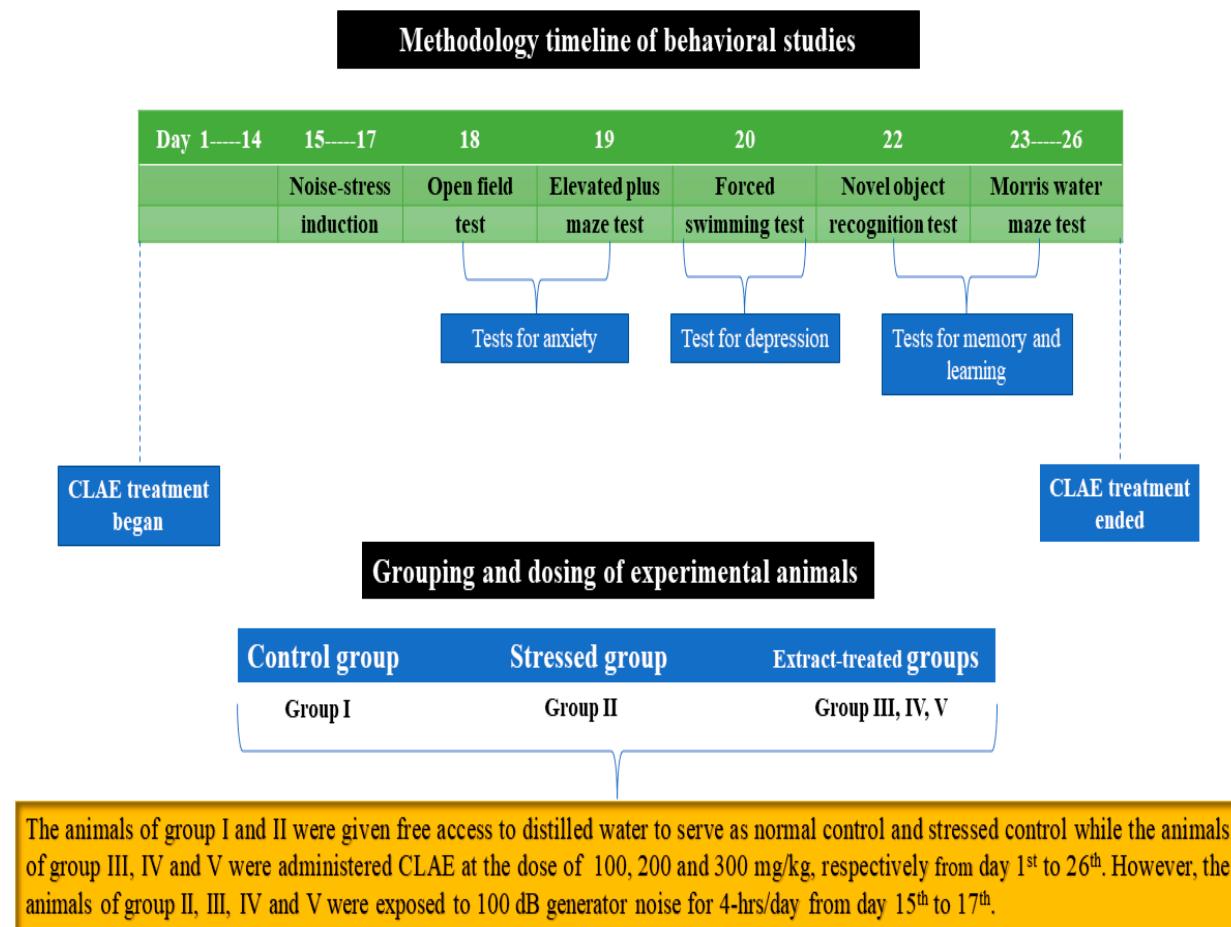
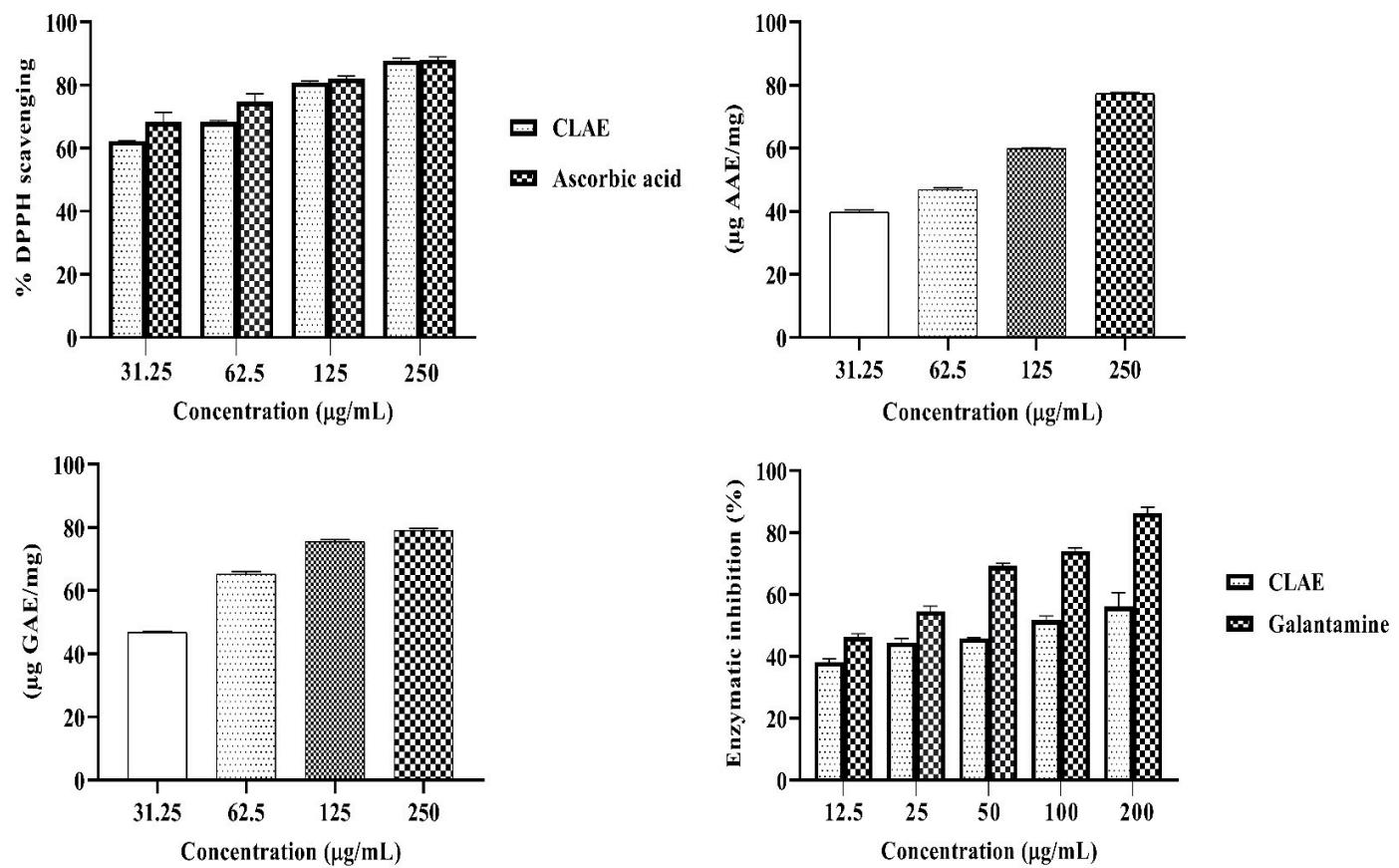


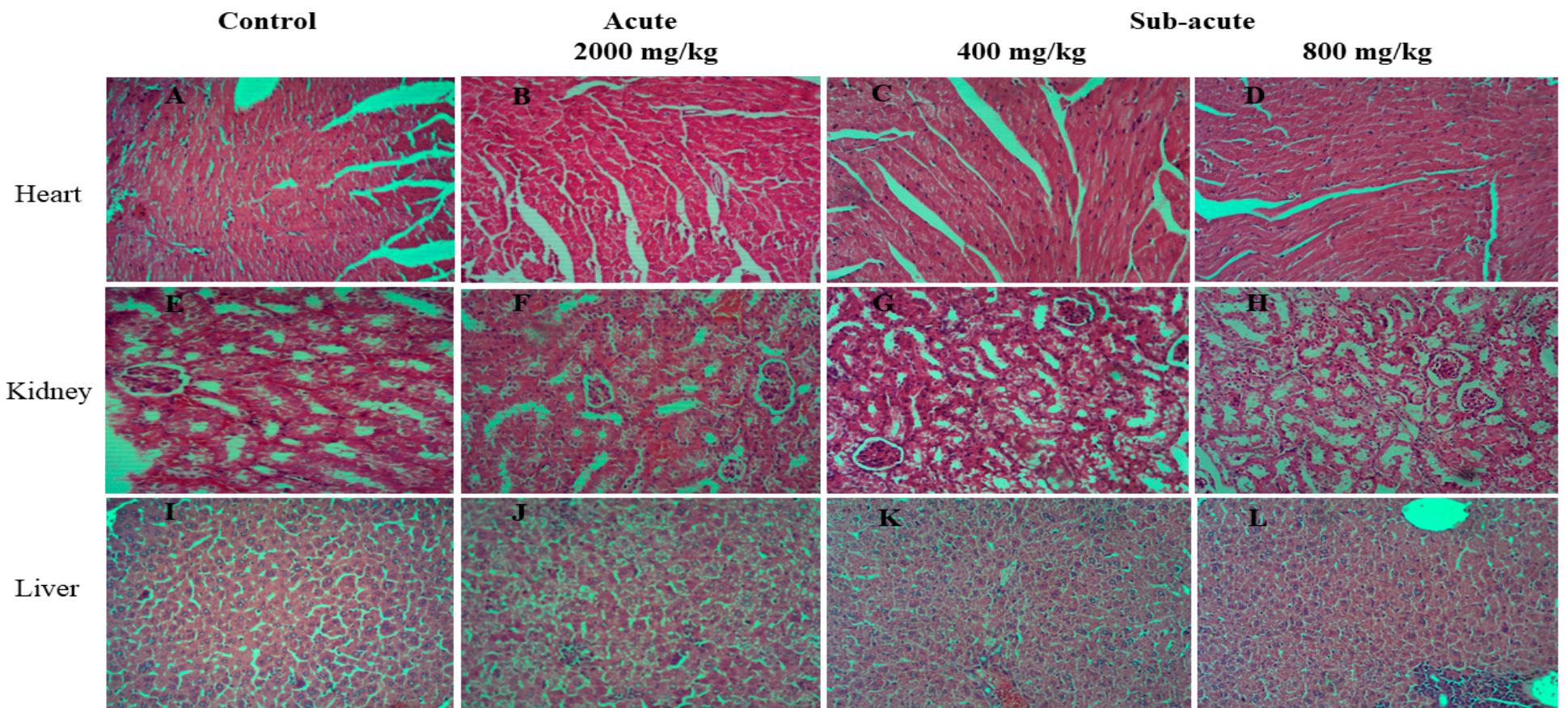
Supplementary Materials

Supplementary Figure S1. Experimental timeline for behavioral studies including animal grouping and group-wise treatments; Supplementary Figure S2. Percentage (%) inhibition of 2,2-Diphenyl-1-picrylhydrazyl (DPPH), total antioxidant capacity (TAC), total reducing power (TRP) ability and acetylcholinesterase (AChE) inhibitory assays; Supplementary Figure S3. Photomicrographs of CLAE effect on the histology of vital organs after 14 and 28 days of toxicity study; Supplementary Figure S4. The track plots of random animals for the exploration of novel object from each group in NOR test; Supplementary Figure S5. The chemical structures and ESI-MS/MS spectra of 53 tentatively identified phytochemicals in negative and positive modes of analysis; Supplementary Figure S6. Venn diagram between CLAE phytochemicals and disease-target genes related to myocardial infarction, anxiety, depression and memory deficits; Supplementary Figure S7. GO biological processes and KEGG analysis of disease-target genes associated with myocardial infarction, anxiety, depression and memory deficits; Table S1. Effects of *Conocarpus lancifolius* aqueous extract (CLAE) in behavioral novel object recognition (NOR) test on the recognition memory of experimental rats; Table S2. Prediction of drug-likeness parameters of selected CLAE phytoconstituents by using SwissADME; Table S3. Prediction of absorption, distribution, metabolism, excretion and toxicity (ADMET) properties of selected CLAE compounds by using pkCSM program; Table S4. Myocardial infarction related pathogenic genes for CLAE; Table S5. Anxiety, depression and impaired memory related pathogenic genes for CLAE; Table S6. Myocardial infarction related pathogenic genes retrieved for the CLAE compounds; Table S7. Anxiety, depression and impaired memory related pathogenic genes retrieved for CLAE compounds; Table S8. Top 20 GO biological process of CLAE phytocompounds for myocardial infarction related target genes; Table S9. Top 20 KEGG pathway of CLAE phytocompounds for myocardial infarction related target genes; Table S10. Top 20 GO biological process of CLAE phytocompounds for anxiety, depression and impaired memory related target genes; Table S11. Top 20 KEGG pathway of CLAE phytocompounds for anxiety, depression and impaired memory related target genes; Table S12. Network analysis of myocardial infarction related target genes interaction with CLAE compounds; Table S13. Network analysis of myocardial infarction related target genes interaction with CLAE compounds and GO biological process (BP); Table S14. Network analysis of myocardial infarction related target genes interaction with CLAE compounds and KEGG pathways; Table S15. Network analysis of anxiety, depression and impaired memory related target genes interaction with CLAE constituents; Table S16. Network analysis of anxiety, depression and impaired memory related target genes interaction with CLAE compounds and GO biological process (BP); Table S17. Network analysis of anxiety, depression and impaired memory related target genes interaction with CLAE constituents and KEGG signaling pathways.

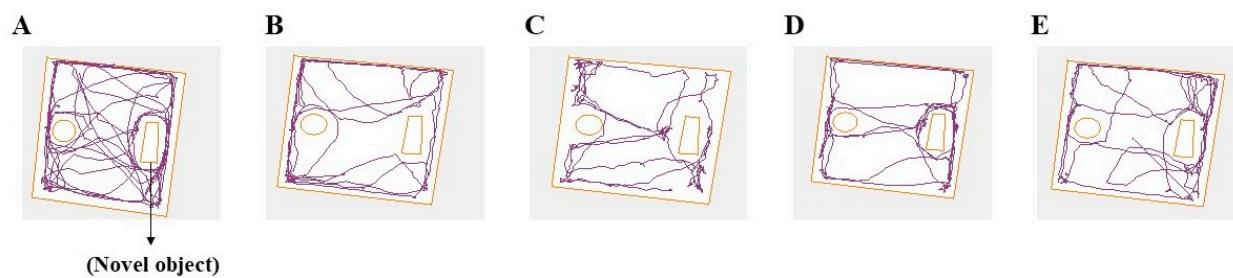


Supplementary Figure S1. Experimental timeline for behavioral studies including animal grouping and group-wise treatments.

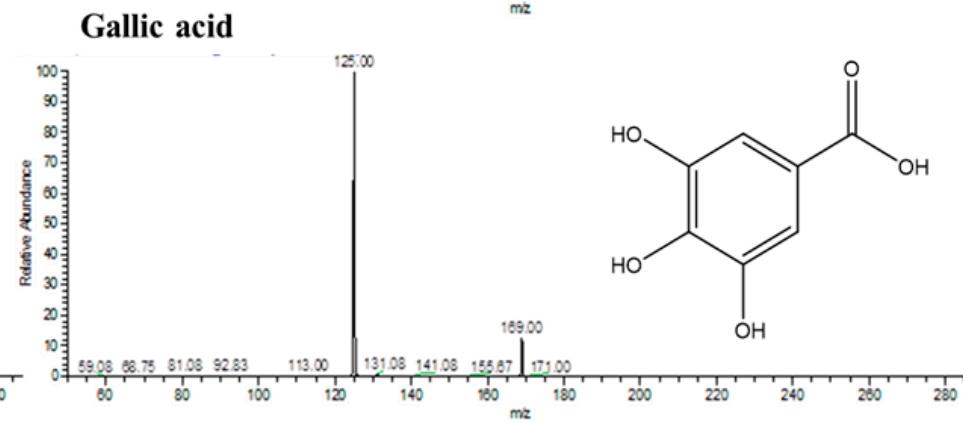
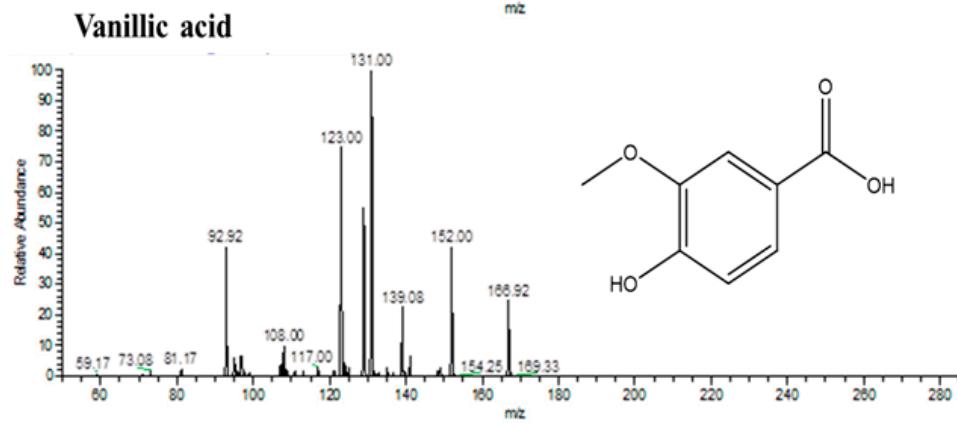
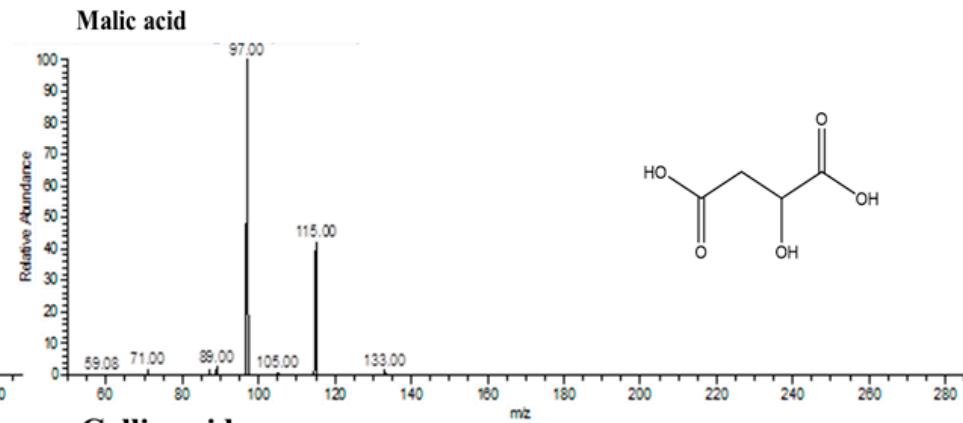
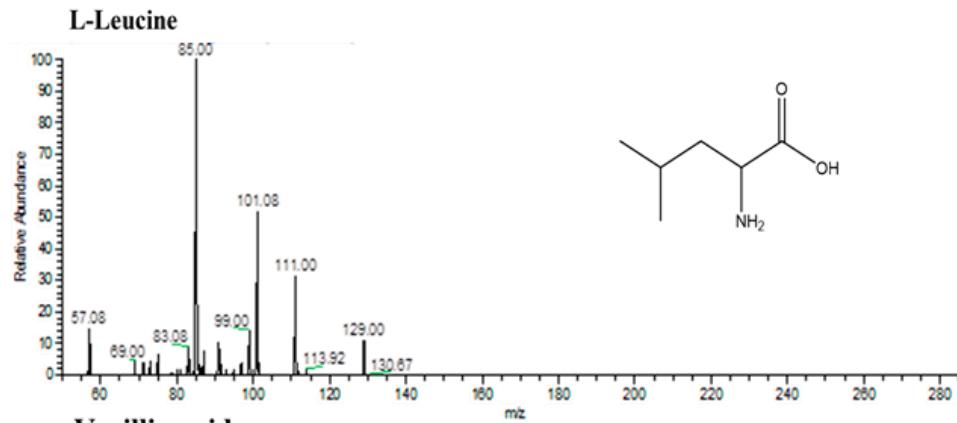


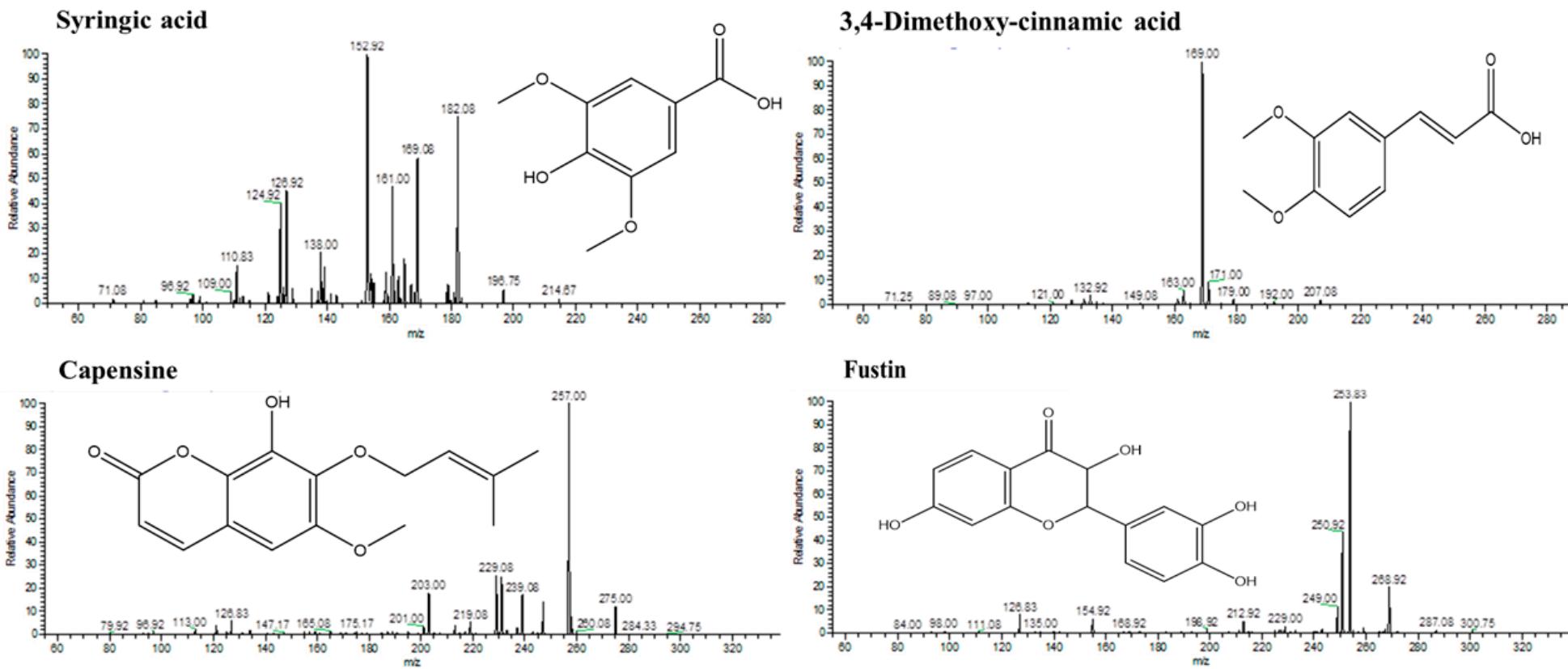


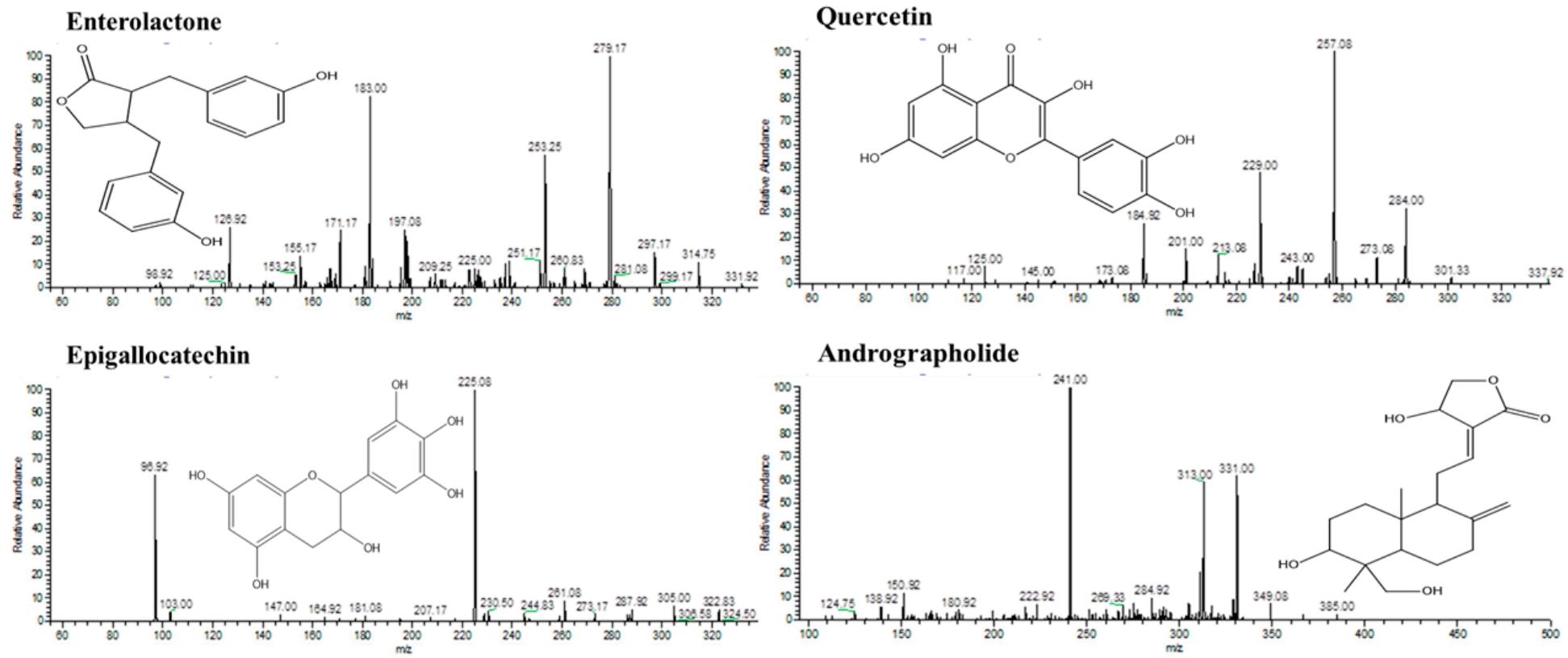
Supplementary Figure S3. Photomicrographs (H&E staining, 10 x magnification) of CLAE effect on the histology of vital organs after 14 and 28 days of toxicity study. (A) control group; (B) 2000 mg/kg CLAE; (C) 400 mg/kg CLAE; and (D) 800 mg/kg CLAE group showed normal heart architecture. In kidney (E) control group and (F) 2000 mg/kg CLAE displayed normal histology whereas existence of cells in the renal tubular lumen, degenerated epithelial cells and mild inflammatory cells infiltration were observed in (G) 400 mg/kg CLAE and (H) 800 mg/kg CLAE treated groups. In liver tissues (I) control group displayed normal structure; (J) 2000 mg/kg CLAE presented mild infiltration of inflammatory cells; (K) 400 mg/kg CLAE showed moderate infiltration of inflammatory cells and (L) 800 mg/kg CLAE treated group displayed severe inflammatory infiltrates.

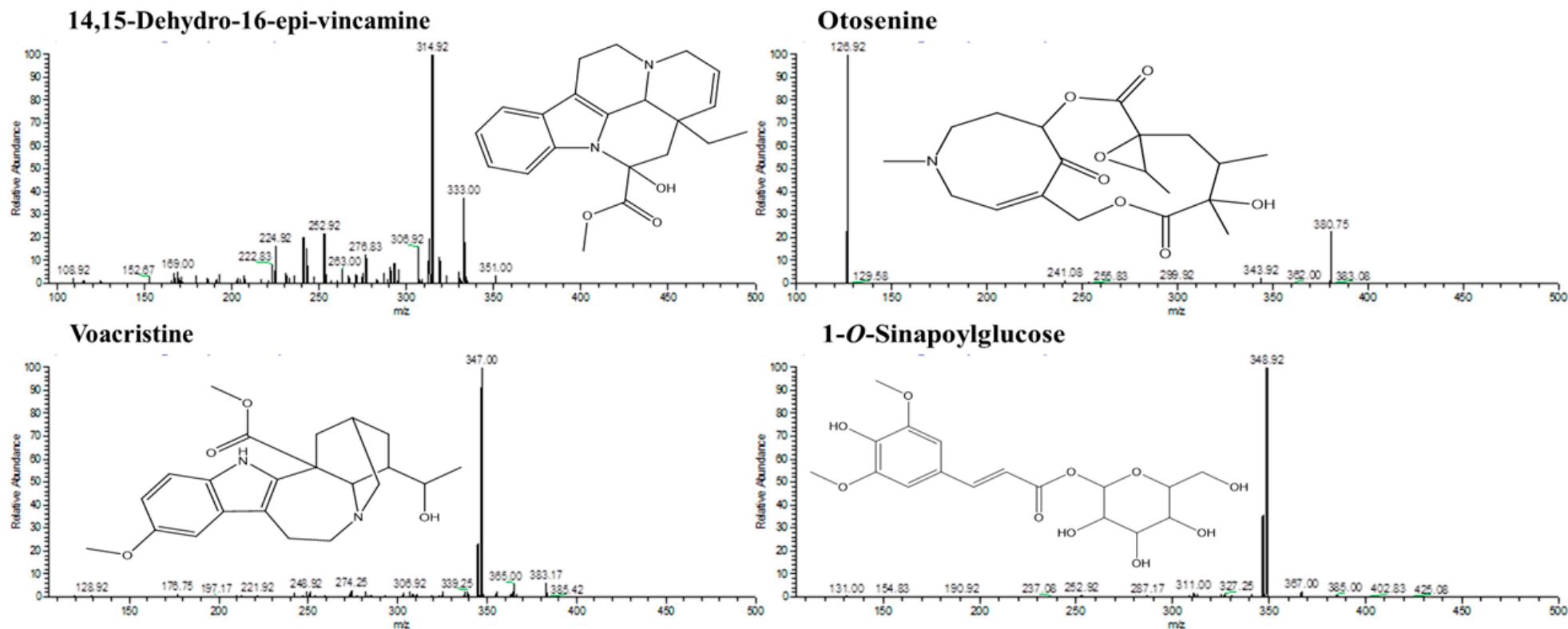


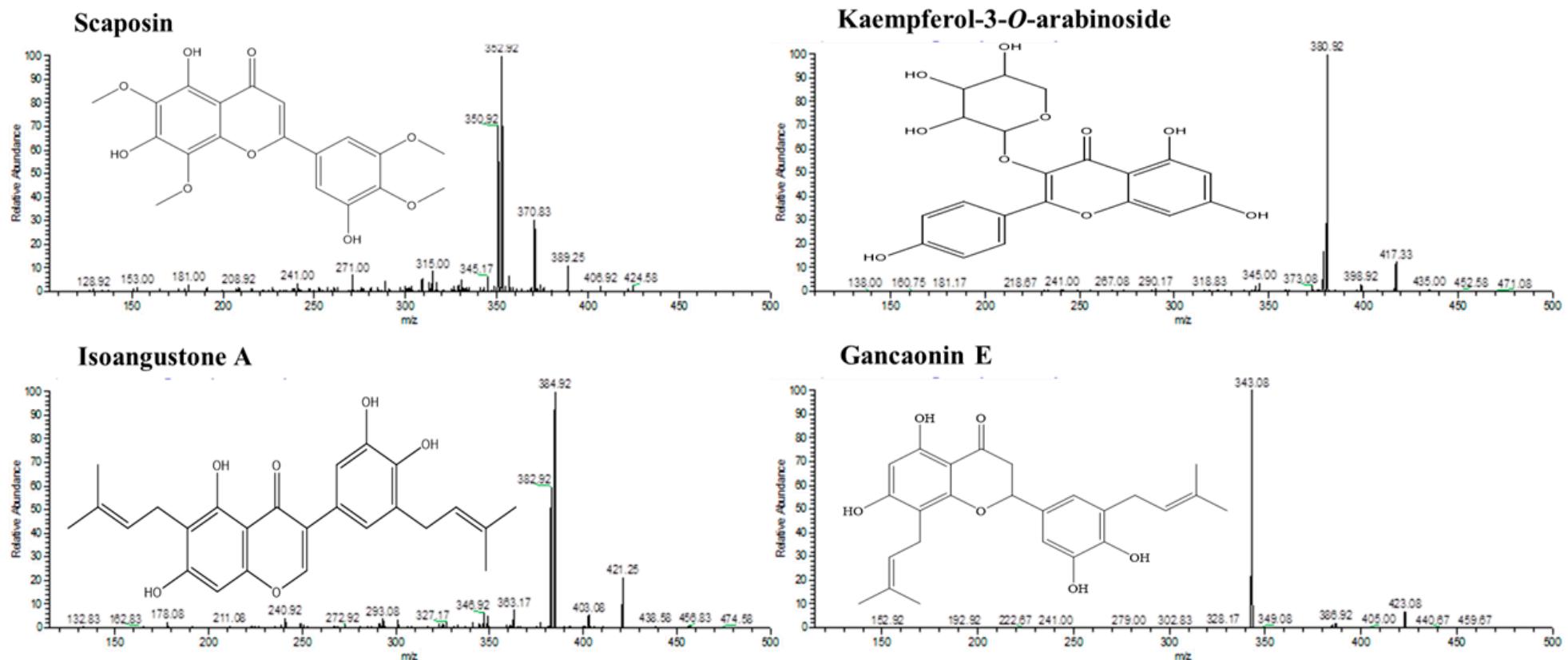
Supplementary Figure S4. The track plots of random animals for the exploration of novel object from each group in NOR test. (A) Control group; (B) Stressed group; (C) 100 mg/kg CLAE; (D) 200 mg/kg CLAE; and (E) 300 mg/kg CLAE. NOR test: Novel object recognition test.

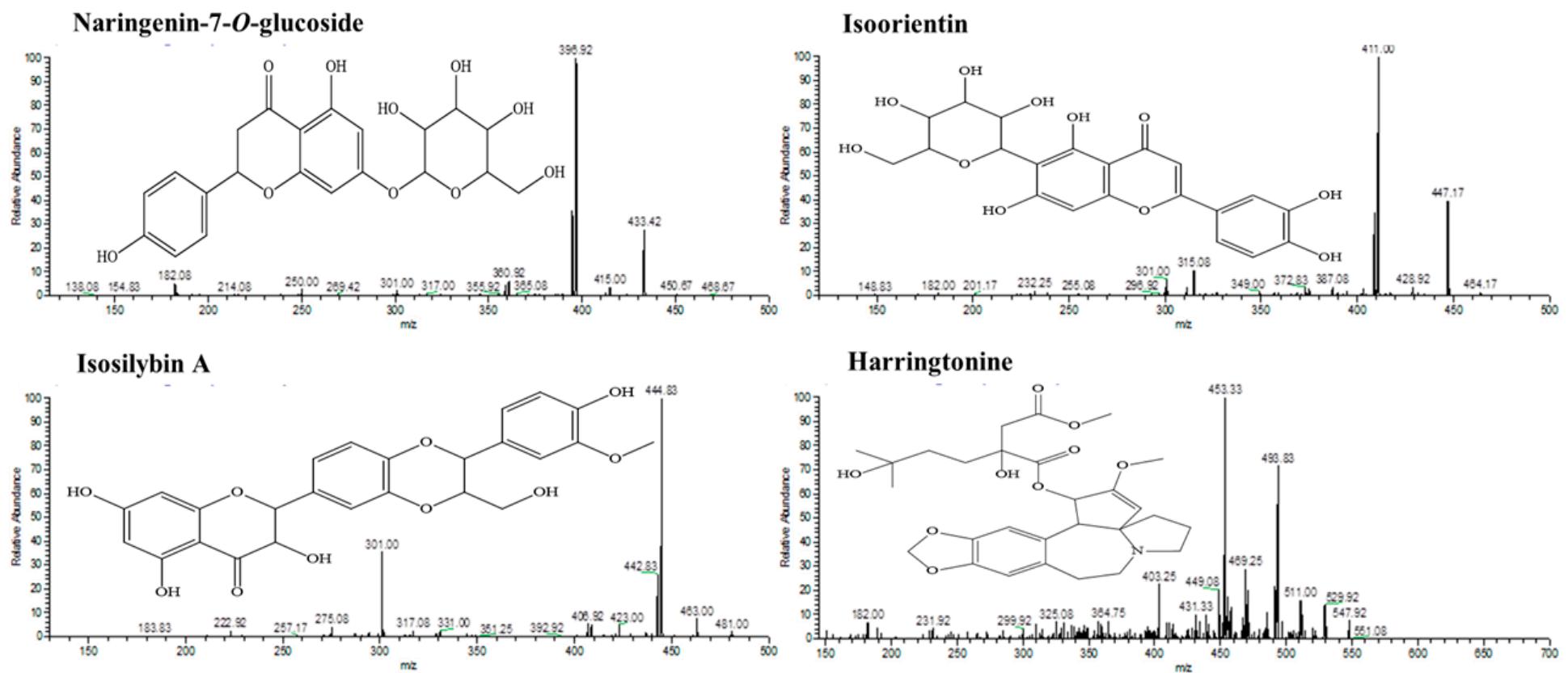


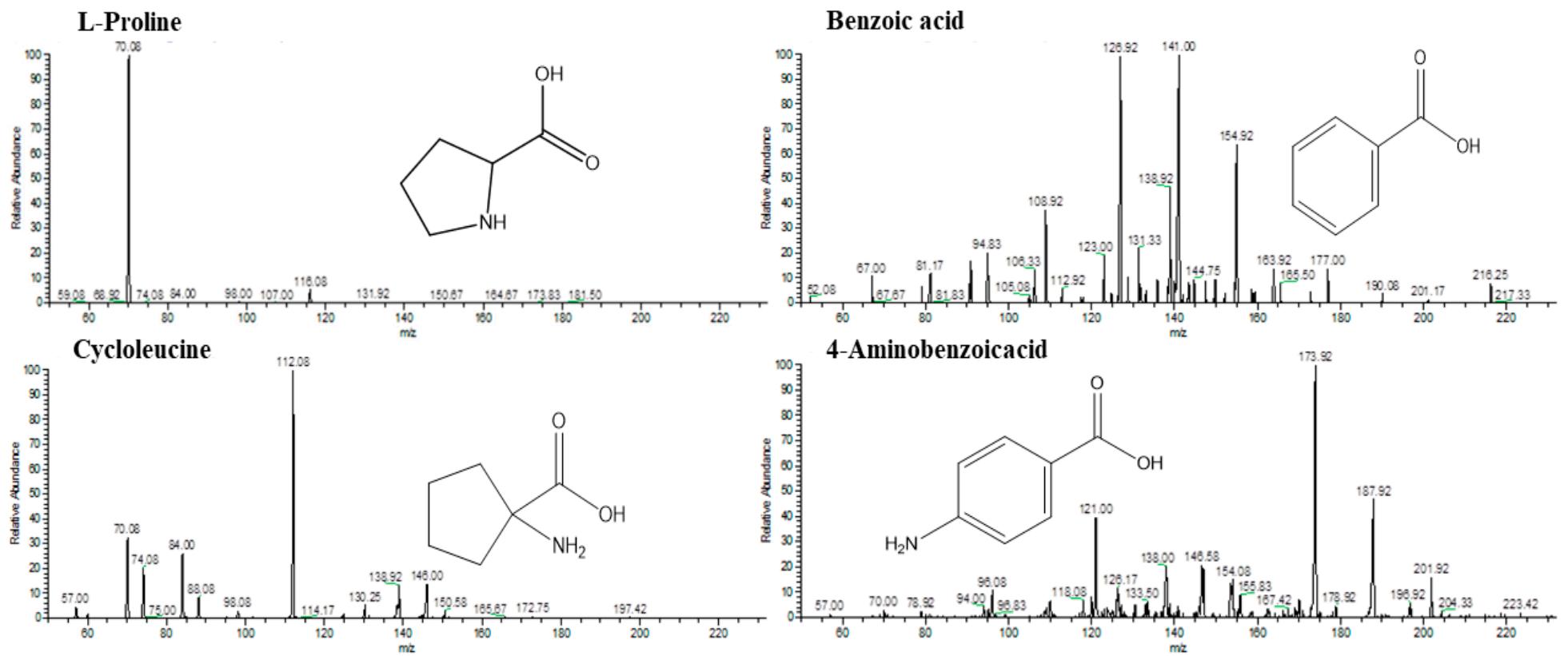


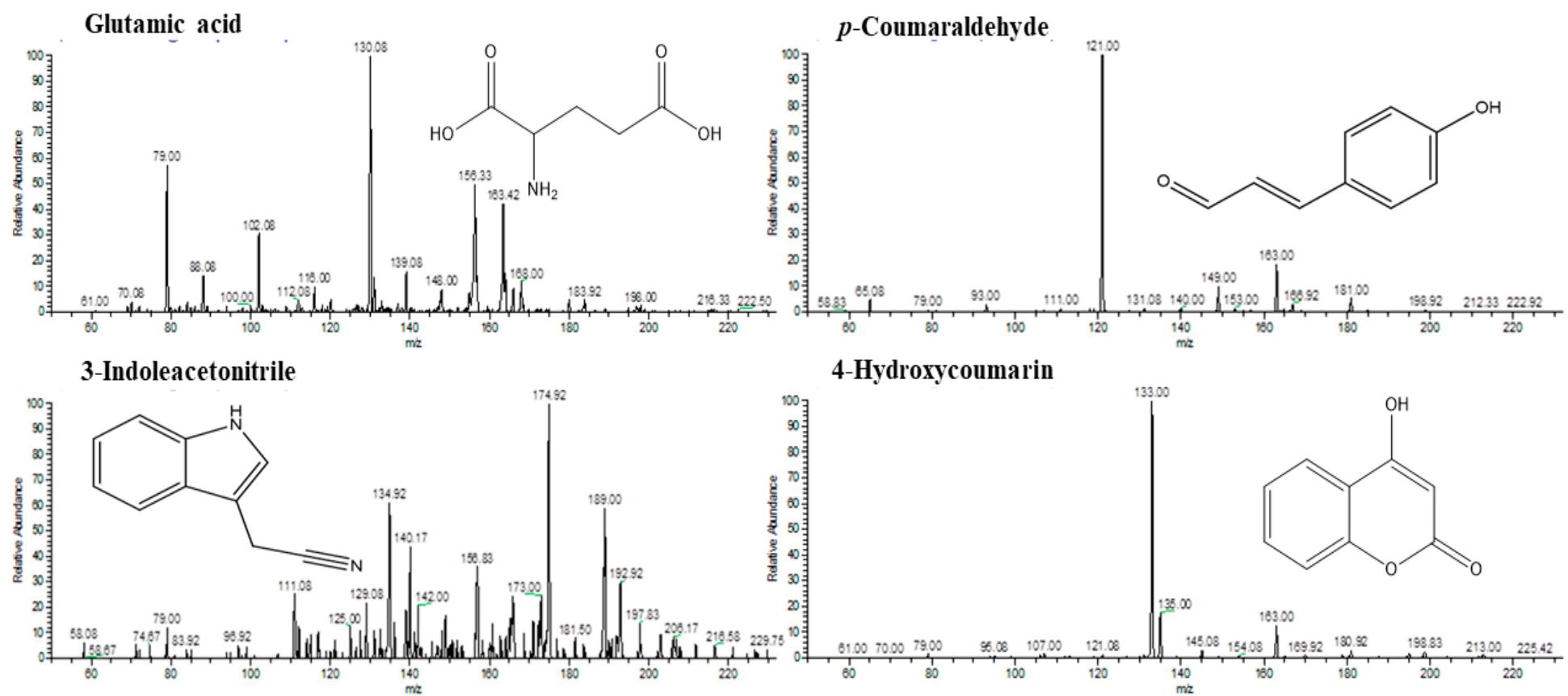


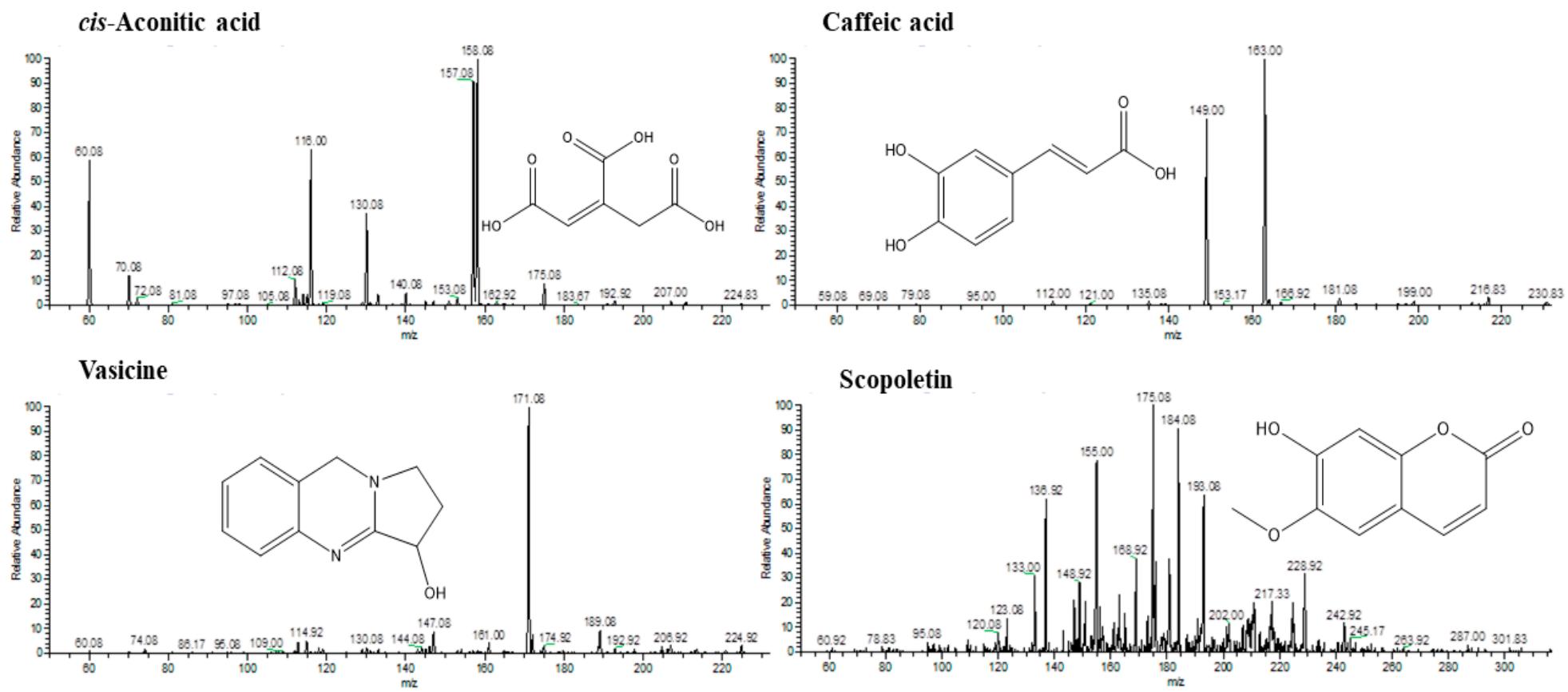


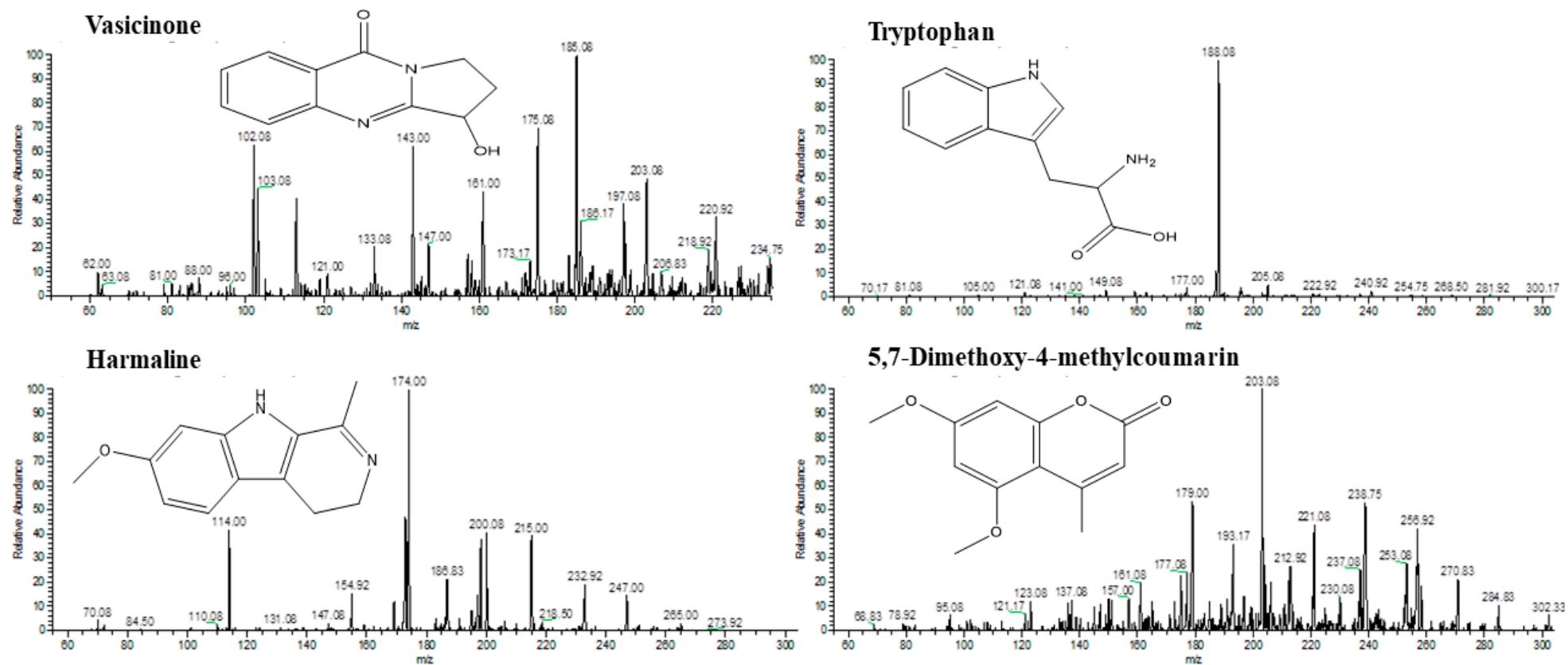




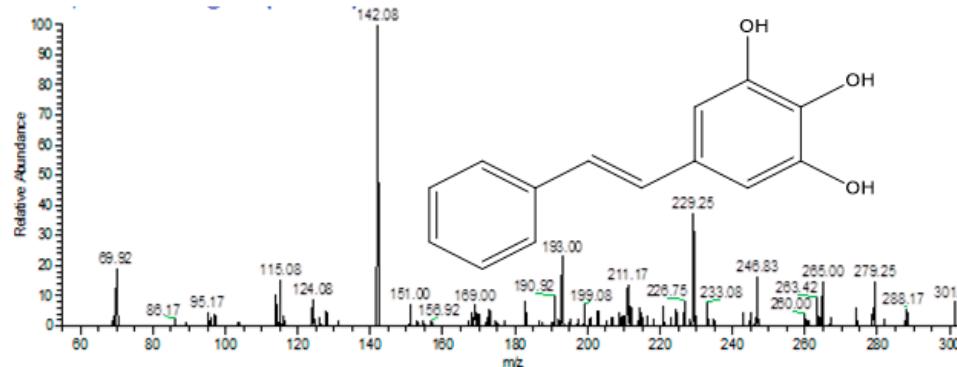




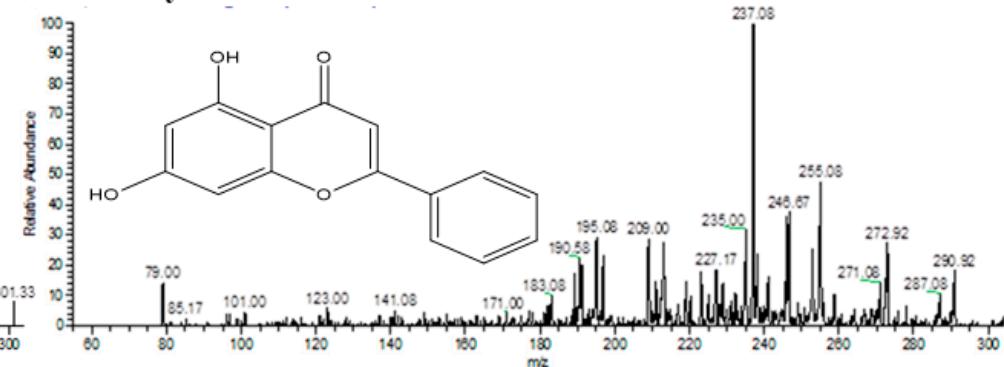




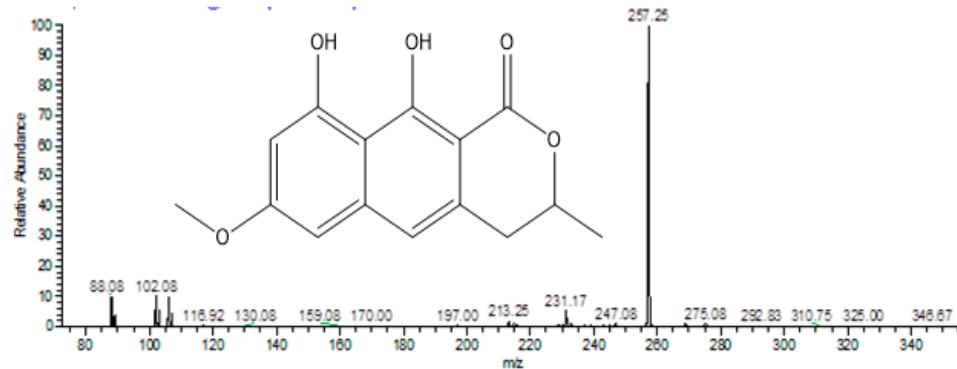
3,4,5-Trihydroxystilbene



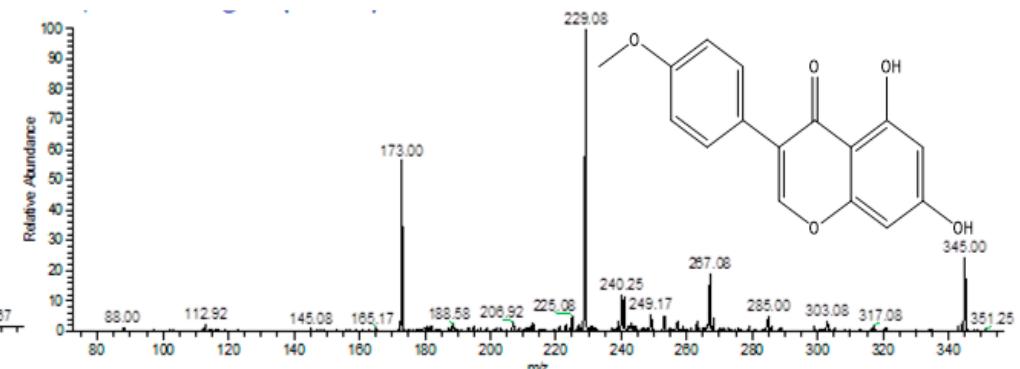
Chrysin

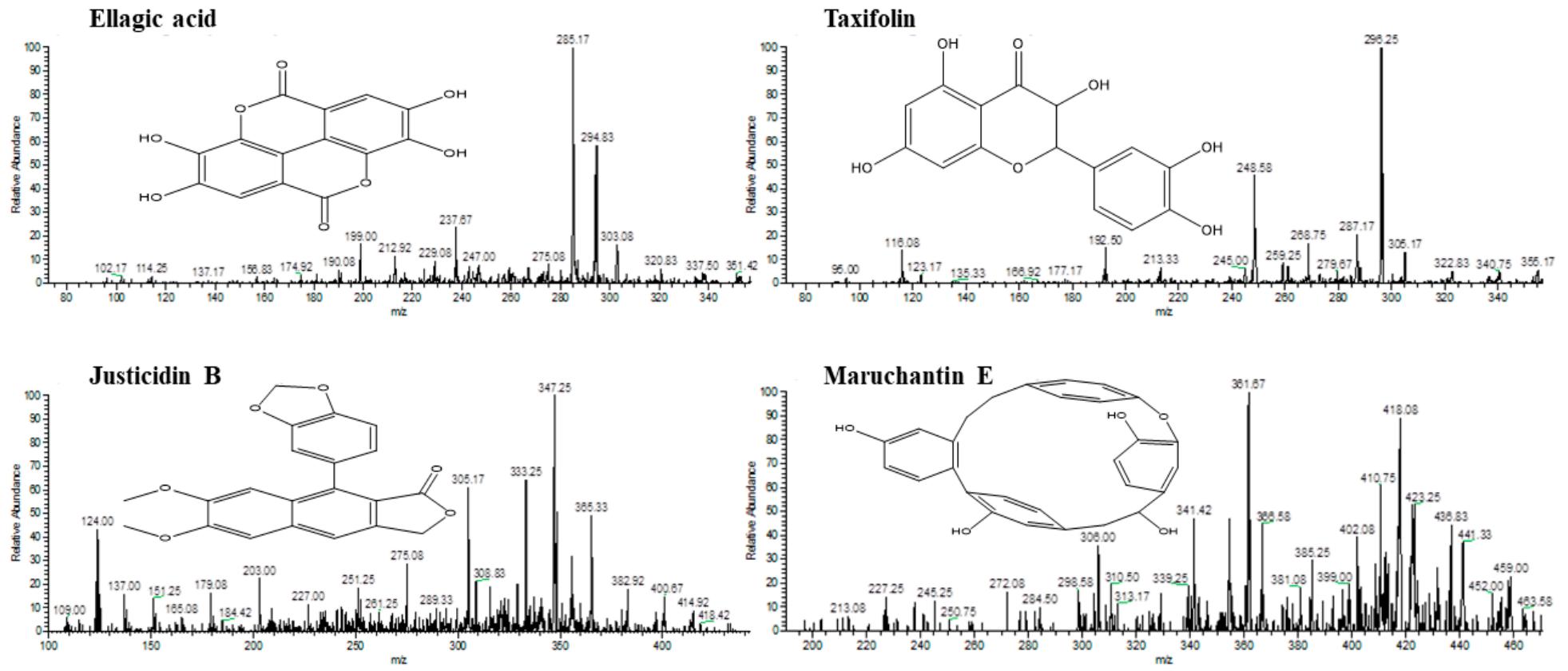


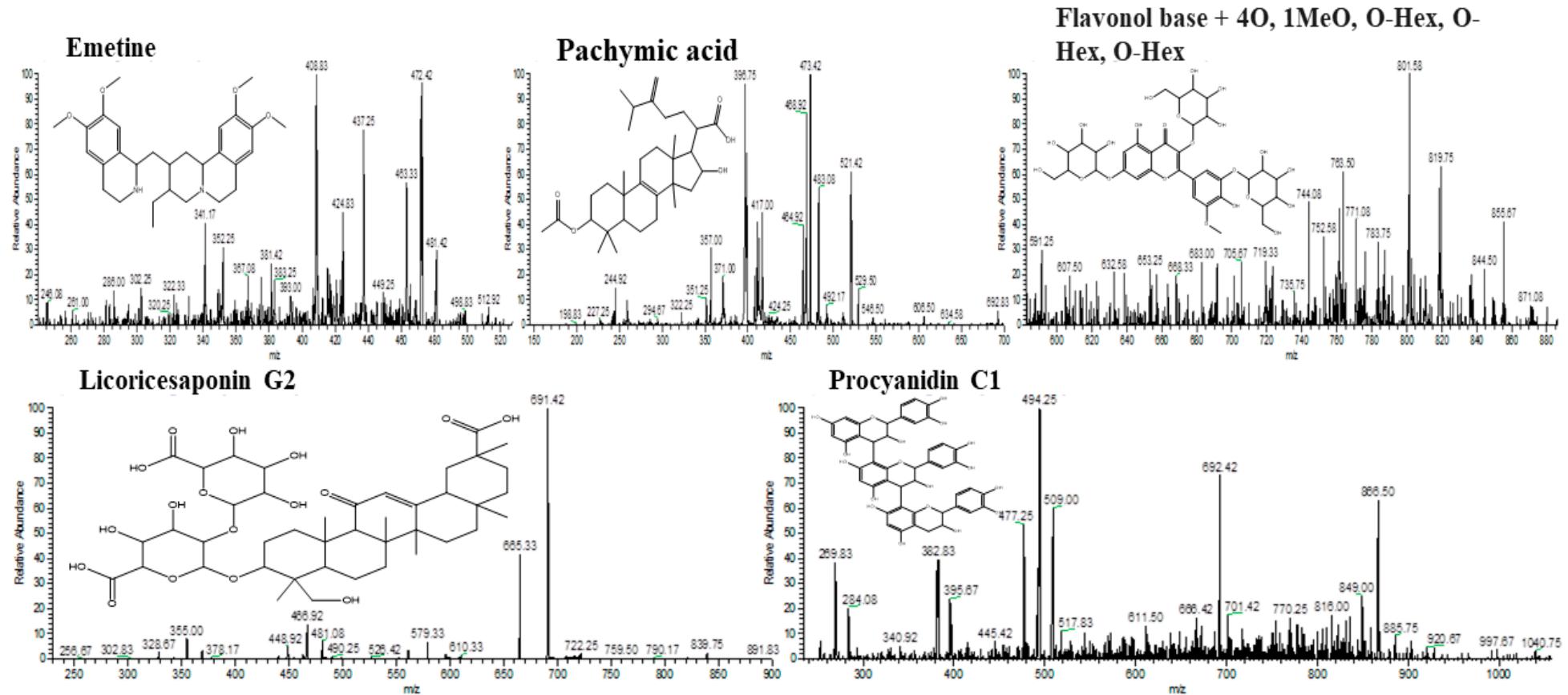
(R)-Semivioxanthin



Biochanin A



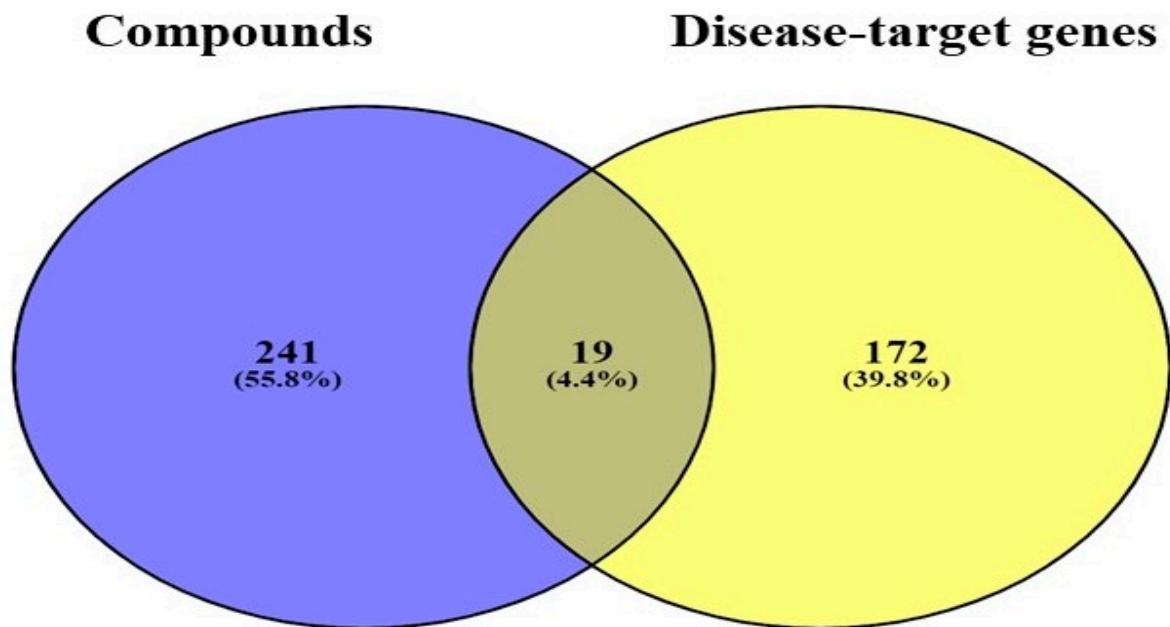




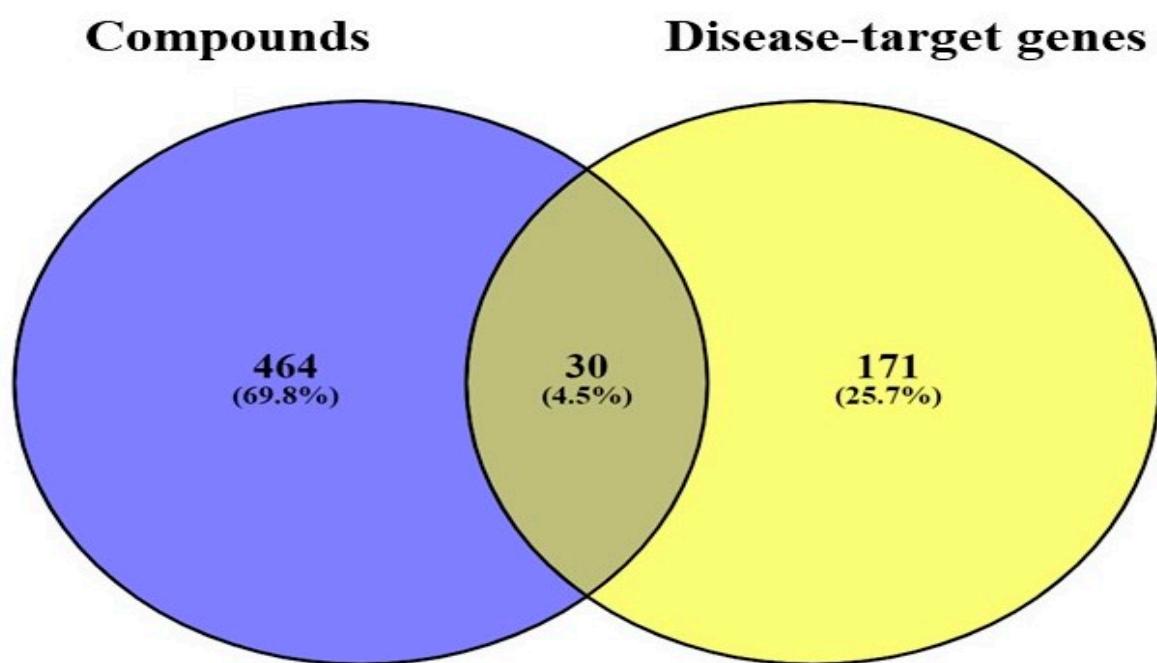
Supplementary Figure S5.

The chemical structures and ESI-MS/MS spectra of 53 tentatively identified phytochemicals in negative and positive modes of analysis.

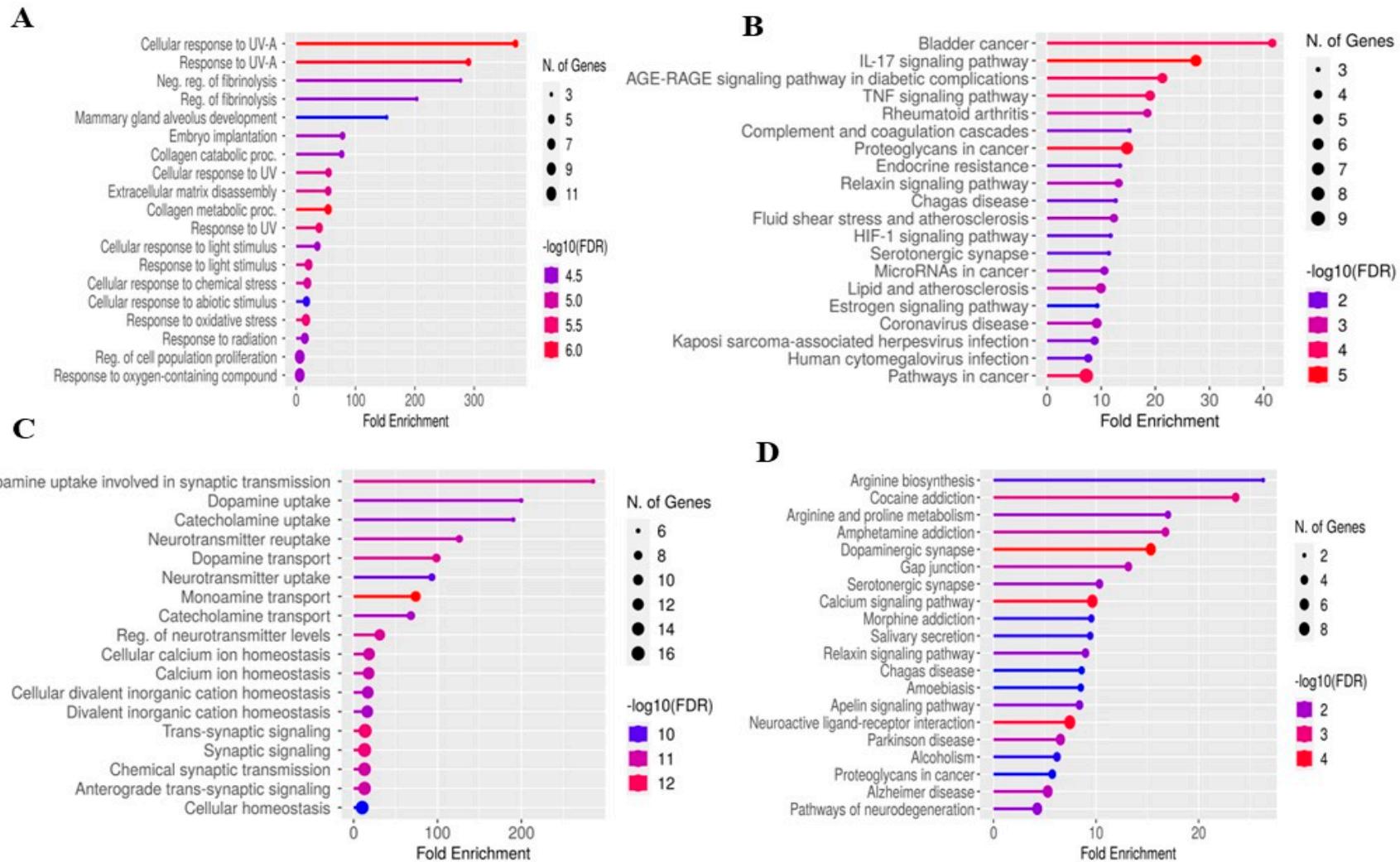
A



B



Supplementary Figure S6. Venn diagram between CLAE phytochemicals and disease-target genes related to myocardial infarction (A.) and anxiety, depression and memory deficits (B.)



Supplementary Figure S7. GO biological processes (**A**) and KEGG analysis (**B**) of disease-target genes associated with myocardial infarction and GO biological processes (**C**) and KEGG analysis (**D**) of disease-target genes related to anxiety, depression and memory deficits.

Table S1. Effects of *Conocarpus lancifolius* aqueous extract (CLAE) in behavioral novel object recognition (NOR) test on the recognition memory of experimental rats.

| Group/Dose | Test Phase | |
|----------------|-------------------------------------|---|
| | Novel object exploration time (sec) | Time spent to explore familiar object (sec) |
| Control | 18.14 ± 3.37 | 5.26 ± 1.71 |
| Stressed | 8.98 ± 4.83 ## | 13.18 ± 8.51 # |
| 100 mg/kg CLAE | 9.62 ± 4.25 | 6.56 ± 2.27 |
| 200 mg/kg CLAE | 11.62 ± 7.06 | 6.32 ± 2.12 |
| 300 mg/kg CLAE | 12.52 ± 12.44 | 5.98 ± 1.97 * |

Results are expressed as mean ± SD (n=5). Data was analyzed by using one way ANOVA followed by Dunnett's multiple comparison test. # $p < 0.05$ and ## $p < 0.01$ comparisons between control and stressed groups; * $p < 0.05$ comparison between stressed and CLAE-treated groups (300 mg/kg).

Table S2. Prediction of drug-likeness parameters of selected CLAE phytoconstituents by using SwissADME.

| Compound name | M.W | HBAs | HBDs | XLOGP3 | Log S (ESOL model) | TPSA (Å ²) | Flexibility RBs | Inhibitors | | PAINS alerts | Ro5 violations |
|--------------------------------|--------|------|------|--------|--------------------------|---------------------------|--------------------|------------|--------|-----------------|-------------------|
| | | | | | | | | CYP2D6 | CYP3A4 | | |
| Malic acid | 134.02 | 5 | 3 | -1.26 | 0.32 | 94.83 | 3 | No | No | 0 | 0 |
| Vanillic acid | 168.04 | 4 | 2 | 1.43 | -2.02 | 66.76 | 2 | No | No | 0 | 0 |
| Gallic acid | 170.02 | 5 | 4 | 0.7 | -1.64 | 97.99 | 1 | No | Yes | 1 | 0 |
| Syringic acid | 198.05 | 5 | 2 | 1.04 | -1.84 | 75.99 | 3 | No | No | 0 | 0 |
| 3,4-Dimethoxycinnamic acid | 208.21 | 4 | 1 | 2.34 | -2.64 | 55.76 | 4 | No | No | 0 | 0 |
| Capensine | 276.09 | 5 | 1 | 3 | -3.55 | 68.9 | 4 | No | No | 0 | 0 |
| Fustin | 288.06 | 6 | 4 | 0.87 | -2.53 | 107.22 | 1 | No | No | 1 | 0 |
| Enterolactone | 298.33 | 4 | 2 | 3.32 | -3.92 | 66.76 | 4 | Yes | No | 0 | 0 |
| Quercetin | 302.04 | 7 | 5 | 1.54 | -3.16 | 131.36 | 1 | Yes | Yes | 1 | 0 |
| Epigallocatechin | 306.07 | 7 | 6 | 0.92 | -2.08 | 130.61 | 1 | No | No | 1 | 1 |
| Andrographolide | 350.20 | 5 | 3 | 2.16 | -3.18 | 86.99 | 3 | No | No | 0 | 0 |
| 14,15-Dehydro-16-epi-vincamine | 352.43 | 4 | 1 | 2.75 | -3.82 | 54.7 | 3 | Yes | No | 0 | 0 |
| Otosenine | 381.17 | 8 | 1 | 0.63 | -2.6 | 105.67 | 0 | No | No | 0 | 0 |
| Voacristine | 384.47 | 5 | 2 | 2.36 | -3.68 | 74.79 | 4 | Yes | No | 0 | 0 |
| 1-O-Sinapoylglucose | 386.35 | 10 | 5 | -0.34 | -1.72 | 155.14 | 7 | No | No | 0 | 0 |
| Scaposin | 390.09 | 9 | 3 | 2.55 | -3.96 | 127.82 | 5 | No | Yes | 0 | 0 |
| Kaempferol-3-O-arabinoside | 418.35 | 10 | 6 | 0.78 | -3.12 | 170.05 | 3 | No | No | 0 | 1 |
| Isoangustone A | 422.17 | 6 | 4 | 6.16 | -6.39 | 111.13 | 5 | No | No | 1 | 1 |
| Gancaonin E | 424.18 | 6 | 4 | 5.89 | -6.14 | 107.22 | 5 | No | Yes | 1 | 1 |
| Naringenin-7-O-glucoside | 434.39 | 10 | 6 | 0.65 | -2.97 | 166.14 | 4 | No | No | 0 | 1 |
| Isoorientin | 448.10 | 11 | 8 | -0.15 | -2.7 | 201.28 | 3 | No | No | 1 | 2 |
| Isosilybin A | 482.12 | 10 | 5 | 1.9 | -4.14 | 155.14 | 4 | No | Yes | 0 | 0 |
| Harringtonine | 531.24 | 10 | 2 | 0.46 | -2.88 | 123.99 | 10 | Yes | Yes | 0 | 1 |
| Benzoic acid | 122.03 | 2 | 1 | 1.87 | -2.2 | 37.3 | 1 | No | No | 0 | 0 |
| 4-Aminobenzoic acid | 137.04 | 2 | 2 | 0.83 | -1.59 | 63.32 | 1 | No | No | 0 | 0 |

| Compound name | M.W | HBAs | HBDs | XLOGP3 | Log S (ESOL model) | TPSA (Å ²) | Flexibility RBs | Inhibitors | | PAINS alerts | Ro5 violations |
|--|--------|------|------|--------|--------------------------|---------------------------|--------------------|------------|--------|-----------------|-------------------|
| | | | | | | | | CYP2D6 | CYP3A4 | | |
| <i>p</i> -Coumaraldehyde | 148.16 | 2 | 1 | 1.75 | -2.13 | 37.3 | 2 | No | No | 0 | 0 |
| 3-Indoleacetonitrile | 156.06 | 1 | 1 | 1.60 | -2.31 | 39.58 | 1 | No | No | 0 | 0 |
| 4-Hydroxycoumarin | 162.03 | 3 | 1 | 1.27 | -2.26 | 50.44 | 0 | No | No | 0 | 0 |
| <i>cis</i> -Aconitic acid | 174.01 | 6 | 3 | -0.97 | -0.04 | 111.9 | 4 | No | No | 0 | 0 |
| Caffeic acid | 180.04 | 4 | 3 | 1.15 | -1.89 | 77.76 | 2 | No | No | 1 | 0 |
| Vasicine | 188.23 | 2 | 1 | 0.44 | -1.6 | 35.83 | 0 | No | No | 0 | 0 |
| Scopoletin | 192.04 | 4 | 1 | 1.53 | -2.46 | 59.67 | 1 | No | No | 0 | 0 |
| Vasinonone | 202.21 | 3 | 1 | 0.52 | -1.91 | 55.12 | 0 | No | No | 0 | 0 |
| Harmaline | 214.11 | 2 | 1 | 2.07 | -2.82 | 37.38 | 1 | Yes | No | 0 | 0 |
| 5,7-Dimethoxy-4-methylcoumarin | 220.22 | 4 | 0 | 1.77 | -2.65 | 48.67 | 2 | No | No | 0 | 0 |
| 3,4,5-Trihydroxystilbene | 228.24 | 3 | 3 | 3.13 | -3.62 | 60.69 | 2 | No | Yes | 1 | 0 |
| Chrysin | 254.05 | 4 | 2 | 3.52 | -4.19 | 70.67 | 1 | Yes | Yes | 0 | 0 |
| (<i>R</i>)-Semivioxanthin | 274.08 | 5 | 2 | 3.3 | -3.92 | 75.99 | 1 | No | No | 0 | 0 |
| Biochanin A | 284.06 | 5 | 2 | 2.99 | -3.92 | 79.9 | 2 | Yes | Yes | 0 | 0 |
| Ellagic acid | 302.19 | 8 | 4 | 1.1 | -2.94 | 141.34 | 0 | No | No | 1 | 0 |
| Taxifolin | 304.25 | 7 | 5 | 0.95 | -2.66 | 127.45 | 1 | No | No | 1 | 0 |
| Justicidin B | 364.09 | 6 | 0 | 3.98 | -4.85 | 63.22 | 3 | Yes | Yes | 0 | 0 |
| Maruchantin E | 440.16 | 5 | 4 | 5.41 | -6.52 | 90.15 | 0 | No | No | 0 | 1 |
| Emetine | 480.29 | 6 | 1 | 4.74 | -5.6 | 52.19 | 7 | No | No | 0 | 0 |
| Pachymic acid | 528.38 | 5 | 2 | 7.23 | -7.15 | 83.83 | 8 | No | Yes | 0 | 3 |
| Flavonol base + 4O, 1MeO, O-Hex-Hex, O-Hex | 818.68 | 23 | 14 | -3.28 | -2.33 | 378.04 | 11 | No | No | 0 | 3 |
| Licoricesaponin G2 | 838.94 | 17 | 9 | 1.58 | -5.51 | 287.27 | 8 | No | No | 0 | 3 |
| Procyanidin C1 | 866.20 | 18 | 15 | 3.31 | -7.39 | 331.14 | 5 | No | No | 1 | 3 |

M.W: Molecular weight (< 500 g/mol); HBAs: Hydrogen bond acceptors (≤ 10); HBDs: Hydrogen bond donors (< 5); For lipophilicity: XLOGP3 between -0.7 and $+5.0$; For solubility: Log S between -6 and $+0.5$; ESOL: Estimated solubility; TPSA: Topological polar surface area ($< 140 \text{ \AA}^2$); Flexibility: no more than 9 rotatable bonds (RBs); PAINS: Pan assay interference compounds; Ro5: Lipinski's rule of five.

Table S3. Prediction of absorption, distribution, metabolism, excretion and toxicity (ADMET) properties of selected CLAE compounds by using pkCSM program.

| Compound name | Absorption | | | Distribution | | Metabolism | | Excretion | | Toxicity | | | | |
|--------------------------------|------------|---------|-----------|------------------|--------|------------|--------|-----------------|---------------|---|-------------------|--------------------|-----------------|------------|
| | C2P | HIA (%) | P-gp sub. | Permeability BBB | CNS | CYP3A4 | CYP2D6 | Total clearance | AMES toxicity | Oral rat acute toxicity (LD ₅₀) | Inhibitors hERG I | Inhibitors hERG II | Hepato-toxicity | Skin sens. |
| Malic acid | -0.395 | 13.831 | No | -0.788 | -3.523 | No | No | 0.81 | No | 1.818 | No | No | No | No |
| Vanillic acid | 0.33 | 78.152 | No | -0.38 | -2.628 | No | No | 0.628 | No | 2.454 | No | No | No | No |
| Gallic acid | -0.081 | 43.374 | No | -1.102 | -3.74 | No | No | 0.518 | No | 2.218 | No | No | No | No |
| Syringic acid 3,4- | 0.495 | 73.076 | Yes | -0.191 | -2.701 | No | No | 0.646 | No | 2.157 | No | No | No | No |
| Dimethoxycinnamic acid | 1.225 | 94.767 | No | 0.502 | -2.518 | No | No | 0.719 | No | 2.186 | No | No | No | No |
| Capensine | 1.103 | 94.652 | Yes | -0.258 | -2.855 | No | No | 0.764 | No | 2.112 | No | No | No | No |
| Fustin | -0.174 | 73.643 | Yes | -0.739 | -3.111 | No | No | -0.067 | Yes | 2.329 | No | No | No | No |
| Enterolactone | 1.045 | 93.934 | Yes | -0.62 | -2.383 | Yes | Yes | 0.161 | No | 2.02 | No | No | No | No |
| Quercetin | -0.229 | 77.207 | Yes | -1.098 | -3.065 | No | No | 0.407 | No | 2.471 | No | No | No | No |
| Epigallocatechin | -0.375 | 54.128 | Yes | -1.377 | -3.507 | No | No | 0.328 | No | 2.492 | No | No | No | No |
| Andrographolide | 1.07 | 95.357 | No | -0.598 | -2.691 | Yes | Yes | 1.183 | No | 2.162 | No | Yes | No | No |
| 14,15-Dehydro-16-epi-vincamine | 0.946 | 90.873 | Yes | 0.74 | -2.127 | Yes | Yes | 0.933 | No | 3.098 | No | No | Yes | No |
| Otosenine | 0.639 | 83.228 | Yes | -0.701 | -3.053 | No | No | 0.627 | Yes | 3.913 | No | Yes | Yes | No |
| Voacristine | 1.02 | 95.72 | Yes | -0.67 | -2.515 | Yes | Yes | 1.088 | No | 3.017 | No | No | No | No |
| 1-O-Sinapoylglucose | 0.172 | 47.505 | Yes | -1.308 | -4.05 | No | No | 0.71 | No | 1.823 | No | No | No | No |
| Scaposin | 1.274 | 94.64 | Yes | -1.546 | -3.643 | No | No | 0.575 | No | 2.316 | No | Yes | No | No |
| Kaempferol-3-O-arabinoside | 0.128 | 59.181 | Yes | -1.243 | -4.053 | No | No | 0.431 | No | 2.607 | No | Yes | No | No |
| Isoangustone A | -0.116 | 89.78 | Yes | -1.025 | -1.929 | Yes | Yes | 0.259 | No | 2.557 | No | No | No | No |
| Gancaonin E | 0.237 | 90.127 | Yes | -0.875 | -2.665 | Yes | Yes | 0.088 | No | 2.408 | No | No | No | No |
| Naringenin-7-O-glucoside | 0.415 | 36.035 | Yes | -1.261 | -4.053 | No | No | 0.378 | No | 2.683 | No | No | No | No |
| Isoorientin | -0.912 | 61.768 | Yes | -1.564 | -3.939 | No | No | 0.372 | No | 2.55 | No | Yes | No | No |
| Isosilybin A | 0.43 | 69.767 | Yes | -1.181 | -3.671 | No | No | -0.106 | No | 2.557 | No | No | Yes | No |
| Harringtonine | 0.601 | 71.074 | Yes | -1.102 | -3.585 | Yes | Yes | 1.299 | No | 2.017 | No | No | No | No |
| Benzoic acid | 1.707 | 100 | No | -0.22 | -2.002 | No | No | 0.707 | No | 2.17 | No | No | No | No |

| Compound name | Absorption | | | Distribution | | Metabolism | | Excretion | | Toxicity | | | | |
|--|------------|---------|-----------|--------------|--------|------------|--------|-----------------|---------------|---|------------|---------|-----------------|------------|
| | C2P | HIA (%) | P-gp sub. | Permeability | | Substrates | | Total clearance | AMES toxicity | Oral rat acute toxicity (LD ₅₀) | Inhibitors | | Hepato-toxicity | Skin sens. |
| | | | | BBB | CNS | CYP3A4 | CYP2D6 | | | | hERG I | hERG II | | |
| 4-Aminobenzoic acid | 0.558 | 81.966 | No | -0.389 | -3.222 | No | No | 0.492 | No | 1.548 | No | No | No | No |
| <i>p</i> -Coumaraldehyde | 1.725 | 92.221 | No | 0.445 | -1.834 | No | No | 0.16 | No | 1.943 | No | No | No | Yes |
| 3-Indoleacetonitrile | 1.491 | 92.011 | No | 0.381 | -1.814 | No | No | 0.529 | Yes | 2.339 | No | No | Yes | Yes |
| 4-Hydroxycoumarin | 1.206 | 94.551 | No | -0.278 | -2.741 | No | No | 0.751 | No | 2.047 | No | No | No | No |
| <i>cis</i> -Aconitic acid | -0.274 | 0 | No | -0.886 | -3.156 | No | No | 0.99 | No | 2.138 | No | No | No | No |
| Caffeic acid | 0.634 | 69.407 | No | -0.647 | -2.608 | No | No | 0.508 | No | 2.383 | No | No | No | No |
| Vasicine | 1.595 | 86.22 | No | -0.127 | -2.159 | Yes | Yes | 0.58 | Yes | 2.697 | No | No | No | No |
| Scopoletin | 1.184 | 95.277 | No | -0.299 | -2.32 | No | No | 0.73 | No | 1.95 | No | No | No | No |
| Vasinonone | 1.172 | 92.532 | Yes | -0.206 | -2.323 | No | No | 0.568 | No | 1.91 | No | No | No | No |
| Harmaline | 1.621 | 93.622 | Yes | 0.39 | -2.017 | No | No | 0.576 | No | 2.452 | No | No | No | No |
| 5,7-Dimethoxy-4-methylcoumarin | 1.298 | 96.974 | Yes | 0.396 | -2.289 | No | No | 0.831 | No | 2.001 | No | No | No | No |
| 3,4,5-Trihydroxystilbene | 1.197 | 90.975 | Yes | 0.5 | -2.075 | Yes | Yes | -0.014 | Yes | 2.486 | No | No | No | No |
| Chrysin | 0.945 | 93.761 | Yes | 0.047 | -1.912 | No | No | 0.405 | No | 2.289 | No | No | No | No |
| (R)-Semivioxanthin | 1.101 | 92.346 | Yes | 0.079 | -2.169 | No | No | 0.49 | No | 1.737 | No | No | No | No |
| Biochanin A | 0.897 | 93.028 | Yes | -0.221 | -2.115 | Yes | Yes | 0.247 | No | 1.851 | No | No | No | No |
| Ellagic acid | 0.335 | 86.684 | Yes | -1.272 | -3.533 | No | No | 0.537 | No | 2.399 | No | No | No | No |
| Taxifolin | 0.924 | 64.709 | Yes | -0.725 | -3.198 | No | No | -0.078 | No | 2.261 | No | Yes | No | No |
| Justicidin B | 1.151 | 99.578 | No | -0.728 | -2.876 | Yes | Yes | 0.34 | Yes | 2.843 | No | Yes | Yes | No |
| Maruchantin E | 0.667 | 97.775 | Yes | -0.826 | -1.469 | Yes | Yes | -0.125 | Yes | 2.59 | No | Yes | No | No |
| Emetine | 0.751 | 91.032 | Yes | -0.394 | -2.067 | Yes | Yes | 0.993 | No | 2.793 | No | No | No | No |
| Pachymic acid | 0.694 | 97.531 | No | -0.293 | -1.748 | Yes | Yes | 0.246 | No | 2.284 | No | Yes | No | No |
| Flavonol base + 4O, 1MeO, O-Hex-Hex, O-Hex | -1.116 | 0 | Yes | -3.22 | -6.434 | No | No | -0.577 | No | 2.482 | No | No | No | No |
| Licoricesaponin G2 | -0.83 | 0 | Yes | -1.644 | -4.613 | No | No | -0.194 | No | 2.481 | No | Yes | No | No |
| Procyanidin C1 | -1.826 | 60.469 | Yes | -2.843 | -4.855 | No | No | -3.326 | No | 2.482 | No | Yes | No | No |

C2P: Caco-2 cell line permeability (log Papp value in 10⁻⁶ cm/s, > 0.90 represents higher permeability); HIA: Human intestinal absorption (< 30% is poorly absorbed); P-gp sub.: P-glycoprotein substrate; BBB: Blood brain barrier (expressed in log BB, logBB value > 0.3 indicates that a compound is considered to be readily cross the blood brain barrier); CNS: Central nervous system permeability is stated in terms of logPS (a compound with logPS > -2 is considered to penetrate the CNS); The predicted total

clearance is expressed as $\log(\text{CL}_{\text{tot}})$ which is measured in $\log(\text{mL}/\text{min}/\text{kg})$; Ames toxicity is the measurement of compound's mutagenic potential using bacteria; Oral rat acute toxicity values are calculated in terms of LD₅₀ (lethal dose, 50%) and its unit is mol/kg; hERG: human ether-a-go-go related gene; Skin sens.: Skin sensitization.

Table S4. Myocardial infarction related pathogenic genes for CLAE.

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|---------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 1. | ACE | Angiotensin I Converting Enzyme | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 4.47 | 15.82% |
| 2. | MIAT | Myocardial Infarction Associated Transcript | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 4.17 | 0.00% |
| 3. | MEF2A | Myocyte Enhancer Factor 2A | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.87 | 68.17% |
| 4. | ITGB3 | Integrin Subunit Beta 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.63 | 58.75% |
| 5. | CRP | C-Reactive Protein | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.57 | 61.71% |
| 6. | PLAT | Plasminogen Activator; Tissue Type | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 4.00 | 53.97% |
| 7. | NPPB | Natriuretic Peptide B | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.52 | 46.17% |
| 8. | APOB | Apolipoprotein B | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.47 | 41.09% |
| 9. | MIR499A | MicroRNA 499a | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.43 | 0.00% |
| 10. | MIR208B | MicroRNA 208b | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.33 | 0.00% |
| 11. | OLR1 | Oxidized Low Density Lipoprotein Receptor 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.70 | 42.84% |
| 12. | IL6 | Interleukin 6 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.22 | 56.07% |
| 13. | TNNT2 | Troponin T2; Cardiac Type | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.19 | 46.22% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|---------------------------------|----------------|---|--------------------------|-----------|------------------------------------|
| 14. | NPPA | Natriuretic Peptide A | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.17 | 21.30% |
| 15. | SERPINE1 | Serpin Family E Member 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.15 | 47.40% |
| 16. | APOE | Apolipoprotein E | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.13 | 30.00% |
| 17. | TNNI3 | Troponin I3; Cardiac Type | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.11 | 58.63% |
| 18. | AGTR1 | Angiotensin II Receptor Type 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.09 | 63.82% |
| 19. | LTA | Lymphotoxin Alpha | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.39 | 12.09% |
| 20. | APOA1 | Apolipoprotein A1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.06 | 70.10% |
| 21. | F7 | Coagulation Factor VII | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.36 | 36.95% |
| 22. | ESR1 | Estrogen Receptor 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.04 | 68.53% |
| 23. | EDN1 | Endothelin 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.03 | 32.66% |
| 24. | MMP9 | Matrix Metallopeptidase 9 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 3.01 | 20.28% |
| 25. | F13A1 | Coagulation Factor XIII A Chain | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.30 | 33.82% |
| 26. | MB | Myoglobin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.27 | 77.88% |
| 27. | THBD | Thrombomodulin | Protein | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.24 | 26.24% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|---|--------------------------|---|--------------------------|-----------|------------------------------------|
| 28. | IL10 | Interleukin 10 | Coding Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.94 | 63.14% |
| 29. | LRP6 | LDL Receptor Related Protein 6 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.88 | 61.60% |
| 30. | TNF | Tumor Necrosis Factor | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.87 | 70.41% |
| 31. | NOS3 | Nitric Oxide Synthase 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.86 | 58.50% |
| 32. | FABP3 | Fatty Acid Binding Protein 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.79 | 52.95% |
| 33. | PON1 | Paraoxonase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.76 | 14.02% |
| 34. | AGT | Angiotensinogen | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.75 | 20.68% |
| 35. | F3 | Coagulation Factor III; Tissue Factor | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 3.00 | 45.38% |
| 36. | LRP8 | LDL Receptor Related Protein 8 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.98 | 50.12% |
| 37. | LPL | Lipoprotein Lipase | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.92 | 25.04% |
| 38. | ITGA2B | Integrin Subunit Alpha 2b | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.70 | 50.67% |
| 39. | ADIPOQ | Adiponectin; C1Q And Collagen Domain Containing | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.70 | 38.10% |
| 40. | SELP | Selectin P | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.91 | 14.14% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 41. | JAK2 | Janus Kinase 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.69 | 71.65% |
| 42. | VEGFA | Vascular Endothelial Growth Factor A | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.68 | 64.83% |
| 43. | CETP | Cholesteryl Ester Transfer Protein | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.65 | 43.59% |
| 44. | VWF | Von Willebrand Factor | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.85 | 1.01% |
| 45. | F2 | Coagulation Factor II; Thrombin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.83 | 56.27% |
| 46. | MMP3 | Matrix Metallopeptidase 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.64 | 52.50% |
| 47. | PCSK9 | Proprotein Convertase Subtilisin/Kexin Type 9 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.82 | 15.35% |
| 48. | MIR210 | MicroRNA 210 | RNA Gene | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.80 | 0.00% |
| 49. | F5 | Coagulation Factor V | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.78 | 3.19% |
| 50. | LDLR | Low Density Lipoprotein Receptor | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.77 | 58.01% |
| 51. | TNFSF4 | TNF Superfamily Member 4 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.77 | 71.26% |
| 52. | REN | Renin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.62 | 75.65% |
| 53. | TGFB1 | Transforming Growth Factor Beta 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.62 | 42.49% |
| 54. | SERPINC1 | Serpin Family C Member 1 | Protein | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.74 | 60.97% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|------------|--|--------------------------|---|--------------------------|-----------|------------------------------------|
| 55. | HFE | Homeostatic Iron Regulator | Coding Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.60 | 22.09% |
| 56. | ADM | Adrenomedullin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.59 | 45.97% |
| 57. | CDKN2B-AS1 | CDKN2B Antisense RNA 1 | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.59 | 0.00% |
| 58. | MTHFR | Methylenetetrahydrofolate Reductase | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.73 | 22.21% |
| 59. | TLR4 | Toll Like Receptor 4 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.71 | 25.45% |
| 60. | LGALS2 | Galectin 2 | Protein Coding | Myocardial Infarction | 1 | 3.08 | 27.24% |
| 61. | MMP2 | Matrix Metallopeptidase 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.57 | 71.78% |
| 62. | MPO | Myeloperoxidase | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.56 | 33.79% |
| 63. | PTGS2 | Prostaglandin-Endoperoxide Synthase 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.55 | 66.54% |
| 64. | PPARG | Peroxisome Proliferator Activated Receptor Gamma | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.54 | 58.38% |
| 65. | ITGA2 | Integrin Subunit Alpha 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.52 | 45.90% |
| 66. | IL1B | Interleukin 1 Beta | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.51 | 81.84% |
| 67. | IGF1 | Insulin Like Growth Factor 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.50 | 50.87% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 68. | LPA | Lipoprotein(A) | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.67 | 3.20% |
| 69. | FGA | Fibrinogen Alpha Chain | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.66 | 63.13% |
| 70. | MYH7 | Myosin Heavy Chain 7 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.50 | 79.57% |
| 71. | ICAM1 | Intercellular Adhesion Molecule 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.49 | 20.08% |
| 72. | ADRB1 | Adrenoceptor Beta 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.48 | 63.76% |
| 73. | IL18 | Interleukin 18 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.48 | 64.91% |
| 74. | ALB | Albumin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.47 | 82.33% |
| 75. | VCAM1 | Vascular Cell Adhesion Molecule 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.47 | 53.48% |
| 76. | SELE | Selectin E | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.65 | 29.04% |
| 77. | INS | Insulin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.46 | 74.53% |
| 78. | CKB | Creatine Kinase B | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.46 | 69.75% |
| 79. | MIR21 | MicroRNA 21 | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.46 | 0.00% |
| 80. | PECAM1 | Platelet And Endothelial Cell Adhesion Molecule 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.63 | 0.00% |
| 81. | CTNNB1 | Catenin Beta 1 | Protein | Myocardial Infarction; Cardiac Hypertrophy; Acute | 3 | 2.45 | 91.86% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|---|--------------------------|---|--------------------------|-----------|------------------------------------|
| 82. | PSMA6 | Proteasome 20S Subunit Alpha 6 | Coding Protein Coding | Myocardial Infarction Myocardial Infarction | 1 | 2.97 | 82.23% |
| 83. | ADRB2 | Adrenoceptor Beta 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.44 | 41.04% |
| 84. | MMP1 | Matrix Metallopeptidase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.44 | 34.17% |
| 85. | TP53 | Tumor Protein P53 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.42 | 72.85% |
| 86. | AGER | Advanced Glycosylation End-Product Specific Receptor | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.42 | 27.13% |
| 87. | ELN | Elastin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.41 | 28.69% |
| 88. | GCLC | Glutamate-Cysteine Ligase Catalytic Subunit | Protein Coding | Myocardial Infarction | 1 | 2.95 | 68.34% |
| 89. | ADAMTS13 | ADAM Metallopeptidase with Thrombospondin Type 1 Motif 13 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.61 | 9.02% |
| 90. | APOC3 | Apolipoprotein C3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.40 | 58.93% |
| 91. | CXCL12 | C-X-C Motif Chemokine Ligand 12 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.60 | 61.77% |
| 92. | AGTR2 | Angiotensin II Receptor Type 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.40 | 41.73% |
| 93. | CBS | Cystathionine Beta-Synthase | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.39 | 54.73% |
| 94. | GCLM | Glutamate-Cysteine Ligase | Protein | Myocardial Infarction | 1 | 2.89 | 78.79% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|---------|--|--------------------------|---|--------------------------|-----------|------------------------------------|
| 95. | GATA4 | Modifier Subunit GATA Binding Protein 4 | Coding Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.39 | 33.78% |
| 96. | CD14 | CD14 Molecule | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.58 | 66.35% |
| 97. | NR3C2 | Nuclear Receptor Subfamily 3 Group C Member 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.38 | 63.80% |
| 98. | ABCA1 | ATP Binding Cassette Subfamily A Member 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.58 | 51.73% |
| 99. | CCL2 | C-C Motif Chemokine Ligand 2 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.56 | 69.23% |
| 100. | PTX3 | Pentraxin 3 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.55 | 30.68% |
| 101. | PPARA | Peroxisome Proliferator Activated Receptor Alpha | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.38 | 36.99% |
| 102. | LGALS3 | Galectin 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.37 | 22.69% |
| 103. | CYP2C19 | Cytochrome P450 Family 2 Subfamily C Member 19 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.53 | 21.81% |
| 104. | CKM | Creatine Kinase; M-Type | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.52 | 71.23% |
| 105. | RETN | Resistin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.36 | 75.34% |
| 106. | FGB | Fibrinogen Beta Chain | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.51 | 42.36% |
| 107. | GUCY1A1 | Guanylate Cyclase 1 Soluble Subunit Alpha 1 | Protein Coding | Myocardial Infarction | 1 | 2.84 | 62.09% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|--------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 108. | PON2 | Paraoxonase 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.36 | 33.29% |
| 109. | GNB3 | G Protein Subunit Beta 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.35 | 65.39% |
| 110. | KNG1 | Kininogen 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.34 | 39.10% |
| 111. | CSF3 | Colony Stimulating Factor 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.34 | 42.61% |
| 112. | ALDH2 | Aldehyde Dehydrogenase 2 Family Member | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.32 | 51.06% |
| 113. | LIPC | Lipase C; Hepatic Type | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.32 | 40.73% |
| 114. | HMOX1 | Heme Oxygenase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.32 | 31.92% |
| 115. | AVP | Arginine Vasopressin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.49 | 0.00% |
| 116. | IFNG | Interferon Gamma | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.31 | 81.00% |
| 117. | PF4 | Platelet Factor 4 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.45 | 71.14% |
| 118. | PAPPA | Pappalysin 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.44 | 60.82% |
| 119. | PLG | Plasminogen | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.43 | 38.18% |
| 120. | CXCL8 | C-X-C Motif Chemokine Ligand 8 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.43 | 70.13% |
| 121. | CLCN1 | Chloride Voltage-Gated | Protein | Myocardial Infarction | 1 | 2.72 | 36.16% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|----------|--|-----------------|---|--------------------------|-----------|------------------------------------|
| 122. | MIR29A | MicroRNA 29a | Coding RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.26 | 0.00% |
| 123. | HP | Haptoglobin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.41 | 32.66% |
| 124. | BDKRB2 | Bradykinin Receptor B2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.26 | 39.75% |
| 125. | GJA4 | Gap Junction Protein Alpha 4 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.41 | 23.73% |
| 126. | TLR2 | Toll Like Receptor 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.25 | 33.06% |
| 127. | HMGB1 | High Mobility Group Box 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.24 | 64.54% |
| 128. | TIMP1 | TIMP Metallopeptidase Inhibitor 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.24 | 13.68% |
| 129. | MIR199A1 | MicroRNA 199a-1 | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.23 | 0.00% |
| 130. | MIR22 | MicroRNA 22 | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.23 | 0.00% |
| 131. | ITGB1 | Integrin Subunit Beta 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.23 | 87.68% |
| 132. | ACE2 | Angiotensin Converting Enzyme 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.22 | 59.57% |
| 133. | HIF1A | Hypoxia Inducible Factor 1 Subunit Alpha | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.22 | 61.97% |
| 134. | MIR146A | MicroRNA 146a | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.22 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|----------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 135. | IL17A | Interleukin 17A | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.22 | 61.60% |
| 136. | STAT3 | Signal Transducer and Activator Of Transcription 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.21 | 78.94% |
| 137. | MEF2C | Myocyte Enhancer Factor 2C | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.21 | 87.81% |
| 138. | NPY | Neuropeptide Y | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.20 | 51.25% |
| 139. | HTR2A | 5-Hydroxytryptamine Receptor 2A | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.20 | 62.08% |
| 140. | CTF1 | Cardiotrophin 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.19 | 0.00% |
| 141. | F10 | Coagulation Factor X | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.38 | 62.81% |
| 142. | CD40LG | CD40 Ligand | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.37 | 63.35% |
| 143. | SERPINA3 | Serpin Family A Member 3 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.37 | 20.59% |
| 144. | CYP11B2 | Cytochrome P450 Family 11 Subfamily B Member 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.18 | 33.11% |
| 145. | IL1RN | Interleukin 1 Receptor Antagonist | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.36 | 79.13% |
| 146. | FAS | Fas Cell Surface Death Receptor | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.17 | 44.27% |
| 147. | ANXA5 | Annexin A5 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.16 | 59.65% |
| 148. | MIR208A | MicroRNA 208a | RNA | Myocardial Infarction; Cardiac Hypertrophy; Acute | 3 | 2.16 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|--------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 149. | CA3 | Carbonic Anhydrase 3 | Gene | Myocardial Infarction | | | |
| | | | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.35 | 32.84% |
| 150. | EPO | Erythropoietin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.16 | 50.01% |
| 151. | GP1BA | Glycoprotein Ib Platelet Subunit Alpha | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.34 | 46.66% |
| 152. | LEP | Leptin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.33 | 59.73% |
| 153. | THBS4 | Thrombospondin 4 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.15 | 41.35% |
| 154. | MIR150 | MicroRNA 150 | RNA Gene | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.33 | 0.00% |
| 155. | HGF | Hepatocyte Growth Factor | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.33 | 70.64% |
| 156. | SLC6A4 | Solute Carrier Family 6 Member 4 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.15 | 72.97% |
| 157. | CD36 | CD36 Molecule | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.15 | 20.40% |
| 158. | THBS1 | Thrombospondin 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.31 | 43.29% |
| 159. | CYP2C9 | Cytochrome P450 Family 2 Subfamily C Member 9 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.31 | 18.56% |
| 160. | MIR223 | MicroRNA 223 | RNA Gene | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.30 | 0.00% |
| 161. | APLN | Apelin | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.13 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|--------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 162. | CST3 | Cystatin C | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.30 | 0.00% |
| 163. | MIR126 | MicroRNA 126 | RNA Gene | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.30 | 0.00% |
| 164. | MIR132 | MicroRNA 132 | RNA Gene | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.13 | 0.00% |
| 165. | NPR1 | Natriuretic Peptide Receptor 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.12 | 40.51% |
| 166. | FLT1 | Fms Related Receptor Tyrosine Kinase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.12 | 77.15% |
| 167. | IL4 | Interleukin 4 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.12 | 68.48% |
| 168. | CXCR4 | C-X-C Motif Chemokine Receptor 4 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.11 | 78.34% |
| 169. | LCN2 | Lipocalin 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.11 | 42.06% |
| 170. | FN1 | Fibronectin 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.29 | 56.86% |
| 171. | MIR34A | MicroRNA 34a | RNA Gene | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.29 | 0.00% |
| 172. | UTS2 | Urotensin 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.11 | 10.48% |
| 173. | PROCR | Protein C Receptor | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.29 | 31.98% |
| 174. | MIR145 | MicroRNA 145 | RNA | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.28 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|--------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 175. | ITGAM | Integrin Subunit Alpha M | Gene | | | | |
| | | | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.10 | 46.05% |
| 176. | APOA2 | Apolipoprotein A2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.10 | 77.05% |
| 177. | CASP3 | Caspase 3 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.10 | 64.18% |
| 178. | KCNQ1 | Potassium Voltage-Gated Channel Subfamily Q Member 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.10 | 73.58% |
| 179. | POSTN | Periostin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.28 | 56.11% |
| 180. | CD40 | CD40 Molecule | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.27 | 60.13% |
| 181. | GDF15 | Growth Differentiation Factor 15 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.27 | 41.31% |
| 182. | APOA5 | Apolipoprotein A5 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.27 | 25.94% |
| 183. | SIRT1 | Sirtuin 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.09 | 73.01% |
| 184. | IGFBP1 | Insulin Like Growth Factor Binding Protein 1 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.26 | 50.90% |
| 185. | CYBA | Cytochrome B-245 Alpha Chain | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.08 | 0.00% |
| 186. | APOH | Apolipoprotein H | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.25 | 25.92% |
| 187. | P2RY12 | Purinergic Receptor P2Y12 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.25 | 67.32% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|------|----------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 188. | MYH6 | Myosin Heavy Chain 6 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy | 2 | 2.25 | 44.00% |
| 189. | AHSG | Alpha 2-HS Glycoprotein | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.07 | 42.52% |
| 190. | WRN | WRN RecQ Like Helicase | Protein Coding | Myocardial Infarction | 1 | 2.50 | 13.62% |
| 191. | NPPC | Natriuretic Peptide C | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.06 | 45.81% |
| 192. | CPB2 | Carboxypeptidase B2 | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.23 | 40.67% |
| 193. | SELL | Selectin L | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.21 | 26.44% |
| 194. | IL1A | Interleukin 1 Alpha | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.20 | 17.73% |
| 195. | FGF2 | Fibroblast Growth Factor 2 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.05 | 65.39% |
| 196. | HSPA4 | Heat Shock Protein Family A (Hsp70) Member 4 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.05 | 63.02% |
| 197. | PTGS1 | Prostaglandin-Endoperoxide Synthase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.04 | 25.27% |
| 198. | ENG | Endoglin | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.19 | 58.11% |
| 199. | TNFRSF1A | TNF Receptor Superfamily Member 1A | Protein Coding | Myocardial Infarction; Acute Myocardial Infarction | 2 | 2.19 | 55.74% |
| 200. | SOD1 | Superoxide Dismutase 1 | Protein Coding | Myocardial Infarction; Cardiac Hypertrophy; Acute Myocardial Infarction | 3 | 2.04 | 77.48% |

Table S5. Anxiety, depression and impaired memory related pathogenic genes for CLAE.

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|--|----------------|--|--------------------------|-----------|------------------------------------|
| 1. | SLC6A4 | Solute Carrier Family 6 Member 4 | Protein Coding | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 4.47 | 72.97% |
| 2. | HTR2A | 5-Hydroxytryptamine Receptor 2A | Protein Coding | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 3.87 | 62.08% |
| 3. | BDNF | Brain Derived Neurotrophic Factor | Protein Coding | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 3.63 | 36.81% |
| 4. | APP | Amyloid Beta Precursor Protein | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 3.70 | 77.65% |
| 5. | PRNP | Prion Protein | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 3.57 | 29.89% |
| 6. | GRN | Granulin Precursor | Protein Coding | Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 4 | 3.43 | 69.69% |
| 7. | DRD2 | Dopamine Receptor D2 | Protein Coding | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 3.17 | 63.33% |
| 8. | OXT | Oxytocin/Neurophysin I Prepropeptide | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 3.22 | 72.30% |
| 9. | CHMP2B | Charged Multivesicular Body Protein 2B | Protein Coding | Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 4 | 3.13 | 63.84% |
| 10. | TMEM106B | Transmembrane Protein 106B | Protein Coding | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 3.08 | 70.63% |
| 11. | DCTN1 | Dynactin Subunit 1 | Protein | Anxiety Disease; Mental Depression; | 4 | 3.11 | 66.27% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 12. | CRHR1 | Corticotropin Releasing Hormone Receptor 1 | Coding Protein | Memory Loss; Memory Impairment Anxiety Disorder; Mental Depression; | 4 | 3.09 | 78.05% |
| 13. | VCP | Valosin Containing Protein | Coding Protein | Memory Loss; Memory Impairment Anxiety Disease; Mental Depression; | 4 | 3.06 | 90.66% |
| 14. | GRIN2A | Glutamate Ionotropic Receptor NMDA Type Subunit 2A | Coding Protein | Memory Loss; Memory Impairment Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; | 5 | 2.92 | 78.30% |
| 15. | FMR1 | Fragile X Messenger Ribonucleoprotein 1 | Coding Protein | Anxiety Disorder; Anxiety Disease; Memory Loss; Memory Impairment | 4 | 3.04 | 46.07% |
| 16. | SLC6A3 | Solute Carrier Family 6 Member 3 | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 3.03 | 84.90% |
| 17. | POMC | Proopiomelanocortin | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 3.00 | 32.82% |
| 18. | TSPO | Translocator Protein | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.94 | 0.00% |
| 19. | SLC6A2 | Solute Carrier Family 6 Member 2 | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 3.01 | 57.52% |
| 20. | SNCA | Synuclein Alpha | Coding Protein | Anxiety Disorder; Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 5 | 2.65 | 65.02% |
| 21. | AKT1 | AKT Serine/Threonine Kinase 1 | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.82 | 90.77% |
| 22. | TPH1 | Tryptophan Hydroxylase 1 | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.97 | 54.69% |
| 23. | H2AC18 | H2A Clustered Histone 18 | Coding Protein | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.76 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 24. | IL1B | Interleukin 1 Beta | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.75 | 81.84% |
| 25. | DRD4 | Dopamine Receptor D4 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.89 | 0.00% |
| 26. | HTR2C | 5-Hydroxytryptamine Receptor 2C | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.85 | 33.28% |
| 27. | CREB1 | CAMP Responsive Element Binding Protein 1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.63 | 63.02% |
| 28. | PDGFB | Platelet Derived Growth Factor Subunit B | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.80 | 54.61% |
| 29. | TNF | Tumor Necrosis Factor | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.61 | 70.41% |
| 30. | INS | Insulin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.60 | 74.53% |
| 31. | HCRT | Hypocretin Neuropeptide Precursor | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.58 | 0.00% |
| 32. | MIR22 | MicroRNA 22 | RNA Gene | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.77 | 0.00% |
| 33. | PDGFRB | Platelet Derived Growth Factor Receptor Beta | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.68 | 62.04% |
| 34. | CSF1R | Colony Stimulating Factor 1 Receptor | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.91 | 39.96% |
| 35. | SQSTM1 | Sequestosome 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.62 | 40.03% |
| 36. | ABCA7 | ATP Binding Cassette Subfamily A Member 7 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.84 | 2.00% |
| 37. | GRIA1 | Glutamate Ionotropic Receptor AMPA Type | Protein | Anxiety Disorder; Mental Depression; | 4 | 2.42 | 61.34% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|--|--------------------|---|--------------------------|-----------|------------------------------------|
| 38. | MIR34A | Subunit 1 MicroRNA 34a | Coding RNA Gene | Memory Loss; Memory Impairment Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.59 | 0.00% |
| 39. | HLA-DQB1 | Major Histocompatibility Complex; Class II; DQ Beta 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.56 | 0.14% |
| 40. | ACHE | Acetylcholinesterase (Cartwright Blood Group) | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.55 | 43.95% |
| 41. | MYORG | Myogenesis Regulating Glycosidase (Putative) | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.79 | 0.00% |
| 42. | NGF | Nerve Growth Factor | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.37 | 35.16% |
| 43. | AARS2 | Alanyl-tRNA Synthetase 2; Mitochondrial | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.74 | 23.96% |
| 44. | DNMT1 | DNA Methyltransferase 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.73 | 73.22% |
| 45. | PVALB | Parvalbumin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.36 | 51.42% |
| 46. | CCK | Cholecystokinin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.48 | 62.52% |
| 47. | TARDBP | TAR DNA Binding Protein | Protein Coding | Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.35 | 86.35% |
| 48. | MDD1 | Major Depressive Disorder | Genetic Locus | Anxiety Disorder; Mental Depression | 2 | 2.67 | 0.00% |
| 49. | SLC25A13 | Solute Carrier Family 25 Member 13 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.64 | 78.03% |
| 50. | OSTF1 | Osteoclast Stimulating Factor 1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.41 | 68.60% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|---|-------------------|---|--------------------------|-----------|------------------------------------|
| 51. | ALB | Albumin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.30 | 82.33% |
| 52. | MIR132 | MicroRNA 132 | RNA Gene | Mental Depression; Memory Loss; Memory Impairment | 3 | 2.38 | 0.00% |
| 53. | GAD2 | Glutamate Decarboxylase 2 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.38 | 66.16% |
| 54. | CCR1 | C-C Motif Chemokine Receptor 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.56 | 61.45% |
| 55. | CYLD | CYLD Lysine 63 Deubiquitinase | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.54 | 88.26% |
| 56. | IL23R | Interleukin 23 Receptor | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.53 | 38.44% |
| 57. | C4A | Complement C4A (Rodgers Blood Group) | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.53 | 0.00% |
| 58. | EIF2B3 | Eukaryotic Translation Initiation Factor 2B Subunit Gamma | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.52 | 49.31% |
| 59. | FRAXA | Fragile Site; Folic Acid Type; Rare; Fra(X) (Q27.3) A | Biological Region | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.31 | 0.00% |
| 60. | MAOB | Monoamine Oxidase B | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.24 | 84.51% |
| 61. | TAC1 | Tachykinin Precursor 1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.23 | 77.26% |
| 62. | STUB1 | STIP1 Homology And U-Box Containing Protein 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.31 | 72.64% |
| 63. | VAMP1 | Vesicle Associated Membrane Protein 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.49 | 68.90% |
| 64. | JPH3 | Junctophilin 3 | Protein | Anxiety Disease; Memory Loss; | 3 | 2.30 | 39.71% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|---|-----------------------------|--|--------------------------|-----------|------------------------------------|
| 65. | IL12A | Interleukin 12A | Coding Protein Coding | Memory Impairment Memory Loss; Memory Impairment | 2 | 2.47 | 67.00% |
| 66. | STAT4 | Signal Transducer and Activator of Transcription 4 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.47 | 73.39% |
| 67. | MEFV | MEFV Innate Immunity Regulator; Pyrin | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.47 | 10.89% |
| 68. | XPR1 | Xenotropic And Polytropic Retrovirus Receptor 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.43 | 88.78% |
| 69. | JAM2 | Junctional Adhesion Molecule 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.42 | 35.69% |
| 70. | MSH2 | MutS Homolog 2 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.29 | 65.16% |
| 71. | NIPA1 | NIPA Magnesium Transporter 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.40 | 60.19% |
| 72. | CNR1 | Cannabinoid Receptor 1 | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.29 | 87.47% |
| 73. | TIA1 | TIA1 Cytotoxic Granule Associated RNA Binding Protein | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.39 | 65.55% |
| 74. | ATXN3 | Ataxin 3 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.39 | 31.68% |
| 75. | HFE | Homeostatic Iron Regulator | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.26 | 22.09% |
| 76. | FUS | FUS RNA Binding Protein | Protein Coding | Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.17 | 75.66% |
| 77. | ACE | Angiotensin I Converting Enzyme | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.25 | 15.82% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 78. | DRD1 | Dopamine Receptor D1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.15 | 73.93% |
| 79. | DRD3 | Dopamine Receptor D3 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.24 | 60.23% |
| 80. | TNFRSF1A | TNF Receptor Superfamily Member 1A | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.36 | 55.74% |
| 81. | CCKBR | Cholecystokinin B Receptor | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 2.23 | 36.96% |
| 82. | AD10 | Alzheimer Disease-10 | Genetic Locus | Memory Loss; Memory Impairment | 2 | 2.35 | 0.00% |
| 83. | SLC20A2 | Solute Carrier Family 20 Member 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.35 | 69.55% |
| 84. | SMARCE1 | SWI/SNF Related; Matrix Associated; Actin Dependent Regulator of Chromatin; Subfamily E; Member 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.35 | 82.41% |
| 85. | EIF2B2 | Eukaryotic Translation Initiation Factor 2B Subunit Beta | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.32 | 73.46% |
| 86. | SORL1 | Sortilin Related Receptor 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.32 | 46.42% |
| 87. | OPRM1 | Opioid Receptor Mu 1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 2.22 | 7.81% |
| 88. | KRAS | KRAS Proto-Oncogene; GTPase | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.21 | 79.60% |
| 89. | GAL | Galanin And GMAP Prepropeptide | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.08 | 44.58% |
| 90. | PTEN | Phosphatase And Tensin Homolog | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.30 | 78.93% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|---------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 91. | FAN1 | FANCD2 And FANCI Associated Nuclease 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.19 | 28.45% |
| 92. | BMPR1A | Bone Morphogenetic Protein Receptor Type 1A | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.19 | 44.71% |
| 93. | MT-TL1 | Mitochondrially Encoded tRNA-Leu (UUA/G) 1 | RNA Gene | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.19 | 0.00% |
| 94. | POLG | DNA Polymerase Gamma; Catalytic Subunit | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.19 | 56.04% |
| 95. | CCR6 | C-C Motif Chemokine Receptor 6 | Protein Coding | Mental Depression; Memory Loss; Memory Impairment | 3 | 2.16 | 81.89% |
| 96. | CD4 | CD4 Molecule | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.03 | 34.31% |
| 97. | AFG3L2 | AFG3 Like Matrix AAA Peptidase Subunit 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.28 | 86.29% |
| 98. | ATXN1 | Ataxin 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.27 | 66.56% |
| 99. | NOD2 | Nucleotide Binding Oligomerization Domain Containing 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.27 | 18.32% |
| 100 | PSTPIP1 | Proline-Serine-Threonine Phosphatase Interacting Protein 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.27 | 24.66% |
| 101 | CP | Ceruloplasmin | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.25 | 20.55% |
| 102 | PPIG | Peptidylprolyl Isomerase G | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 2.01 | 47.60% |
| 103 | MT-ND4 | Mitochondrially Encoded NADH: Ubiquinone Oxidoreductase Core Subunit 4 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.12 | 0.00% |
| 104 | EPCAM | Epithelial Cell Adhesion Molecule | Protein | Anxiety Disease; Memory Loss; | 3 | 2.12 | 11.96% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|--|-------------------|--|--------------------------|-----------|------------------------------------|
| 105 | TGFBR2 | Transforming Growth Factor Beta Receptor 2 | Coding Protein | Memory Impairment Anxiety Disease; Memory Loss; | 3 | 2.12 | 61.24% |
| | | | Coding | Memory Impairment | | | |
| 106 | MT-CO3 | Mitochondrially Encoded Cytochrome C Oxidase III | Protein | Anxiety Disease; Memory Loss; | 3 | 2.12 | 0.00% |
| | | | Coding | Memory Impairment | | | |
| 107 | MLH3 | MutL Homolog 3 | Protein | Anxiety Disease; Memory Loss; | 3 | 2.12 | 10.60% |
| | | | Coding | Memory Impairment | | | |
| 108 | PAND1 | Panic Disorder 1 | Genetic Locus | Anxiety Disorder | 1 | 2.50 | 0.00% |
| 109 | HTR1D | 5-Hydroxytryptamine Receptor 1D | Protein | Anxiety Disorder; Mental Depression | 2 | 2.24 | 43.78% |
| | | | Coding | | | | |
| 110 | ATN1 | Atrophin 1 | Protein | Memory Loss; Memory Impairment | 2 | 2.23 | 59.89% |
| | | | Coding | | | | |
| 111 | SOD1 | Superoxide Dismutase 1 | Protein | Anxiety Disease; Memory Loss; | 3 | 2.08 | 77.48% |
| | | | Coding | Memory Impairment | | | |
| 112 | HTR7 | 5-Hydroxytryptamine Receptor 7 | Protein | Anxiety Disorder; Mental Depression | 2 | 2.23 | 82.77% |
| | | | Coding | | | | |
| 113 | NOS1 | Nitric Oxide Synthase 1 | Protein | Anxiety Disorder; Mental Depression; | 4 | 1.99 | 50.65% |
| | | | Coding | Memory Loss; Memory Impairment | | | |
| 114 | GRIK2 | Glutamate Ionotropic Receptor Kainate Type Subunit 2 | Protein | Anxiety Disorder; Anxiety Disease; | 4 | 1.98 | 75.34% |
| | | | Coding | Mental Depression; Memory Impairment | | | |
| 115 | SPG11 | SPG11 Vesicle Trafficking Associated; Spatacsin | Protein | Memory Loss; Memory Impairment | 2 | 2.20 | 49.61% |
| | | | Coding | | | | |
| 116 | HTRA1 | HtrA Serine Peptidase 1 | Protein | Memory Loss; Memory Impairment | 2 | 2.19 | 63.08% |
| | | | Coding | | | | |
| 117 | TOMM40 | Translocase Of Outer Mitochondrial Membrane | Protein | Memory Loss; Memory Impairment | 2 | 2.19 | 72.15% |
| | | | Coding | | | | |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|---------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 118 | ACTB | Actin Beta | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 1.96 | 93.46% |
| 119 | SCN1A | Sodium Voltage-Gated Channel Alpha Subunit 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 2.01 | 75.96% |
| 120 | CACNA1C | Calcium Voltage-Gated Channel Subunit Alpha1 C | Protein Coding | Mental Depression; Memory Loss; Memory Impairment | 3 | 2.01 | 70.84% |
| 121 | IL4 | Interleukin 4 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 1.95 | 68.48% |
| 122 | ANKLE2 | Ankyrin Repeat and LEM Domain Containing 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.15 | 33.55% |
| 123 | PLAU | Plasminogen Activator; Urokinase | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.14 | 32.24% |
| 124 | NEFL | Neurofilament Light Chain | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.13 | 0.00% |
| 125 | UBQLN2 | Ubiquilin 2 | Protein Coding | Anxiety Disease; Mental Depression; Memory Loss; Memory Impairment | 4 | 1.94 | 89.57% |
| 126 | CA4 | Carbonic Anhydrase 4 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 1.93 | 44.21% |
| 127 | NIPA2 | NIPA Magnesium Transporter 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.13 | 67.44% |
| 128 | MOG | Myelin Oligodendrocyte Glycoprotein | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.98 | 31.84% |
| 129 | PSAP | Prosaposin | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.13 | 69.37% |
| 130 | PAH | Phenylalanine Hydroxylase | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.09 | 48.92% |
| 131 | CACNA1H | Calcium Voltage-Gated Channel Subunit | Protein | Anxiety Disease; Memory Loss; | 3 | 1.98 | 40.67% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|--------|---|-----------------------------|--|--------------------------|-----------|------------------------------------|
| 132 | TACR1 | Alpha1 H Tachykinin Receptor 1 | Coding Protein Coding | Memory Impairment Anxiety Disorder; Mental Depression; Memory Loss | 3 | 1.97 | 79.39% |
| 133 | HM13 | Histocompatibility Minor 13 | Protein Coding | Anxiety Disorder; Memory Loss | 2 | 2.07 | 78.83% |
| 134 | AMY1A | Amylase Alpha 1A | Protein Coding | Anxiety Disorder; Mental Depression | 2 | 2.07 | 0.00% |
| 135 | LEP | Leptin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.96 | 59.73% |
| 136 | PRKACA | Protein Kinase CAMP-Activated Catalytic Subunit Alpha | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.06 | 88.75% |
| 137 | PICALM | Phosphatidylinositol Binding Clathrin Assembly Protein | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.95 | 79.10% |
| 138 | SETD2 | SET Domain Containing 2; Histone Lysine Methyltransferase | Protein Coding | Anxiety Disorder; Anxiety Disease; Memory Impairment | 3 | 1.95 | 51.01% |
| 139 | UGT1A1 | UDP Glucuronosyltransferase Family 1 Member A1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.02 | 63.13% |
| 140 | USP8 | Ubiquitin Specific Peptidase 8 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.02 | 31.98% |
| 141 | MYD88 | MYD88 Innate Immune Signal Transduction Adaptor | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.02 | 75.67% |
| 142 | SIM1 | SIM BHLH Transcription Factor 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.02 | 51.36% |
| 143 | SNCB | Synuclein Beta | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.01 | 76.69% |
| 144 | CRHBP | Corticotropin Releasing Hormone Binding Protein | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.93 | 53.95% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|--|----------------|---|--------------------------|-----------|------------------------------------|
| 145 | MIRLET7D | MicroRNA Let-7d | RNA Gene | Mental Depression; Memory Loss | 2 | 2.00 | 0.00% |
| 146 | MIR142 | MicroRNA 142 | RNA Gene | Mental Depression; Memory Loss | 2 | 2.00 | 0.00% |
| 147 | SLC18A2 | Solute Carrier Family 18 Member A2 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss; Memory Impairment | 4 | 1.89 | 78.94% |
| 148 | DNMT3A | DNA Methyltransferase 3 Alpha | Protein Coding | Anxiety Disorder; Anxiety Disease; Memory Loss; Memory Impairment | 4 | 1.87 | 86.72% |
| 149 | GRM3 | Glutamate Metabotropic Receptor 3 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.92 | 80.24% |
| 150 | S100B | S100 Calcium Binding Protein B | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.92 | 72.81% |
| 151 | AARS1 | Alanyl-tRNA Synthetase 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.00 | 58.77% |
| 152 | GFAP | Glial Fibrillary Acidic Protein | Protein Coding | Memory Loss; Memory Impairment | 2 | 2.00 | 40.30% |
| 153 | DTNBP1 | Dystrobrevin Binding Protein 1 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.91 | 47.57% |
| 154 | HTR4 | 5-Hydroxytryptamine Receptor 4 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 1.91 | 61.76% |
| 155 | MIR155 | MicroRNA 155 | RNA Gene | Mental Depression; Memory Impairment | 2 | 1.99 | 0.00% |
| 156 | ASS1 | Argininosuccinate Synthase 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.98 | 63.54% |
| 157 | XK | X-Linked Kx Blood Group Antigen; Kell and VPS13A Binding Protein | Protein Coding | Anxiety Disorder; Anxiety Disease; Memory Impairment | 3 | 1.90 | 85.78% |
| 158 | CHAT | Choline O-Acetyltransferase | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.96 | 7.28% |
| 159 | HCRTTR1 | Hypocretin Receptor 1 | Protein Coding | Anxiety Disorder; Mental Depression | 2 | 1.96 | 21.33% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|---------|---|----------------|---|--------------------------|-----------|------------------------------------|
| 160 | AD6 | Alzheimer Disease 6 | Genetic Locus | Memory Loss | 1 | 2.16 | 0.00% |
| 161 | TP53 | Tumor Protein P53 | Protein Coding | Anxiety Disorder; Anxiety Disease; Memory Loss; Memory Impairment | 4 | 1.83 | 72.85% |
| 162 | AMY1B | Amylase Alpha 1B | Protein Coding | Anxiety Disorder; Mental Depression | 2 | 1.94 | 0.00% |
| 163 | MME | Membrane Metalloendopeptidase | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.93 | 69.79% |
| 164 | CXCL8 | C-X-C Motif Chemokine Ligand 8 | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.85 | 70.13% |
| 165 | ATP13A2 | ATPase Cation Transporting 13A2 | Protein Coding | Mental Depression; Memory Loss; Memory Impairment | 3 | 1.85 | 67.39% |
| 166 | ITGB2 | Integrin Subunit Beta 2 | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.85 | 71.45% |
| 167 | MIR21 | MicroRNA 21 | RNA Gene | Memory Loss; Memory Impairment | 2 | 1.91 | 0.00% |
| 168 | SYP | Synaptophysin | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.91 | 66.45% |
| 169 | CHRN2 | Cholinergic Receptor Nicotinic Beta 2 Subunit | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 1.84 | 84.82% |
| 170 | LRP8 | LDL Receptor Related Protein 8 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Loss | 3 | 1.84 | 50.12% |
| 171 | AD5 | Alzheimer Disease 5 | Genetic Locus | Memory Loss | 1 | 2.06 | 0.00% |
| 172 | AD8 | Alzheimer Disease 8 | Genetic Locus | Memory Loss | 1 | 2.06 | 0.00% |
| 173 | MIR298 | MicroRNA 298 | RNA Gene | Memory Loss | 1 | 2.06 | 0.00% |
| 174 | MIR29B1 | MicroRNA 29b-1 | RNA Gene | Memory Loss | 1 | 2.06 | 0.00% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|----------|---|----------------|--|--------------------------|-----------|------------------------------------|
| 175 | AD11 | Alzheimer Disease-11 | Genetic Locus | Memory Loss | 1 | 2.06 | 0.00% |
| 176 | AD13 | Alzheimer Disease-13 | Genetic Locus | Memory Loss | 1 | 2.06 | 0.00% |
| 177 | MIR107 | MicroRNA 107 | RNA Gene | Memory Loss | 1 | 2.06 | 0.00% |
| 178 | MIR106B | MicroRNA 106b | RNA Gene | Memory Loss | 1 | 2.06 | 0.00% |
| 179 | MIR146A | MicroRNA 146a | RNA Gene | Memory Loss | 1 | 2.06 | 0.00% |
| 180 | AD16 | Alzheimer Disease 16 | Genetic Locus | Memory Loss | 1 | 2.06 | 0.00% |
| 181 | AIF1 | Allograft Inflammatory Factor 1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.91 | 22.37% |
| 182 | PINK1 | PTEN Induced Kinase 1 | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 1.83 | 16.06% |
| 183 | C19orf12 | Chromosome 19 Open Reading Frame 12 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.89 | 47.95% |
| 184 | ATP1A2 | ATPase Na+/K+ Transporting Subunit Alpha 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.89 | 85.48% |
| 185 | ASMT | Acetyl serotonin O-Methyltransferase | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.83 | 10.57% |
| 186 | NR3C2 | Nuclear Receptor Subfamily 3 Group C Member 2 | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.83 | 63.80% |
| 187 | BCHE | Butyrylcholinesterase | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.89 | 17.99% |
| 188 | ENO2 | Enolase 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.89 | 86.64% |
| 189 | CREBBP | CREB Binding Protein | Protein Coding | Anxiety Disorder; Memory Loss; Memory Impairment | 3 | 1.77 | 69.94% |

| No. | Symbol | Description | Category | Matched phenotypes | Matched phenotypes count | -LOG10(P) | Average disease-causing likelihood |
|-----|---------|--|----------------|--|--------------------------|-----------|------------------------------------|
| 190 | AIP | Aryl Hydrocarbon Receptor Interacting Protein | Protein Coding | Anxiety Disease; Memory Impairment | 2 | 1.87 | 51.53% |
| 191 | CST3 | Cystatin C | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.86 | 0.00% |
| 192 | RNASEH1 | Ribonuclease H1 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.86 | 82.83% |
| 193 | YY1 | YY1 Transcription Factor | Protein Coding | Anxiety Disease; Memory Loss; Memory Impairment | 3 | 1.76 | 55.78% |
| 194 | NOS2 | Nitric Oxide Synthase 2 | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.86 | 46.59% |
| 195 | RHO | Rhodopsin | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.76 | 73.02% |
| 196 | RORA | RAR Related Orphan Receptor A | Protein Coding | Anxiety Disorder; Mental Depression; Memory Impairment | 3 | 1.76 | 86.61% |
| 197 | SPTLC1 | Serine Palmitoyl transferase Long Chain Base Subunit 1 | Protein Coding | Memory Impairment | 1 | 1.99 | 65.31% |
| 198 | DLGAP2 | DLG Associated Protein 2 | Protein Coding | Anxiety Disorder | 1 | 1.99 | 0.00% |
| 199 | PSENEN | Presenilin Enhancer; Gamma-Secretase Subunit | Protein Coding | Memory Loss; Memory Impairment | 2 | 1.85 | 68.50% |
| 200 | CDK5 | Cyclin Dependent Kinase 5 | Protein Coding | "Memory Loss", "Memory Impairment" | 2 | 1.85 | 83.41% |

Table S6. Myocardial infarction related pathogenic genes retrieved for the CLAE compounds.

| Compounds | Common name |
|---------------|---|
| Isooientin | AKR1B1, CA7, CA12, TNF, IL2, AKT1, ABCB1, ALOX5, NOX4, CDK5R1 CDK5, XDH, MAOA, FLT3, CA2, CCNB3 CDK1 CCNB1 CCNB2, GLO1, APP, SYK, GSK3B, PARP1, TTR, MMP9, MMP2, CA4, MMP12, CD38, CYP1B1, ABCG2, AKR1B10, TNKS2, TNKS, ADORA1, ARG1, HIF1A, ABCC1, RPS6KA3, EGFR, PTPRS, SLC29A1, PRKCG, PRKCB, PRKCZ, SQLE, PLG, MAPT, KDM4E, GPR35, AVPR2, TOP2A, IGF1R, CYP19A1, INSR, F2, PIM1, AURKB, DRD4, ACHE, MYLK, MPO, PIK3R1, DAPK1, PYGL, CA1, SRC, PTK2, HSD17B2, KDR, MMP13, MMP3, CA3, ALOX15, PLK1, CA6, CDK1, PIK3CG, PKN1, CA14, CA9, CSNK2A1, ALOX12, MET, NEK2, CXCR1, CAMK2B, ALK, NEK6, PLA2G1B, CA5A, AXL, APEX1, NUAK1, AKR1C2, AKR1C1, AKR1C3, AKR1C4, CA13, ADORA2A, AKR1A1, PRKACA, BCL2L1. |
| Isosilybin A | CA2, CA7, CA1, CA3, CA6, CA12, CA4, CA13, CA5B, ABCB1, CA5A, MMP13, MMP12, CYP1B1, TAS2R31, KLK1, KLK2, CYP19A1, KIT, MMP2, MMP14, PTGS1, MAPT, TERT, PGD, ST3GAL3, FUT7, FUT4, STAT1, SQLE, HIF1A, GABRA1 GABRB2 GABRG2, BCL2, ESR2, ABCG2, ABCC1, SHBG, CBR1, MAOB, KDR, RXRA, KCNH2, MET, ADORA3, MT-ND4, ADORA1, SRC, CA9, FGFR1, APP, BACE1, FFAR1, DNMT1, MMP8, ESR1, PLA2G1B, CES1, CES2, HSD17B1, PTGS2, MAPK14, MAP2K1, CYP2C19, MMP9, DYRK1A, NADK, GRM2, PGF, VEGFA, PRKACA, F2, IRAK4, AURKA, ADORA2A, EIF4A1, PIK3C2A, PIK3C3, TYMS, SYK, MTOR, MAP3K9, PARP1, PIK3CD, PIK3CB, PIK3CG, PIK3CA, FGR, PIK3C2B, TNKS2, TNKS, ADAM10, CHRM4, CHRM5, CHRM2, CHRM1, CHRM3, POLB, ADORA2B, AKR1C3, PLA2G2A. |
| Vanillic acid | CA2, CA7, CA1, CA12, CA14, CA9, CA3, CA6, CA5A, CA4, TPMT, TTR, CA5B, CA13, FUT7, KDM4E, KDM4A, KDM3A, KDM6B, FTO, KDM4C, FYN, LCK, FBP1, AKR1C3, KDM2A, MMP9, MMP1, MMP2, MMP8, SQLE, POLA1, POLB, SERPINE1, TUBB1, NGFR, KMO, TYMS, PTPRB, LDHA, LDHB, LAP3, GPR17, MIF, IDO1, CTBP2, IGF1R, ALK, SRD5A2, PLA2G4B, ELANE, ERN1, LIG1, ACHE, FUCA1, GRM2, DPP4, SLC13A5, OGA, MAOA, MAOB, HSP90AA1, COMT, AKR1B1, BCL2L1, ESR2, CNR2, SLC29A1, CPA1, ALB, DTYMK, CASP3, SHBG, PIN1, RXRB, RXRG, RXRA, APEX1, CDA, TYR, ACE, ADA, NAALAD2, AMPD3, TRPM8, FABP4, FABP3, FABP5, MCL1, GGH, ECE1, ESR1, TBXAS1, MME, ST14, PLAU, HMGCR, DBF4 CDC7, SLC16A1, AURKB. |

Table S7. Anxiety, depression and impaired memory related pathogenic genes retrieved for CLAE compounds.

| Compound name | Genes |
|--------------------------------|---|
| 14,15-Dehydro-16-epi-vincamine | CYP17A1, SLC6A2, KCNA5, PARP1, MDM2, CTSS, CAPN2, CAPN1, CCNE2 CDK2 CCNE1, CCNB3 CDK1 CCNB1 CCNB2, ALOX5, CTSK, SCN9A, CYP19A1, JAK3, HSD17B2, CASP1, FNTA FNTB, ADORA1, PGGT1B, PPOX, CTSB, CASP3, CASP6, CASP7, CASP8, PTK2B, DUSP3, MCL1, TLR9, NR3C2, NR3C1, MAPK8, MMP9, MMP2, MMP8, TNNC1 TNNT2 TNNI3, TERT, STAT3, HSD11B1, AURKA, DUT, TTR, ERBB2, JAK2, GRM5, HMOX1, NTRK1, ADAMTS5, MET, PGGT1B FNTA, PER2, HCRTR2, HCRTR1, BACE1, EIF2AK1, LRRK2, CTSL, PAK4, PAK1, STK3, STK26, FAAH, AGTR1, MMP1, NPY5R, PRCP, MAPK10, HIF1A, PTGS2, MAPK14, GSK3B, SRC, SOAT1, MMP3, ADAM17, MMP7, QRFPR, CHRM4, CCNE1 CDK2, HRH2, FLT3, CHRM5, RET, CHRM2, CHRM3, PTAFR, BACE2, LCK, FGFR3, MUSK, NR4A1, AURKB, TACR1, ADORA2A, ITK, NOS1, NPY2R, KCNA3, NOS3. |
| Biochanin A | CYP19A1, CA7, HSD17B2, CA12, CA4, CBR1, ABCB1, HSD17B1, ESR1, ESR2, ALOX12, EGFR, ABCG2, ALDH2, TBXAS1, MAOA, MGAM, HTR2A, HTR2C, ADORA1, ADORA2A, ESRRA, ESRRB, IL2, PTGS1, SLC6A2, ALOX15, XDH, TYR, MIF, CA2, PTPRS, PPARA, TLR9, CA1, CYP1B1, PFKFB3, PON1, CA5B, MAOB, NOX4, STS, ACHE, PTPN1, HSP90AB1, CA9, CDC7, GCGR, PLAT, F10, PLAU, MCL1, GPR84, DUSP3, CDC25B, ABCC1, HSP90B1, BAD, TBXA2R, CHEK1, WEE1, ALPL, HSP90AA1, CA3, CA6, CA14, CA13, CA5A, IGFBP3, PPARG, TNNC1 TNNT2 TNNI3, SNCA, PTK6, BCL2, TLR8, SORT1, BACE1, PRMT1, IGFBP6, IGFBP4, IGFBP5, IGFBP2, IGFBP1, GRIN2B, AKR1B1, KIF11, CCND1 CDK4, PRSS1, CCR4, CHEK2, TNF, RPS6KA3, PDE10A, OPRD1, PLA2G4A, RAF1, COMT, NTRK1, PIM2, BRAF. |
| Ellagic Acid | GPR35, ERBB2, AKR1B1, CCND1 CDK4, PDGFRB, FLT4, IGF1R, INSR, EGFR, CA2, CDK2 CCNA1 CCNA2, AURKB, CA7, CA1, GSK3B, SRC, PTK2, KDR, PLK1, CA6, CA12, CA14, CA9, CSNK2A1, MET, CA4, PLK4, CA13, TEK, AKT1, AURKA, CA5A, BACE1, MAP3K8, BRAF, EPHB4, HSPA1A, NUAK1, SQLE, FGR, LYN, GSR, TNNC1 TNNT2 TNNI3, XDH, DAO, PTGS2, ESR1, ESR2, MAOA, HSD17B3, PTPN1, ALOX5, CBR1, CDK5R1 CDK5, CES2, CA5B, SNCA, ACHE, CYP1A2, ALDH2, GRK6, SRD5A1, CA3, KCNA3, MAOB, AKR1C3, AKR1C1, STS, PIM1, ALK, AXL, MIF, ERN1, CNR1, CNR2, NFKB1, KCNA5, APEX1, FYN, LCK, PON1, DYRK1A, BCHE, AR, ALOX15, PFKFB3, NQO1, SHBG, OPRK1, CYP19A1, PDE4D, IKBKB, NTRK2, TTR, CYP1B1, SLC6A3, SLC16A3, SIRT1, TERT, GPR55. |
| Enterolactone | CYP19A1, SHBG, MAP2K1, HSD17B2, NR1H3, ESR1, ESR2, PPARD, SLC6A3, SLC6A2, F2, LYPLA1, LYPLA2, ALPL, PRSS1, ALOX5, HSD17B1, HSP90AA1, CAPN1, PARP1, CDK2 CCNA1 CCNA2, MYLK, MAPK14, TGFBR1, GSTA1, NQO2, CHRNA4 CHRN2, ADORA2A, MMP3, MMP7, HSD11B1, NOX4, ADORA2B, JUN, PSEN2 PSENEN NCSTN APH1A PSEN1 APH1B, KIT, FLT4, FLT3, PDGFRA, MAP2K2, PITRM1, BRAF, CPA1, CPA3, CPB2, ABL1, MAP2, CCKBR, GCGR, MTNR1B, DRD1, BCL2, JAK2, RET, ALB, RIPK2, FTO, SGK1, HDAC5, GSK3B, HDAC7, ROCK2, ROCK1, LIMK1, CDC42BPA, TNK2, DMPK, RAF1, PDPK1, MAPK8, CDK2, PLK1, NOS1, FGFR1, MKNK2, NOS2, PAK4, |

| Compound name | Genes |
|----------------------|---|
| Gancaonin E | CHEK1, PTGFR, LRRK2, GRK7, ERBB2, CCNE1 CDK2, ANPEP, JAK3, DYRK1A, CAMK1, RPS6KA1, CAMK2D, JAK1, PKN2, JAK3 JAK1, JAK1 JAK2, TYK2 JAK2 JAK1, TYK2 JAK1, TYK2 JAK2, PKN1, PLA2G7, TYK2, RPS6KA2. |
| Isoorientin | ABCG2, ESR1, ESR2, CYP19A1, ACHE, PPARG, CES2, CA7, CA12, PLA2G1B, BCHE, HSD17B1, CA4, CYP1B1, SLC5A2, BACE1, MMP12, MMP13, CES1, RXRA, PTGS1, PTPN1, ODC1, ADORA1, ADORA3, MAOB, SHBG, CTSL, KLK2, TAS2R31, EPHB4, ABL1, EPHA2, EPHB2, EPHA5, EPHA4, EPHA8, EPHA7, EPHB3, EPHA3, EPHB1, EPHA1, RPS6KB1, AURKA, MMP3, ABCC1, KLK1, CBR1, HSD17B2, WEE1, RAF1, BCL2L1, BRAF, SERPINE1, CA6, CA13, CA5B, CA5A, PDGFRB, SRC, AKR1B10, HSP90AA1, CA2, CA1, DRD5, DRD1, DRD4, DRD3, F3, ESRRA, ESRRB, TRPM8, CAPN1, CHEK1, MET, HDAC3, GCGR, HDAC9, CCNE1 CDK2, CCNE1 CDK3, POLB, ANPEP, PDK1, NOX4, CDK1 CCNB1, MYLK, GRK2, KIT, PDE7A, CDK1, CA14, MMP8, PLA2G5, PLA2G10, HDAC7, MTOR, MMP1, ADAM17, FYN, YES1. |
| Isosilybin A | AKR1B1, CA7, CA12, TNF, IL2, AKT1, ABCB1, ALOX5, NOX4, CDK5R1 CDK5, XDH, MAOA, FLT3, CA2, CCNB3 CDK1 CCNB1 CCNB2, GLO1, APP, SYK, GSK3B, PARP1, TTR, MMP9, MMP2, CA4, MMP12, CD38, CYP1B1, ABCG2, AKR1B10, TNKS2, TNKS, ADORA1, ARG1, HIF1A, ABCC1, RPS6KA3, EGFR, PTPRS, SLC29A1, PRKCG, PRKCB, PRKCZ, SQLE, PLG, MAPT, KDM4E, GPR35, AVPR2, TOP2A, IGF1R, CYP19A1, INSR, F2, PIM1, AURKB, DRD4, ACHE, MYLK, MPO, PIK3R1, DAPK1, PYGL, CA1, SRC, PTK2, HSD17B2, KDR, MMP13, MMP3, CA3, ALOX15, PLK1, CA6, CDK1, PIK3CG, PKN1, CA14, CA9, CSNK2A1, ALOX12, MET, NEK2, CXCR1, CAMK2B, ALK, NEK6, PLA2G1B, CA5A, AXL, APEX1, NUAK1, AKR1C2, AKR1C1, AKR1C3, AKR1C4, CA13, ADORA2A, AKR1A1, PRKACA, BCL2L1. |
| Quercetin | CA2, CA7, CA1, CA3, CA6, CA12, CA4, CA13, CA5B, ABCB1, CA5A, MMP13, MMP12, CYP1B1, TAS2R31, KLK1, KLK2, CYP19A1, KIT, MMP2, MMP14, PTGS1, MAPT, TERT, PGD, ST3GAL3, FUT7, FUT4, STAT1, SQLE, HIF1A, GABRA1 GABRB2 GABRG2, BCL2, ESR2, ABCG2, ABCC1, SHBG, CBR1, MAOB, KDR, RXRA, KCNH2, MET, ADORA3, MT-ND4, ADORA1, SRC, CA9, FGFR1, APP, BACE1, FFAR1, DNMT1, MMP8, ESR1, PLA2G1B, CES1, CES2, HSD17B1, PTGS2, MAPK14, MAP2K1, CYP2C19, MMP9, DYRK1A, NADK, GRM2, PGF, VEGFA, PRKACA, F2, IRAK4, AURKA, ADORA2A, EIF4A1, PIK3C2A, PIK3C3, TYMS, SYK, MTOR, MAP3K9, PARP1, PIK3CD, PIK3CB, PIK3CG, PIK3CA, FGR, PIK3C2B, TNKS2, TNKS, ADAM10, CHRM4, CHRM5, CHRM2, CHRM1, CHRM3, POLB, ADORA2B, AKR1C3, PLA2G2A. |

| Compound name | Genes |
|----------------------|---|
| Scaposin | PIK3CG, APEX1, PTPRS, ESR2, MPG, SLC22A12, CDK5R1 CDK5, CCNB3 CDK1 CCNB1 CCNB2, ARG1, CDK6, CDK2, TYR, HSD17B1, AHR, ESRRRA, APP, PARP1, TTR, MMP12, CD38, AKR1B10, TNKS2, TNKS, TOP1, TERT. |
| Scopoletin | AKR1B1, ABCG2, OPRD1, KIT, CA2, CA4, NOS2, OPRM1, ABCC1, NOX4, PTGS2, ADORA3, XDH, PLA2G2A, ALOX5, CA12, CYP1B1, PFKFB3, CA9, MCL1, CA7, MAPT, KDM4E, TOP2A, DRD4, GLO1, MYLK, MPO, PIK3R1, DAPK1, PYGL, SYK, MMP3, CA3, CA6, CSNK2A1, CA13, PLA2G1B, CA5A, APEX1, AKR1C2, AKR1C1, AKR1C3, AKR1C4, AKR1A1, APP, GSK3B, BACE1, CDK1, PARP1, TTR, MMP12, CD38, AKR1B10, TNKS2, TNKS, TOP1, ARG1, ABCB1, ALOX15, ALOX12, PIM1, AKT1, F2, CYP1A1, CYP1A2, MMP9, MMP2, PLG, ESR2, TERT, AMY1A, HSD17B2, FLT3, TYR, AHR, ESRRRA, AXL, CA1, ADORA2A, IKBKB, IGF1R, AURKB, SRC, PTK2, KDR, PLK1, PKN1, MET, NEK2, ALK, NEK6, NUAK1, ADORA1, NTRK2, CYP19A1, PIK3CG, INSR, EGFR, MPG. |
| Vasicine | CA7, CA12, CA9, CA13, CA1, CA14, CA6, CA4, EGFR, CA5A, XDH, CA2, MAOA, CBR1, SRD5A1, CDK2 CCNA1 CCNA2, CA3, CCND1 CDK4, FLT4, INSR, PTK2, TEK, MAP3K8, HSPA1A, NUAK1, FGR, ESR2, AKR1C1, ALOX5, CA5B, GSK3B, DAO, KCNA3, GSR, KDR, ACHE, PTGS2, KCNA5, HSD17B3, SRC, CYP1A2, MAOB, NAT1, SQLE, PTPN1, KCNMA1, MB, BACE1, ERBB2, ESR1, PARP1, AKR1C3, MET, ALPG, PLAA, ALPL, COMT, GPR35, AURKA, CDK9 CCNT1, HMGCR, CSNK2A1, AKR1B1, PLEC, CSNK1A1, CSNK1D, AOC3, AURKB, AKT1, APEX1, CHRM1, CISD1, ALDH5A1, ABAT, BRAF, IGF1R, PIK3CG, PTPRC, GRK6, HTR2B, CXCR1, CLK1, DYRK1B, TNNC1 TNNT2 TNNI3, TAAR1, EPHB4, F2, ADRA2A, ADRA2C, ADRA2B, TERT, NISCH, CHEK1, WEE1, PLK1, PNP, PDGFRB, LYN, PLK4, CHRNA7, BCHE, ACHE, HRH3, NOS1, NOS2, NOS3, JAK1, JAK2, HMGCR, JAK3, SYK, ZAP70, STAT5A, AR, PSEN2 PSENEN NCSTN APH1A PSEN1 APH1B, ADORA1, ADORA3, ADRB2, ADRB1, ADRB3, ADRA1D, ADRA1A, ADRA1B, CYP19A1, CHEK1, PYGL, NR3C1, CA7, SERPINA6, CA1, CA12, CA9, CA13, SCN9A, PGR, SHBG, SLC6A3, PRKCA, PRKDC, MAPK1, ADORA2A, TTR, PIM1, PIM3, OPRK1, MMP3, MMP9, MMP1, MMP2, MMP7, MMP8, LIMK2, CYP11B1, CYP11B2, NEK1, MAPK14, CDC25A, CA2, TYK2, CDK2 CCNA1 CCNA2, LRRK2, CHRNA3 CHRN4, GABRB3 GABRA3 GABRG2, GABRB3 GABRG2 GABRA1, GABRB3 GABRG2 GABRA5, GABRA2 GABRB3 GABRG2, PDE7A, CDK2, ADAM17, AKR1C3, POLA1, DPP4, MAP2K1, DPP8, FAP, DPP9, TTL, IMPDH1, IMPDH2, EGFR, DRD1, GSK3B, IKBKB, OPRL1, HLCS, PARP1, MMP13, TK1, PER2, HSD11B1, PDE10A, ADAM10, ESR2, ADK, DRD3, EDNRA, KDR, HRH4, MAP3K7, COMT. |

Table S8. Top 20 GO biological process of CLAE phytocompounds for myocardial infarction related target genes.

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|---|---|
| 1. | 4.12E-07 | 4 | 11 | 369.67 | Cellular response to UV-A | MMP2, MMP9, MMP3, MMP1 |
| 2. | 5.59E-07 | 6 | 113 | 53.98 | Collagen metabolic process | MMP2, HIF1A, MMP9, MMP3, F2, MMP1 |
| 3. | 5.59E-07 | 4 | 14 | 290.45 | Response to UV-A | MMP2, MMP9, MMP3, MMP1 |
| 4. | 3.05E-06 | 6 | 157 | 38.85 | Response to UV | PTGS2, MMP2, MMP9, MMP3, CASP3, MMP1 |
| 5. | 3.59E-06 | 8 | 490 | 16.60 | Response to oxidative stress | MPO, PTGS2, MMP2, HIF1A, MMP9, MMP3, CASP3, CA3 |
| 6. | 6.33E-06 | 7 | 339 | 20.99 | Response to light stimulus | PTGS2, MMP2, HIF1A, MMP9, MMP3, CASP3, MMP1 |
| 7. | 6.33E-06 | 5 | 94 | 54.07 | Extracellular matrix disassembly | MMP2, MMP9, PLG, MMP3, MMP1 |
| 8. | 6.33E-06 | 5 | 93 | 54.65 | Cellular response to UV | PTGS2, MMP2, MMP9, MMP3, MMP1 |
| 9. | 8.44E-06 | 7 | 375 | 18.98 | Cellular response to chemical stress | MPO, PTGS2, MMP2, HIF1A, MMP9, MMP3, CASP3 |
| 10. | 2.48E-05 | 3 | 11 | 277.25 | Negative regulation of fibrinolysis | SERPINE1, PLG, F2 |
| 11. | 2.66E-05 | 4 | 52 | 78.20 | Embryo implantation | PTGS2, MMP2, MMP9, VEGFA |
| 12. | 2.66E-05 | 7 | 483 | 14.73 | Response to radiation | PTGS2, MMP2, HIF1A, MMP9, MMP3, CASP3, MMP1 |
| 13. | 2.66E-05 | 4 | 53 | 76.72 | Collagen catabolic process | MMP2, MMP9, MMP3, MMP1 |
| 14. | 2.66E-05 | 11 | 1817 | 6.15 | Regulation of cell population proliferation | PTGS2, MMP2, ESR1, HIF1A, MMP9, VEGFA, FABP3, PLG, ACE, CASP3, F2 |

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|--|--|
| 15. | 2.66E-05 | 5 | 142 | 35.80 | Cellular response to light stimulus | PTGS2, MMP2, MMP9, MMP3, MMP1 |
| 16. | 2.66E-05 | 11 | 1832 | 6.10 | Response to oxygen-containing compound | MPO, PTGS2, MMP2, ESR1, HIF1A, MMP9, SERPINE1, FABP3, MMP3, CASP3, CA3 |
| 17. | 4.02E-05 | 3 | 15 | 203.32 | Regulation of fibrinolysis | SERPINE1, PLG, F2 |
| 18. | 7.44E-05 | 6 | 350 | 17.43 | Cellular response to abiotic stimulus | PTGS2, MMP2, MMP9, MMP3, CASP3, MMP1 |
| 19. | 7.44E-05 | 6 | 350 | 17.43 | Cellular response to environmental stimulus Mammary gland | PTGS2, MMP2, MMP9, MMP3, CASP3, MMP1 |
| 20. | 8.12E-05 | 3 | 20 | 152.49 | alveolus development | ESR1, HIF1A, VEGFA |

Table S9. Top 20 KEGG pathway of CLAE phytocompounds for myocardial infarction related target genes.

| No. | Enrichment FDR | No. of genes | Pathway genes | Fold enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|--|--|
| 1. | 6.57E-06 | 6 | 93 | 27.50 | IL-17 signaling pathway | PTGS2, MMP9, MMP3, CASP3, MMP1, TNF |
| 2. | 1.48E-05 | 7 | 202 | 14.77 | Proteoglycans in cancer | MMP2, ESR1, HIF1A, MMP9, VEGFA, CASP3, TNF |
| 3. | 4.91E-05 | 9 | 530 | 7.24 | Pathways in cancer | PTGS2, MMP2, ESR1, HIF1A, MMP9, VEGFA, CASP3, F2, MMP1 |
| 4. | 7.26E-05 | 4 | 41 | 41.58 | Bladder cancer | MMP2, MMP9, VEGFA, MMP1 |
| 5. | 7.37E-05 | 5 | 100 | 21.31 | AGE-RAGE signaling pathway in diabetic complications | MMP2, SERPINE1, VEGFA, CASP3, TNF |
| 6. | 1.08E-04 | 5 | 112 | 19.03 | TNF signaling pathway | PTGS2, MMP9, MMP3, CASP3, TNF |
| 7. | 1.06E-03 | 4 | 92 | 18.53 | Rheumatoid arthritis | VEGFA, MMP3, MMP1, TNF |
| 8. | 1.85E-03 | 5 | 214 | 9.96 | Lipid and atherosclerosis | MMP9, MMP3, CASP3, MMP1, TNF |
| 9. | 2.41E-03 | 5 | 232 | 9.19 | Coronavirus disease | MMP3, ACE, F2, MMP1, TNF |
| 10. | 2.77E-03 | 4 | 129 | 13.22 | Relaxin signaling pathway | MMP2, MMP9, VEGFA, MMP1 |
| 11. | 3.26E-03 | 4 | 138 | 12.35 | Fluid shear stress and atherosclerosis | MMP2, MMP9, VEGFA, TNF |
| 12. | 5.39E-03 | 4 | 161 | 10.59 | MicroRNAs in cancer | PTGS2, MMP9, VEGFA, CASP3 |
| 13. | 9.33E-03 | 3 | 84 | 15.22 | Complement and coagulation cascades | SERPINE1, PLG, F2 |
| 14. | 9.33E-03 | 4 | 194 | 8.79 | Kaposi sarcoma-associated herpesvirus infection | PTGS2, HIF1A, VEGFA, CASP3 |
| 15. | 1.23E-02 | 3 | 95 | 13.46 | Endocrine resistance | MMP2, ESR1, MMP9 |
| 16. | 1.31E-02 | 3 | 101 | 12.66 | Chagas disease | SERPINE1, ACE, TNF |
| 17. | 1.31E-02 | 4 | 224 | 7.61 | Human cytomegalovirus infection | PTGS2, VEGFA, CASP3, TNF |
| 18. | 1.53E-02 | 3 | 109 | 11.73 | HIF-1 signaling pathway | HIF1A, SERPINE1, VEGFA |
| 19. | 1.56E-02 | 3 | 112 | 11.42 | Serotonergic synapse | PTGS2, CASP3, CYP2C19 |
| 20. | 2.69E-02 | 3 | 138 | 9.27 | Estrogen signaling pathway | MMP2, ESR1, MMP9 |

Table S10. Top 20 GO biological process of CLAE phytocompounds for anxiety, depression and impaired memory related target genes.

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|--|---|
| 1. | 1.23E-13 | 10 | 90 | 74.00 | Monoamine transport | MAOB, NOS1, HTR2A, SLC6A2, CNR1, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 2. | 1.89E-12 | 16 | 776 | 13.73 | Trans-synaptic signaling | ACHE, NOS1, HTR2A, SLC6A2, OPRM1, BCHE, CNR1, HCRTR1, APP, AKT1, SNCA, DRD3, DRD1, DRD4, SLC6A3, PRKACA |
| 3. | 2.71E-12 | 16 | 815 | 13.08 | Synaptic signaling | ACHE, NOS1, HTR2A, SLC6A2, OPRM1, BCHE, CNR1, HCRTR1, APP, AKT1, SNCA, DRD3, DRD1, DRD4, SLC6A3, PRKACA |
| 4. | 5.10E-12 | 8 | 54 | 98.67 | Dopamine transport | HTR2A, SLC6A2, CNR1, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 5. | 6.42E-12 | 11 | 235 | 31.18 | Regulation of neurotransmitter levels | MAOB, ACHE, NOS1, HTR2A, SLC6A2, CNR1, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 6. | 6.42E-12 | 6 | 14 | 285.44 | Dopamine uptake involved in synaptic transmission | SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 7. | 6.42E-12 | 6 | 14 | 285.44 | Catecholamine uptake involved in synaptic transmission | SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 8. | 9.70E-12 | 13 | 470 | 18.42 | Cellular calcium ion homeostasis | NOS1, HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |
| 9. | 9.70E-12 | 15 | 767 | 13.03 | Chemical synaptic transmission | ACHE, HTR2A, SLC6A2, OPRM1, BCHE, CNR1, HCRTR1, APP, AKT1, SNCA, DRD3, DRD1, DRD4, SLC6A3, PRKACA |
| 10. | 9.70E-12 | 15 | 767 | 13.03 | Anterograde trans-synaptic signaling | ACHE, HTR2A, SLC6A2, OPRM1, BCHE, CNR1, HCRTR1, APP, AKT1, SNCA, DRD3, DRD1, DRD4, SLC6A3, PRKACA |
| 11. | 1.22E-11 | 13 | 482 | 17.96 | Calcium ion homeostasis | NOS1, HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |
| 12. | 1.50E-11 | 7 | 37 | 126.01 | Neurotransmitter reuptake | NOS1, SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 13. | 2.23E-11 | 13 | 512 | 16.91 | Cellular divalent inorganic cation homeostasis | NOS1, HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|---------------------------------------|---|
| 14. | 3.07E-11 | 8 | 78 | 68.31 | Catecholamine transport | HTR2A, SLC6A2, CNR1, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 15. | 3.07E-11 | 13 | 531 | 16.31 | Divalent inorganic cation homeostasis | NOS1, HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |
| 16. | 3.60E-11 | 6 | 20 | 199.81 | Dopamine uptake | SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 17. | 4.75E-11 | 6 | 21 | 190.30 | Catecholamine uptake | SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 18. | 9.56E-11 | 7 | 50 | 93.24 | Neurotransmitter uptake | NOS1, SLC6A2, SNCA, DRD3, DRD1, DRD4, SLC6A3 |
| 19. | 1.53E-10 | 13 | 616 | 14.06 | Cellular metal ion homeostasis | NOS1, HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |
| 20. | 1.53E-10 | 15 | 979 | 10.20 | Cellular homeostasis | NOS2, NOS1, HTR2A, SLC6A2, CCKBR, OPRM1, TACR1, CNR1, HCRTR1, APP, SNCA, DRD3, DRD1, DRD4, PRKACA |

Table S11. Top 20 KEGG pathway of CLAE phytocompounds for anxiety, depression and impaired memory related target genes.

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|---|---|
| 1. | 4.64E-05 | 7 | 132 | 15.34 | Dopaminergic synapse | MAOB, AKT1, DRD3, DRD1, DRD4, SLC6A3, PRKACA |
| 2. | 9.86E-05 | 8 | 240 | 9.64 | Calcium signaling pathway | NOS2, NOS1, HTR2A, CCKBR, PDGFRB, TACR1, DRD1, PRKACA |
| 3. | 1.05E-04 | 9 | 350 | 7.44 | Neuroactive ligand-receptor interaction | HTR2A, CCKBR, OPRM1, TACR1, CNR1, HCRT1, DRD3, DRD1, DRD4 |
| 4. | 1.09E-03 | 4 | 49 | 23.61 | Cocaine addiction | MAOB, DRD1, SLC6A3, PRKACA |
| 5. | 3.39E-03 | 4 | 69 | 16.77 | Amphetamine addiction | MAOB, DRD1, SLC6A3, PRKACA |
| 6. | 6.25E-03 | 4 | 88 | 13.15 | Gap junction | HTR2A, PDGFRB, DRD1, PRKACA |
| 7. | 6.25E-03 | 7 | 383 | 5.29 | Alzheimer disease | NOS2, NOS1, APP, AKT1, SNCA, MT-ND4, TNF |
| 8. | 6.25E-03 | 6 | 266 | 6.52 | Parkinson disease | MAOB, SNCA, DRD1, MT-ND4, SLC6A3, PRKACA |
| 9. | 1.22E-02 | 4 | 112 | 10.33 | Serotonergic synapse | MAOB, HTR2A, APP, PRKACA |
| 10. | 1.38E-02 | 3 | 51 | 17.01 | Arginine and proline metabolism | NOS2, MAOB, NOS1 |
| 11. | 1.56E-02 | 4 | 129 | 8.97 | Relaxin signaling pathway | NOS2, NOS1, AKT1, PRKACA |
| 12. | 1.56E-02 | 7 | 475 | 4.26 | Pathways of neurodegeneration | NOS2, NOS1, APP, SNCA, MT-ND4, TNF, SLC6A3 |
| 13. | 1.85E-02 | 4 | 138 | 8.38 | Apelin signaling pathway | NOS2, NOS1, AKT1, PRKACA |
| 14. | 3.65E-02 | 2 | 22 | 26.29 | Arginine biosynthesis | NOS2, NOS1 |
| 15. | 4.45E-02 | 3 | 92 | 9.43 | Salivary secretion | NOS1, AMY1A, PRKACA |
| 16. | 4.45E-02 | 3 | 91 | 9.53 | Morphine addiction | OPRM1, DRD1, PRKACA |
| 17. | 4.45E-02 | 4 | 187 | 6.19 | Alcoholism | MAOB, DRD1, SLC6A3, PRKACA |
| 18. | 4.82E-02 | 3 | 101 | 8.59 | Chagas disease | NOS2, AKT1, TNF |
| 19. | 4.82E-02 | 3 | 102 | 8.51 | Amoebiasis | NOS2, TNF, PRKACA |

| No. | Enrichment FDR | No. of genes | Pathway Genes | Fold Enrichment | Pathway | Genes |
|-----|----------------|--------------|---------------|-----------------|-------------------------|-------------------------|
| 20. | 4.82E-02 | 4 | 202 | 5.73 | Proteoglycans in cancer | PLAU, AKT1, TNF, PRKACA |

Table S12. Network analysis of myocardial infarction related target genes interaction with CLAE compounds.

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|----------------|------------------------|----------------------|--------|-------------------------|----------|
| 1. | FABP3 | 0 | 0.259259259 | 1 | 0 | Gene |
| 2. | ACE | 0 | 0.259259259 | 1 | 0 | Gene |
| 3. | CASP3 | 0 | 0.259259259 | 1 | 0 | Gene |
| 4. | ALB | 0 | 0.259259259 | 1 | 0 | Gene |
| 5. | SERPINE1 | 0 | 0.355932203 | 1 | 0 | Gene |
| 6. | MMP1 | 0 | 0.355932203 | 1 | 0 | Gene |
| 7. | VEGFA | 0 | 0.355932203 | 1 | 0 | Gene |
| 8. | CYP2C19 | 0 | 0.355932203 | 1 | 0 | Gene |
| 9. | PTGS2 | 0 | 0.355932203 | 1 | 0 | Gene |
| 10. | Vanilllic acid | 0.352381 | 0.344262295 | 5 | 0.2 | Compound |
| 11. | ESR1 | 0.380952 | 0.428571429 | 2 | 0.5 | Gene |
| 12. | CA3 | 0.057143 | 0.428571429 | 2 | 0.642857 | Gene |
| 13. | MMP3 | 0 | 0.287671233 | 1 | 0 | Gene |
| 14. | MPO | 0 | 0.287671233 | 1 | 0 | Gene |
| 15. | F2 | 0.057143 | 0.428571429 | 2 | 0.642857 | Gene |
| 16. | PLG | 0 | 0.287671233 | 1 | 0 | Gene |
| 17. | HIF1A | 0.057143 | 0.428571429 | 2 | 0.642857 | Gene |
| 18. | MMP2 | 0.057143 | 0.428571429 | 2 | 0.642857 | Gene |
| 19. | Isosilybin A | 0.738095 | 0.538461538 | 11 | 0.272727 | Compound |
| 20. | MMP9 | 0.057143 | 0.428571429 | 2 | 0.642857 | Gene |
| 21. | Isoorientin | 0.37619 | 0.396226415 | 9 | 0.555556 | Compound |
| 22. | TNF | 0 | 0.287671233 | 1 | 0 | Gene |

Table S13. Network analysis of myocardial infarction related target genes interaction with CLAE compounds and GO biological process (BP).

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|---|------------------------|----------------------|--------|-------------------------|----------|
| 1. | Vanillic acid | 0.077978 | 0.513514 | 9 | 0.368687 | Compound |
| 2. | Isosilybin A | 0.048745 | 0.5 | 8 | 0.426136 | Compound |
| 3. | Isooientin | 0.054599 | 0.5 | 8 | 0.443182 | Compound |
| 4. | Mammary gland alveolus development | 0.003216 | 0.351852 | 3 | 0.484848 | Pathway |
| 5. | Cellular response to environmental stimulus | 0.005936 | 0.44186 | 6 | 0.754386 | Pathway |
| 6. | Cellular response to abiotic stimulus | 0.005936 | 0.44186 | 6 | 0.754386 | Pathway |
| 7. | Regulation of fibrinolysis | 0.003329 | 0.333333 | 3 | 0.5 | Pathway |
| 8. | Response to oxygen-containing compound | 0.094609 | 0.542857 | 11 | 0.409091 | Pathway |
| 9. | Cellular response to light stimulus | 0.003356 | 0.431818 | 5 | 0.810526 | Pathway |
| 10. | ACE | 0.000802 | 0.383838 | 2 | 0.692308 | Gene |
| 11. | FABP3 | 0.002216 | 0.408602 | 3 | 0.622222 | Gene |
| 12. | ESR1 | 0.017878 | 0.426966 | 5 | 0.493333 | Gene |
| 13. | Regulation of cell population proliferation | 0.122507 | 0.542857 | 11 | 0.359504 | Pathway |
| 14. | Collagen catabolic process | 0.001631 | 0.422222 | 4 | 0.855263 | Pathway |
| 15. | Response to radiation | 0.012079 | 0.463415 | 7 | 0.678571 | Pathway |
| 16. | VEGFA | 0.010355 | 0.383838 | 4 | 0.5 | Gene |
| 17. | Embryo implantation | 0.010501 | 0.431818 | 4 | 0.6625 | Pathway |
| 18. | Negative regulation of fibrinolysis | 0.003329 | 0.333333 | 3 | 0.5 | Pathway |
| 19. | SERPINE1 | 0.027789 | 0.408602 | 4 | 0.392857 | Gene |
| 20. | Cellular response to chemical stress | 0.017393 | 0.463415 | 7 | 0.614286 | Pathway |
| 21. | Cellular response to UV | 0.003356 | 0.431818 | 5 | 0.810526 | Pathway |
| 22. | PLG | 0.034321 | 0.426966 | 5 | 0.333333 | Gene |
| 23. | Extracellular matrix disassembly | 0.018788 | 0.452381 | 5 | 0.657143 | Pathway |
| 24. | Response to light stimulus | 0.012079 | 0.463415 | 7 | 0.678571 | Pathway |
| 25. | CA3 | 0.008135 | 0.426966 | 5 | 0.52 | Gene |
| 26. | Response to oxidative stress | 0.025699 | 0.475 | 8 | 0.5625 | Pathway |

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|----------------------------|------------------------|----------------------|--------|-------------------------|---------|
| 27. | MPO | 0.003436 | 0.391753 | 4 | 0.625 | Gene |
| 28. | CASP3 | 0.03214 | 0.481013 | 10 | 0.453333 | Gene |
| 29. | Response to UV | 0.005936 | 0.44186 | 6 | 0.754386 | Pathway |
| 30. | PTGS2 | 0.05708 | 0.520548 | 13 | 0.4 | Gene |
| 31. | Response to UV-A | 0.001631 | 0.422222 | 4 | 0.855263 | Pathway |
| 32. | F2 | 0.047877 | 0.436782 | 6 | 0.366667 | Gene |
| 33. | HIF1A | 0.057391 | 0.481013 | 10 | 0.44 | Gene |
| 34. | Collagen metabolic process | 0.023342 | 0.475 | 6 | 0.598485 | Pathway |
| 35. | MMP1 | 0.046216 | 0.493506 | 13 | 0.360947 | Gene |
| 36. | MMP3 | 0.076103 | 0.535211 | 16 | 0.399038 | Gene |
| 37. | MMP9 | 0.16253 | 0.644068 | 20 | 0.37 | Gene |
| 38. | Cellular response to UV-A | 0.001631 | 0.422222 | 4 | 0.855263 | Pathway |
| 39. | MMP2 | 0.16253 | 0.644068 | 20 | 0.37 | Gene |

Table S14. Network analysis of myocardial infarction related target genes interaction with CLAE compounds and KEGG pathways.

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|--|------------------------|----------------------|--------|-------------------------|-----------|
| 1. | Vanillic acid | 0.078589 | 0.493333 | 7 | 0.331169 | Compounds |
| 2. | Isooientin | 0.086283 | 0.480519 | 7 | 0.326531 | Compounds |
| 3. | Isosilybin A | 0.089004 | 0.493333 | 8 | 0.333333 | Compounds |
| 4. | Estrogen signaling pathway | 0.002494 | 0.373737 | 3 | 0.666667 | Pathway |
| 5. | CYP2C19 | 0.003567 | 0.345794 | 2 | 0.5625 | Gene |
| 6. | Serotonergic synapse | 0.010853 | 0.345794 | 3 | 0.545455 | Pathway |
| 7. | HIF-1 signaling pathway | 0.010598 | 0.381443 | 3 | 0.444444 | Pathway |
| 8. | Human cytomegalovirus infection | 0.01099 | 0.425287 | 4 | 0.5 | Pathway |
| 9. | Chagas disease | 0.011439 | 0.359223 | 3 | 0.410256 | Pathway |
| 10. | Endocrine resistance | 0.002494 | 0.373737 | 3 | 0.666667 | Pathway |
| 11. | Kaposi sarcoma-associated herpesvirus infection | 0.008886 | 0.406593 | 4 | 0.485294 | Pathway |
| 12. | PLG | 0.005037 | 0.33945 | 2 | 0.571429 | Gene |
| 13. | Complement and coagulation cascades | 0.01149 | 0.333333 | 3 | 0.375 | Pathway |
| 14. | MicroRNAs in cancer | 0.008884 | 0.425287 | 4 | 0.539474 | Pathway |
| 15. | Fluid shear stress and atherosclerosis | 0.009854 | 0.435294 | 4 | 0.55 | Pathway |
| 16. | Relaxin signaling pathway | 0.008129 | 0.425287 | 4 | 0.539474 | Pathway |
| 17. | ACE | 0.008095 | 0.366337 | 3 | 0.444444 | Gene |
| 18. | Coronavirus disease | 0.027828 | 0.406593 | 5 | 0.35 | Pathway |
| 19. | Lipid and atherosclerosis | 0.017424 | 0.445783 | 5 | 0.45 | Pathway |
| 20. | Rheumatoid arthritis | 0.012353 | 0.41573 | 4 | 0.458333 | Pathway |
| 21. | TNF signaling pathway | 0.020224 | 0.445783 | 5 | 0.45 | Pathway |
| 22. | SERPINE1 | 0.039859 | 0.397849 | 5 | 0.290909 | Gene |
| 23. | AGE-RAGE signaling pathway in diabetic complications | 0.031677 | 0.468354 | 5 | 0.409091 | Pathway |
| 24. | Bladder cancer | 0.008129 | 0.425287 | 4 | 0.539474 | Pathway |

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|-------------------------|------------------------|----------------------|--------|-------------------------|---------|
| 25. | F2 | 0.047056 | 0.425287 | 5 | 0.385714 | Gene |
| 26. | Pathways in cancer | 0.076829 | 0.506849 | 9 | 0.380952 | Pathway |
| 27. | VEGFA | 0.111641 | 0.480519 | 12 | 0.333333 | Gene |
| 28. | HIF1A | 0.032107 | 0.425287 | 6 | 0.410256 | Gene |
| 29. | ESR1 | 0.023215 | 0.41573 | 6 | 0.430556 | Gene |
| 30. | Proteoglycans in cancer | 0.039391 | 0.480519 | 7 | 0.435374 | Pathway |
| 31. | MMP2 | 0.088208 | 0.493333 | 11 | 0.324675 | Gene |
| 32. | TNF | 0.112643 | 0.480519 | 11 | 0.307692 | Gene |
| 33. | MMP1 | 0.04458 | 0.435294 | 8 | 0.375 | Gene |
| 34. | CASP3 | 0.098944 | 0.480519 | 11 | 0.335664 | Gene |
| 35. | MMP3 | 0.021558 | 0.406593 | 6 | 0.393939 | Gene |
| 36. | MMP9 | 0.152187 | 0.536232 | 14 | 0.316327 | Gene |
| 37. | IL-17 signaling pathway | 0.028769 | 0.45679 | 6 | 0.433333 | Pathway |
| 38. | PTGS2 | 0.046139 | 0.425287 | 8 | 0.397727 | Gene |

Table S15. Network analysis of anxiety, depression and impaired memory related target genes interaction with CLAE constituents.

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|------------------------------------|------------------------|----------------------|--------|-------------------------|-----------|
| 1. | AMY1A | 0 | 0.277027027 | 1 | 0 | Gene |
| 2. | OPRM1 | 0 | 0.277027027 | 1 | 0 | Gene |
| 3. | MT-ND4 | 0 | 0.259493671 | 1 | 0 | Gene |
| 4. | PRKACA | 0.004378121 | 0.284722222 | 2 | 0.611111111 | Gene |
| 5. | APP | 0.028845002 | 0.3203125 | 4 | 0.4375 | Gene |
| 6. | DRD3 | 0.003698078 | 0.315384615 | 2 | 0.65 | Gene |
| 7. | DRD4 | 0.018468104 | 0.325396825 | 4 | 0.410714286 | Gene |
| 8. | DNMT1 | 0.048780488 | 0.262820513 | 2 | 0.5 | Gene |
| 9. | NOS2 | 0.062510063 | 0.347457627 | 3 | 0.4 | Gene |
| 10. | ALB | 0 | 0.262820513 | 1 | 0 | Gene |
| 11. | DRD1 | 0.029694403 | 0.336065574 | 3 | 0.487179487 | Gene |
| 12. | CCKBR | 0 | 0.262820513 | 1 | 0 | Gene |
| 13. | SLC6A3 | 0.039730535 | 0.347457627 | 3 | 0.444444444 | Gene |
| 14. | BCHE | 0.012298072 | 0.336065574 | 3 | 0.538461538 | Gene |
| 15. | CNR1 | 0 | 0.284722222 | 1 | 0 | Gene |
| 16. | AKT1 | 0.029763503 | 0.336065574 | 5 | 0.373333333 | Gene |
| 17. | PDGFRB | 0.00455241 | 0.305970149 | 3 | 0.575757576 | Gene |
| 18. | TNF | 0.008852841 | 0.325396825 | 2 | 0.583333333 | Gene |
| 19. | SNCA | 0.007601722 | 0.330645161 | 2 | 0.615384615 | Gene |
| 20. | PLAU | 0 | 0.301470588 | 1 | 0 | Gene |
| 21. | ACHE | 0.118744555 | 0.41 | 7 | 0.307142857 | Gene |
| 22. | MAOB | 0.092031434 | 0.401960784 | 5 | 0.32 | Gene |
| 23. | HTR2C | 0 | 0.301470588 | 1 | 0 | Gene |
| 24. | HTR2A | 0 | 0.301470588 | 1 | 0 | Gene |
| 25. | Scopoletin | 0.019701531 | 0.347457627 | 5 | 0.575 | Compound |
| 26. | Scaposin | 0.146525192 | 0.37962963 | 7 | 0.301587302 | Compound |
| 27. | Quercetin | 0.021167229 | 0.347457627 | 5 | 0.575 | Compound |
| 28. | Isosilybin A | 0.16325299 | 0.347457627 | 6 | 0.333333333 | Compound |
| 29. | Isoorientin | 0.073714884 | 0.359649123 | 7 | 0.446428571 | Compound |
| 30. | Gancaonin E | 0.110287341 | 0.386792453 | 8 | 0.375 | Compound |
| 31. | Ellagic Acid | 0.149186773 | 0.394230769 | 9 | 0.345679012 | Compound |
| 32. | CA4 | 0.201238297 | 0.455555556 | 8 | 0.260869565 | Gene |
| 33. | Vasicine | 0.111117197 | 0.37962963 | 7 | 0.26984127 | Compound |
| 34. | NOS1 | 0.065515371 | 0.310606061 | 3 | 0.444444444 | Gene |
| 35. | TACR1 | 0 | 0.227777778 | 1 | 0 | Gene |
| 36. | HCRTTR1 | 0 | 0.227777778 | 1 | 0 | Gene |
| 37. | NR3C2 | 0 | 0.227777778 | 1 | 0 | Gene |
| 38. | Enterolactone | 0.148789729 | 0.353448276 | 7 | 0.238095238 | Compounds |
| 39. | Biochanin A | 0.28927684 | 0.427083333 | 9 | 0.233333333 | Compounds |
| 40. | 14,15-Dehydro- 16-epi-vincamine | 0.146248588 | 0.292857143 | 5 | 0.266666667 | Compounds |

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|--------|------------------------|----------------------|--------|-------------------------|------|
| 41. | SLC6A2 | 0.152565294 | 0.359649123 | 3 | 0.352941176 | Gene |

Table S16. Network analysis of anxiety, depression and impaired memory related target genes interaction with CLAE compounds and GO biological process (BP).

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|--|------------------------|----------------------|--------|-------------------------|---------|
| 1. | MAOB | 0.018413 | 0.393701 | 7 | 0.387755102 | Gene |
| 2. | Monoamine transport | 0.018139 | 0.5 | 10 | 0.56 | Pathway |
| 3. | NOS1 | 0.036584 | 0.49505 | 15 | 0.522807018 | Gene |
| 4. | HTR2A | 0.025688 | 0.49505 | 15 | 0.592982456 | Gene |
| 5. | SLC6A2 | 0.056211 | 0.526316 | 18 | 0.435672515 | Gene |
| 6. | CNR1 | 0.025396 | 0.49505 | 15 | 0.6 | Gene |
| 7. | SNCA | 0.06932 | 0.574713 | 22 | 0.495215311 | Gene |
| 8. | DRD3 | 0.063845 | 0.574713 | 22 | 0.497607656 | Gene |
| 9. | DRD1 | 0.075672 | 0.588235 | 23 | 0.487414188 | Gene |
| 10. | DRD4 | 0.108737 | 0.60241 | 24 | 0.467105263 | Gene |
| 11. | SLC6A3 | 0.040689 | 0.505051 | 17 | 0.45751634 | Gene |
| 12. | ACHE | 0.04241 | 0.45045 | 12 | 0.480392157 | Gene |
| 13. | Trans-synaptic signaling | 0.045514 | 0.568182 | 16 | 0.48125 | Pathway |
| 14. | OPRM1 | 0.012112 | 0.45045 | 11 | 0.686868687 | Gene |
| 15. | BCHE | 0.006052 | 0.413223 | 7 | 0.630252101 | Gene |
| 16. | HCRT1 | 0.014307 | 0.45045 | 11 | 0.681818182 | Gene |
| 17. | APP | 0.043354 | 0.485437 | 14 | 0.545112782 | Gene |
| 18. | AKT1 | 0.025143 | 0.42735 | 9 | 0.503267974 | Gene |
| 19. | PRKACA | 0.026287 | 0.46729 | 12 | 0.605263158 | Gene |
| 20. | Synaptic signaling | 0.045514 | 0.568182 | 16 | 0.48125 | Pathway |
| 21. | Dopamine transport | 0.0046 | 0.462963 | 8 | 0.660714286 | Pathway |
| 22. | Regulation of neurotransmitter levels | 0.024173 | 0.510204 | 11 | 0.542424242 | Pathway |
| 23. | Dopamine uptake involved in synaptic transmission | 0.002126 | 0.446429 | 6 | 0.714285714 | Pathway |
| 24. | Catecholamine uptake involved in synaptic transmission | 0.002126 | 0.446429 | 6 | 0.714285714 | Pathway |

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|--|------------------------|----------------------|--------|-------------------------|----------|
| 25. | Cellular calcium ion homeostasis | 0.023578 | 0.520833 | 13 | 0.49071618 | Pathway |
| 26. | CCKBR | 0.004423 | 0.393701 | 7 | 0.752380952 | Gene |
| 27. | TACR1 | 0.005002 | 0.387597 | 7 | 0.785714286 | Gene |
| 28. | Chemical synaptic transmission | 0.039752 | 0.555556 | 15 | 0.482222222 | Pathway |
| 29. | Anterograde trans-synaptic signaling | 0.039752 | 0.555556 | 15 | 0.482222222 | Pathway |
| 30. | Calcium ion homeostasis | 0.023578 | 0.520833 | 13 | 0.49071618 | Pathway |
| 31. | Neurotransmitter reuptake | 0.003586 | 0.454545 | 7 | 0.683673469 | Pathway |
| 32. | Cellular divalent inorganic cation homeostasis | 0.023578 | 0.520833 | 13 | 0.49071618 | Pathway |
| 33. | Catecholamine transport | 0.0046 | 0.462963 | 8 | 0.660714286 | Pathway |
| 34. | Divalent inorganic cation homeostasis | 0.023578 | 0.520833 | 13 | 0.49071618 | Pathway |
| 35. | Dopamine uptake | 0.002126 | 0.446429 | 6 | 0.714285714 | Pathway |
| 36. | Catecholamine uptake | 0.002126 | 0.446429 | 6 | 0.714285714 | Pathway |
| 37. | Neurotransmitter uptake | 0.003586 | 0.454545 | 7 | 0.683673469 | Pathway |
| 38. | Cellular metal ion homeostasis | 0.023578 | 0.520833 | 13 | 0.49071618 | Pathway |
| 39. | NOS2 | 0.004028 | 0.4 | 4 | 0.402777778 | Gene |
| 40. | Cellular homeostasis | 0.048098 | 0.543478 | 15 | 0.471264368 | Pathway |
| 41. | Biochanin A | 0.00638 | 0.446429 | 5 | 0.475862069 | Compound |
| 42. | Ellagic Acid | 0.01214 | 0.462963 | 7 | 0.403940887 | Compound |
| 43. | Gancaonin E | 0.009884 | 0.454545 | 6 | 0.511494253 | Compound |
| 44. | Isosilybin A | 0.003372 | 0.367647 | 3 | 0.526315789 | Compound |
| 45. | Scopoletin | 0.001767 | 0.333333 | 3 | 0.595238095 | Compound |
| 46. | 14,15-Dehydro-16-epi-vincamine | 0.002287 | 0.396825 | 4 | 0.510869565 | Compound |
| 47. | Enterolactone | 0.009966 | 0.431034 | 6 | 0.5 | Compound |
| 48. | Vasicine | 0.014557 | 0.462963 | 7 | 0.458128079 | Compound |
| 49. | Isoorientin | 0.004311 | 0.438596 | 5 | 0.471428571 | Compound |
| 50. | Quercetin | 0.002749 | 0.431034 | 4 | 0.491071429 | Compound |
| 51. | Scaposin | 0.008066 | 0.438596 | 5 | 0.407142857 | Compound |

Table S17. Network analysis of anxiety, depression, and impaired memory related target genes interaction with CLAE constituents and KEGG signaling pathways.

| No. | Name | Betweenness centrality | Closeness centrality | Degree | Topological coefficient | Type |
|-----|---|------------------------|----------------------|--------|-------------------------|---------|
| 1. | MAOB | 0.089248 | 0.429752 | 12 | 0.223958 | Gene |
| 2. | Dopaminergic synapse | 0.045737 | 0.448276 | 7 | 0.321429 | Pathway |
| 3. | AKT1 | 0.095618 | 0.429752 | 11 | 0.219251 | Gene |
| 4. | DRD3 | 0.00971 | 0.374101 | 4 | 0.366667 | Gene |
| 5. | DRD1 | 0.092533 | 0.436975 | 12 | 0.254902 | Gene |
| 6. | DRD4 | 0.037368 | 0.396947 | 6 | 0.284314 | Gene |
| 7. | SLC6A3 | 0.040099 | 0.403101 | 9 | 0.288889 | Gene |
| 8. | PRKACA | 0.18071 | 0.485981 | 16 | 0.180921 | Gene |
| 9. | NOS2 | 0.101069 | 0.444444 | 12 | 0.208333 | Gene |
| 10. | Calcium signaling pathway | 0.084369 | 0.464286 | 8 | 0.25431 | Pathway |
| 11. | NOS1 | 0.101235 | 0.429752 | 11 | 0.213904 | Gene |
| 12. | HTR2A | 0.029342 | 0.390977 | 5 | 0.294118 | Gene |
| 13. | CCKBR | 0.005295 | 0.358621 | 3 | 0.487179 | Gene |
| 14. | PDGFRB | 0.017379 | 0.374101 | 5 | 0.3 | Gene |
| 15. | TACR1 | 0.009231 | 0.353741 | 3 | 0.472222 | Gene |
| 16. | Neuroactive ligand-receptor interaction | 0.089018 | 0.393939 | 9 | 0.191358 | Pathway |
| 17. | OPRM1 | 0.009559 | 0.358621 | 3 | 0.384615 | Gene |
| 18. | CNR1 | 0.004796 | 0.339869 | 2 | 0.5 | Gene |
| 19. | HCRTR1 | 0.003698 | 0.315152 | 2 | 0.555556 | Gene |
| 20. | Cocaine addiction | 0.007502 | 0.4 | 4 | 0.46875 | Pathway |
| 21. | Amphetamine addiction | 0.007502 | 0.4 | 4 | 0.46875 | Pathway |
| 22. | Gap junction | 0.011559 | 0.38806 | 4 | 0.386364 | Pathway |
| 23. | Alzheimer disease | 0.042049 | 0.412698 | 7 | 0.310559 | Pathway |
| 24. | APP | 0.032558 | 0.379562 | 7 | 0.318681 | Gene |
| 25. | SNCA | 0.016356 | 0.374101 | 5 | 0.371429 | Gene |

| | | | | | | |
|-----|---------------------------------|----------|----------|---|----------|----------|
| 26. | MT-ND4 | 0.005854 | 0.348993 | 4 | 0.5 | Gene |
| 27. | TNF | 0.029695 | 0.374101 | 7 | 0.321429 | Gene |
| 28. | Parkinson disease | 0.02986 | 0.419355 | 6 | 0.346667 | Pathway |
| 29. | Serotonergic synapse | 0.014749 | 0.40625 | 4 | 0.36 | Pathway |
| 30. | Arginine and proline metabolism | 0.010019 | 0.393939 | 3 | 0.444444 | Pathway |
| 31. | Relaxin signaling pathway | 0.013673 | 0.419355 | 4 | 0.425926 | Pathway |
| 32. | Pathways of neurodegeneration | 0.041866 | 0.42623 | 7 | 0.274286 | Pathway |
| 33. | Apelin signaling pathway | 0.013673 | 0.419355 | 4 | 0.425926 | Pathway |
| 34. | Arginine biosynthesis | 0.000638 | 0.325 | 2 | 0.807692 | Pathway |
| 35. | Salivary secretion | 0.019438 | 0.382353 | 3 | 0.376812 | Pathway |
| 36. | AMY1A | 0.00227 | 0.322981 | 2 | 0.5 | Gene |
| 37. | Morphine addiction | 0.010639 | 0.371429 | 3 | 0.466667 | Pathway |
| 38. | Alcoholism | 0.007502 | 0.4 | 4 | 0.46875 | Pathway |
| 39. | Chagas disease | 0.005121 | 0.356164 | 3 | 0.5 | Pathway |
| 40. | Amoebiasis | 0.007253 | 0.382353 | 3 | 0.444444 | Pathway |
| 41. | PLAU | 0.001159 | 0.307692 | 2 | 0.583333 | Gene |
| 42. | Proteoglycans in cancer | 0.026405 | 0.38806 | 4 | 0.347826 | Pathway |
| 43. | Biochanin A | 0.032857 | 0.376812 | 5 | 0.26 | Compound |
| 44. | Ellagic Acid | 0.041912 | 0.419355 | 6 | 0.253333 | Compound |
| 45. | Gancaonin E | 0.017952 | 0.382353 | 5 | 0.34 | Compound |
| 46. | Isosilybin A | 0.013203 | 0.393939 | 4 | 0.364583 | Compound |
| 47. | Scopoletin | 0.00664 | 0.371429 | 3 | 0.396825 | Compound |
| 48. | Isoorientin | 0.021882 | 0.412698 | 5 | 0.336 | Compound |
| 49. | Quercetin | 0.004495 | 0.346667 | 3 | 0.466667 | Compound |
| 50. | Scaposin | 0.05207 | 0.40625 | 6 | 0.253623 | Compound |
| 51. | Vasicine | 0.022334 | 0.393939 | 5 | 0.373913 | Compound |
| 52. | Enterolactone | 0.021728 | 0.393939 | 5 | 0.365217 | Compound |
| 53. | 14,15-Dehydro-16-epi-vincamine | 0.014666 | 0.325 | 3 | 0.393939 | Compound |