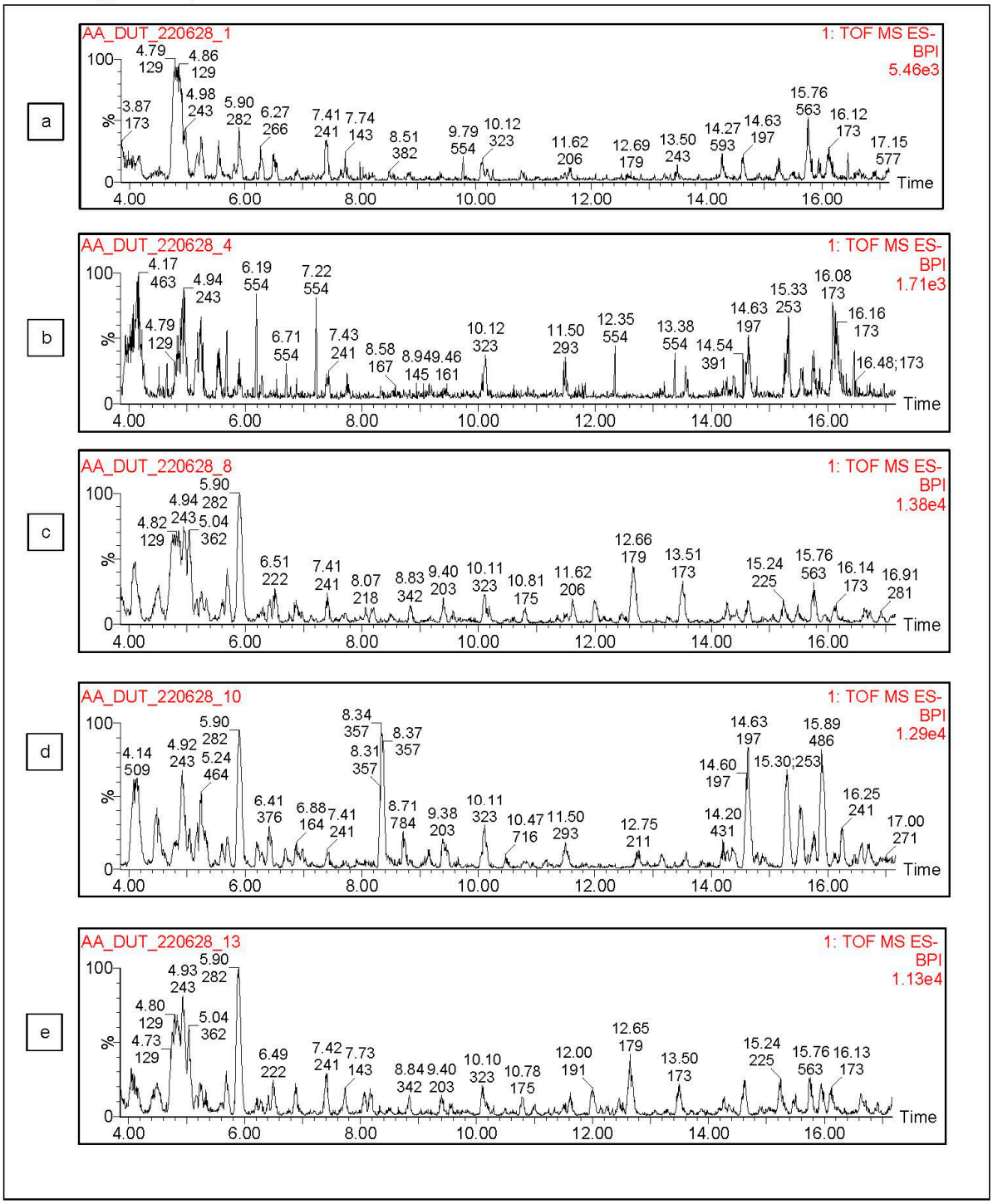
Supplementary materials



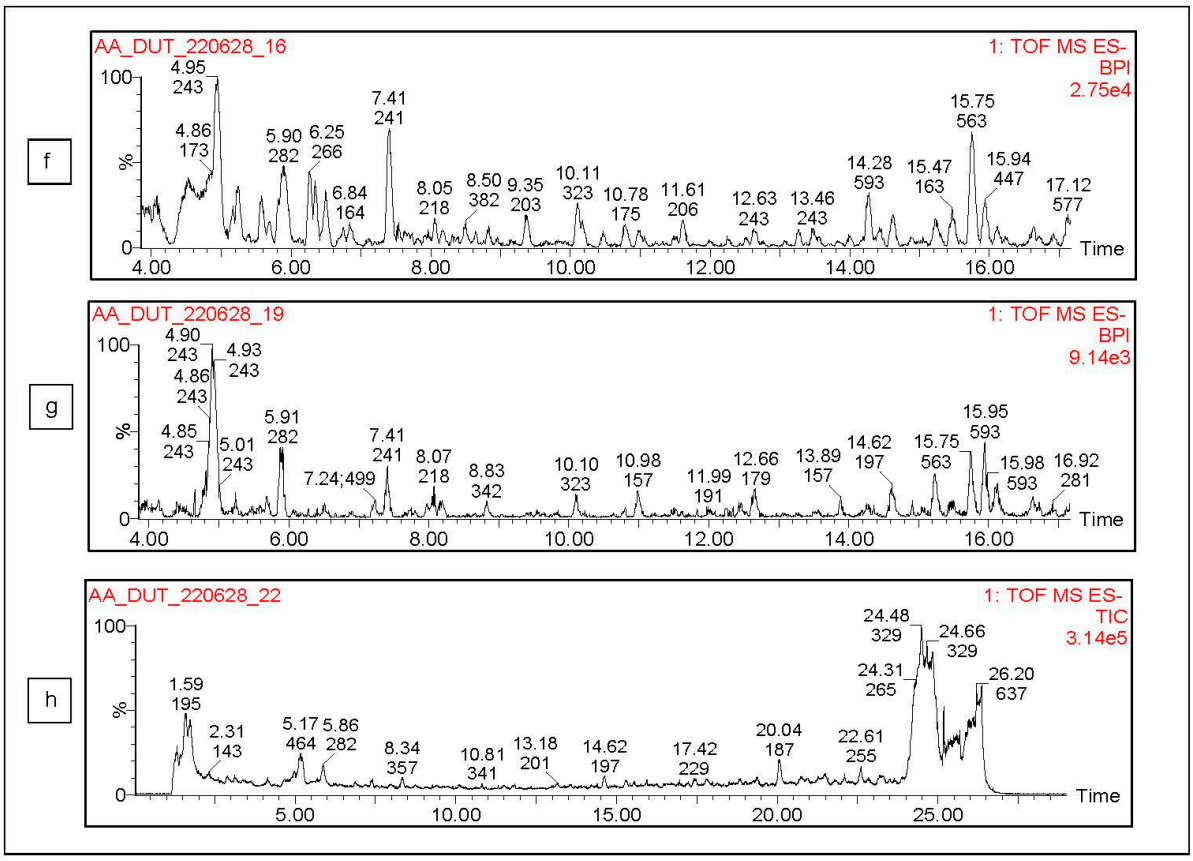



Figure S1: Examples of chromatograms produced showing mass to charge and retention times of compounds found in a) raw premature CS, b) raw mature cs as well as CS extracts; c) aqueous premature, d) aqueous mature, e) hydroethanolic premature, f) hydroethanolic mature, g) ethanolic premature and h) ethanolic mature.

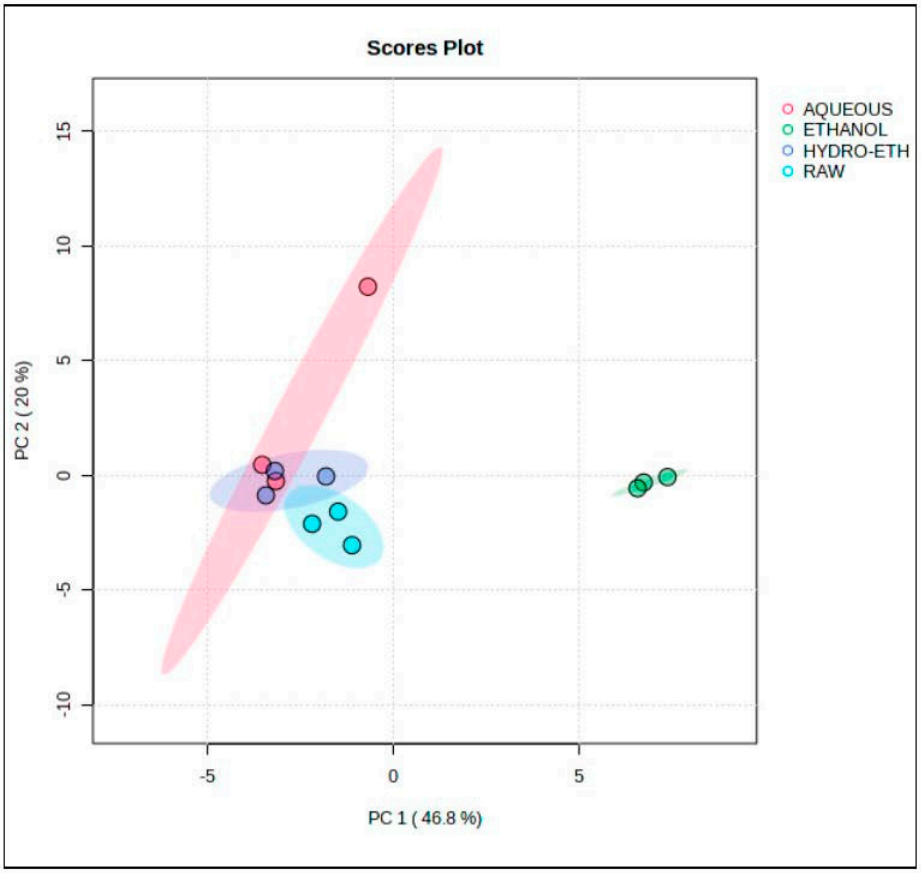
Table S1: Bioactive secondary metabolites identified in various extracts of CS through UPLC-MS analysis

| Compound number | Identity | Average retention time (minute) | m/z [M - H]$^-$ |
|---|---|---|---|
| 1 | (7'R)-(+)-Lyoniresinol 9'-glucoside | 4,071 | 581,2203 |
| 2 | Estriol-16-Glucuronide | 4,149 | 509,2002 |
| 3 | Ascorbic acid | 4,307 | 175,0235 |
| 4 | Methylisocitric acid | 4,389 | 205,0338 |
| 5 | Citraconic acid | 4,524 | 129,0178 |
| 6 | Oxalosuccinic acid | 4,984 | 189,0053 |
| 7 | Pinocembrin 7-apiosyl-(1->5)-apiosyl-(1->2)-glucoside;5,7-Dihydroxyflavanone 7-apiosyl-(1->5)-apiosyl-(1->2)-glucoside | 4,988 | 681,2069 |
| 8 | Mevalonic acid | 5,089 | 147,0657 |
| 9 | D-2-Hydroxyglutaric acid | 5,176 | 147,0287 |
| 10 | (2R,3S)-2,3-dimethylmalic acid | 5,236 | 161,0445 |
| 11 | UNPD109129 | 6,348 | 251,0772 |
| 12 | Glutaric acid | 6,152 | 131,0349 |
| 13 | Cinnamic acid | 6,849 | 147,0448 |
| 14 | (6E)-1-(4-hydroxyphenyl)-7-phenylhepta-4,6-dien-3-one | 8,452 | 277,1251 |
| 15 | Vanillic acid | 8,553 | 167,0338 |
| 16 | 1-O-vanilloyl-beta-D-glucose | 8,553 | 329,0892 |
| 17 | Isorhamnetin 3-(6''-malonylglucoside) | 8,642 | 563,1026 |
| 18 | Saccharumoside C | 9,081 | 461,1286 |
| 19 | 7-hydroxy-4-{3-oxo-3H-benzo[f]chromen-2-yl}-2H-chromen-2-one | 9,14 | 355,0631 |
| 20 | Sarmentose | 9,447 | 161,0809 |
| 21 | CNP0447999 | 9,571 | 353,084 |
| 22 | 1-O-Caffeoylglucose | 9,75 | 341,0882 |
| 23 | 1-O-Galloylglycerol | 10,05 | 243,0488 |
| 24 | C00051555 | 10,106 | 323,1328 |
| 25 | 3-Isopropylmalate | 10,789 | 175,0606 |
| 26 | Diaportinic acid | 10,819 | 279,0534 |
| 27 | Benzyl beta-D-glucopyranoside;(-)-Benzyl-O-beta-D-glucopyranoside | 11,147 | 269,103 |
| 28 | Domesticoside | 11,354 | 343,1013 |
| 29 | Dihydrophaseic acid 4'-O-beta-D-glucopyranoside | 11,369 | 443,1937 |
| 30 | Ketoleucine | 11,471 | 129,0549 |
| 31 | Aesculin | 11,471 | 339,0728 |
| 32 | Chlorogenic acid | 11,997 | 353,0874 |
| 33 | Quinic acid | 12,004 | 191,055 |
| 34 | Cudraphenone A | 12,229 | 363,1627 |
| 35 | Pimelic acid | 12,255 | 159,0653 |
| 36 | (-)-6-((2S,3R,4R,5S,6R)-3,4-dihydroxy-6-(hydroxymethyl)-5-methoxytetrahydro-2H-pyran-2-yloxy)-8-hydroxy-3-methyl-1H-isochromen-1-one | 12,458 | 367,1035 |

| | | | |
|---|---|---|---|
| 37 | (-)-11-hydroxy-9,10-dihydrojasmonic acid 11-beta-D-glucoside | 12,515 | 389,1799 |
| 38 | Caffeic acid | 12,653 | 179,0349 |
| 39 | 5-Carboxyvanillic acid | 12,729 | 211,0234 |
| 40 | Phellodendric acid A;(+)-Phellodendric acid A | 12,754 | 203,0944 |
| 41 | (-)-Epigallocatechin | 13,267 | 305,0676 |
| 42 | D-Leucic acid | 13,289 | 131,0713 |
| 43 | cis-Aconitic acid | 13,501 | 173,0094 |
| 44 | MINEs-320976 | 14,199 | 431,1909 |
| 45 | Loganic acid | 14,248 | 375,1276 |
| 46 | Astragalin 7-rhamnoside | 14,269 | 593,1522 |
| 47 | Quing hau sau; quinghaosu; artemisinin | 14,353 | 281,1399 |
| 48 | 3-Hydroxy-4-butanolide | 14,432 | 263,0786 |
| 49 | Annularin A;(+)-Annularin A | 14,623 | 197,081 |
| 50 | Traumatic acid | 14,781 | 227,1267 |
| 51 | Methyl geranate | 14,869 | 181,1236 |
| 52 | 3-Hydroxytetradecanedioic acid | 14,873 | 273,1726 |
| 53 | Dihydrophaseic acid | 14,937 | 281,1376 |
| 54 | Tuberonic acid | 15,238 | 225,1111 |
| 55 | Daldiniapyrone | 15,294 | 253,1071 |
| 56 | 4-Hydroxycinnamic acid | 15,479 | 163,0386 |
| 57 | Monascusone A | 15,536 | 253,106 |
| 58 | Acetovanillone;Apocynin | 15,596 | 165,0547 |
| 59 | Apiin | 15,756 | 563,1376 |
| 60 | Quercitrin | 15,953 | 447,0915 |
| 61 | 2-Hydroxydecanedioic acid | 16,176 | 217,1065 |
| 62 | UNPD221406 | 16,241 | 241,1083 |
| 63 | Cichorioside M;(+)-Cichorioside M | 16,618 | 427,1946 |
| 64 | Austricin;8-Deacetylmatricarin;Desacetylmatricarin | 16,714 | 261,1154 |
| 65 | trans-Ferulic acid | 17,086 | 193,0499 |
| 66 | UNPD19396 | 17,122 | 577,15 |
| 67 | UNPD77208 | 17,208 | 271,1529 |
| 68 | Nepetaside | 17,236 | 345,1552 |
| 69 | Dodecanedioic acid | 17,417 | 229,1427 |
| 70 | Kaempferitrin | 17,554 | 577,1528 |
| 71 | Chrysoeriol 4',7-diglucuronide | 17,675 | 651,118 |
| 72 | erythronolide B | 17,734 | 401,2548 |
| 73 | UNPD230015 | 17,818 | 263,0574 |
| 74 | 3-Hydroxysebacic acid | 17,836 | 217,106 |
| 75 | Tricin 7-diglucuronoside | 17,958 | 681,1317 |
| 76 | Esculetin | 18,079 | 177,0172 |
| 77 | ethyl 5-[(2,5-dimethylphenyl)methoxy]-2-phenyl-1-benzofuran-3-carboxylate | 18,087 | 399,1613 |
| 78 | xi-2,2,6-Trimethyl-1,4-cyclohexanedione | 18,254 | 153,0928 |
| 79 | Quercetin 3-(2'',3'',4''-triacetylgalactoside) | 18,307 | 589,1204 |
| 80 | [4]-Gingerol | 18,844 | 265,1428 |
| 81 | Phaseic acid | 18,558 | 279,1234 |
| 82 | Diaportinol | 18,603 | 265,0729 |
| 83 | Herbacetin 7-(6''-quinoylglucoside) | 18,677 | 637,1406 |

| | | | |
|---|---|---|---|
| 84 | 12-deoxyerythronolide A | 19,046 | 401,253 |
| 85 | UNPD156113 | 19,094 | 605,1201 |
| 86 | Mirificin | 19,148 | 547,1448 |
| 87 | Phaseolic acid | 19,244 | 261,1326 |
| 88 | Curvularol | 19,367 | 265,1433 |
| 89 | (+)-(S)-Carvone | 19,645 | 149,0958 |
| 90 | Kaempferol 3-rhamnoside 7-galacturonide | 19,868 | 607,1331 |
| 91 | Azelaic acid | 20,074 | 187,0968 |
| 92 | Kaempferol 3-rhamnoside 7-galacturonide | 20,286 | 607,1347 |
| 93 | Stagonolide F;(-)-Stagonolide F | 20,677 | 183,1045 |
| 94 | Isowertin 2''-rhamnoside | 20,732 | 1183,344 |
| 95 | UNPD223815 | 20,864 | 255,1598 |
| 96 | 9-hydroxynonanoic acid | 20,885 | 173,1173 |
| 97 | Maysin | 20,941 | 1151,286 |
| 98 | 5,7,4'-Trihydroxy-3'-methoxyflavone; Luteolin 3'-methyl ether 7-glucuronide | 21,005 | 475,085 |
| 99 | Quercetin 3-O-(6''-acetyl-glucoside) | 21,144 | 505,0988 |
| 100 | Blennin D | 21,154 | 265,1425 |
| 101 | 10-Deoxygeniposidic acid | 21,271 | 357,1225 |
| 102 | Gallicynoic acid F;(-)-Gallicynoic acid F | 21,409 | 343,2093 |
| 103 | Pandangolide 1a;(-)-Pandangolide 1a | 21,459 | 243,1215 |
| 104 | 4-Hydroxynonenal | 21,569 | 155,1078 |
| 105 | Tetradecanedioic acid | 21,764 | 257,1747 |
| 106 | (R)-7-butyl-6,8-dihydroxy-3-[(3E)-pent-3-en-1-yl]-3,4-dihydroisochromen-1-one | 21,818 | 303,1627 |
| 107 | Genistin | 21,815 | 431,0959 |
| 108 | p-Coumaroyl malic acid | 20,852 | 282,1126 |
| 109 | Kaempferol 3-[2'''-acetyl-alpha-L-arabinopyranosyl-(1->6)-galactoside] | 21,942 | 621,1427 |
| 110 | Cyperine | 22,091 | 259,0962 |
| 111 | (+)-Cnicin; Cnicin | 22,111 | 377,1621 |
| 112 | (S)-Abscisic acid | 22,202 | 263,1284 |
| 113 | Sydnic acid; Sydonic acid | 22,233 | 265,1424 |
| 114 | Gallicynoic acid A;(+)-Gallicynoic acid A | 22,806 | 253,1445 |
| 115 | Apigenin 7-O-(6''-O-acetylglucoside) | 22,847 | 473,1057 |
| 116 | UNPD127537 | 23,18 | 255,1597 |
| 117 | Olivetol | 23,205 | 179,1065 |
| 118 | Ginsenoyne E | 23,293 | 303,1604 |
| 119 | Caffeoyl tartaric acid | 23,326 | 312,1225 |
| 120 | Luteolin 3'-methyl ether 7-glucuronide | 23,476 | 265,1425 |
| 121 | UNPD205010 | 23,478 | 343,1748 |
| 122 | Maysin 3'-methyl ether | 23,505 | 589,1541 |
| 123 | Artemin | 23,657 | 265,1458 |
| 124 | Gallicynoic acid B | 23,687 | 267,159 |
| 125 | Aspergillide A | 23,804 | 253,1443 |
| 126 | (S)-Oleuropeic acid | 23,889 | 183,1018 |
| 127 | Sebacic acid | 23,894 | 201,1113 |
| 128 | 7-Acetoxy-5,6-dimethoxycoumarin | 17,818 | 263,0574 |

a


Scores Plot
AQUEOUS
ETHANOL
HYDRO-ETH
RAW
PC 2 ( 20 %)
PC 1 ( 46.8 %)
15
10
5
0
-5
-10
-5
0
5

b

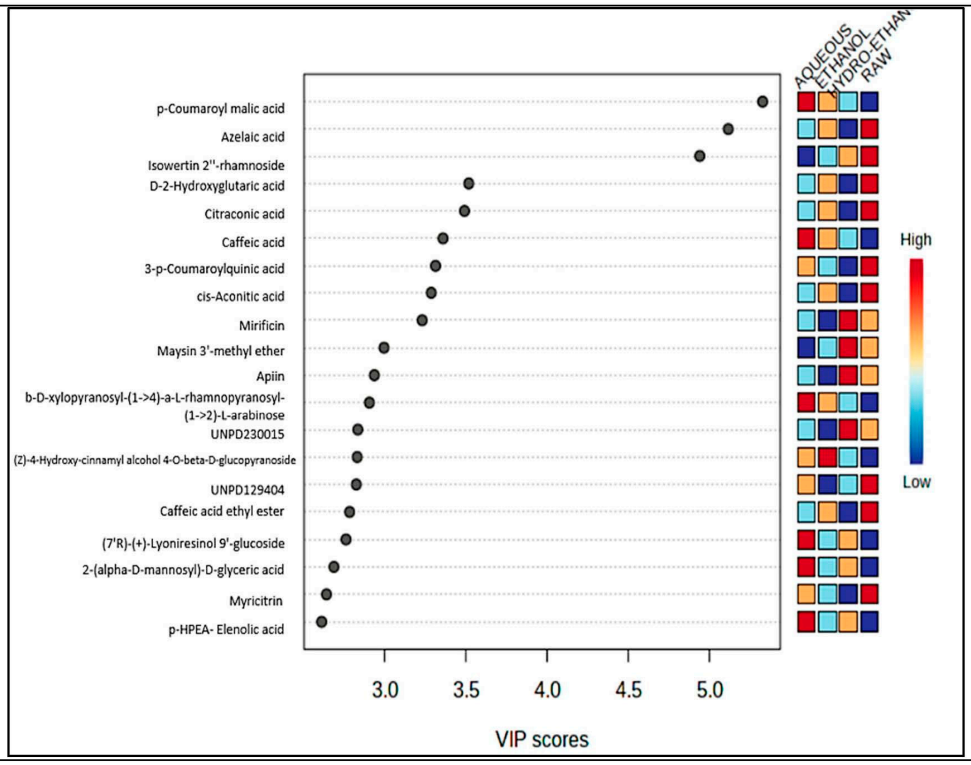

AQUEOUS
ETHANOL
HYDRO-ETHAN
RAW
p-Coumaroyl malic acid
Azelaic acid
Isowertin 2''-rhamnoside
D-2-Hydroxyglutaric acid
Citraconic acid
Caffeic acid
3-p-Coumaroylquinic acid
cis-Aconitic acid
Mirificin
Maysin 3'-methyl ether
Apiin
b-D-xylopyranosyl-(1->4)-a-L-rhamnopyranosyl-(1->2)-L-arabinose
UNPD230015
(Z)-4-Hydroxy-cinnamyl alcohol 4-O-beta-D-glucopyranoside
UNPD129404
Caffeic acid ethyl ester
(7'R)-(+)-Lyoniresinol 9'-glucoside
2-(alpha-D-mannosyl)-D-glyceric acid
Myricitrin
p-HPEA- Elenolic acid
High
Low
3.0
3.5
4.0
4.5
5.0
VIP scores

Figure S2: a) Principal component analysis scores plot showing variance in CS secondary metabolites between the four extracts; b) Partial least square discriminant analysis (PLS-DA) loadings plot showing the differences in the amount of secondary metabolites present in the four samples of CS.

Table S2: Number of Lipinski's violations of CS bioactive compounds

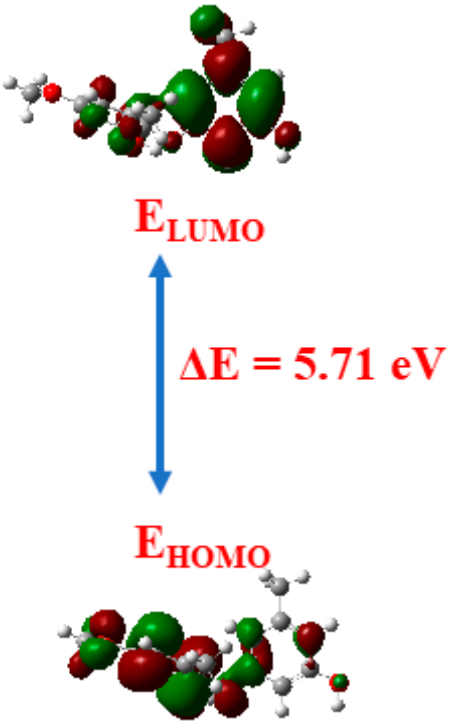
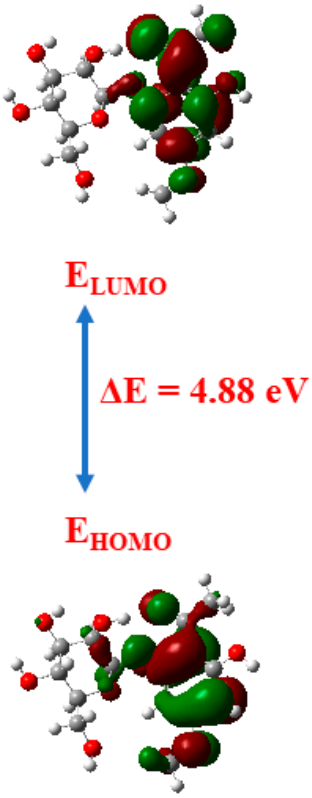
| | Formula | Molecular weight (g/mol) | #H-bond acceptors | #H-bond donors | iLOGP (octanol/ water partition coefficient ) | Lipinski #violations |
|---|---|---|---|---|---|---|
| 1 | C28H38O13 | 582.59 | 13 | 7 | 4.71 | 3 |
| 2 | C24H32O9 | 464.51 | 9 | 6 | 1.67 | 1 |
| 3 | C6H8O6 | 176.12 | 6 | 4 | 0.39 | 0 |
| 4 | C7H10O7 | 206.15 | 7 | 4 | -0.94 | 0 |
| 5 | C5H6O4 | 130.10 | 4 | 2 | 0.46 | 0 |
| 6 | C6H6O7 | 190.11 | 7 | 3 | -0.71 | 0 |
| 7 | C31H38O17 | 682.62 | 17 | 9 | 2.27 | 3 |
| 8 | C6H12O4 | 148.16 | 4 | 3 | 0.39 | 0 |
| 9 | C5H8O5 | 148.11 | 5 | 3 | 0.18 | 0 |
| 10 | C6H10O5 | 162.14 | 5 | 3 | 0.34 | 0 |
| 11 | C9H16O8 | 252.22 | 8 | 5 | 0.37 | 0 |
| 12 | C5H8O4 | 132.11 | 4 | 2 | 0.45 | 0 |
| 13 | C9H8O2 | 148.16 | 2 | 1 | 1.55 | 0 |
| 14 | C19H18O2 | 278.35 | 2 | 1 | 2.79 | 0 |
| 15 | C8H8O4 | 168.15 | 4 | 2 | 1.40 | 0 |
| 16 | C14H18O9 | 330.29 | 9 | 5 | 1.88 | 0 |
| 17 | C25H24O15 | 564.45 | 15 | 7 | 1.77 | 3 |
| 18 | C19H26O13 | 462.40 | 13 | 7 | 1.35 | 2 |
| 19 | C22H12O5 | 356.33 | 5 | 1 | 2.52 | 0 |
| 20 | C7H14O4 | 162.18 | 4 | 2 | 0.94 | 0 |
| 21 | C23H14O4 | 354.35 | 4 | 1 | 2.41 | 0 |
| 22 | C15H18O9 | 342.30 | 9 | 6 | 0.23 | 1 |
| 23 | C10H12O7 | 244.20 | 7 | 5 | 0.63 | 0 |
| 24 | C13H24O9 | 324.32 | 9 | 5 | 1.95 | 0 |
| 25 | C7H12O5 | 176.17 | 5 | 3 | 0.24 | 0 |
| 26 | C13H12O7 | 280.23 | 7 | 3 | 1.54 | 0 |
| 27 | C13H18O6 | 270.28 | 6 | 4 | 1.60 | 0 |
| 28 | C15H20O9 | 344.31 | 9 | 5 | 2.05 | 0 |
| 29 | C21H32O10 | 444.47 | 10 | 6 | 1.89 | 1 |
| 30 | C6H10O3 | 130.14 | 3 | 1 | 1.06 | 0 |
| 31 | C15H16O9 | 340.28 | 9 | 5 | 1.04 | 0 |
| 32 | C16H18O9 | 354.31 | 9 | 6 | 0.96 | 1 |
| 33 | C7H12O6 | 192.17 | 6 | 5 | -0.12 | 0 |
| 34 | C23H24O4 | 364.43 | 4 | 2 | 3.70 | 0 |
| 35 | C7H12O4 | 160.17 | 4 | 2 | 0.94 | 0 |
| 36 | C17H20O9 | 368.34 | 9 | 4 | 2.54 | 0 |
| 37 | C18H30O9 | 390.43 | 9 | 5 | 2.35 | 0 |
| 38 | C9H8O4 | 180.16 | 4 | 3 | 0.97 | 0 |
| 39 | C9H8O6 | 212.16 | 6 | 3 | 0.24 | 0 |
| 40 | C9H16O5 | 204.22 | 5 | 2 | 1.55 | 0 |
| 41 | C15H14O7 | 306.27 | 7 | 6 | 0.98 | 1 |
| 42 | C6H12O3 | 132.16 | 3 | 2 | 1.17 | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 43 | C6H6O6 | 174.11 | 6 | 3 | -0.13 | 0 |
| 44 | C20H32O10 | 432.46 | 10 | 6 | 1.57 | 1 |
| 45 | C16H24O10 | 376.36 | 10 | 6 | 1.26 | 1 |
| 46 | C27H30O15 | 594.52 | 15 | 9 | 1.80 | 3 |
| 47 | C15H22O5 | 282.33 | 5 | 0 | 2.75 | 0 |
| 48 | C10H16O8 | 264.23 | 8 | 4 | 0.97 | 0 |
| 49 | C10H14O4 | 198.22 | 4 | 1 | 2.32 | 0 |
| 50 | C12H20O4 | 228.28 | 4 | 2 | 2.04 | 0 |
| 51 | C11H18O2 | 182.26 | 2 | 0 | 3.05 | 0 |
| 52 | C14H26O5 | 274.35 | 5 | 3 | 2.34 | 0 |
| 53 | C15H22O5 | 282.33 | 5 | 3 | 2.09 | 0 |
| 54 | C12H18O4 | 226.27 | 4 | 2 | 1.46 | 0 |
| 55 | C13H18O5 | 254.28 | 5 | 0 | 3.07 | 0 |
| 56 | C9H8O3 | 164.16 | 3 | 2 | 0.95 | 0 |
| 57 | C13H18O5 | 254.28 | 5 | 3 | 1.82 | 0 |
| 58 | C9H10O3 | 166.17 | 3 | 1 | 1.77 | 0 |
| 59 | C26H28O14 | 564.49 | 14 | 8 | 2.11 | 3 |
| 60 | C21H20O11 | 448.38 | 11 | 7 | 1.27 | 2 |
| 61 | C10H18O5 | 218.25 | 5 | 3 | 0.96 | 0 |
| 62 | C12H18O5 | 242.27 | 5 | 2 | 1.81 | 0 |
| 63 | C21H32O9 | 428.47 | 9 | 5 | 1.97 | 0 |
| 64 | C15H18O4 | 262.30 | 4 | 1 | 2.03 | 0 |
| 65 | C10H10O4 | 194.18 | 4 | 2 | 1.62 | 0 |
| 66 | C34H26O9 | 578.56 | 9 | 6 | 3.45 | 2 |
| 67 | C14H24O5 | 272.34 | 5 | 1 | 2.71 | 0 |
| 68 | C16H26O8 | 346.37 | 8 | 4 | 2.06 | 0 |
| 69 | C12H22O4 | 230.30 | 4 | 2 | 1.83 | 0 |
| 70 | C27H30O14 | 578.52 | 14 | 8 | 1.89 | 3 |
| 71 | C28H28O18 | 652.51 | 18 | 9 | 0.94 | 3 |
| 72 | C21H38O7 | 402.52 | 7 | 4 | 2.83 | 0 |
| 73 | C13H12O6 | 264.23 | 6 | 3 | 1.70 | 0 |
| 74 | C10H18O5 | 218.25 | 5 | 3 | 1.32 | 0 |
| 75 | C29H30O19 | 682.54 | 19 | 9 | 1.95 | 3 |
| 76 | C9H6O4 | 178.14 | 4 | 2 | 1.25 | 0 |
| 77 | C26H24O4 | 400.47 | 4 | 0 | 4.45 | 1 |
| 78 | C9H14O2 | 154.21 | 2 | 0 | 1.63 | 0 |
| 79 | C27H26O15 | 590.49 | 15 | 5 | 1.94 | 2 |
| 80 | C15H22O4 | 266.33 | 4 | 2 | 2.38 | 0 |
| 81 | C15H20O5 | 280.32 | 5 | 2 | 1.76 | 0 |
| 82 | C13H14O6 | 266.25 | 6 | 3 | 2.33 | 0 |
| 83 | C28H30O17 | 638.53 | 17 | 11 | 1.81 | 3 |
| 84 | C21H38O7 | 402.52 | 7 | 4 | 2.83 | 0 |
| 85 | C27H26O16 | 606.49 | 16 | 9 | 2.59 | 3 |
| 86 | C26H28O13 | 548.49 | 13 | 8 | 0.66 | 3 |
| 87 | C12H22O6 | 262.30 | 6 | 4 | 1.32 | 0 |
| 88 | C15H22O4 | 266.33 | 4 | 2 | 2.35 | 0 |
| 89 | C10H14O | 150.22 | 1 | 0 | 2.27 | 0 |
| 90 | C27H28O16 | 608.50 | 16 | 9 | 1.66 | 3 |
| 91 | C9H16O4 | 188.22 | 4 | 2 | 1.44 | 0 |
| 92 | C27H28O16 | 608.50 | 16 | 9 | 1.66 | 3 |
| 93 | C10H16O3 | 184.23 | 3 | 1 | 2.03 | 0 |
| 94 | C28H32O14 | 592.55 | 14 | 8 | 0.80 | 3 |
| 95 | C14H24O4 | 256.34 | 4 | 1 | 3.26 | 0 |
| 96 | C9H18O3 | 174.24 | 3 | 2 | 1.83 | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 97 | C27H28O14 | 576.50 | 14 | 8 | 1.95 | 3 |
| 98 | C22H20O12 | 476.39 | 12 | 6 | 2.02 | 2 |
| 99 | C23H22O13 | 506.41 | 13 | 7 | 1.61 | 3 |
| 100 | C15H22O4 | 266.33 | 4 | 2 | 2.46 | 0 |
| 101 | C16H22O9 | 358.34 | 9 | 5 | 1.24 | 0 |
| 102 | C18H32O6 | 344.44 | 6 | 5 | 2.95 | 0 |
| 103 | C12H20O5 | 244.28 | 5 | 2 | 1.91 | 0 |
| 104 | C9H16O2 | 156.22 | 2 | 1 | 2.15 | 0 |
| 105 | C14H26O4 | 258.35 | 4 | 2 | 2.49 | 0 |
| 106 | C18H24O4 | 304.38 | 4 | 2 | 3.45 | 0 |
| 107 | C21H20O10 | 432.38 | 10 | 6 | 2.11 | 1 |
| 108 | C13H12O7 | 280.23 | 7 | 3 | 0.62 | 0 |
| 109 | C28H30O16 | 622.53 | 16 | 8 | 1.81 | 3 |
| 110 | C15H16O4 | 260.29 | 4 | 2 | 2.73 | 0 |
| 111 | C20H26O7 | 378.42 | 7 | 3 | 1.97 | 0 |
| 112 | C15H20O4 | 264.32 | 4 | 2 | 1.97 | 0 |
| 113 | C15H22O4 | 266.33 | 4 | 3 | 2.59 | 0 |
| 114 | C14H22O4 | 254.32 | 4 | 3 | 2.19 | 0 |
| 115 | C23H22O11 | 474.41 | 11 | 5 | 2.31 | 1 |
| 116 | C14H24O4 | 256.34 | 4 | 2 | 2.66 | 0 |
| 117 | C11H16O2 | 180.24 | 2 | 2 | 2.04 | 0 |
| 118 | C17H22O2 | 258.36 | 2 | 0 | 4.10 | 0 |
| 119 | C13H12O9 | 312.23 | 9 | 5 | 0.55 | 0 |
| 120 | C28H30O16 | 622.50 | 4 | 3 | 2.59 | 1 |
| 121 | C17H28O7 | 344.40 | 7 | 2 | 2.59 | 0 |
| 122 | C28H30O14 | 590.53 | 14 | 7 | 1.76 | 3 |
| 123 | C15H22O4 | 266.33 | 4 | 2 | 2.19 | 0 |
| 124 | C15H24O4 | 268.35 | 4 | 3 | 2.87 | 0 |
| 125 | C14H22O4 | 254.32 | 4 | 1 | 2.59 | 0 |
| 126 | C10H16O3 | 184.23 | 3 | 2 | 1.65 | 0 |
| 127 | C10H18O4 | 202.25 | 4 | 2 | 1.77 | 0 |
| 128 | C13H12O6 | 264.23 | 6 | 3 | 1.70 | 1 |

Table S3: Frontier molecular orbitals for the top-scoring compounds against ADORA1, HCAR2, GABBR1

| Compound | Frontier molecular orbital |
|---|---|
| ADORA1 | |

| | |
|---|---|
| Cyperine |  |
| Domesticoside |  |

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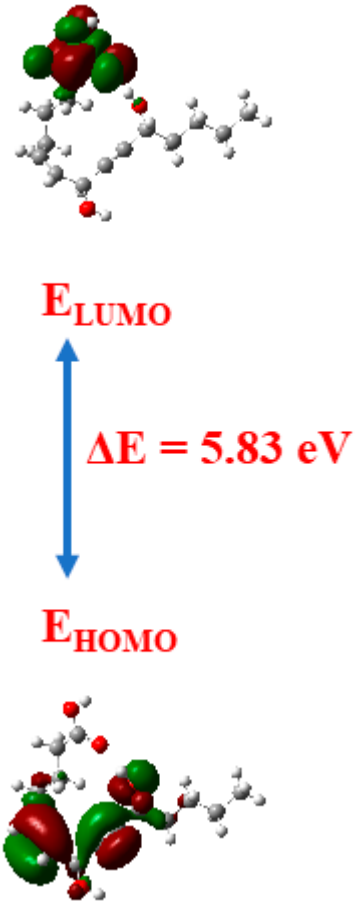
| Gallicynoic acid B |  |

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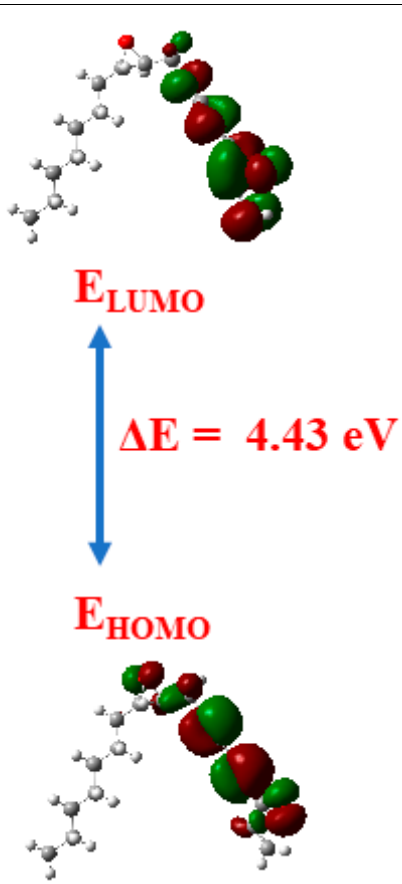
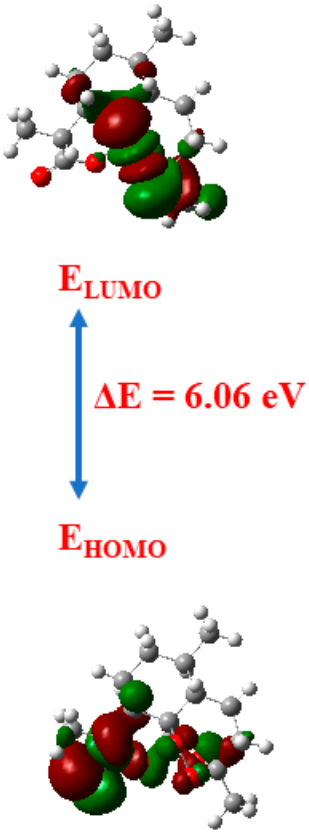
| Ginsenoyne E |  |
| Quing hau sau |  |

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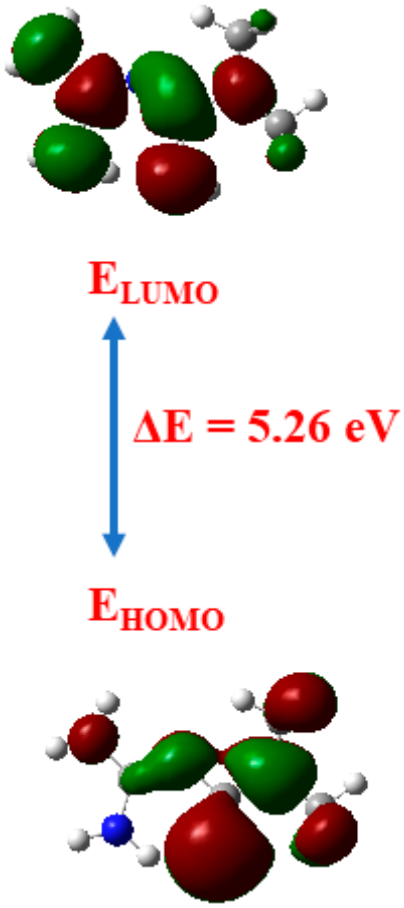
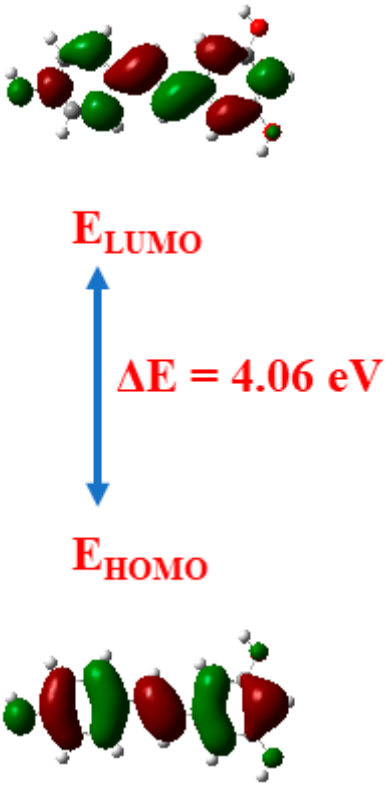
| Metformin |  |
| Reservatrol |  |

| **HCAR2** | |
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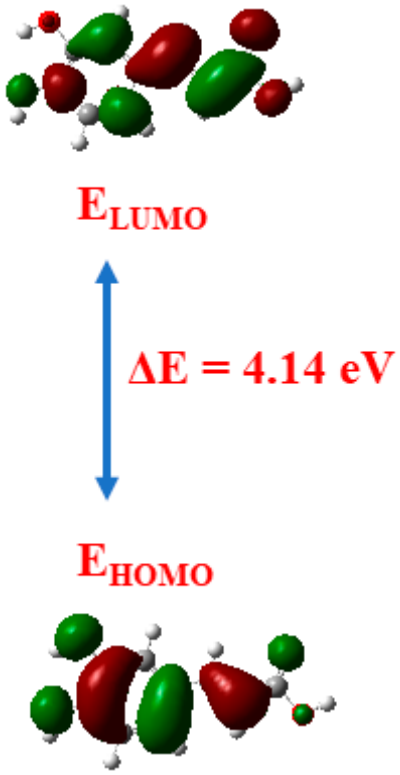
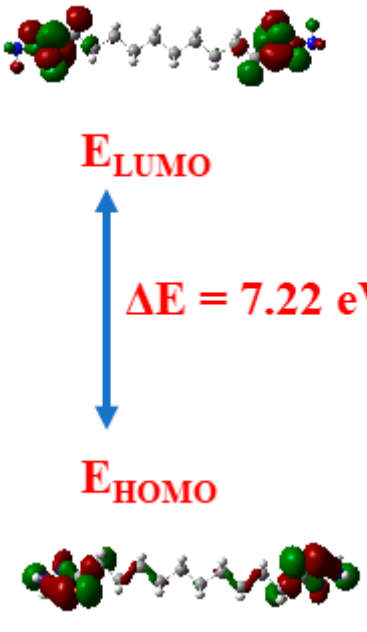
| Caffeic acid |  |
| Dodecanedioc acid |  |

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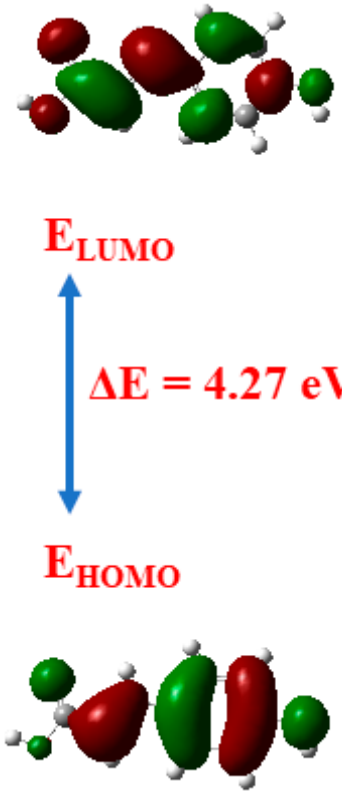
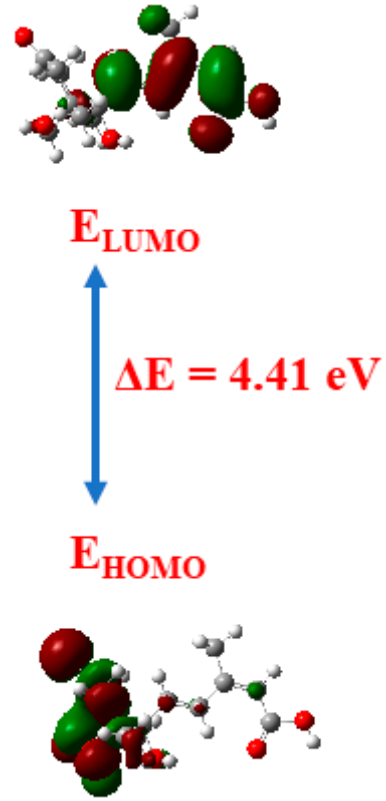
| 4-Hydroxycinnamic acid |  |
| Phaseic acid |  |

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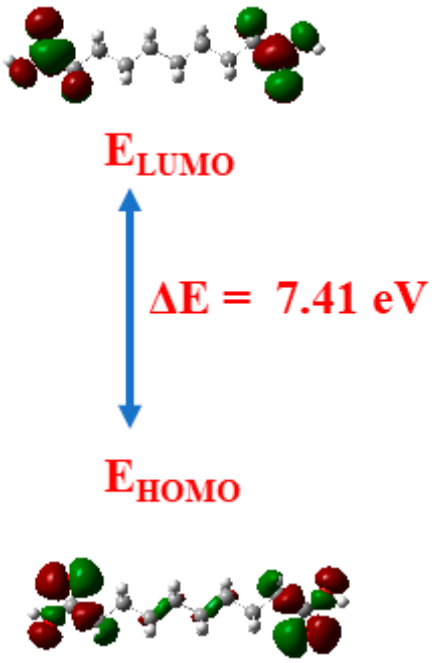
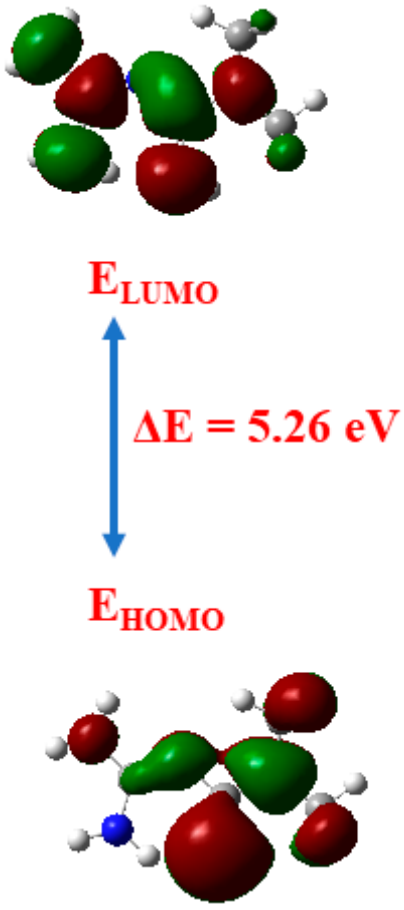
| Sebaic acid |  |
| Metformin |  |

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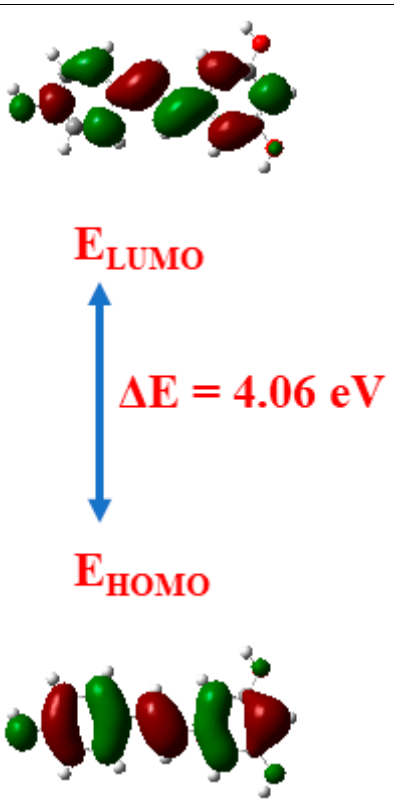
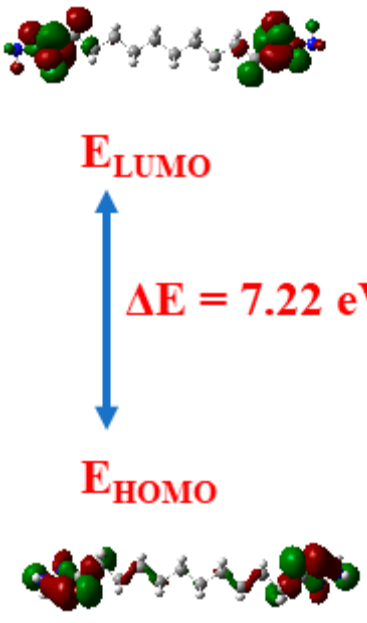
| Reservatrol |  |
| **GABBR1** | |
| Dodecanedioc acid |  |

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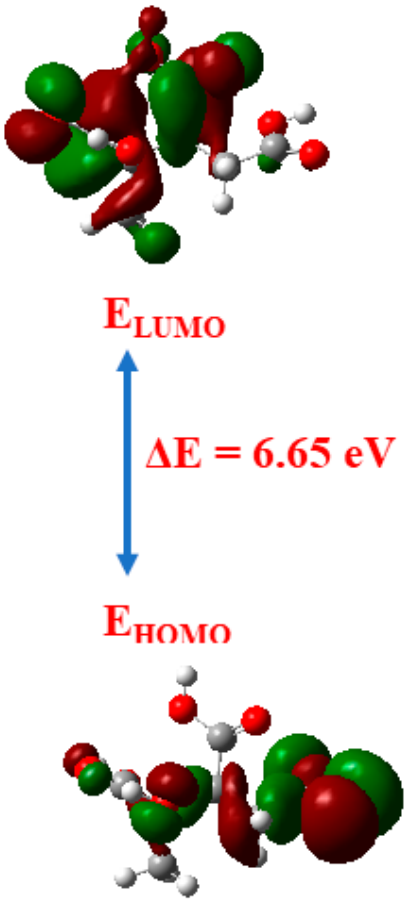
| Methylisocitric acid |  |

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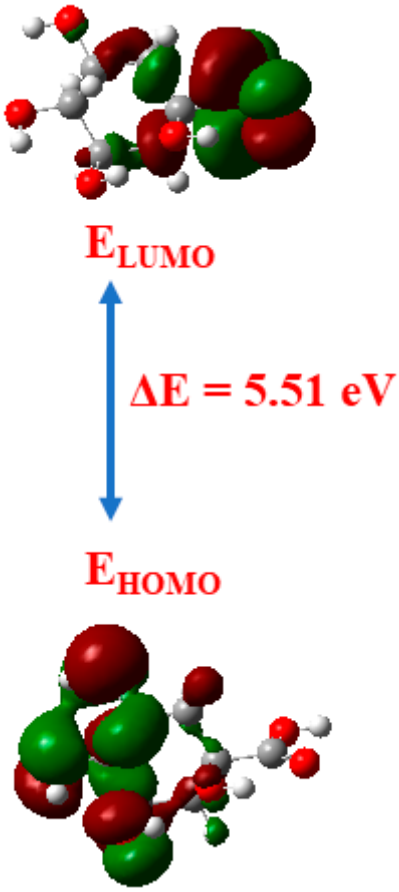
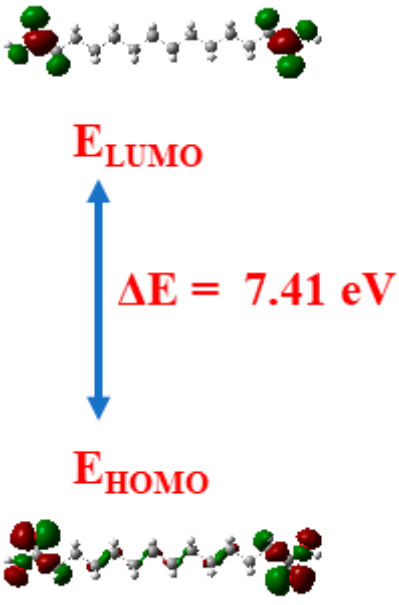
| Quinic acid |  |
| Tetradecanedioc acid |  |

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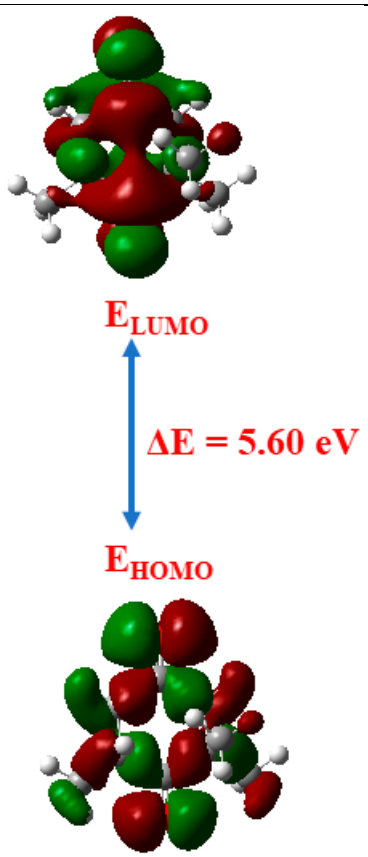
| Xi-2,2,6-Trimethyl-1,4-Cyclohexanedione |  |

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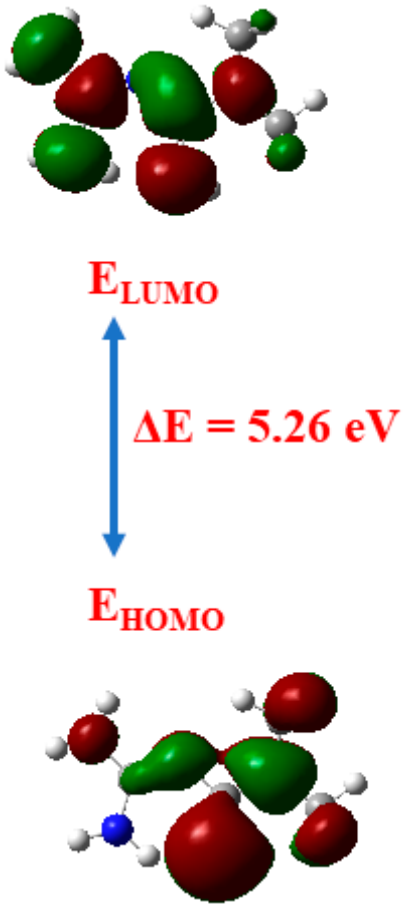
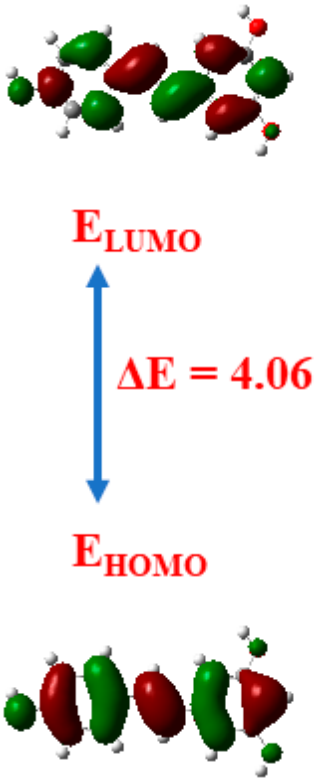
|---|---|
| Metformin |  |
| Reservatrol |  |

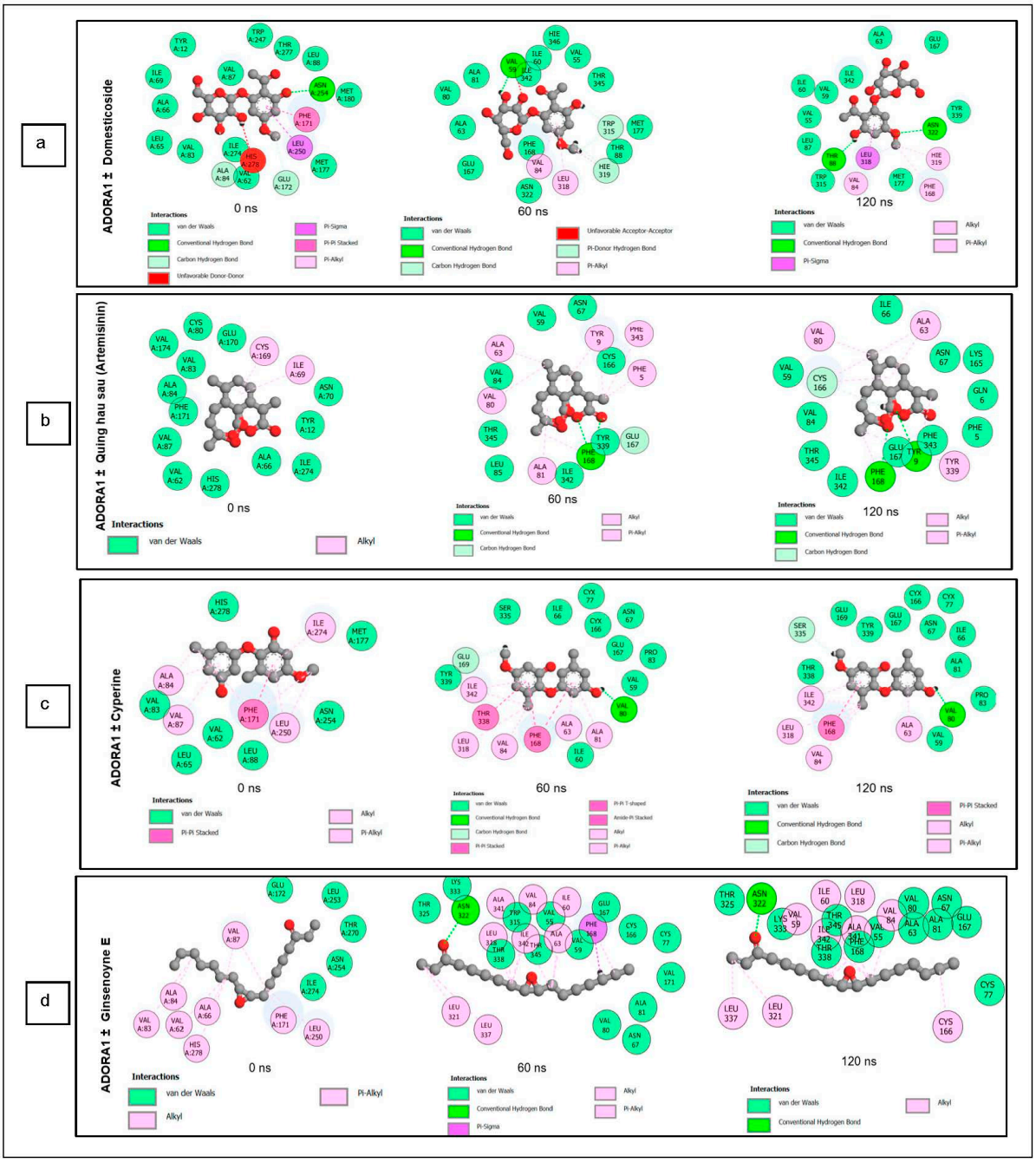



Figure S3: a) domesticoside, b) quing hau sau, c) cyperine and d) ginsenoyne E, over a 120 ns simulation

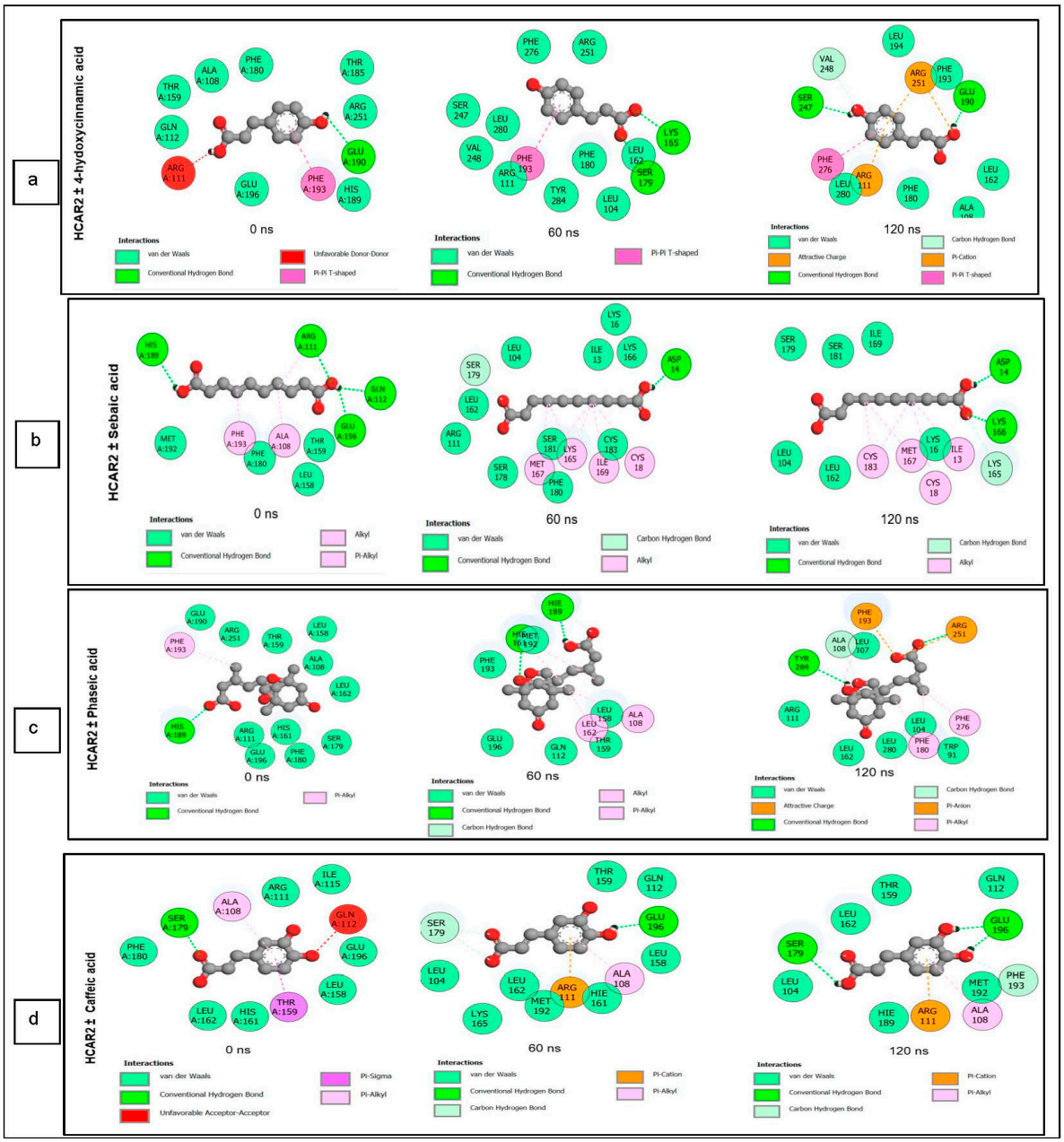



Figure S4: 2-D interaction plots of target gene HCAR2 with bioactive constituents present in CS: a) 4-hydroxycinnamic acid, b) sebacic acid, c) phaseic acid and d) caffeic acid over a 120 ns simulation

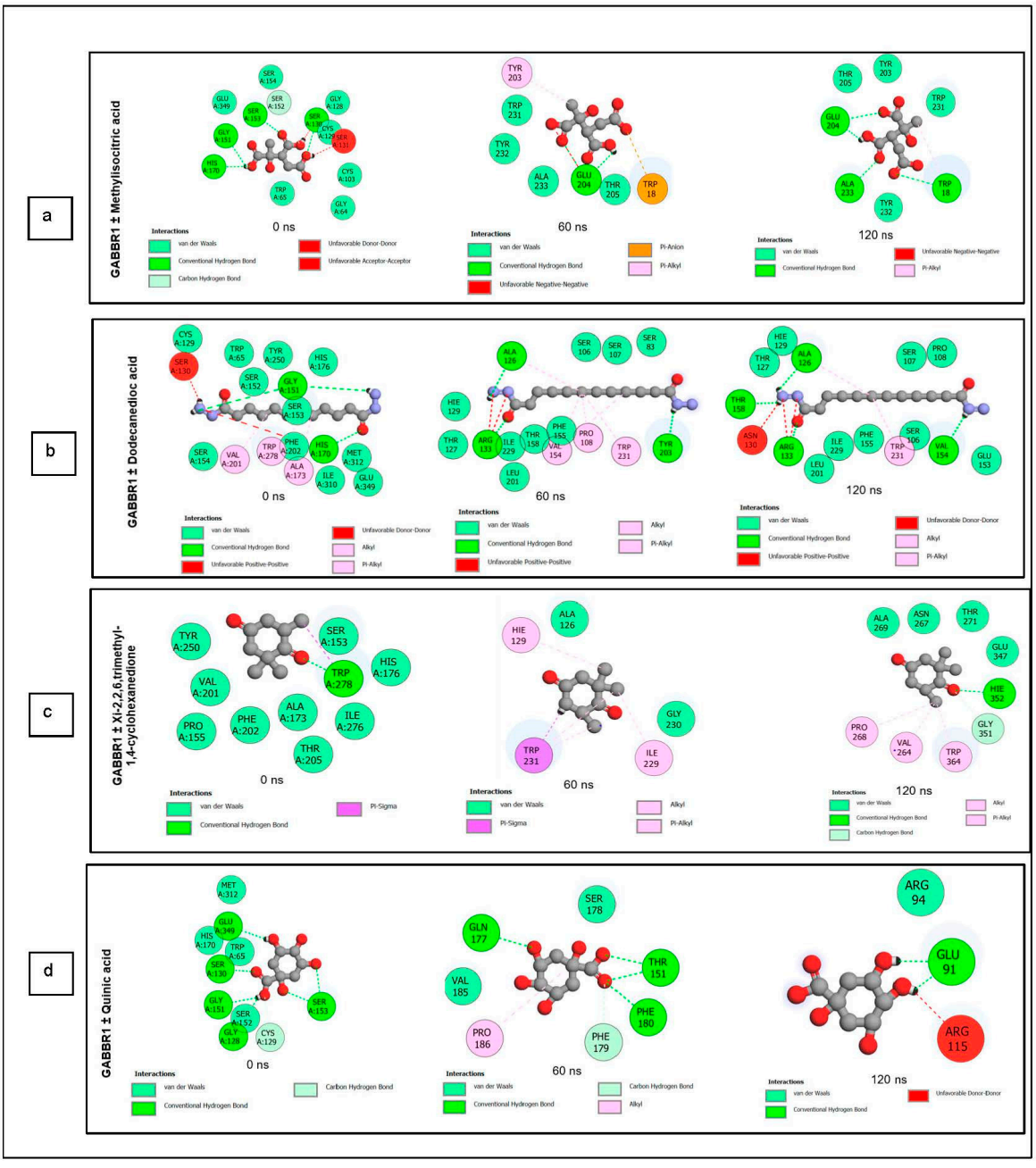



Figure S5: 2-D interaction plots of target gene GABBR1 with bioactive constituents present in CS: a) methylisocitric acid, b) dodecanedioc acid, c) xi-2,2,6,trimethyl-1,4-cyclohexanedione and d) quinic acid, over a 120 ns simulation.