Supplementary Material

Study of Ganshu Nuodan in protecting against alcohol liver disease using proteomics and network pharmacology

# Supplementary Table 1. Compounds identified in Ganshu Nuodan using HPLC-QTOF-MS

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No | tR  min | Predicted formula | | Neutral  mass | Observed  m/z | mass error  （mDa） | MS/MS | Adduct | Component name | Herb | Structure |
| 1 | 4.11 | | C20H18O10 | 418.0900 | 419.0971 | -0.1 | 299.0538 [C16H11O6]+, 137.0230[C7H5O3]+ | +H | Bifendate | LZ | others |
| 2 | 4.41 | | C17H12O6 | 312.0634 | 313.0710 | 0.3 | 133.0281 [C8H5O2]+, 110.0252 [C6H6O2]+ | +H | Tournefolic acid A | HQ | organic acid |
| 3 | 4.92 | | C21H20O9 | 416.1180 | 417.1180 | 0.2 | 255.0652 [C15H11O4]+, 137.0233 [C7H5O3]+, 93.0335 [C6H5O]+ | +H, +Na | Puerarin | GG | flavonoid |
| 4 | 5.7 | | C16H14O4 | 270.0892 | 269.0812 | -0.7 | 150.0307 [C8H6O3]-, 243.0653 [C14H11O4]-, 177.0549 [C10H9O3]- | -H | Isoimperatorin | DS | coumarin |
| 5 | 6.77 | | C22H22O9 | 430.1264 | 431.1336 | -0.1 | 139.0388 [C7H7O3]+, 267.0648 [C16H11O4]+,239.0692 [C15H11O3]+ | +H, +Na | Ononin | DS | flavonoid |
| 6 | 6.97 | | C15H10O5 | 270.0528 | 271.0602 | 0.1 | 253.0492 [C15H9O4]+, 137.023 [C7H5O3]+ | +H | 7,8,4'-Trihydroxyisoflavone | LZ | flavonoid |
| 7 | 7.08 | | C18H16O8 | 360.0845 | 361.0913 | -0.5 | 163.0391 [C9H7O3]+, 145.0281 [C9H5O2]+ | +H, +Na | Rosmarinic acid | DS | organic acid |
| 8 | 7.12 | | C11H10O4 | 206.0579 | 207.0650 | -0.2 | 153.0533 [C8H9O3]+, 163.0391[C9H7O3]+ | +H | Scoparone | DS | coumarin |
| 9 | 7.14 | | C18H12O7 | 340.0583 | 341.0656 | 0.1 | 295.0599 [C17H11O5]+, 279.0648 [C17H11O4]+ | +H | salvianolic acid | DS | organic acid |
| 10 | 7.34 | | C29H38O16 | 642.216 | 641.2083 | -0.4 | 193.0503 [C10H9O4]-, 317.1014 [C17H17O6]- | -H | 5'-hydroxyiso-muronulatol-2',5'-di-O-glucoside | LZ | flavonoid |
| 11 | 7.4 | | C18H16O5 | 312.0998 | 313.1064 | -0.7 | 249.0545 [C16H9O3]+, 111.0437 [C6H7O2]+, 137.023 [C7H5O3]+ | +H | przewaquinone f | DS | quinone |
| 12 | 7.44 | | C27H22O12 | 538.1111 | 539.1181 | -0.3 | 323.0551 [C18H11O6]+，295.0604 [C17H11O5]+ | +H | salvianolic acid j | DS | organic acid |
| 13 | 7.54 | | C18H18O5 | 314.1154 | 315.1224 | -0.3 | 283.0594 [C16H11O5]+, 283.0602[C16H11O5]+, 253.0494[C15H9O4]+ | +H, +Na | 3,9-di-O-methylnissolin | LZ | flavonoid |
| 14 | 7.71 | | C21H18O11 | 446.0849 | 447.0933 | 1.1 | 269.0425 [C15H9O5]+，146.0348 [C9H6O2]+ | +H | Baicalin | LZ | flavonoid |
| 15 | 7.84 | | C15H10O4 | 254.0579 | 255.0652 | 0.1 | 137.0231 [C7H5O3]+, 119.0485 [C8H7O]+, 109.0278 [C6H5O2]+ | +H, +Na | Daidzein | LZ | flavonoid |
| 16 | 8.17 | | C29H38O15 | 626.2211 | 625.2121 | -1.7 | 267.0655 [C16H11O4]-, 299.0911 [C17H15O5]-, 282.0526 [C16H10O5]- | -H, +HCOO | isomucronulatol-7,2'-di-O-glucosiole | DS | flavonoid |
| 17 | 8.21 | | C23H26O10 | 462.1526 | 485.1422 | 0.4 | 299.0911 [C17H15O5]+, 284.0679 [C16H12O5]+ | +Na | 9,10-dimethoxypterocarpan-3-O-β-D-glucoside | LZ | flavonoid |
| 18 | 8.31 | | C16H12O5 | 284.0685 | 285.076 | 0.3 | 253.0495 [C15H9O4]+, 269.0442 [C15H9O5]+, 133.0279 [C8H5O2]+ | +H, +Na | 3'-Methoxydaidzein | LZ | flavonoid |
| 19 | 8.31 | | C16H12O5 | 284.0685 | 283.0611 | -0.1 | 268.0374 [C15H8O5]-, 135.0082 [C7H3O3]-, 132.0213 [C8H4O2]- | -H | Calycosin | LZ | flavonoid |
| 20 | 8.54 | | C17H14O6 | 314.079 | 315.0863 | 0 | 300.0628 [C16H12O6]+, 167.0339 [C8H7O4]+ | +H, +Na | Jaranol | DS | flavonoid |
| 21 | 8.76 | | C18H16O5 | 312.0998 | 313.1068 | -0.2 | 221.0956 [C16H13O]+, 285.0755[C16H13O5]+, 267.1012[C17H15O3]+ | +H, +Na | (6S,7R)-6,7-dihydroxy-1,6-dimethyl-8,9-dihydro-7H-naphtho[8,7-g]benzofuran-10,11-dione | LZ | quinone |
| 22 | 8.76 | | C17H14O3 | 266.0943 | 267.1012 | -0.3 | 202.0770 [C16H10]+, 221.0956 [C16H13O]+, 249.0907 [C17H13O2]+ | +H | dihydrotanshinlactone | DS | coumarin |
| 23 | 9.06 | | C15H10O5 | 270.0528 | 271.0603 | 0.2 | 253.0490 [C15H9O4]+, 145.0278 [C9H5O2]+, 119.0489 [C8H7O]+ | +H | Genistein | DS | flavonoid |
| 24 | 9.27 | | C18H16O4 | 296.1049 | 297.1118 | -0.3 | 255.0652 [C15H11O4]+, 269.0806 [C16H13O4]+ | +H, +Na | przewaquinone c | DS | quinone |
| 25 | 9.36 | | C17H16O6 | 316.0947 | 315.0861 | -1.3 | 284.0311 [C15H8O6]-, 119.0496 [C8H7O]-, 137.0236 [C7H5O3]- | -H | isoflavanone | DS | flavonoid |
| 26 | 9.44 | | C18H16O4 | 296.1049 | 297.1116 | -0.5 | 249.09 [C17H13O2]+, 202.0775 [C16H10]+ | +H, +Na | tanshinone Ⅵ | DS | quinone |
| 27 | 9.68 | | C30H46O2 | 438.3498 | 439.3563 | -0.7 | 421.3455 [C30H45O]+, 145.10045 [C11H13]+ | +H | Lucialdehyde A | DS | terpenoid |
| 28 | 9.75 | | C19H20O4 | 312.1362 | 313.1437 | 0.3 | 249.0908 [C17H13O2]+, 225.0530 [C14H9O3]+ | +H | miltionone Ⅱ | DS | quinone |
| 29 | 10.08 | | C19H20O4 | 312.1362 | 313.1433 | -0.2 | 251.1062 [C17H15O2]+, 225.0539 [C14H9O3]+ | +H, +Na | miltionone Ⅰ | DS | quinone |
| 30 | 10.32 | | C16H12O4 | 268.0736 | 269.0812 | 0.3 | 254.0564 [C15H10O4]+, 118.0490 [C8H6O]+, 137.0229 [C7H5O3]+, | +H, +Na | Formononetin | GG  HQ | flavonoid |
| 31 | 10.54 | | C30H48O4 | 472.3553 | 473.3623 | -0.2 | 297.2212 [C21H29O]+, 437.3412 [C30H45O2]+, 455.3516 [C30H47O3]+ | +H | Epoxyganoderiol A | DS | terpenoid |
| 32 | 10.54 | | C30H46O3 | 454.3447 | 455.3518 | -0.2 | 143.1064 [C8H15O2]+, 437.3412 [C30H45O2]+, 419.3304 [C30H43O]+ | +H | Ganoderic acid Y | DS | organic acid |
| 33 | 10.56 | | C18H12O4 | 292.0736 | 293.0807 | -0.2 | 205.0646 [C15H9O]+, 219.0789 [C16H11O]+ | +H | Przewaquinone B | DS | quinone |
| 34 | 10.6 | | C17H16O5 | 300.0998 | 301.1073 | 0.2 | 152.0462 [C8H8O3]+, 167.0704 [C9H11O3]+, 134.0359 [C8H6O2]+ | +H, +Na | Methylnissolin | DS | flavonoid |
| 35 | 10.81 | | C17H18O5 | 302.1154 | 303.1224 | -0.3 | 149.0590 [C9H9O2]+, 106.0404 [C7H6O]+ | +H | Isomucrnulatol | DS | flavonoid |
| 36 | 10.91 | | C18H14O4 | 294.0892 | 295.0965 | 0 | 169.0640 [C12H9O]+, 221.0944 [C16H13O]+ | +H, +Na | 3-beta-Hydroxymethyllenetanshiquinone | LZ | quinone |
| 37 | 10.91 | | C27H38O6 | 458.2668 | 457.2582 | -1.4 | 253.1220 [C17H17O2]-, 267.1009 [C17H15O3]-, 211.1332 [C12H19O3]- | -H | lucidenic acid A | DS | organic acid |
| 38 | 10.94 | | C30H42O8 | 530.2880 | 529.2798 | -0.8 | 357.1693 [C21H25O5]-, 511.2688 [C30H39O7­]-, 457.2586 [C27H37O6]- | -H | Ganoderic acid C6 | DS | organic acid |
| 39 | 11.2 | | C28H42O6 | 474.2981 | 497.289 | 1.6 | 437.3412 [C30H45O2]+, 256.1105 [C16H16O3]+ | +Na | Methyl lucidenate Q | DS | terpenoid |
| 40 | 11.24 | | C18H20O3 | 284.1412 | 285.1483 | -0.2 | 142.0760 [C11H10]+, 85.0282 [C4H5O2]+ | +H | epidanshenspiroketallactone | DS | others |
| 41 | 11.46 | | C18H20O5 | 316.1311 | 339.1221 | 1.9 | 177.0902 [C11H13O2]+, 143.1064 [C8H15O2]+, 125.0958 [C8H13O]+ | +Na | 7-O-ethylisomucronulatol | LZ | flavonoid |
| 42 | 11.46 | | C20H20O6 | 356.126 | 355.1176 | -1.1 | 239.0334 [C14H7O4]-, 295.0600 [C17­H­11O5]-, 323.0912 [C19H15O5]- | -H | 2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-3-benzofurancarboxaldehyde | DS | others |
| 43 | 11.52 | | C30H44O6 | 500.3138 | 499.3054 | -1.1 | 437.3044 [C29H41O3]-, 285.1842 [C19H25O2]-, 481.2943 [C30H41O5]- | -H | Ganoderic acid beta | DS | organic acid |
| 44 | 11.61 | | C17H12O4 | 280.0736 | 281.0805 | -0.3 | 224.0815 [C15H12O2]+, 225.0537 [C14H9O3]+ | +H, +Na | Nortanshinone | DS | quinone |
| 45 | 11.64 | | C30H44O9 | 548.2985 | 571.2895 | 1.8 | 407.2786 [C24H39O5]+, 321.1850 [C22H25O2]+ | +Na | 20-Hydroxyganoderic acid G | LZ | organic acid |
| 46 | 11.69 | | C18H18O3 | 282.1256 | 283.1324 | -0.5 | 265.1220 [C18H17O2]+, 185.0977 [C13H13O]+, 208.0868 [C15H12O]+ | +H | danshenspiroketallactone | DS | quinone |
| 47 | 11.84 | | C19H18O4 | 310.1205 | 311.128 | 0.3 | 293.1165 [C19H17O3]+, 141.0696 [C11H9]+ | +H, +Na | 3α-hydroxytanshinoneⅡa | LZ | quinone |
| 48 | 11.87 | | C19H16O3 | 292.1099 | 293.1168 | -0.4 | 219.0794 [C16H11O]+, 235.1110 [C17H15O]+ | +H | Dehydrotanshinone II A | DS | quinone |
| 49 | 11.95 | | C19H18O4 | 310.1205 | 311.1281 | 0.3 | 185.0955 [C13H13O]+, 252.1141 [C17H16O2]+, 237.0904 [C16H13O2]+ | +H | TanshinoneIIB | DS | quinone |
| 50 | 12.16 | | C30H46O3 | 454.3447 | 455.3509 | -1 | 297.2206 [C21H29O]+, 437.3409 [C­30H45O2]+, 419.3302 [C30H43O]+ | +H | 15alpha,26-Dihydroxy-5alpha-lanosta-7,9(11),24-triene-3-one | LZ | others |
| 51 | 12.46 | | C30H46O5 | 486.3345 | 485.3265 | -0.8 | 277.2161 [C18H29O2]-, 171.10208 [C9H15O3]-, 221.1540 [C14H21O2]- | -H, +HCOO | 3α,15α,22α-trihydroxylanosta-7,9(11),24-trien-26-oic acid | LZ | organic acid |
| 52 | 12.6 | | C19H16O4 | 308.1049 | 309.1121 | -0.1 | 265.0844 [C17H13O3]+, 279.1008 [C18H15O3]+ | +H | tanshinaldehyde | DS | quinone |
| 53 | 12.88 | | C28H46O3 | 430.3447 | 453.3352 | 1.3 | 201.1632 [C15H21]+, 205.1582 [C14H21O]+, 187,1475 [C14H19]+ | +Na | ergosta-7,22-dien-3β,5α,6α-triol | DS | others |
| 54 | 12.88 | | C29H46O3 | 442.3447 | 487.3424 | -0.5 | 269.1164 [C17H17O3]-, 237.0917 [C16H13O2]-, 221.0617 [C15H9­O2]- | +HCOO | ergosta-7,9(11),22-trien-3β,5α,6α-triol | DS | others |
| 55 | 13.05 | | C19H22O4 | 314.1518 | 337.1407 | -0.3 | 269.1529 [C18H21O2]+, 297.1481 [C19H21O3]+ | +Na, +H | neocryptotanshinone | DS | quinone |
| 56 | 13.05 | | C19H20O3 | 296.1412 | 297.1484 | -0.1 | 143.0835 [C11H11]+, 269.1534 [C18H21O2]+, 141.0693 [C11H9]+ | +H | Cryptotanshinone | LZ | quinone |
| 57 | 13.34 | | C19H22O3 | 298.1569 | 299.1637 | -0.4 | 269.1532 [C18H21O2]+, 252.113 [C17H16O2]+, 239.1056 [C16H15O2]+ | +H, +Na | deoxyneocryptotanshinone | DS | quinone |
| 58 | 13.5 | | C18H14O3 | 278.0943 | 279.1014 | -0.2 | 261.0907 [C18H13O2]+, 221.0583 [C15H9O2]+ | +H, +Na | dihydrotanshinoneⅠ | DS | quinone |
| 59 | 14 | | C18H16O3 | 280.1099 | 281.117 | -0.2 | 263.1059 [C18H15O2]+, 127.0539 [C10H7]+ | +H, +Na | 1,2,5,6-tetrahydrotanshinone | DS | quinone |
| 60 | 14.06 | | C20H26O2 | 298.1933 | 297.1848 | -1.2 | 282.1610 [C19H22O2]- | -H | microstegiol | DS | others |
| 61 | 14.47 | | C19H24O3 | 300.1725 | 301.1792 | -0.6 | 241.1216 [C16H17O2]+, 271.1689 [C18H23O2]+,  256.1451 [C17H20O2]+ | +H | miltipolone | DS | others |
| 62 | 15.16 | | C19H20O3 | 296.1412 | 297.1486 | 0.1 | 279.1379 [C19H19O2]+, 254.0934 [C16H14O3]+ | +H, +Na | isocryptotanshi-none | DS | quinone |
| 63 | 15.31 | | C20H28O2 | 300.2089 | 301.2159 | -0.3 | 259.1690 [C17H23O2]+, 213.1267 [C15H17O]+, 95.08518 [C7H11]+ | +H | sugiol | DS | terpenoid |
| 64 | 15.68 | | C23H26O6 | 398.1729 | 421.1637 | 1.5 | 319.0961 [C20H15O4]+, 281.0462 [C16H9O5]+­, 337.1054 [C20H17O5]+ | +Na | przewalskin a | DS | terpenoid |
| 65 | 16.19 | | C18H20O2 | 268.1463 | 269.1535 | -0.1 | 239.1062 [C16H15O2]+, 141.0694 [C11H9]+, 254.1295 [C17H18O2]+ | +H | Salviolone | DS | others |
| 66 | 16.86 | | C19H18O3 | 294.1256 | 295.1329 | -0.2 | 265.1223 [C18H17O2]+, 261.0910 [C18H13O2]+, 249.1274 [C18H16O]+ | +H, +Na | Tanshinone IIA | DS | quinone |
| 67 | 17.37 | | C19H22O2 | 282.162 | 283.1694 | 0.1 | 269.0805 [C16H13O4]+, 239.1061 [C16H15O2]+ | +H, +Na | Miltrione | DS | others |
| 68 | 18.1 | | C31H48O6 | 516.3451 | 515.3366 | -1.2 | 169.0861 [C9H13O3]-, 453.2995 [C29H41O4]-, 125.0967 [C8H13O]- | -H | ganolucidate B | DS | terpenoid |
| 69 | 18.37 | | C30H48O3 | 456.3604 | 455.3518 | -1.3 | 255.2328 [C16H31O2]-, 277.2165 [C18H29O2]-, 299.2002 [C20H27­O2]- | -H, +HCOO | Ganodermanondiol | DS | terpenoid |
| 70 | 18.73 | | C20H30O | 286.2297 | 331.2276 | -0.3 | 135.0808 [C9H11O]-, 219.1750 [C15H23O]-, 161.0965 [C11H13O]- | +HCOO | Ferruginol | DS | others |
| 71 | 18.84 | | C30H48O3 | 456.3604 | 455.3525 | -0.5 | 277.2166 [C18H29O2]-, 325.2523 [C23H33O]-, 409.2737 [C27H37­O3]- | -H, +HCOO | Betulinic acid | LZ | organic acid |
| 72 | 19.94 | | C30H46O3 | 454.3447 | 453.3376 | 0.2 | 125.0968 [C8H13O]-, 261.2222 [C18H29O]-, 275.2003 [C18H27O]- | -H, +HCOO | ganoderan B | DS | others |
| 73 | 20.12 | | C28H44O4 | 444.3240 | 489.3214 | -0.8 | 239.1429 [C17H19O]-, 369.2780 [C26H37O2]-, 283.1321 [C18H19O3]- | +HCOO | Peroxyergosterol | DS | others |
| 74 | 21.13 | | C28H40O2 | 408.3028 | 409.309 | -1.1 | 283.1693 [C19H23O2]+ | +H | Ganodosterone | DS | others |
| 75 | 21.46 | | C20H36O2 | 308.2715 | 307.2648 | 0.5 | 125.0971 [C8H13O]- | -H | Sclareol | DS | others |
| 76 | 24.32 | | C28H40O | 392.3079 | 393.3155 | 0.3 | 268.1823 [C19H24O]+, 253.1585 [C18H21O]+, 224.1555 [C17H20]+ | +H | Ergosta-4,6,8(14),22-tetraen-3-one | DS | others |

\* LZ represents G. lucidum, GG represents P. montana, DS represents S. miltiorrhiza, HQ represents A. membranaceus

**Supplementary** **Table 2.** The binding energy of targets and compounds

|  |  |  |
| --- | --- | --- |
| **targets** | **compounds** | **binding energy**  **(kcal/mol)** |
| Map2k1 | Methylnissolin | -8.904 |
| Map2k1 | 2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-7-benzofurancarboxaldehyde | -8.331 |
| Map2k1 | 9,10-dimethoxypterocarpan-3-O-β-D-glucoside | -7.57 |
| Map2k1 | isoflavanone | -6.982 |
| Map2k1 | TanshinoneIIB | -6.971 |
| Map2k1 | przewaquinone c | -6.599 |
| Map2k1 | 3,9-di-O-methylnissolin | -6.034 |
| Map2k1 | Methyl lucidenate Q | -4.752 |
| Map2k1 | ergosta-7,9(11),22-trien-3β,5α,6α-triol | -4.283 |
| Map2k1 | Epoxyganoderiol A | -4.138 |
| Mtor | 2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-6-benzofurancarboxaldehyde | -8.773 |
| Mtor | Methylnissolin | -8.289 |
| Mtor | epidanshenspiroketallactone | -6.96 |
| Mtor | 3,9-di-O-methylnissolin | -6.885 |
| Mtor | 20-Hydroxyganoderic acid G | -6.585 |
| Mtor | ganolucidate B | -6.546 |
| Mtor | Isoimperatorin | -6.536 |
| Mtor | TanshinoneIIB | -6.411 |
| Mtor | Epoxyganoderiol A | -6.016 |
| Mtor | Ganoderic acid beta | -5.623 |
| Mtor | Methyl lucidenate Q | -5.363 |
| Mtor | Peroxyergosterol | -5.331 |
| Mtor | 15alpha,26-Dihydroxy-5alpha-lanosta-7,9 | -5.187 |
| Mtor | ergosta-7,22-dien-3β,5α,6α-triol | -4.934 |
| Mtor | ergosta-7,9(11),22-trien-3β,5α,6α-triol | -4.869 |
| Mtor | Ganoderic acid C6 | -4.181 |
| Ephx2 | 3,9-di-O-methylnissolin | -7.639 |
| Ephx2 | Salviolone | -7.198 |
| Ephx2 | Cryptotanshinone | -7.084 |
| Ephx2 | isocryptotanshi-none | -6.584 |
| Stat3 | isoflavanone | -5.139 |
| Stat3 | Methyl lucidenate Q | -4.453 |
| Stat3 | 1,2,5,6-tetrahydrotanshinone | -4.285 |
| Stat3 | Miltrione | -4.244 |
| Stat3 | 20-Hydroxyganoderic acid G | -4.227 |
| Stat3 | dihydrotanshinoneⅠ | -4.123 |
| Stat3 | Cryptotanshinone | -3.87 |
| Stat3 | 3,9-di-O-methylnissolin | -3.794 |
| Stat3 | neocryptotanshinone | -3.476 |
| Dgat1 | Methylnissolin | -5.785 |
| Dgat1 | 20-Hydroxyganoderic acid G | -5.001 |
| Dgat1 | ganolucidate B | -4.163 |
| Dgat1 | lucidenic acid A | -4.078 |
| Lta4h | Ganoderic acid C6 | -6.427 |
| Lta4h | tanshinone Ⅵ | -5.989 |
| Lta4h | Sclareol | -4.091 |