**High-Performance Liquid Chromatography - Electrospray Ionization-tandem Mass Spectrometry (HPLC-ESI/$MS^n$)**

The HPLC-ESI/$MS^n$ analysis was done on the Agilent Infinity 1260 coupled with a High-Resolution Mass Spectrometry Agilent 6520 B equipped with Quadrupole Time of Flight (QTOF) and electrospray ionization (ESI), according to the methodology described by Justino *et al*. 2018. The extract and fractions were injected on an Agilent Zorbax C18 column (100 mm x 2.1 mm, 2.7 µm) at 1.0 mg/mL. The mobile phase consisted of water acidified with formic acid (0.1 % v/v) (A) and methanol (B), as follows: 2% B (0 min), 98% B (0-15 min); 98% B (15-17 min); 2% B (17-22 min) at a flow 0.4 mL/min. High purity nitrogen ($N_2$) was used as drying gas (8.0 L/min) and as nebulizing gas at pressure of 58 PSI. The nebulizer temperature was 220 ºC with a potential of 4.5 kV used on the capillary. The mass spectra of the ions (MS and $MS^2$) were acquired in negative mode in the range of *m/z* 100–1000. Different collision energies were adjusted automatically according to the precursor *m/z* to obtain the fragmentation spectra ($MS^2$). Identification of compounds in each sample was performed by high resolution mass and fragmentation spectra $MS^2$ analysis, comparing with data from the literature and METLIN metabolite database.

## HPLC-ESI/MS$^n$ analysis

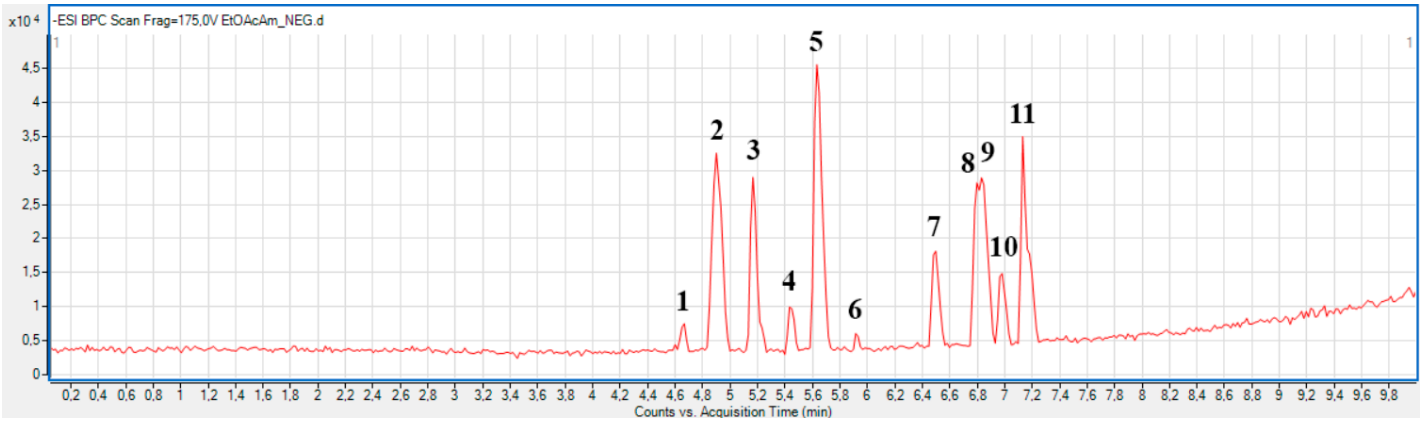


**Figure S1.** ESI-MS chromatogram of the ethyl acetate fraction (EtOAC.f) from *Annona muricata* leaf (negative mode). Numbers corresponding to major peaks and their respective compounds are shown in Supplementary Table S1.

| Peak | Compound (tentative identification) | Retention time (min) | Formula $[M-H]^-$ | Mass calculated for $[M-H]^-$ | *m/z* of $[M-H]^-$ | Error (ppm) | *m/z* of fragments of $[M-H]^-$ | References |
|---|---|---|---|---|---|---|---|---|
| 1 | Chlorogenic acid | 4.6 | $C_{16}H_{17}O_9^-$ | 353.0878 | 353.0864 | 3.9 | 191, 161, 127, 125 | doi: 10.3390/12030679 |
| 2 | Procyanidin B2 | 4.8 | $C_{30}H_{25}O_{12}^-$ | 577.1351 | 577.1340 | -1.9 | 451, 407, 289, 203, 161, 125 | Justino 2018 |
| 3 | Procyanidin C1 | 5.2 | $C_{45}H_{37}O_{18}^-$ | 865.1985 | 865.1985 | 0.0 | 739, 577, 503, 451, 407, 289, 243, 125 | Justino 2018 |
| 4 | Caffeic acid | 5.4 | $C_9H_7O_4^-$ | 179.0350 | 179.0343 | 3.9 | 176, 135 | doi: 10.3390/ijms13010260 |
| 5 | (Epi)catechin | 5.6 | $C_{15}H_{13}O_6^-$ | 289.0718 | 289.0711 | -2.4 | 271, 245, 203, 179, 125 | Justino 2018 |
| 6 | Quercetin-diglucoside | 5.9 | $C_{27}H_{29}O_{17}^-$ | 625.1410 | 625.1409 | -0.1 | 463, 301, 300, 179 | Justino 2018 |
| 7 | Quercetin-glucosyl-pentoside | 6.5 | $C_{26}H_{27}O_{16}^-$ | 595.1305 | 595.1304 | -0.1 | 427, 301, 300, 271, 229, 179 | Justino 2018 |
| 8 | Quercetin-glucoside | 6.8 | $C_{12}H_{19}O_{12}^-$ | 463.0877 | 463.0875 | -0.4 | 301, 300, 271, 125 | Justino 2018 |
| 9 | Rutin | 6.8 | $C_{27}H_{29}O_{16}^-$ | 609.1461 | 609.1462 | 0.1 | 565, 463, 301, 300, 179 | Justino 2018 |
| 10 | Quercetin-pentoside | 6.9 | $C_{20}H_{17}O_{11}^-$ | 433.0776 | 433.0759 | -3.9 | 301, 300, 271, 233, 165 | Chen 2012. |
| 11 | Quercetin-rhamnoside | 7.2 | $C_{21}H_{19}O_{11}^-$ | 447.0933 | 447.0911 | -4.9 | 341, 301, 300, 285, 284 | Justino 2018 |

**Table S1.** Compounds identified in the ethyl acetate fraction from *Annona muricata* leaf (EtOAc) by HPLC-ESI-MS/MS (negative mode).

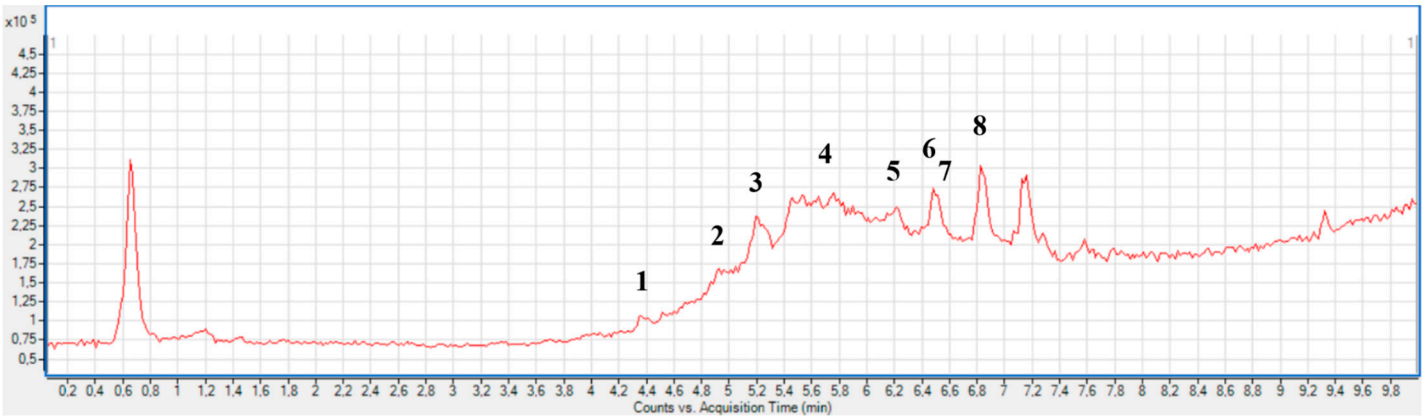


**Figure S2.** ESI-MS chromatogram of the n-butanol (BuOH.f) from *Annona muricata* leaf (negative mode). Numbers corresponding to major peaks and their respective compounds are shown in Table S2**.**

| Peak | Compound (tentative identification) | Retention time (min) | Formula $[M-H]^-$ | Mass calculated for $[M-H]^-$ | *m/z* of $[M-H]^-$ | Error (ppm) | *m/z* of fragments of $[M-H]^-$ | References |
|---|---|---|---|---|---|---|---|---|
| 1 | Chlorogenic acid | 4.4 | $C_{16}H_{17}O_9^-$ | 353.0878 | 353.0864 | 3.9 | 191, 161, 127, 125 | doi: 10.3390/12030679 |
| 2 | Procyanidin B2 | 4.9 | $C_{30}H_{25}O_{12}^-$ | 577.1351 | 577.1340 | -1.9 | 451, 407, 289, 203, 161, 125 | Justino 2018 |
| 3 | Procyanidin C1 | 5.2 | $C_{45}H_{37}O_{18}^-$ | 865.1985 | 865.1985 | 0.0 | 739, 577, 503, 451, 407, 289, 243, 125 | Justino 2018 |
| 4 | (Epi)catechin | 5.6 | $C_{15}H_{13}O_6^-$ | 289.0718 | 289.0711 | -2.4 | 271, 245, 203, 179, 125 | Justino 2018 |
| 5 | Quercetin-diglucoside | 6.2 | $C_{27}H_{29}O_{17}^-$ | 625.1410 | 625.1409 | -0.1 | 463, 301, 300, 179 | Justino 2018 |
| 6 | Quercetin-glucosyl-pentoside | 6.4 | $C_{26}H_{27}O_{16}^-$ | 595.1305 | 595.1304 | -0.1 | 427, 301, 300, 271, 229, 179 | Justino 2018 |
| 7 | Quercetin-xyloside-rutinoside | 6.4 | $C_{32}H_{37}O_{20}^-$ | 741.1883 | 741.1851 | 4,31 | 653,487, 301, 300 | doi: 10.3390/molecules200611490 |
| 8 | Rutin | 6.8 | $C_{27}H_{29}O_{16}^-$ | 609.1461 | 609.1462 | 0.1 | 565, 463, 301, 300, 179 | Justino 2018 |

**Table S2.** Compounds identified in the n-butanol fraction (BuOH.f) from *Annona muricata* leaf (BuOH.f) by HPLC-ESI-MS/MS (negative mode).