|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S1: (a) XIC chromatogram , (b) MS1, and (c) MS2 spectra of apigenin (65)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S2: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectraof apigenin 8-*C*-glucoside (46)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S3: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of apigenin 7-*O*-glucoside (57)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S4: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of luteolin (26)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S5: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of luteolin 6-*C*-glucoside (44)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S6: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of luteolin 7-*O*-glucoside (52)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S7: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of quercetin (33)** |

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| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S8: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of quercitrin (32)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S9: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of quercetin 4'-*O*-glucoside (49)** |

|  |
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| **(a)** |
| **(b)** |
| **Fig. S10: (a) XIC chromatogram and (b) MS2 spectrum of quercetin 3-D-xyloside (31)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S11: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of naringenin 7-*O*-glucoside (54)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **Fig. S12: (a) XIC chromatogram and (b) MS2 spectrum of kaempferol 3-*O*--L-arabinoside (27)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S13: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of kaempferol 3-*O*- -L-rhamnoside (43)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S14: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of okanin 4'-*O*-glucoside (34)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S15: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of isorhamnetin 3-*O*-glucoside (55)** |

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| **(a)** |
| **(b)** |
| **Fig. S16: (a) XIC chromatogram and (b) MS2 spectrum of myricitrin (56)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S17: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of punicalagin (13)** |

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| --- |
| **(b)**  **(a)** |
|  |
| **(c)** |
| **Fig. S18: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of digalloylglucose (21)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S19: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of monogalloylglucose (28)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **Fig. S20: (a) XIC chromatogram, and (b) MS2 spectrumof 3,4,3'-tri-*O*-methylellagic acid (29)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S21: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of ellagic acid (3)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S22: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of chlorogenic acid (15)** |

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| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S23: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of gallic acid (10)** |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S24: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of shikimic acid (9)** |
| **(a)** |
| **(b)** |
| **Fig. S25: (a) XIC chromatogram and (b) MS2 spectrum of 3,4-dihydroxybenzoic acid (19)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **Fig. S26: (a) XIC chromatogram and (b) MS2 spectrm of daphnetin (42)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **Fig. S27: (a) XIC chromatogram and (b) MS2 spectrum of 6,7-dihydroxycoumarin (66)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **(c)** |
| **Fig. S28: (a) XIC chromatogram, (b) MS1, and (c) MS2 spectra of quinic acid (11)** |

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| **(a)** |
| **(b)** |
| **Fig. S29: (a) XIC chromatogram and (b) MS2 spectrum of gallagylglucose (punicalin, 7)** |

|  |
| --- |
| **(a)** |
| **(b)** |
| **Fig. S30: (a) XIC chromatogram and (b) MS2 spectrum of apigenin 6-*C*-glucoside -7-*O*-glucoside (13)** |

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| --- |
| **(a)** |
| **(b)** |
| **Fig. S31: (a) XIC chromatogram and (b) MS2 spectrum of vitexin 2''-*O*-rhamnoside (20)** |

**Table S1 Cytotoxicity of the different extracts against Vero cell line expressed as CC50 values (M±SE)**

|  |  |
| --- | --- |
| **ID** | **Cytotoxicity (CC50), μg/ml** |
| **Doxo** | 31.73 ± 0.83C |
| **L** | 968.2 ± 26.2C |
| **F** | Nd |
| **S** | Nd |

**Doxo.:** Doxorubicin; Groups that share letters are non-significantly different, while different letters express significant differences. Nd= Not detected

**Table** S2 **Cytotoxicity of different extracts against Vero, Caco2, HepG2, Panc1 and MCF-7 cell lines expressed as CC50 values (M±SE)**

**Cytotoxicity(IC50)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ID** | **Vero** | **Caco-2** | | **HepG-2** | | **Panc-1** | | **MCF-7** | |
| **CC50, μg/ml** | **IC50**  **μg/ml** | **SI** | **IC50**  **μg/ml** | **SI** | **IC50**  **μg/ml** | **SI** | **IC50**  **μg/ml** | **SI** |
| **Doxo** | 31.73 ± 0.83C | 31.91± 0.81D | 1 | 5.4± 0.22C | 5.8 | 19.07± 0.2D | 1.6 | 15.48±0.84C | 2 |
| **L** | 968.2 ± 26.2C | 81.78 ± 0.43C | 11.83 | 221.71 ± 4.44B | 4.3 | 435.35 ± 11.1B | 2.2 | 491.67 ± 17.56A | 2 |
| **F** | Nd | 162.07 ± 8.63A | - | 329.35 ± 9.27A | - | 568.11 ± 6.37A | - | 288 ± 20.1B | - |
| **S** | Nd | 110.33 ± 3.23B | - | 203.3 ± 5.33B | - | 390.39 ± 5.64C | - | 428.9 ± 23.9A | - |

**Doxo.: Doxorubicin**; Groups that share letters are non-significantly different, while different letters express significant differences. Nd= Not detected IC50 ˃ 1000 μg/ml

**Table S3 Determination of MNTCs and CC50 of the L, F, and S extracts vs. acyclovir (Ac)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ID** | **μg/ml** | **OD** | | | **Mean OD** | **SE** | **Viability, %** | **Toxicity, %** | **CC50 μg/ml** | **MNTC, μg/ml** |
| **Vero** | - | 0.482 | 0.473 | 0.458 | 0.471 | 0.007 | 100 | 0 | - | - |
| **Ac** | 1000 | 0.038 | 0.048 | 0.04 | 0.042 | 0.003055 | 10.9947644 | 89.0052356 | 360.92 | 62.5 |
| 500 | 0.092 | 0.105 | 0.129 | 0.108667 | 0.010837 | 28.44677138 | 71.55322862 |
| 250 | 0.274 | 0.271 | 0.246 | 0.263667 | 0.008876 | 69.02268761 | 30.97731239 |
| 125 | 0.314 | 0.293 | 0.326 | 0.311 | 0.00644 | 81.41361257 | 18.58638743 |
| 62.5 | 0.365 | 0.388 | 0.391 | 0.381333 | 0.008212 | 99.82547993 | 0.17452007 |
| 31.25 | 0.371 | 0.381 | 0.388 | 0.38 | 0.004933 | 99.47643979 | 0.523560209 |
| **L** | 1000 | 0.182 | 0.215 | 0.195 | 0.19733 | 0.00959 | 46.3223787 | 53.6776212 | 965.6 | 500 |
| 500 | 0.425 | 0.429 | 0.418 | 0.424 | 0.003215 | 99.53051643 | 0.469483568 |
| 250 | 0.436 | 0.421 | 0.412 | 0.423 | 0.005686 | 99.29577465 | 0.704225352 |
| 125 | 0.428 | 0.422 | 0.415 | 0.421667 | 0.003756 | 98.9827856 | 1.017214397 |
| 62.5 | 0.426 | 0.421 | 0.415 | 0.420667 | 0.00318 | 98.74804382 | 1.251956182 |
| 31.25 | 0.433 | 0.419 | 0.42 | 0.424 | 0.004509 | 99.53051643 | 0.469483568 |
| **F** | 1000 | 0.385 | 0.405 | 0.415 | 0.400667 | 0.00809 | 94.05320814 | 5.946791862 | - | 500 |
| 500 | 0.426 | 0.421 | 0.43 | 0.425667 | 0.002603 | 99.92175274 | 0.078247261 |
| 250 | 0.419 | 0.425 | 0.427 | 0.423667 | 0.002404 | 99.45226917 | 0.547730829 |
| 125 | 0.413 | 0.427 | 0.419 | 0.419667 | 0.004055 | 98.51330203 | 1.486697966 |
| 62.5 | 0.423 | 0.420 | 0.431 | 0.424667 | 0.003283 | 99.68701095 | 0.312989045 |
| 31.25 | 0.428 | 0.421 | 0.416 | 0.421667 | 0.00348 | 98.9827856 | 1.017214397 |
| **S** | 1000 | 0.415 | 0.418 | 0.422 | 0.418333 | 0.002028 | 98.20031299 | 1.799687011 | - | 1000 |
| 500 | 0.426 | 0.421 | 0.43 | 0.425667 | 0.002603 | 99.92175274 | 0.078247261 |
| 250 | 0.418 | 0.422 | 0.425 | 0.421667 | 0.002028 | 98.9827856 | 1.017214397 |
| 125 | 0.417 | 0.43 | 0.431 | 0.426 | 0.004509 | 100 | 0 |
| 62.5 | 0.421 | 0.424 | 0.425 | 0.423333 | 0.001202 | 99.37402191 | 0.625978091 |
| 31.25 | 0.429 | 0.422 | 0.418 | 0.423 | 0.003215 | 99.29577465 | 0.704225352 |

**OD = optical density, SE = standard error**

**Table S4 Antiviral activity of the different extracts against HSV1 vs. acyclovir (Ac), using different protocols expressed as antiviral activity% values (M±SE)**

|  |  |  |  |
| --- | --- | --- | --- |
| **ID** | **Antiviral activity %** | | |
| **Protocol A** | **Protocol B** | **Protocol C** |
| **Ac** | 83.76 ± 5.67A | 92.69 ± 1.32A | 68.44 ± 7.62AB |
| **L** | 38.19 ± 5.38D | 36.46 ± 4.09D | 55.42 ± 4.86CD |
| **F** | 46.66 ± 3.85BCD | 40.94 ± 5.79CD | 65.53 ± 3.24BC |
| **S** | 6.28 ± 5.25EF | 2.17 ± 1.09F | 31.74 ± 9.73DE |

Groups that share letters are non-significantly different, while different letters express significant differences.

**Table S5 Antiviral activity of the different extracts against HAV using different protocols expressed as antiviral activity% values (M±SE)**

**Antiviral activity( IC50)**

|  |  |  |  |
| --- | --- | --- | --- |
| **ID** | **Antiviral activity %** | | |
| **Protocol A** | **Protocol B** | **Protocol C** |
| **L** | 73.19 ± 3.1AB | 63.63 ± 1.98ABC | 82.99 ± 1.56A |
| **F** | 40.6 ± 2.61CDE | 22.84 ± 1.17EFG | 54.16 ± 3.13ABCD |
| **S** | 17.36 ± 4.39FG | 9.73 ± 1.35G | 31.11 ± 5.51DEF |

Groups that share letters are non-significantly different, while different letters express significant differences.