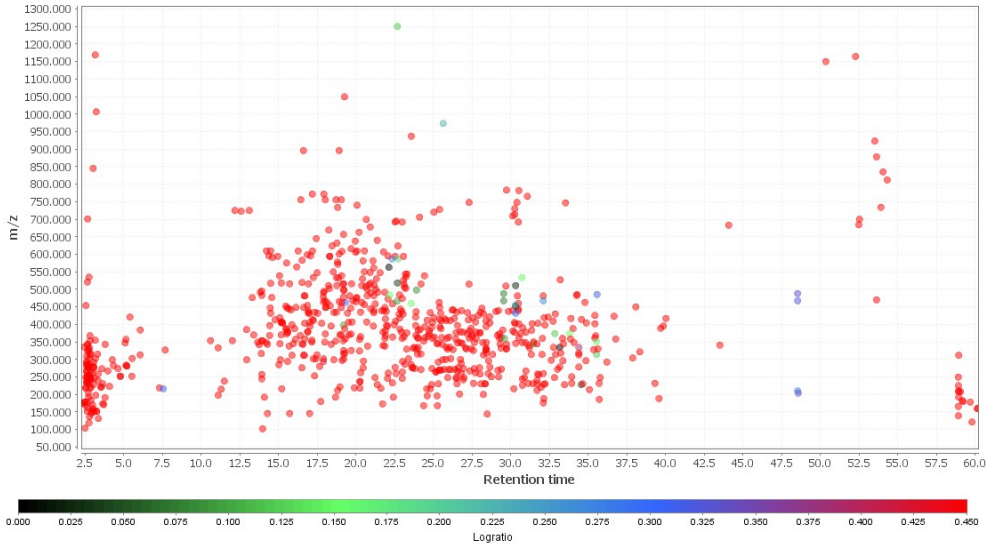
**Figure S4.** The Principal Component Analysis—Expanded PCA plot of the positive (**A**) and negative; (**B**) mode MS datasets (before data treatment) for sample (#33) injected in the beginning, middle and end of the injection sequence indicates the reproducibility of the HPLC-ESI-HRMS analysis. The triplicate samples for extract #33 (indicated by the arrows) overlapped or grouped very near of each other.




**(A)**

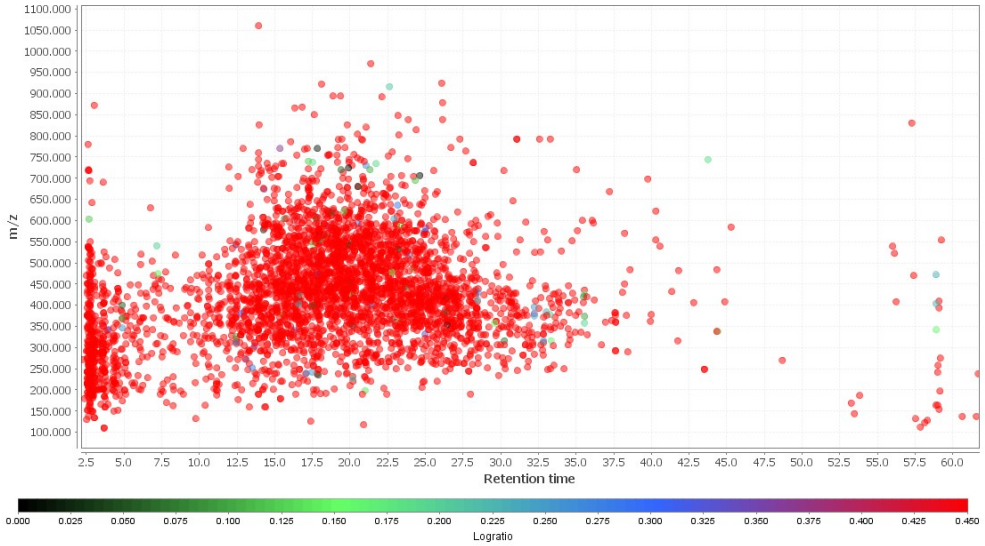



**(B)**




**(C)**

**Figure S5.** *Cont.*




**(D)**

**Figure S5.** The correlation of variation analysis performed with the data from the three replicate injections of extract #33 (injected in the beginning, middle and end of the injection sequence of 57 extracts; before data treatment) validated the reproducibility of the results from the HPLC-ESI-HRMS analysis. Few attributes demonstrated variation as indicated by a log ratio > 0.40 (colored red on the heat bar), most of the peaks gained the green color (log ratio < 0.25) on the heat bar representing small variation as exhibited by the positive (**A**) and negative (**B**) mode datasets. The correlation of variation plots for the MS data with all the 57 samples (**C** for positive mode and **D** for negative mode) showed that almost all attributes afforded a log ratio > 0.4 and this result is coherent because variation between the different sample extracts must occur.

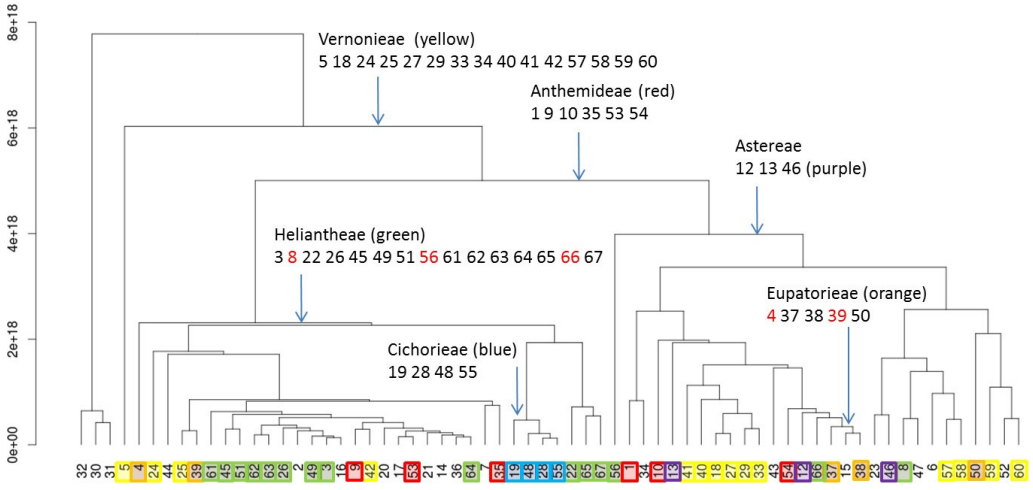



**Figure S6.** Hierarchical Cluster Analysis (HCA) of the metabolomics data of all Asteraceae species evaluated ($n$ = 66, which included root, stem and flower parts for some species). Red highlighted sample codes represent extracts with unique chemistry when compared with other extracts within their respective taxa.

**Table S1.** A summary of available literature information on the chemistry of different plant species used in this study and AI activity [31] of their crude extracts. Those shown to exhibit dual inhibition of COX and LOX were highlighted in red.

| Species | Sample Codes | Chemistry Investigated/AI Evidence | Tribes | 5-LOX [31] (μg/mL) | COX-1 [31] (μg/mL) |
|---|---|---|---|---|---|
| *Achillea millefolium* Ledeb. [yarrow] | 1 | Yes/Yes | Anthemideae Cass. | (−) | (−) |
| *Achyrocline satureioides* (Lam.) DC. [macela] | 2 | Yes/Yes | Gnaphalieae (Cass.) Lecoq&Juill. | (−) | (−) |
| *Acmella oleracea* (L.) R.K. Jansen [toothache plant] | 3 | Yes/Yes | Heliantheae Cass. | (−) | (−) |
| *Ageratum conyzoides* L. [billygoat-weed] | 4 | No/Yes | Eupatorieae Cass. | (−) | (−) |
| *Anteremanthus hatschbachii* H. Rob. | 5 | No/No | Vernonieae Cass. | (−) | (−) |
| *Arctium lappa* L. [greater burdock] | 6 | Yes/Yes | Cynareae Less. | (+) | (−) |
| *Arnica montana* L. [arnica] | 8 | Yes /Yes | Heliantheae Cass. | (+) | (−) |
| *Artemisia absinthium* L. [wormwood] | 9 | Yes/Yes | Anthemideae Cass. | (+) | (−) |
| *Artemisia annua* L. [sweet wormwood] | 10 | Yes/Yes | Anthemideae Cass. | (−) | (−) |
| *Baccharis dracunculifolia* D.C. [alecrim do campo] | 12 | Yes/Yes | Astereae Cass. | (−) | (−) |
| *Baccharis trimera* (Less.) DC. [carqueja] | 13 | Yes/Yes | Astereae Cass. | (−) | (−) |
| *Bidens pilosa* L. [beggar-ticks] | 14 | Yes/Yes | Coreopsideae Lindl. | (−) | (−) |
| *Calea cuneifolia* DC. | 15 | No/No | Neurolaeneae Rydb. | (−) | (−) |
| *Calendula officinalis* L. [marigold] | 16 | Yes/Yes | Calenduleae Cass. | (−) | (+) |
| *Chronopappus bifrons* (DC. ex Pers.) DC. | 18 | No/No | Vernonieae Cass. | (−) | (+) |
| *Cichorium intybus* L. [chicory] | 19 | Yes/Yes | Cichorieae Lam. & DC. | (+) | (+) |
| *Cynara scolymus* L. [artichoke] | 20 | Yes/No | Cardueae Cass. | (−) | (+) |
| *Dasyphyllum brasiliense var. latifolium (D.Don) Cabrera* [espinho agulha] | 21 | No/Yes | BarnadesieaeD.Don | (−) | (+) |
| *Echinacea purpurea* (L.) Moench [purple cone flower] | 22 | Yes/Yes | Heliantheae Cass. | (+) | (−) |
| *Emilia sonchifolia* L. DC [lilac tassel flower] | 23 | No/No | Senecioneae Cass. | (−) | (−) |
| *Eremanthus polycephalus* (DC.) MacLeish | 24 | No/No | Vernonieae Cass. | (−) | (+) |
| *Helianthus annuus* L. [sunflower] | 26 | Yes/No | Heliantheae Cass. | (−) | (−) |
| *Heterocoma gracilis* Loeuille, J. N. Nakaj. & Semir | 27 | No/No | Vernonieae Cass. | (−) | (+) |
| *Lactuca sativa* L. [common lettuce] | 28 | Yes/No | Cichorieae Lam. & DC. | (+) | (−) |
| *Lychnophora diamantinana* Coile & S.B. Jones | 29 | No/No | Vernonieae Cass. | (+) | (−) |
| *Lychnophora ericoides* Mart. [arnica da serra] | 33 | Yes/Yes | Vernonieae Cass. | (+) | (−) |
| *Lychnophora tomentosa* (Mart. ex DC.) Sch. Bip. | 34 | No/No | Vernonieae Cass. | (+) | (−) |
| *Matricaria chamomilla* L. [chamomile] | 35 | Yes/Yes | Anthemideae Cass. | (+) | (−) |
| *Mikania glomerata* Sprengl. [guaco] | 37 | No/No | Eupatorieae Cass. | (+) | (−) |
| *Mikania hirsutissima* DC. [cipó cabeludo] | 38 | No/No | Eupatorieae Cass. | (+) | (−) |
| *Mikania laevigata* Schultz Bip. ex Baker [guaco] | 39 | No/No | Eupatorieae Cass. | (+) | (−) |
| *Minasia scapigera* H. Rob. | 40 | No/No | Vernonieae Cass. | (+) | (+) |
| *Piptolepis monticola* Loeuille | 41 | No/No | Vernonieae Cass. | (+) | (+) |
| *Prestelia eriopus* Sch. Bip. | 42 | No/No | Vernonieae Cass. | (+) | (+) |
| *Pluchea quitoc* D.C. | 43 | No/No | Inuleae Cass. | (−) | (−) |
| *Smallanthus sonchifolius* (Poepp. &Endl.) H. Robinson [yacon] | 45 | No/Yes | Heliantheae Cass. | (−) | (+) |
| *Solidago microglossa* DC. [arnica do campo] | 46 | No/Yes | Astereae Cass. | (+) | (+) |

**Table S1.** *Cont.*

| Species | Sample Codes | Chemistry Investigated/AI Evidence | Tribes | 5-LOX [31] (µg/mL) | COX-1 [31] (µg/mL) |
|---|---|---|---|---|---|
| *Sonchus oleraceus* L. [sowthistle] | 48 | No/No | Cichorieae Lam. & DC. | (+) | (−) |
| *Sphagneticola trilobata* (L.) Pruskei | 49 | No/No | Heliantheae Cass. | (+) | (+) |
| *Stevia rebaudiana* (Bertoni) Bertoni [sweetleaf] | 50 | Yes/No | Eupatorieae Cass. | (+) | (−) |
| *Tridax procumbens* L. [tridax daisy] | 51 | No/No | Heliantheae Cass. | (+) | (−) |
| *Tanacetum parthenium* L. (feverfew)[34,36,37,69] | 53 | Yes/Yes | Anthemideae Cass. | (+) | (−) |
| *Tanacetum vulgaris* L. [tansy] | 54 | No/Yes | Anthemideae Cass. | (−) | (−) |
| *Taraxacum officinale* Weber ex FH Wigg. [dandelion] | 55 | Yes/Yes | Cichorieae Lam. &DC. | (−) | (+) |
| *Tithonia diversifolia* (Hemsl.) A. Gray [tree marigold] | 56 | No/Yes | Heliantheae Cass. | (+) | (+) |
| *Vernonia condensata* Baker [boldo baiano] | 25 | No/Yes | Vernonieae Cass. | (−) | (−) |
| *Vernonia herbacea* (Vell.) Rusby | 57 | No/No | Vernonieae Cass. | (+) | (+) |
| *Vernonia platensis* (Spreng.) Less. | 58 | Yes/No | Vernonieae Cass. | (+) | (+) |
| *Vernonia polyanthes* Less. [assa peixe] | 59 | Yes/No | Vernonieae Cass. | (+) | (+) |
| *Vernonia rubriramea* Mart. Ex DC. | 60 | No/No | Vernonieae Cass. | (+) | (+) |
| *Viguiera arenaria* Baker | 61 | No/No | Heliantheae Cass. | (+) | (−) |
| *Viguiera bracteata* Gardner | 62 | No/No | Heliantheae Cass. | (+) | (−) |
| *Viguiera discolor* Baker | 63 | No/No | Heliantheae Cass. | (+) | (−) |
| *Viguiera filifolia* Sch. Bip. Ex Baker | 64 | No/No | Heliantheae Cass. | (+) | (−) |
| *Viguiera linearifolia* Chodat & Hassl. | 65 | No/No | Heliantheae Cass. | (−) | (−) |
| *Viguiera robusta* Gardner | 66 | No/Yes | Heliantheae Cass. | (+) | (+) |
| *Viguiera trichophylla* Dusén | 67 | No/No | Heliantheae Cass. | (+) | (+) |
| **Reference inhibitors (RI)** | | | | | |
| Indomethacin (Sigma-Aldrich®) | | | RI of COX-1 | (−) | (+) |
| Nordihydroguaiaretic acid (Sigma-Aldrich®) | | | RI of 5-LOX | (+) | (−) |

**Table S2.** Peak area of the biomarkers of dual inhibition.

| | Sample | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **ID** | **19** | **40** | **41** | **42** | **46** | **49** | **56** | **57** | **58** | **59** | **60** | **66** | **67** |
| Negative Mode | | | | | | | | | | | | | |
| 671 | 0 | 1.78E+3 | 1.92E+6 | 3.70E+6 | 3.78E+2 | 1.11E+3 | 6.49E+3 | 2.01E+3 | 1.03E+4 | 3.16E+6 | 3.97E+6 | 1.51E+4 | 6.64E+2 |
| 694 | 0 | 5.14E+3 | 7.70E+3 | 4.80E+3 | 6.68E+1 | 1.14E+2 | 6.31E+2 | 1.41E+3 | 7.39E+2 | 5.12E+2 | 2.02E+2 | 3.91E+3 | 1.92E+2 |
| 2054 | 5.40E+2 | 4.57E+3 | 1.50E+3 | 5.92E+4 | 2.79E+3 | 1.87E+3 | 1.48E+7 | 1.86E+7 | 1.38E+4 | 5.46E+7 | 2.06E+7 | 2.81E+7 | 3.33E+6 |
| 2488 | 0 | 1.18E+3 | 1.69E+3 | 1.05E+3 | 0 | 5.70E+1 | 0 | 5.31E+1 | 1.17E+2 | 1.75E+2 | 6.47E+2 | 6.75E+1 | 2.22E+1 |
| 3913 | 1.02E+4 | 2.43E+3 | 1.04E+4 | 1.77E+4 | 1.03E+4 | 1.03E+4 | 2.48E+4 | 6.55E+6 | 6.43E+6 | 6.90E+6 | 3.60E+6 | 7.64E+6 | 3.64E+4 |
| 5001 | 2.63E+3 | 1.07E+3 | 1.50E+4 | 6.92E+3 | 2.00E+3 | 3.08E+4 | 2.70E+4 | 3.21E+4 | 7.06E+3 | 2.15E+3 | 8.24E+3 | 2.10E+4 | 1.25E+4 |
| Positive Mode | | | | | | | | | | | | | |
| 1190 | 0 | 9.06E+3 | 1.22E+2 | 2.39E+3 | 1.08E+1 | 0 | 0 | 3.18E+1 | 0 | 0 | 0 | 0 | 0 |
| 1273 | 0 | 2.27E+4 | 4.86E+4 | 1.61E+4 | 0 | 9.65E+1 | 7.17E+1 | 0 | 0 | 2.12E+1 | 1.40E+1 | 0 | 0 |
| 1282 | 0 | 1.54E+3 | 3.23E+3 | 2.39E+3 | 8.50 | 1.70E+1 | 9.36E+1 | 0 | 8.98 | 0 | 0 | 1.13E+3 | 0 |
| 1436 | 0 | 2.19E+2 | 4.45E+2 | 6.31E+3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1615 | 0 | 1.97E+3 | 4.31E+7 | 1.03E+5 | 6.07 | 1.88E+3 | 1.77E+3 | 9.46E+1 | 0 | 1.21E+2 | 4.15E+1 | 0 | 3.76E+1 |
| 1623 | 0 | 4.02E+2 | 1.25E+7 | 2.42E+3 | 0 | 2.20E+2 | 2.50E+1 | 0 | 0 | 1.04E+2 | 4.39E+1 | 0 | 0 |
| 1637 | 0 | 1.70E+3 | 6.59E+6 | 1.24E+3 | 0 | 3.74E+2 | 5.14E+6 | 0 | 0 | 0 | 0 | 9 | 0 |