

## *Supplementary Materials*

### **Network pharmacology-based investigation of the system-level molecular mechanisms of the hematopoietic activity of Samul-tang, a traditional Korean herbal formula**

Ho-Sung Lee<sup>1</sup>, In-Hee Lee<sup>1</sup>, Sang-In Park<sup>2</sup>, and Dae-Yeon Lee<sup>1,3,\*</sup>

<sup>1</sup>The Fore, 87 Ogeum-ro, Songpa-gu, Seoul 05542, Republic of Korea.

<sup>2</sup>Forestheal Hospital, 173 Ogeum-ro, Songpa-gu, Seoul 05641, Republic of Korea.

<sup>3</sup>Forest Hospital, 129 Ogeum-ro, Songpa-gu, Seoul 05549, Republic of Korea.

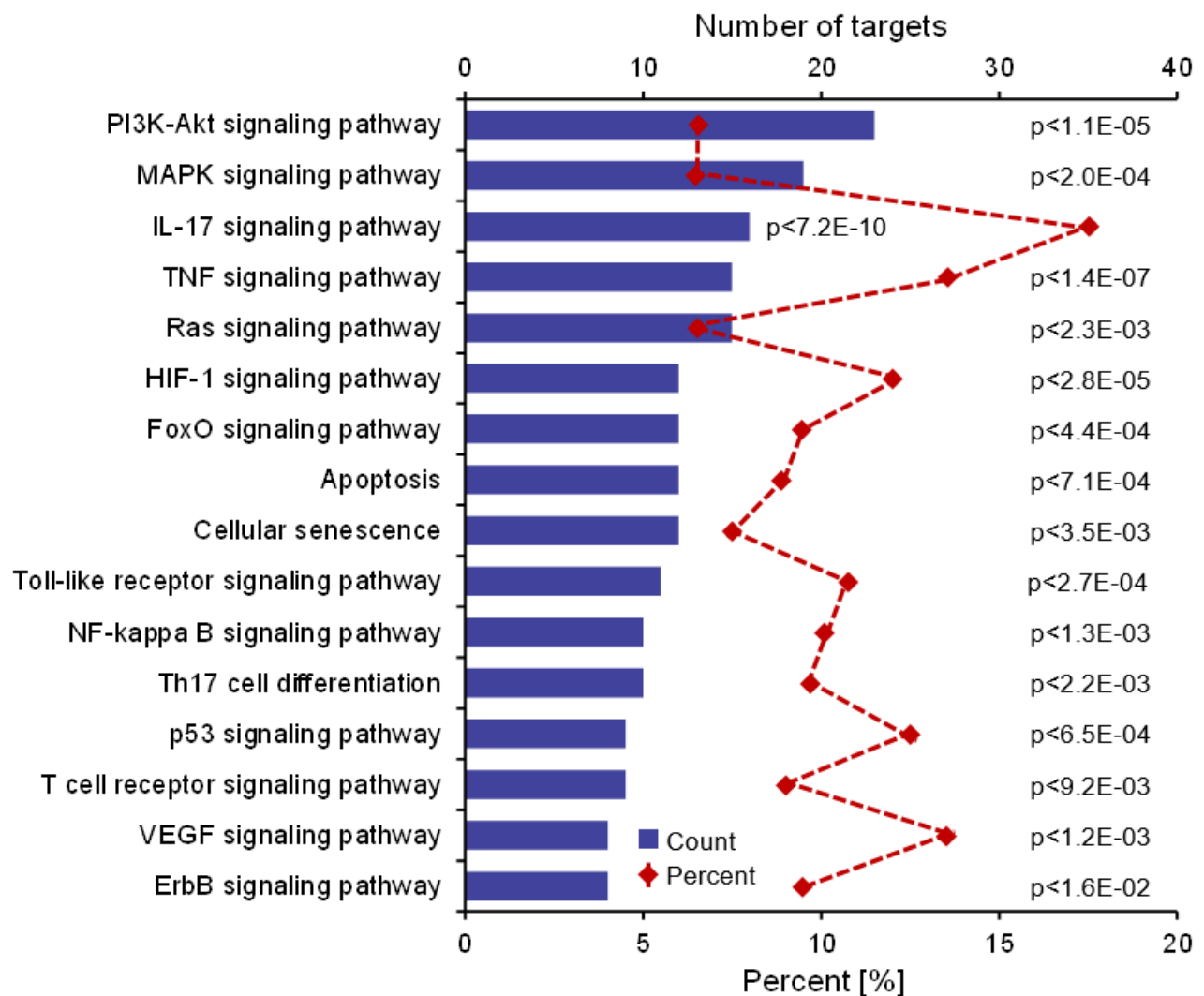
\*Correspondence should be addressed to Dae-Yeon Lee; foresthrnd@gmail.com

## Supplementary Figures

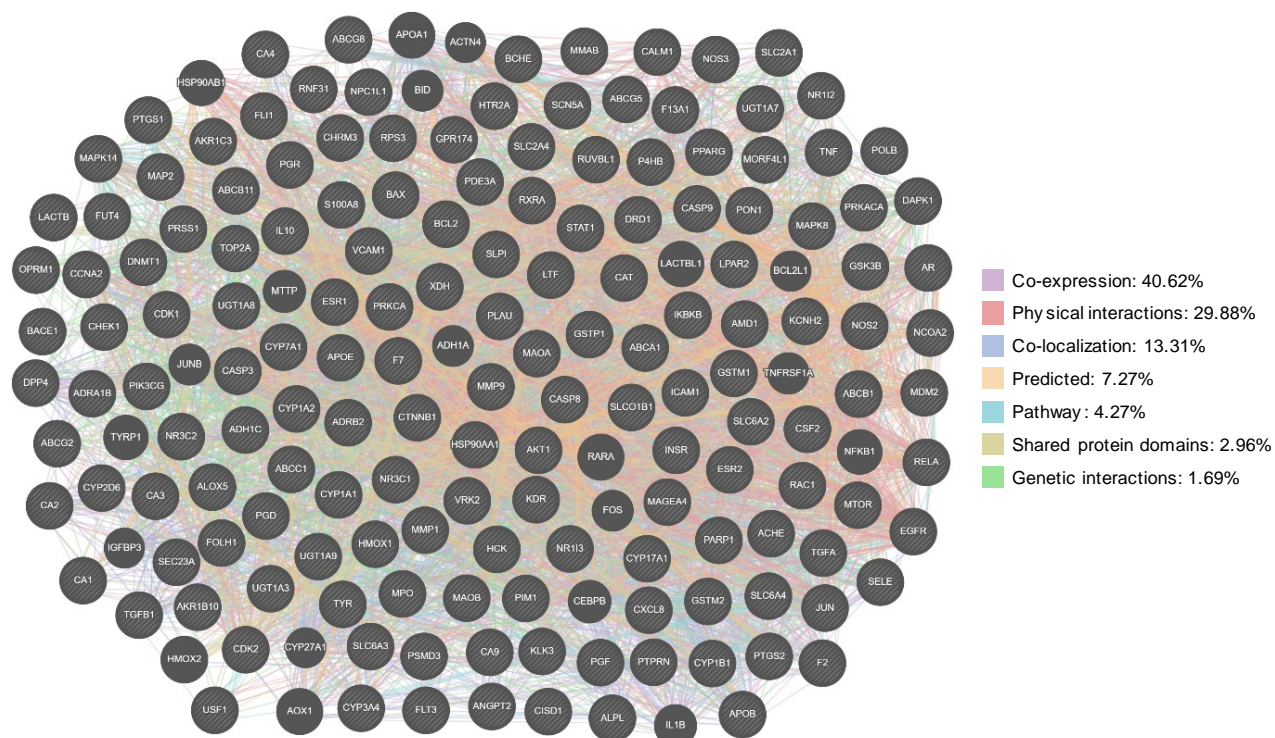
|               | Category           | Term   | Count | Percent [%] | p-value  |
|---------------|--------------------|--|-------|-------------|----------|
| Gene ontology | Biological process | Cell activation involved in immune response      | 19    | 2.69        | 3.41E-02 |
|               |                    | Cytokine production                              | 20    | 2.57        | 3.97E-02 |
|               |                    | Hematopoietic or lymphoid organ development      | 29    | 3.08        | 7.94E-06 |
|               |                    | Hemopoiesis                                      | 27    | 2.99        | 5.22E-05 |
|               |                    | Immune response-regulating signaling pathway     | 20    | 2.97        | 4.68E-03 |
|               |                    | Immune system development                        | 29    | 2.93        | 2.41E-05 |
|               |                    | Leukocyte activation                             | 34    | 2.63        | 1.54E-05 |
|               |                    | Leukocyte activation involved in immune response | 19    | 2.71        | 3.15E-02 |
|               |                    | Leukocyte cell-cell adhesion                     | 13    | 3.83        | 2.20E-02 |
|               |                    | Leukocyte degranulation                          | 16    | 3.01        | 4.39E-02 |
|               |                    | Leukocyte differentiation                        | 19    | 3.64        | 4.06E-04 |
|               |                    | Leukocyte homeostasis                            | 7     | 7.87        | 2.95E-02 |
|               |                    | Lymphocyte homeostasis                           | 6     | 9.52        | 4.13E-02 |
|               |                    | Myeloid cell differentiation                     | 18    | 4.31        | 7.13E-05 |
|               |                    | Myeloid leukocyte activation                     | 21    | 3.23        | 6.59E-04 |
|               |                    | Myeloid leukocyte differentiation                | 14    | 6.76        | 9.66E-06 |
|               |                    | Regulation of apoptotic process                  | 53    | 3.32        | 8.96E-15 |
|               |                    | Regulation of apoptotic signaling pathway        | 22    | 5.37        | 2.80E-08 |
|               |                    | Regulation of blood circulation                  | 15    | 4.98        | 1.61E-04 |
|               |                    | Regulation of cell cycle                         | 30    | 2.47        | 5.39E-04 |
|               |                    | Regulation of cell death                         | 53    | 3.03        | 4.83E-13 |
|               |                    | Regulation of cell differentiation               | 40    | 2.11        | 2.77E-04 |
|               |                    | Regulation of cell migration                     | 28    | 2.99        | 2.80E-05 |
|               |                    | Regulation of cell motility                      | 28    | 2.81        | 1.07E-04 |
|               |                    | Regulation of cell population proliferation      | 57    | 3.32        | 3.26E-16 |
|               |                    | Regulation of immune response                    | 31    | 2.82        | 1.60E-05 |
|               |                    | Regulation of immune system process              | 43    | 2.61        | 1.06E-07 |
|               |                    | Regulation of inflammatory response              | 17    | 4.57        | 7.44E-05 |
|               |                    | Regulation of ion transport                      | 27    | 3.88        | 1.93E-07 |
|               |                    | Regulation of leukocyte migration                | 10    | 5.24        | 1.67E-02 |
|               |                    | Regulation of metal ion transport                | 18    | 4.60        | 2.56E-05 |
|               |                    | Regulation of myeloid cell differentiation       | 12    | 4.72        | 5.93E-03 |
|               |                    | Regulation of myeloid leukocyte differentiation  | 9     | 7.50        | 2.54E-03 |
|               |                    | Regulation of protein kinase activity            | 22    | 2.77        | 4.30E-03 |
|               |                    | Regulation of signal transduction                | 72    | 2.14        | 2.69E-11 |
|               |                    | Regulation of signaling                          | 81    | 2.16        | 8.97E-14 |
|               |                    | Response to chemical                             | 131   | 2.74        | 4.15E-46 |
|               |                    | Response to cytokine                             | 47    | 3.89        | 2.65E-15 |
|               |                    | Response to drug                                 | 65    | 6.18        | 4.03E-35 |
|               |                    | Response to growth factor                        | 25    | 3.37        | 1.83E-05 |
|               |                    | Response to iron ion                             | 5     | 14.71       | 2.42E-02 |
|               |                    | Response to metal ion                            | 27    | 7.18        | 7.67E-14 |
|               |                    | Response to toxic substance                      | 39    | 7.26        | 1.54E-21 |
|               |                    | T cell activation                                | 15    | 3.23        | 3.58E-02 |
|               |                    | T cell homeostasis                               | 6     | 15.38       | 2.36E-03 |

|               | Category            | Term                                 | Count | Percent [%] | p-value  |
|---------------|---------------------|--------------------------------------|-------|-------------|----------|
| Gene ontology | Cellular components | Blood microparticle                  | 9     | 6.29        | 1.08E-03 |
|               |                     | Cytoplasmic part                     | 126   | 1.30        | 4.64E-11 |
|               |                     | Cytoplasmic vesicle part             | 32    | 2.15        | 2.15E-04 |
|               |                     | Cytosol                              | 68    | 1.34        | 3.10E-03 |
|               |                     | Endoplasmic reticulum membrane       | 27    | 2.54        | 7.75E-05 |
|               |                     | Endoplasmic reticulum part           | 34    | 2.52        | 1.80E-06 |
|               |                     | Extracellular organelle              | 43    | 1.98        | 1.48E-05 |
|               |                     | Extracellular region part            | 64    | 1.71        | 5.90E-07 |
|               |                     | Extracellular vesicle                | 43    | 1.99        | 1.44E-05 |
|               |                     | Intracellular organelle part         | 109   | 1.17        | 1.37E-04 |
|               |                     | Intracellular part                   | 141   | 0.97        | 1.92E-02 |
|               |                     | Intracellular vesicle                | 46    | 1.99        | 3.59E-06 |
|               |                     | Membrane part                        | 88    | 1.24        | 1.10E-03 |
|               |                     | Organelle part                       | 111   | 1.16        | 1.96E-04 |
|               |                     | Plasma membrane part                 | 54    | 1.88        | 9.64E-07 |
|               | Molecular function  | Drug binding                         | 48    | 2.74        | 1.74E-10 |
|               |                     | Enzyme binding                       | 66    | 3.00        | 3.46E-18 |
|               |                     | Heme binding                         | 14    | 10.14       | 1.14E-08 |
|               |                     | Ion binding                          | 108   | 1.73        | 2.66E-15 |
|               |                     | Iron ion binding                     | 10    | 6.45        | 7.05E-04 |
|               |                     | Kinase activity                      | 22    | 2.66        | 2.04E-03 |
|               |                     | Kinase binding                       | 26    | 3.58        | 5.80E-07 |
|               |                     | Metal ion binding                    | 66    | 1.57        | 9.84E-05 |
|               |                     | Nuclear receptor activity            | 9     | 19.15       | 1.58E-07 |
|               |                     | Protein binding                      | 138   | 1.10        | 8.70E-05 |
|               |                     | Protein kinase activity              | 21    | 3.42        | 6.08E-05 |
|               |                     | Protein kinase binding               | 25    | 3.86        | 2.60E-07 |
|               |                     | Signaling receptor binding           | 43    | 2.60        | 2.33E-08 |
|               |                     | Transcription factor binding         | 22    | 3.36        | 3.90E-05 |
|               |                     | Zinc ion binding                     | 24    | 2.91        | 1.38E-04 |
| Pathway       | KEGG                | PI3K-Akt signaling pathway           | 23    | 6.55        | 1.10E-05 |
|               |                     | MAPK signaling pathway               | 19    | 6.46        | 1.92E-04 |
|               |                     | IL-17 signaling pathway              | 16    | 17.58       | 7.14E-10 |
|               |                     | TNF signaling pathway                | 15    | 13.64       | 1.39E-07 |
|               |                     | Ras signaling pathway                | 15    | 6.52        | 2.23E-03 |
|               |                     | HIF-1 signaling pathway              | 12    | 12.00       | 2.79E-05 |
|               |                     | FoxO signaling pathway               | 12    | 9.30        | 4.38E-04 |
|               |                     | Apoptosis                            | 12    | 8.89        | 7.03E-04 |
|               |                     | Cellular senescence                  | 12    | 7.59        | 3.47E-03 |
|               |                     | Toll-like receptor signaling pathway | 11    | 10.78       | 2.61E-04 |
|               |                     | NF-kappa B signaling pathway         | 10    | 10.20       | 1.24E-03 |
|               |                     | Th17 cell differentiation            | 10    | 9.62        | 2.10E-03 |
|               |                     | p53 signaling pathway                | 9     | 12.50       | 6.43E-04 |
|               |                     | T cell receptor signaling pathway    | 9     | 9.00        | 9.22E-03 |
|               |                     | VEGF signaling pathway               | 8     | 13.56       | 1.15E-03 |
|               |                     | ErbB signaling pathway               | 8     | 9.52        | 1.53E-02 |

**Supplementary Figure S1. Functional enrichment analysis of the myelosuppression-related targets of SMT.** A table showing the result of functional enrichment analysis of the myelosuppression-related targets of SMT.



**Supplementary Figure S2. Pathway enrichment analysis of the myelosuppression-related targets of SMT.** A graph depicting the result of KEGG pathway enrichment analysis of the myelosuppression-related targets of SMT.



**Supplementary Figure S3. Functional interaction analysis of the myelosuppression-related targets of SMT.** Black nodes, myelosuppression-related targets; colored edges, different types of functional interaction between the targets.

## Supplementary Tables

**Supplementary Table S1. Molecular properties of chemical compounds in SMT.**

| Herbal medicines | Compounds                        | MW     | OB    | Caco-2 | DL   |
|------------------|----------------------------------|--------|-------|--------|------|
| AGR              | Hemo-sol                         | 136.26 | 39.84 | 1.83   | 0.02 |
| AGR              | Scopoletol                       | 192.18 | 27.77 | 0.71   | 0.08 |
| AGR              | Decanal                          | 156.30 | 29.81 | 1.34   | 0.02 |
| AGR              | beta-Chamigrene                  | 204.39 | 31.99 | 1.82   | 0.08 |
| AGR              | Safrol                           | 162.20 | 45.34 | 1.44   | 0.05 |
| AGR              | ()-alpha-Terpineol               | 154.28 | 46.30 | 1.28   | 0.03 |
| AGR              | o-Thymol                         | 150.24 | 43.28 | 1.58   | 0.03 |
| AGR              | D-Galacturonic acid, homopolymer | 194.16 | 29.75 | -2.00  | 0.04 |
| AGR              | FERULIC ACID (CIS)               | 194.20 | 54.97 | 0.53   | 0.06 |
| AGR              | nicotinic acid                   | 123.12 | 47.65 | 0.34   | 0.02 |
| AGR              | Eucarvone                        | 150.24 | 53.14 | 1.35   | 0.03 |
| AGR              | Farnesene                        | 204.39 | 17.42 | 1.95   | 0.05 |

|     |  |        |       |       |      |
|-----|--|--------|-------|-------|------|
| AGR | (1S,4aR,8aR)-1-isopropyl-7-methyl-4-methylene-2,3,4a,5,6,8a-hexahydro-1H-naphthalene | 204.39 | 19.80 | 1.86  | 0.08 |
| AGR | Dodekan  | 170.38 | 17.74 | 1.79  | 0.02 |
| AGR | bergamotene  | 204.39 | 28.51 | 1.86  | 0.09 |
| AGR | cuminal  | 148.22 | 38.29 | 1.39  | 0.03 |
| AGR | Loxanol V  | 214.44 | 14.19 | 1.27  | 0.05 |
| AGR | Tridecylene  | 182.39 | 17.69 | 1.83  | 0.03 |
| AGR | 80-57-9  | 150.24 | 50.63 | 1.27  | 0.06 |
| AGR | Usaf hc-1  | 202.28 | 16.23 | -0.01 | 0.05 |
| AGR | Azelex   | 188.25 | 16.90 | -0.04 | 0.04 |
| AGR | (+)-Ledol  | 222.41 | 16.96 | 1.43  | 0.12 |
| AGR | Hypnon   | 120.16 | 48.19 | 1.36  | 0.02 |
| AGR | NON  | 172.30 | 26.74 | 0.96  | 0.03 |
| AGR | Marmesin   | 246.28 | 50.28 | 0.52  | 0.18 |
| AGR | ()-Cuparene  | 202.37 | 38.26 | 1.88  | 0.07 |

|     |  |        |       |      |      |
|-----|--|--------|-------|------|------|
| AGR | cis-Thujopsene   | 204.39 | 56.43 | 1.84 | 0.12 |
| AGR | Methylbutenol  | 86.15  | 54.58 | 1.12 | 0.01 |
| AGR | PCR  | 108.15 | 51.99 | 1.56 | 0.01 |
| AGR | (4S)-1-methyl-4-(6-methylhepta-1,5-dien-2-yl)cyclohexene | 204.39 | 20.30 | 1.89 | 0.06 |
| AGR | Guasol   | 124.15 | 51.60 | 1.28 | 0.02 |
| AGR | IPH  | 94.12  | 36.05 | 1.50 | 0.01 |
| AGR | CADINENE   | 204.39 | 17.12 | 1.88 | 0.08 |
| AGR | Acoradiene   | 204.39 | 36.73 | 1.85 | 0.07 |
| AGR | Maruzen M  | 122.18 | 48.44 | 1.57 | 0.02 |
| AGR | o-cresol   | 108.15 | 62.45 | 1.57 | 0.02 |
| AGR | 6,7,3',8'-diligustilide                                  | 380.52 | 9.83  | 0.79 | 0.70 |
| AGR | beta-Terpinene   | 136.26 | 42.29 | 1.85 | 0.02 |
| AGR | Butal  | 72.12  | 68.66 | 1.18 | 0.00 |
| AGR | Ethol  | 242.50 | 13.32 | 1.31 | 0.08 |
| AGR | ANN  | 152.16 | 29.69 | 0.69 | 0.03 |



|     |   |        |       |       |      |
|-----|---|--------|-------|-------|------|
| AGR | h-Met-h   | 149.24 | 70.87 | 0.06  | 0.01 |
| AGR | 3,4-DIMETHYLBENZALDEHYDE                                      | 134.19 | 39.99 | 1.40  | 0.02 |
| AGR | ETHYLBENZALDEHYDE   | 134.19 | 40.95 | 1.40  | 0.02 |
| AGR | TMHYDROP  | 152.21 | 54.42 | 1.21  | 0.03 |
| AGR | bicycloelemene  | 204.39 | 20.89 | 1.88  | 0.08 |
| AGR | WLN: QR CQ DV1  | 152.16 | 36.49 | 0.67  | 0.03 |
| AGR | WLN: QVR BVQ  | 166.14 | 17.74 | -0.05 | 0.04 |
| AGR | (1R,2S,4R)-1-ethyl-1-methyl-2,4-bis(1-methylethyl)cyclohexane | 210.45 | 15.01 | 1.80  | 0.06 |
| AGR | DODECENE  | 168.36 | 17.74 | 1.80  | 0.02 |
| AGR | phosphatdic acid  | 228.11 | 19.32 | -1.22 | 0.05 |
| AGR | L-beta,gamma-Dimyristoyl-alpha-cephalin                       | 635.97 | 20.69 | -0.43 | 0.47 |
| AGR | phosphatidylinositol  | 390.27 | 4.63  | -2.34 | 0.29 |
| AGR | phosphatidylinositol_qt                                       | 228.11 | 12.66 | -1.15 | 0.05 |
| AGR | ESEN  | 148.12 | 47.31 | 0.56  | 0.04 |
| AGR | sedanolide  | 194.30 | 62.46 | 1.24  | 0.07 |

|     |   |        |       |       |      |
|-----|---|--------|-------|-------|------|
| AGR | senkyunolide  | 192.28 | 68.28 | 1.28  | 0.07 |
| AGR | sphingomyelin   | 493.73 | 0.31  | -0.46 | 0.51 |
| AGR | Isotetandrine   | 622.82 | 10.42 | 0.95  | 0.10 |
| AGR | $\alpha$ -acoradiene  | 204.39 | 40.98 | 1.82  | 0.07 |
| AGR | InChI=1/C15H24/c1-10-7-8-15-9-12(10)14(3,4)13(15)6-5-11(15)2/h7,11-13H,5-6,8-9H2,1-4H | 204.39 | 55.56 | 1.79  | 0.10 |
| AGR | $\alpha$ -copaene   | 204.39 | 29.33 | 1.83  | 0.12 |
| AGR | (1R,4R,5S)-4-isopropenyl-1,8-dimethylspiro[4.5]dec-8-ene                              | 204.39 | 40.65 | 1.83  | 0.07 |
| AGR | 2,6-di(phenyl)thiopyran-4-thione  | 280.43 | 69.13 | 1.74  | 0.15 |
| AGR | o-Xylenol   | 122.18 | 53.13 | 1.62  | 0.02 |
| AGR | 2,4,6-trimethyl-Octane  | 156.35 | 29.14 | 1.81  | 0.02 |
| AGR | Mesitaldehyde   | 148.22 | 37.80 | 1.54  | 0.03 |
| AGR | Isoxylaldehyde  | 134.19 | 38.85 | 1.39  | 0.02 |
| AGR | (E)-octadec-3-ene   | 252.54 | 19.50 | 1.86  | 0.09 |
| AGR | 2-valerylbenzoic acid   | 206.26 | 78.26 | 0.61  | 0.06 |

|     |  |        |       |       |      |
|-----|--|--------|-------|-------|------|
| AGR | (Z)-2-Hexenyl hexanoate  | 198.34 | 19.39 | 1.26  | 0.04 |
| AGR | 2-Methylhexadecanoic acid  | 270.51 | 20.23 | 1.07  | 0.11 |
| AGR | cis-Isoeugenol   | 164.22 | 20.73 | 1.43  | 0.04 |
| AGR | 2-methyl-5-decanone  | 310.63 | 20.40 | 1.42  | 0.11 |
| AGR | 2-methyldodecan-5-one  | 198.39 | 13.16 | 1.43  | 0.04 |
| AGR | 3,7-dimethyl-nonane  | 156.35 | 16.97 | 1.78  | 0.02 |
| AGR | 1,1,5-trimethyl-2-formylcyclohexa-2,5-diene-4-one  | 164.22 | 48.94 | 0.82  | 0.04 |
| AGR | 4-Methyl-6-hepten-3-one  | 126.22 | 78.38 | 1.39  | 0.01 |
| AGR | 6-Ethylresorcinol  | 138.18 | 46.45 | 1.13  | 0.03 |
| AGR | 5-Indolol  | 133.16 | 63.14 | 1.38  | 0.03 |
| AGR | Undecanol-6  | 172.35 | 25.77 | 1.19  | 0.02 |
| AGR | 7,10-PENTADECADIYNOIC ACID   | 234.37 | 41.50 | 1.32  | 0.09 |
| AGR | 4-chloro-N-[1-methyl-5-[[1-methyl-5-[[1-methyl-5-(2-morpholinoethylcarbamoyl)pyrrol-3-yl]carbamoyl]pyrrol-3-yl]carbamoyl]pyrrol-3-yl]-5-[2-(2-pyridyl)ethylamino]isothiazole-3-carboxamide | 762.38 | 7.18  | -0.21 | 0.31 |

|     |   |        |       |      |      |
|-----|---|--------|-------|------|------|
| AGR | Amyl ketone   | 170.33 | 18.65 | 1.31 | 0.02 |
| AGR | Isoamylbenzene  | 148.27 | 35.69 | 1.84 | 0.03 |
| AGR | (Z)-2-[[ (Z)-2-methylbut-2-enoyl]oxymethyl]but-2-enoic acid | 198.24 | 77.10 | 0.49 | 0.04 |
| AGR | Tropone   | 106.13 | 47.41 | 1.25 | 0.01 |
| AGR | aromadendrene   | 204.39 | 18.21 | 1.83 | 0.10 |
| AGR | BUA   | 88.12  | 21.62 | 0.69 | 0.00 |
| AGR | (3S)-3-butyl-3H-isobenzofuran-1-one                         | 190.26 | 55.05 | 1.30 | 0.07 |
| AGR | ()-Camphoric acid   | 200.26 | 99.13 | 0.10 | 0.07 |
| AGR | (3E)-3-butyldiene-7-hydroxy-2-benzofuran-1-one              | 204.24 | 42.17 | 1.03 | 0.08 |
| AGR | Coniferyl ferulate  | 356.40 | 4.54  | 0.71 | 0.39 |
| AGR | lecithin  | 678.06 | 0.31  | 0.16 | 0.40 |
| AGR | 2,4-Xylylaldehyde   | 134.19 | 39.33 | 1.42 | 0.03 |
| AGR | m-Ethylphenol   | 122.18 | 51.30 | 1.55 | 0.02 |
| AGR | 1,5,5,6-tetramethyl-1,3-Cyclohexadiene                      | 136.26 | 39.22 | 1.82 | 0.03 |
| AGR | Decursin  | 328.39 | 39.27 | 0.77 | 0.38 |

|        |                                 |        |       |       |      |
|--------|---------------------------------|--------|-------|-------|------|
| AGR    | Lomatin                         | 246.28 | 23.36 | 0.48  | 0.18 |
| AGR/CR | beta-Selinene                   | 204.39 | 24.39 | 1.83  | 0.08 |
| AGR/CR | palmitic acid                   | 256.48 | 19.30 | 1.09  | 0.10 |
| AGR/CR | Nonanal                         | 142.27 | 40.28 | 1.31  | 0.02 |
| AGR/CR | Cymol                           | 134.24 | 27.20 | 1.86  | 0.02 |
| AGR/CR | (-)-alpha-Pinene                | 136.26 | 46.25 | 1.85  | 0.05 |
| AGR/CR | Myrcene                         | 136.26 | 24.96 | 1.84  | 0.02 |
| AGR/CR | p-Ocimene                       | 136.26 | 15.06 | 1.85  | 0.02 |
| AGR/CR | Moslene                         | 136.26 | 33.02 | 1.88  | 0.02 |
| AGR/CR | CHEBI:7                         | 136.26 | 45.20 | 1.84  | 0.04 |
| AGR/CR | vanillin                        | 152.16 | 52.00 | 0.68  | 0.03 |
| AGR/CR | WLN: VH6                        | 114.21 | 19.59 | 1.29  | 0.01 |
| AGR/CR | o-Acetyl-p-cresol               | 150.19 | 24.96 | 1.02  | 0.03 |
| AGR/CR | adenine                         | 135.15 | 62.81 | -0.30 | 0.03 |
| AGR/CR | 3-Butylidene-7-hydroxyphthalide | 204.24 | 62.68 | 1.00  | 0.08 |

|                |                                  |        |       |       |      |
|----------------|----------------------------------|--------|-------|-------|------|
| AGR/CR         | Levistolid A                     | 380.52 | 2.15  | 0.94  | 0.82 |
| AGR/CR         | Allocymene                       | 136.26 | 14.89 | 1.85  | 0.02 |
| AGR/CR         | BdPh                             | 188.24 | 42.44 | 1.32  | 0.07 |
| AGR/CR         | senkyunolide-C                   | 204.24 | 46.80 | 0.87  | 0.08 |
| AGR/CR         | senkyunolide-D                   | 222.26 | 79.13 | 0.12  | 0.10 |
| AGR/CR         | senkyunolide-E                   | 204.24 | 34.40 | 0.55  | 0.08 |
| AGR/CR         | (6R)-6-butylcyclohepta-1,4-diene | 150.29 | 31.69 | 1.85  | 0.02 |
| AGR/CR         | cis-ligustilide                  | 190.26 | 51.30 | 1.30  | 0.07 |
| AGR/PRA        | $\beta$ -Sitosterol              | 414.79 | 36.91 | 1.32  | 0.75 |
| AGR/RRP        | succinic acid                    | 118.10 | 29.62 | -0.44 | 0.01 |
| AGR/RRP        | FER                              | 194.20 | 39.56 | 0.47  | 0.06 |
| AGR/RRP/PRA/CR | Sitogluside                      | 576.95 | 20.63 | -0.14 | 0.62 |
| RRP            | MTL                              | 182.20 | 17.73 | -1.58 | 0.03 |
| RRP            | Arachic acid                     | 312.60 | 16.66 | 1.18  | 0.19 |
| RRP            | lauric acid                      | 200.36 | 23.59 | 1.02  | 0.04 |

|     |                                      |        |       |       |      |
|-----|--------------------------------------|--------|-------|-------|------|
| RRP | Docosanoate                          | 340.66 | 15.69 | 1.21  | 0.26 |
| RRP | Caffeate                             | 180.17 | 54.97 | 0.27  | 0.05 |
| RRP | Stigmasterol                         | 412.77 | 43.83 | 1.44  | 0.76 |
| RRP | Stachyose                            | 666.66 | 3.25  | -5.54 | 0.59 |
| RRP | HMF                                  | 126.12 | 45.07 | 0.05  | 0.02 |
| RRP | raffinose                            | 504.50 | 11.79 | -3.91 | 0.66 |
| RRP | leonuride                            | 348.39 | 2.60  | -1.72 | 0.33 |
| RRP | Daturic acid                         | 270.51 | 18.51 | 1.12  | 0.12 |
| RRP | methyl (2E,4E)-hexadeca-2,4-dienoate | 266.47 | 41.57 | 1.37  | 0.12 |
| RRP | zoomaric acid                        | 254.46 | 35.78 | 1.18  | 0.10 |
| RRP | Sumiki's acid                        | 142.12 | 52.44 | -0.21 | 0.03 |
| RRP | Dihydro-beta-ionone                  | 194.35 | 26.25 | 1.35  | 0.05 |
| RRP | Pca                                  | 129.13 | 96.25 | -0.20 | 0.02 |
| RRP | catalpol                             | 362.37 | 5.07  | -1.72 | 0.44 |
| RRP | catapol_qt                           | 200.21 | 44.69 | -0.63 | 0.10 |

|     |   |        |       |       |      |
|-----|---|--------|-------|-------|------|
| RRP | 8-epi-Loganic acid  | 376.40 | 4.43  | -1.78 | 0.40 |
| RRP | Forsythiaside   | 624.65 | 3.05  | -1.92 | 0.61 |
| RRP | acteoside   | 624.65 | 2.94  | -1.89 | 0.62 |
| RRP | 2-(4-hydroxyphenyl)ethyl hexacosanoate  | 516.94 | 13.12 | 1.31  | 0.53 |
| RRP | aeginetic acid  | 268.39 | 48.31 | 0.13  | 0.13 |
| RRP | Ajugol  | 348.39 | 16.87 | -1.03 | 0.32 |
| RRP | Ajugoside   | 390.43 | 12.15 | -1.03 | 0.45 |
| RRP | Ajugoside_qt  | 212.27 | 81.68 | 0.24  | 0.08 |
| RRP | Cerebrosid  | 266.29 | 13.81 | -2.69 | 0.11 |
| RRP | Cistanoside A   | 800.84 | 3.40  | -2.72 | 0.33 |
| RRP | Cistanoside F   | 488.49 | 4.74  | -2.11 | 0.69 |
| RRP | methyl 9,10-methylene-hexadecanoate   | 282.52 | 22.94 | 1.43  | 0.15 |
| RRP | (2S,3R,4R,5S,6R)-2-[[[(1S,4aS,5R,7aR)-4a,5-dihydroxy-7-methylol-5,7a-dihydro-1H-cyclopenta[c]pyran-1-yl]oxy]-6-methylol-tetrahydropyran-3,4,5-triol | 362.37 | 3.10  | -2.12 | 0.37 |
| RRP | melittoside_qt  | 200.21 | 40.00 | -0.74 | 0.08 |



|     |   |        |       |       |      |
|-----|---|--------|-------|-------|------|
| RRP | Dihydrocatalpol   | 364.39 | 3.58  | -2.24 | 0.44 |
| RRP | geniposide  | 388.41 | 3.78  | -2.02 | 0.44 |
| RRP | geniposide_qt   | 226.25 | 39.71 | -0.92 | 0.10 |
| RRP | glutinoside   | 398.83 | 21.33 | -2.35 | 0.52 |
| RRP | Jiofuran  | 184.21 | 54.91 | -0.38 | 0.06 |
| RRP | jioglutin A   | 250.70 | 90.70 | 0.00  | 0.13 |
| RRP | jioglutin B   | 250.70 | 90.71 | -0.01 | 0.13 |
| RRP | jioglutin C   | 232.26 | 2.55  | -0.54 | 0.13 |
| RRP | jioglutin D   | 246.29 | 39.02 | -0.22 | 0.14 |
| RRP | jioglutin E   | 232.31 | 81.90 | -0.04 | 0.10 |
| RRP | jioglutolide  | 186.23 | 86.95 | -0.15 | 0.06 |
| RRP | Jioglutoside A  | 346.37 | 3.92  | -1.82 | 0.39 |
| RRP | methyl (1S,4aS,7aS)-7-methylene-1-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[[(2R,3R,4R,5S,6R)-3,4,5-trihydroxy-6-methyl-tetrahydropyran-2-yl]oxymethyl]tetrahydropyran-2-yl]oxy-4a,5,6,7a-tetrahydro-1H-cyclopenta[d]pyran-4-carboxylate | 518.57 | 28.27 | -1.55 | 0.84 |

|     |   |        |       |       |      |
|-----|---|--------|-------|-------|------|
| RRP | Jioglutoside B_qt   | 210.25 | 89.22 | 0.29  | 0.08 |
| RRP | Jionoside A   | 800.84 | 3.62  | -2.92 | 0.36 |
| RRP | Jionoside B   | 814.87 | 4.27  | -2.53 | 0.35 |
| RRP | Melittoside   | 524.53 | 19.20 | -2.94 | 0.80 |
| RRP | METHYL PALMITOLEATE   | 268.49 | 34.61 | 1.38  | 0.12 |
| RRP | 6-O-p-coumaroylajugol   | 524.57 | 26.13 | -1.51 | 0.85 |
| RRP | methyl-2,6,10-trimethyltridecanoate   | 269.50 | 24.86 | 0.85  | 0.10 |
| RRP | Purpureaside C  | 786.81 | 3.14  | -2.79 | 0.38 |
| RRP | Rehmaglutin B   | 236.67 | 64.62 | -0.55 | 0.11 |
| RRP | (3aS,4R,6aS)-4-hydroxy-6,6a-dimethylol-3a,4-dihydro-3H-cyclopenta[d]furan-2-one   | 200.21 | 29.92 | -1.10 | 0.08 |
| RRP | (2S,3R,4S,5S,6R)-2-[(1R,2R)-2-hydroxy-2-[(E,3S)-3-hydroxybut-1-enyl]-1,3,3-trimethylcyclohexoxy]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol | 390.53 | 8.43  | -1.22 | 0.33 |
| RRP | (2S,3R,4S,5S,6R)-2-[(1R,2R)-2-hydroxy-2-[(E,3R)-3-hydroxybut-1-enyl]-1,3,3-trimethylcyclohexoxy]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol | 390.53 | 3.24  | -1.21 | 0.33 |

|         |   |        |       |       |      |
|---------|---|--------|-------|-------|------|
| RRP     | Rehmaionoside C   | 388.51 | 12.89 | -1.18 | 0.34 |
| RRP     | rehmannioside B   | 524.53 | 2.05  | -3.18 | 0.88 |
| RRP     | rehmannioside C   | 510.55 | 10.23 | -2.81 | 0.86 |
| RRP     | 6-O-p-hydroxybenzoylajugol  | 468.50 | 4.53  | -1.66 | 0.81 |
| RRP     | (3R)-2,6,6-trimethyl-3-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxycyclohexene-1-carboxylic acid | 346.42 | 13.59 | -1.28 | 0.26 |
| RRP     | Rehmannioside A   | 524.53 | 25.95 | -3.00 | 0.87 |
| RRP     | Rehmaglutin A   | 202.23 | 29.70 | -0.82 | 0.10 |
| RRP     | Rehmaglutin D   | 220.67 | 57.03 | -0.17 | 0.10 |
| RRP     | 6-O-vanilloylajugol   | 484.50 | 23.44 | -1.26 | 0.84 |
| RRP     | echinacoside  | 786.81 | 3.14  | -2.91 | 0.38 |
| RRP     | aucubin   | 346.37 | 4.17  | -1.83 | 0.33 |
| RRP     | Acetylcatalpol  | 402.44 | 5.53  | -1.57 | 0.58 |
| RRP/CR  | EIC   | 280.50 | 41.90 | 1.16  | 0.14 |
| RRP/PRA | PENTADECYLIC ACID   | 242.45 | 20.18 | 1.08  | 0.08 |

|            |                              |        |       |       |      |
|------------|------------------------------|--------|-------|-------|------|
| RRP/PRA/CR | Sitosterol                   | 414.79 | 36.91 | 1.32  | 0.75 |
| RRP/PRA/CR | sucrose                      | 342.34 | 7.17  | -2.89 | 0.23 |
| PRA        | PYG                          | 126.12 | 22.98 | 0.69  | 0.02 |
| PRA        | Mairin                       | 456.78 | 55.38 | 0.73  | 0.78 |
| PRA        | BOX                          | 121.12 | 31.55 | 0.54  | 0.02 |
| PRA        | oleanolic acid               | 456.78 | 29.02 | 0.59  | 0.76 |
| PRA        | Kaempferol                   | 286.25 | 41.88 | 0.26  | 0.24 |
| PRA        | (+)-Catechin                 | 290.29 | 54.83 | -0.03 | 0.24 |
| PRA        | 3,4,5-trihydroxybenzoic acid | 170.13 | 31.69 | -0.09 | 0.04 |
| PRA        | Hederagenol                  | 472.78 | 22.42 | 0.10  | 0.74 |
| PRA        | Astragalin                   | 448.41 | 14.03 | -1.34 | 0.74 |
| PRA        | TRD                          | 184.41 | 17.89 | 1.78  | 0.03 |
| PRA        | (-)-alpha-cedrene            | 204.39 | 55.56 | 1.81  | 0.10 |
| PRA        | DBP                          | 278.38 | 64.54 | 0.80  | 0.13 |
| PRA        | EEE                          | 88.12  | 45.02 | 1.07  | 0.00 |

|     |  |        |       |      |      |
|-----|--|--------|-------|------|------|
| PRA | Heptadekan                                 | 240.53 | 8.64  | 1.84 | 0.07 |
| PRA | LFA  | 282.62 | 8.46  | 1.83 | 0.13 |
| PRA | Henicosane                                 | 296.65 | 8.41  | 1.84 | 0.15 |
| PRA | paeonol                                    | 166.19 | 28.79 | 0.93 | 0.04 |
| PRA | Cedrol                                     | 222.41 | 16.23 | 1.35 | 0.12 |
| PRA | (6R,10R)-6,10,14-trimethylpentadecan-2-one | 268.54 | 23.30 | 1.41 | 0.10 |
| PRA | Pisol                                      | 186.38 | 18.50 | 1.23 | 0.03 |
| PRA | Satol                                      | 268.54 | 27.27 | 1.34 | 0.11 |
| PRA | (1R)-()-Nopinone                           | 138.23 | 57.86 | 1.23 | 0.05 |
| PRA | myristic acid                              | 228.42 | 21.18 | 1.07 | 0.07 |
| PRA | Octacosane                                 | 394.86 | 8.15  | 1.91 | 0.37 |
| PRA | Dodecanal                                  | 184.36 | 21.52 | 1.40 | 0.03 |
| PRA | salicylic acid                             | 138.13 | 32.13 | 0.63 | 0.03 |
| PRA | 2,2-dimethylcyclohexanol                   | 128.24 | 82.54 | 1.22 | 0.02 |
| PRA | Methyl linolelaidate                       | 294.53 | 41.93 | 1.46 | 0.17 |

|     |   |        |       |      |      |
|-----|---|--------|-------|------|------|
| PRA | octadec-9-ene   | 252.54 | 19.50 | 1.87 | 0.09 |
| PRA | 9-methylenefluorene                                       | 178.24 | 26.87 | 1.95 | 0.09 |
| PRA | Dipropyl phthalate  | 250.32 | 66.30 | 0.78 | 0.10 |
| PRA | BU3   | 90.14  | 34.87 | 0.19 | 0.01 |
| PRA | Bicetyl   | 450.98 | 8.03  | 1.96 | 0.46 |
| PRA | Dibutylphenol   | 206.36 | 38.90 | 1.73 | 0.06 |
| PRA | bicyclo[3.1.1]hept-2-ene-2-methanol, 6,6-dimethyl-        | 152.26 | 49.79 | 1.23 | 0.06 |
| PRA | (-)-trans-Myrtanol  | 154.28 | 49.66 | 1.17 | 0.06 |
| PRA | Acetyl oxide  | 102.10 | 45.13 | 0.65 | 0.01 |
| PRA | ZINC02169908  | 268.54 | 23.30 | 1.42 | 0.10 |
| PRA | Pulchrenoside A <sub>qt</sub>                             | 472.78 | 16.91 | 0.12 | 0.77 |
| PRA | 24-Methylenecycloartanol                                  | 440.83 | 10.40 | 1.42 | 0.79 |
| PRA | 3 $\beta$ ,23-dihydroxy-oleana-11,13(18)-dien-28-oic acid | 470.76 | 21.53 | 0.10 | 0.75 |
| PRA | 3 $\beta$ -hydroxy-11-oxo-olean-12-en-28-oic acid         | 470.76 | 13.49 | 0.21 | 0.74 |
| PRA | 2 - methyl - 3 - (2 - propenyl) - phenol                  | 148.22 | 52.06 | 1.64 | 0.03 |

|     |   |         |       |       |      |
|-----|---|---------|-------|-------|------|
| PRA | 3 $\beta$ -hydroxy-oleana-11,13(18)-dien-28-oic acid?                                 | 454.76  | 17.11 | 0.55  | 0.76 |
| PRA | Methylgallate   | 184.16  | 30.91 | 0.26  | 0.05 |
| PRA | Progallin A   | 198.19  | 25.61 | 0.33  | 0.06 |
| PRA | (Z)-(1S,5R)-beta-pinen-10-yl-beta-vicianoside   | 446.55  | 5.74  | -1.56 | 0.67 |
| PRA | (Z)-(1S,5R)-beta-pinen-10-yl-beta-vicianoside_qt                                      | 152.26  | 50.32 | 1.52  | 0.06 |
| PRA | 11alpha,12alpha-epoxy-3beta-23-dihydroxy-30-norolean-20-en-28,12beta-olide            | 470.71  | 64.77 | 0.09  | 0.38 |
| PRA | albiflorin R1   | 480.51  | 21.29 | -1.53 | 0.82 |
| PRA | albiflorin R1_qt  | 318.35  | 26.18 | -0.46 | 0.34 |
| PRA | propyl (2R)-2-hydroxypropanoate   | 132.18  | 25.50 | 0.44  | 0.01 |
| PRA | gallotannin   | 1701.27 | 7.36  | -5.47 | 0.03 |
| PRA | paeonoside  | 610.57  | 3.47  | -2.71 | 0.71 |
| PRA | (3S,3aR,5S,6S,7aR)-5,6-dihydroxy-3,6-dimethyl-3,3a,4,5,7,7a-hexahydrobenzofuran-2-one | 200.26  | 96.64 | -0.16 | 0.07 |
| PRA | Paeoniflorigenone   | 318.35  | 87.59 | -0.09 | 0.37 |
| PRA | Palbinone   | 358.52  | 43.56 | 0.00  | 0.53 |

|     |   |        |        |       |      |
|-----|---|--------|--------|-------|------|
| PRA | Lactiflorin   | 462.49 | 49.12  | -1.13 | 0.80 |
| PRA | 2-Hexyl-1-decanol   | 242.50 | 17.08  | 1.29  | 0.07 |
| PRA | [(3S,3aR,6S,7aR)-6-hydroxy-6-methyl-2,5-dioxo-3a,4,7,7a-tetrahydro-3H-benzofuran-3-yl]methyl benzoate | 318.35 | 17.84  | -0.17 | 0.30 |
| PRA | Paeoniflorin  | 480.51 | 53.87  | -1.47 | 0.79 |
| PRA | Paeoniflorin_qt   | 318.35 | 68.18  | -0.34 | 0.40 |
| PRA | 1,2,3,6-tetra-O-galloylglucose  | 788.62 | 3.01   | -2.97 | 0.34 |
| PRA | albiflorin  | 480.51 | 12.09  | -1.54 | 0.77 |
| PRA | albiflorin_qt   | 318.35 | 66.64  | -0.49 | 0.33 |
| PRA | alexandrin  | 576.95 | 20.63  | -0.29 | 0.62 |
| PRA | benzoyl paeoniflorin  | 584.62 | 31.27  | -0.69 | 0.75 |
| PRA | 4-Chlorobutyric acid  | 122.56 | 85.82  | 0.74  | 0.01 |
| PRA | galloylpaeoniflorin   | 632.62 | 3.03   | -1.77 | 0.42 |
| PRA | oxypaeoniflorin   | 496.51 | 21.88  | -1.88 | 0.78 |
| PRA | (3R,3aR,6S,7aR)-6-hydroxy-3,6-dimethyl-3a,4,7,7a-tetrahydro-3H-benzofuran-2,5-dione                   | 198.24 | 104.94 | -0.08 | 0.08 |



|        |  |        |       |       |      |
|--------|--|--------|-------|-------|------|
| PRA    | (3aR,6S,7aR)-6-hydroxy-6-methyl-3-methylene-3a,4,7,7a-tetrahydrobenzofuran-2,5-dione | 196.22 | 97.79 | -0.01 | 0.08 |
| PRA    | cis-5-Octen-1-ol   | 128.24 | 31.84 | 1.16  | 0.01 |
| PRA    | 24253-30-3   | 98.16  | 74.20 | 1.33  | 0.01 |
| PRA    | acetic acid  | 60.06  | 47.87 | 0.42  | 0.00 |
| PRA    | Oxypaeoniflorin  | 496.51 | 8.38  | -1.62 | 0.78 |
| PRA    | 10-Methylnonadecane  | 282.62 | 10.28 | 1.84  | 0.12 |
| PRA    | Ethylisobutyrate   | 116.18 | 83.67 | 1.24  | 0.01 |
| PRA    | Pentagalloylglucose  | 940.72 | 3.01  | -3.08 | 0.21 |
| PRA/CR | stearic acid   | 284.54 | 17.83 | 1.15  | 0.14 |
| CR     | D-Camphene   | 136.26 | 34.98 | 1.81  | 0.04 |
| CR     | alpha-humulene   | 204.39 | 22.98 | 1.88  | 0.06 |
| CR     | alpha-Curcumene  | 202.37 | 4.68  | 1.93  | 0.06 |
| CR     | 2-[(1R,3S,4S)-3-isopropenyl-4-methyl-4-vinylcyclohexyl]propan-2-ol                   | 222.41 | 19.03 | 1.37  | 0.07 |
| CR     | PHB  | 138.13 | 30.15 | 0.39  | 0.03 |

|    |  |        |       |      |      |
|----|--|--------|-------|------|------|
| CR | vanillic acid  | 168.16 | 35.47 | 0.43 | 0.04 |
| CR | (L)-alpha-Terpineol  | 154.28 | 48.80 | 1.39 | 0.03 |
| CR | 1,8-cineole  | 154.28 | 39.73 | 1.57 | 0.05 |
| CR | (-)-nopinene   | 136.26 | 44.84 | 1.80 | 0.05 |
| CR | 2-[(2S,5S,6S)-6,10-dimethylspiro[4.5]dec-9-en-2-yl]propan-2-ol | 222.41 | 37.62 | 1.44 | 0.09 |
| CR | Furol  | 96.09  | 34.35 | 1.08 | 0.01 |
| CR | L-Bornyl acetate   | 196.32 | 65.52 | 1.29 | 0.08 |
| CR | (R)-linalool   | 154.28 | 39.80 | 1.33 | 0.02 |
| CR | (S)-(+)-alpha-Phellandrene                                     | 136.26 | 27.90 | 1.87 | 0.02 |
| CR | -cis-.beta.-Elemene diastereomer                               | 204.39 | 28.62 | 1.85 | 0.06 |
| CR | Methyleugenol  | 178.25 | 73.36 | 1.47 | 0.04 |
| CR | ()-Aromadendrene   | 204.39 | 55.74 | 1.81 | 0.10 |
| CR | caffeic acid   | 180.17 | 25.76 | 0.21 | 0.05 |
| CR | L-Limonen  | 136.26 | 38.09 | 1.83 | 0.02 |
| CR | Tereben  | 136.26 | 29.62 | 1.86 | 0.02 |

|    |   |        |       |       |      |
|----|---|--------|-------|-------|------|
| CR | (1S,5S)-1-isopropyl-4-methylenebicyclo[3.1.0]hexane | 136.26 | 46.21 | 1.83  | 0.04 |
| CR | Undekansaeure                                       | 186.33 | 30.14 | 0.98  | 0.03 |
| CR | FA  | 441.45 | 68.96 | -1.50 | 0.71 |
| CR | ()-Terpinen-4-ol                                    | 154.28 | 81.41 | 1.36  | 0.03 |
| CR | hexanal   | 100.18 | 55.71 | 1.25  | 0.01 |
| CR | PENTYLFURAN   | 138.23 | 54.59 | 1.72  | 0.02 |
| CR | oleic acid  | 282.52 | 33.13 | 1.17  | 0.14 |
| CR | (R)-(-)-alpha-Phellandrene                          | 136.26 | 27.51 | 1.86  | 0.02 |
| CR | OYA   | 128.24 | 19.07 | 1.30  | 0.01 |
| CR | o-Cymol   | 134.24 | 51.89 | 1.88  | 0.02 |
| CR | MYS   | 212.47 | 13.98 | 1.81  | 0.05 |
| CR | methyl palmitate                                    | 270.51 | 18.09 | 1.37  | 0.12 |
| CR | tetradecane   | 198.44 | 15.94 | 1.79  | 0.04 |
| CR | beta-elemene  | 204.39 | 25.63 | 1.84  | 0.06 |
| CR | Terpilene   | 136.26 | 33.95 | 1.84  | 0.02 |

|    |   |        |       |      |      |
|----|---|--------|-------|------|------|
| CR | (R)-p-Menth-1-en-4-ol   | 154.28 | 32.16 | 1.33 | 0.03 |
| CR | alpha-Farnesene   | 204.39 | 21.70 | 1.97 | 0.05 |
| CR | .gamma.-Bisabolene  | 204.39 | 20.78 | 1.94 | 0.06 |
| CR | 58870_FLUKA   | 204.39 | 49.01 | 1.82 | 0.10 |
| CR | Ethylpalmitate  | 284.54 | 18.99 | 1.41 | 0.14 |
| CR | 5-isopropyl-2-methylbicyclo[3.1.0]hex-2-ene                             | 136.26 | 47.19 | 1.82 | 0.04 |
| CR | (1R,5R,7S)-4,7-dimethyl-7-(4-methylpent-3-enyl)bicyclo[3.1.1]hept-3-ene | 204.39 | 16.23 | 1.86 | 0.09 |
| CR | (4S)-4-isopropylcyclohexene-1-carbaldehyde                              | 152.26 | 40.36 | 1.36 | 0.03 |
| CR | (S)-2,2,3-Trimethylcyclopent-3-ene-1-acetaldehyde                       | 152.26 | 45.18 | 1.32 | 0.03 |
| CR | WLN: Q1R  | 108.15 | 58.68 | 1.08 | 0.01 |
| CR | 49070_FLUKA   | 222.41 | 85.51 | 1.29 | 0.12 |
| CR | Mandenol  | 308.56 | 42.00 | 1.46 | 0.19 |
| CR | germacrene  | 208.43 | 15.06 | 1.82 | 0.06 |
| CR | METHYL LINOLEATE  | 294.53 | 41.93 | 1.44 | 0.17 |

|    |   |        |       |       |      |
|----|---|--------|-------|-------|------|
| CR | Crysophanol   | 254.25 | 18.64 | 0.62  | 0.21 |
| CR | uracil  | 112.10 | 42.53 | 0.05  | 0.02 |
| CR | EUG   | 150.19 | 38.39 | 1.36  | 0.03 |
| CR | ADO   | 267.28 | 15.98 | -1.56 | 0.18 |
| CR | METHYL PENTADECANOATE   | 256.48 | 18.82 | 1.37  | 0.10 |
| CR | (+)-beta-Phellandrene   | 136.26 | 40.30 | 1.83  | 0.02 |
| CR | thymol  | 150.24 | 41.47 | 1.60  | 0.03 |
| CR | alpha-Cubebene  | 204.39 | 16.73 | 1.83  | 0.11 |
| CR | (+)-ALPHA-FUNEBRENE   | 204.39 | 52.87 | 1.79  | 0.10 |
| CR | gem-Dimethylcyclopentane  | 98.21  | 41.22 | 1.78  | 0.01 |
| CR | Senkyunolide-K  | 208.28 | 61.75 | 0.52  | 0.08 |
| CR | (3Z,6S,7R)-3-butylidene-6-butyryl-7-hydroxy-4,5,6,7-tetrahydroisobenzofuran-1-one | 278.38 | 3.41  | 0.08  | 0.16 |
| CR | Senkyunolide-N  | 226.30 | 37.27 | -0.15 | 0.10 |
| CR | Senkyunolide-P  | 382.54 | 9.38  | 0.92  | 0.81 |

|    |   |        |       |       |      |
|----|---|--------|-------|-------|------|
| CR | Senkyunolide-Q  | 278.38 | 26.84 | 0.42  | 0.16 |
| CR | Senkyunolide-R  | 240.28 | 13.14 | -0.76 | 0.11 |
| CR | 1,1-Diethoxybutane  | 146.26 | 29.28 | 1.30  | 0.01 |
| CR | Valerophenone   | 162.25 | 42.58 | 1.46  | 0.03 |
| CR | (1S,5S)-7,7-dimethyl-2-methylenebicyclo[3.1.1]hept-3-ene          | 134.24 | 37.71 | 1.80  | 0.05 |
| CR | Z-6,8',7,3'-diligustilide   | 380.52 | 11.98 | 0.74  | 0.70 |
| CR | alpha-Selinene  | 218.42 | 31.81 | 1.82  | 0.10 |
| CR | 1,2,3,4,4a,7-Hexahydro-1,6-dimethyl-4-(1-methylethyl)-naphthalene | 162.30 | 19.03 | 1.88  | 0.05 |
| CR | augustic-acid   | 472.78 | 21.08 | 0.18  | 0.74 |
| CR | m-Ethyltoluene  | 120.21 | 50.77 | 1.87  | 0.02 |
| CR | (1R,4S,5R)-4-isopropenyl-1,8-dimethylspiro[4.5]dec-8-ene          | 204.39 | 40.01 | 1.85  | 0.07 |
| CR | $\beta$ -sesquiphellandrene                                       | 204.39 | 23.68 | 1.89  | 0.06 |
| CR | (4aS,7S,8aR)-7-isopropenyl-4a-methyl-1-methylenedecalin           | 204.39 | 23.65 | 1.83  | 0.08 |
| CR | Artemisia triene  | 136.26 | 42.10 | 1.84  | 0.02 |
| CR | betea-CUBEBENE  | 204.39 | 32.16 | 1.82  | 0.11 |

|    |   |        |       |      |      |
|----|---|--------|-------|------|------|
| CR | (1S,4E,8E,10R)-4,8,11,11-tetramethylbicyclo[8.1.0]undeca-4,8-diene        | 204.39 | 21.69 | 1.86 | 0.08 |
| CR | (Z)-Ligustilide   | 188.24 | 53.72 | 1.30 | 0.07 |
| CR | Chuanxiongol  | 218.27 | 22.19 | 0.94 | 0.10 |
| CR | beta-asarone  | 208.28 | 35.61 | 1.45 | 0.06 |
| CR | cis-Piperitol   | 154.28 | 43.26 | 1.27 | 0.03 |
| CR | (1S,4R,5R)-1-isopropyl-4-methyl-4-bicyclo[3.1.0]hexanol                   | 154.28 | 27.22 | 1.17 | 0.05 |
| CR | Cnidilide   | 194.30 | 77.55 | 1.21 | 0.07 |
| CR | 1,3,8-p-Menthatriene  | 134.24 | 35.86 | 1.86 | 0.02 |
| CR | CYCLODODECENE   | 166.34 | 47.89 | 1.84 | 0.03 |
| CR | cyclohexane,1,1,2,3-tetramethyl-  | 140.30 | 48.08 | 1.77 | 0.03 |
| CR | 2,9-Dimethyldecane  | 170.38 | 9.93  | 1.82 | 0.02 |
| CR | (2R,4aR)-2-isopropenyl-4a,8-dimethyl-2,3,4,5,6,7-hexahydro-1H-naphthalene | 204.39 | 22.13 | 1.86 | 0.08 |
| CR | 1,5,5-trimethyl-6-methylenecyclohexene                                    | 136.26 | 46.08 | 1.83 | 0.03 |
| CR | Isobutyrophenone  | 148.22 | 80.37 | 1.46 | 0.03 |

|    |                         |        |       |       |      |
|----|-------------------------|--------|-------|-------|------|
| CR | Myricanone              | 356.45 | 40.60 | 0.67  | 0.51 |
| CR | neocnidilide            | 194.30 | 83.83 | 1.23  | 0.07 |
| CR | OCT                     | 114.26 | 29.72 | 1.78  | 0.01 |
| CR | p-Cymen-8-ol            | 150.24 | 32.26 | 1.33  | 0.03 |
| CR | APH                     | 150.20 | 24.76 | 1.17  | 0.03 |
| CR | Perlolyrine             | 264.30 | 65.95 | 0.88  | 0.27 |
| CR | PLO                     | 316.53 | 14.07 | 0.69  | 0.43 |
| CR | sedanoic-acid           | 210.30 | 44.69 | 0.37  | 0.06 |
| CR | senkyunolide-F          | 206.26 | 40.35 | 0.61  | 0.08 |
| CR | senkyunolide-J          | 226.30 | 21.14 | 0.02  | 0.10 |
| CR | senkyunolide-L          | 242.72 | 29.64 | 0.63  | 0.09 |
| CR | senkyunolide-S          | 240.33 | 20.61 | -0.46 | 0.11 |
| CR | 1-Acetyl-beta-carboline | 210.25 | 67.12 | 1.18  | 0.13 |
| CR | Senkyunone              | 326.52 | 47.66 | 1.15  | 0.24 |
| CR | sinapic acid            | 224.23 | 64.15 | 0.48  | 0.08 |



|    |  |        |       |      |      |
|----|--|--------|-------|------|------|
| CR | 1H-Cycloprop(e)azulen-7-ol, decahydro-1,1,7-trimethyl-4-methylene-,<br>(1aR-(1aalpha,4aalpha,7beta,7abeta,7balphalpha))- | 220.39 | 82.33 | 1.37 | 0.12 |
| CR | trans-2-Nonen-1-ol   | 142.27 | 19.96 | 1.17 | 0.02 |
| CR | TML  | 59.13  | 59.98 | 1.78 | 0.00 |
| CR | Wallichilide   | 412.57 | 42.31 | 0.82 | 0.71 |
| CR | xiongterpene   | 574.87 | 23.77 | 0.44 | 0.42 |
| CR | 1-Octanol,2,7-dimethyl-  | 158.32 | 24.43 | 1.25 | 0.02 |
| CR | 1-terpineol  | 154.28 | 49.83 | 1.24 | 0.03 |
| CR | 1-beta-ethylacrylate-7-aldehyde-beta-carboline   | 294.33 | 28.53 | 0.45 | 0.31 |
| CR | 2-Propionylfuran   | 124.15 | 63.12 | 1.21 | 0.02 |
| CR | WLN: 2VR   | 134.19 | 60.17 | 1.45 | 0.02 |
| CR | 2,2,3-Trimethylcyclopent-3-ene-1-carboxaldehyde  | 138.23 | 42.64 | 1.31 | 0.03 |
| CR | methyl 2-pentanoylbenzoate   | 220.29 | 69.28 | 0.91 | 0.07 |
| CR | ISOHEPTANE   | 100.23 | 59.94 | 1.81 | 0.01 |
| CR | WLN: T5OJ BVO1   | 126.12 | 49.41 | 1.12 | 0.02 |

|    |   |        |        |      |      |
|----|---|--------|--------|------|------|
| CR | 2-Methyl-1-phenylpropene                    | 132.22 | 20.17  | 1.89 | 0.02 |
| CR | 2-methyl-5-(1-methylene)-1,3-cyclohexadiene | 106.18 | 39.91  | 1.83 | 0.03 |
| CR | (4S,6S)-cis-Carveol                         | 152.26 | 32.50  | 1.22 | 0.03 |
| CR | 2-Methylbenzoxazol                          | 133.16 | 65.25  | 1.31 | 0.03 |
| CR | (5S,6R)-5,6-dimethyltetrahydropyran-2-one   | 128.19 | 48.07  | 1.15 | 0.02 |
| CR | 3(S)-3-Butyl-4,5-dihydrophthalide           | 194.30 | 25.76  | 1.28 | 0.07 |
| CR | 3,4-epoxy-2,2,7,7-tetramethyl-octane        | 184.36 | 66.87  | 1.56 | 0.05 |
| CR | 3-cyclohexen-1-ol                           | 98.16  | 70.57  | 1.14 | 0.01 |
| CR | Methyl 3-furoate                            | 126.12 | 77.82  | 1.03 | 0.02 |
| CR | trans-Piperitol                             | 154.28 | 47.83  | 1.19 | 0.03 |
| CR | 4,7-Dihydroxy-3-butylphthalide              | 222.26 | 106.09 | 0.69 | 0.10 |
| CR | 4-iodoindoline                              | 245.07 | 26.88  | 1.79 | 0.03 |
| CR | 4-Octanone                                  | 128.24 | 19.37  | 1.37 | 0.01 |
| CR | 4-hydroxy-3-butylphthalide                  | 206.26 | 70.31  | 0.90 | 0.08 |
| CR | (-)-spathulenol                             | 220.39 | 25.82  | 1.45 | 0.12 |

|    |  |        |        |       |      |
|----|--|--------|--------|-------|------|
| CR | 5-Propyl-2-thiouracil                                      | 170.26 | 77.60  | 0.93  | 0.03 |
| CR | 7-oxabicyclo-2.2.1-heptane,1-methyl-4-[1-methylethyl]-     | 154.28 | 60.92  | 1.53  | 0.04 |
| CR | Aromadendrene oxide 2                                      | 220.39 | 65.10  | 1.56  | 0.14 |
| CR | Amylbenzene  | 148.27 | 34.34  | 1.88  | 0.03 |
| CR | Dimethyl D-malate  | 162.16 | 11.47  | 0.11  | 0.03 |
| CR | dl-3n-butylphthalide                                       | 190.26 | 47.90  | 1.30  | 0.07 |
| CR | Cedrene  | 204.39 | 51.14  | 1.82  | 0.11 |
| CR | carotol  | 222.41 | 149.03 | 1.46  | 0.09 |
| CR | Coniferylferulate  | 356.40 | 4.54   | 0.67  | 0.39 |
| CR | Cerulignol   | 166.24 | 62.43  | 1.42  | 0.04 |
| CR | Decahydro-1,6-bis(methylene)-4-(1-methylethyl)-naphthalene | 204.39 | 28.34  | 1.84  | 0.08 |
| CR | Hexaphenone  | 176.28 | 19.88  | 1.49  | 0.04 |
| CR | (E,E)-1,3,5-Undecatriene                                   | 150.29 | 34.61  | 1.84  | 0.02 |
| CR | Heptan   | 100.23 | 41.80  | 1.77  | 0.00 |
| CR | L-valyl-L-valine-acylhydride                               | 214.35 | 40.18  | -0.15 | 0.05 |

|    |   |        |       |      |      |
|----|---|--------|-------|------|------|
| CR | Levistolide-A   | 380.52 | 9.96  | 0.96 | 0.82 |
| CR | tetramethylpyrazine   | 136.22 | 20.01 | 1.19 | 0.03 |
| CR | Exceparl M-OL   | 296.55 | 31.90 | 1.39 | 0.16 |
| CR | 506-43-4  | 266.52 | 37.76 | 1.41 | 0.12 |
| CR | Octatriacontane   | 535.16 | 7.91  | 1.99 | 0.37 |
| CR | (2-amylphenyl)methanol  | 178.30 | 55.59 | 1.26 | 0.04 |
| CR | 1(3H)-Isobenzofuranone, 3-butyl-3a,4,5,6-tetrahydro-, cis-(-)-              | 194.30 | 65.03 | 1.25 | 0.07 |
| CR | Senkyunolide A  | 192.28 | 26.56 | 1.30 | 0.07 |
| CR | Senkyunolide G  | 208.28 | 39.52 | 0.63 | 0.08 |
| CR | (3Z,6S,7S)-3-butylidene-6,7-dihydroxy-4,5,6,7-tetrahydroisobenzofuran-1-one | 224.28 | 26.78 | 0.00 | 0.10 |
| CR | Germacrene D  | 204.39 | 19.22 | 1.83 | 0.06 |

---

AGR: *Angelicae Gigantis Radix*, RRP: *Rehmanniae Radix Preparata*, PRA: *Paeoniae Radix Alba*, CR: *Cnidii Rhizoma*, MW: molecular weight, OB: oral bioavailability, Caco-2: Caco-2 cell permeability, DL: drug-likeness score.

**Supplementary Table S2. Molecular properties of active chemical compounds in SMT.**

| Herbal medicines | Compound   | MW     | OB    | Caco-2 | DL   |
|------------------|--|--------|-------|--------|------|
| AGR              | Marmesin   | 246.28 | 50.28 | 0.52   | 0.18 |
| AGR              | Decursin   | 328.39 | 39.27 | 0.77   | 0.38 |
| AGR/PRA          | $\beta$ -Sitosterol  | 414.79 | 36.91 | 1.32   | 0.75 |
| RRP              | Stigmasterol   | 412.77 | 43.83 | 1.44   | 0.76 |
| RRP/PRA/CR       | Sitosterol   | 414.79 | 36.91 | 1.32   | 0.75 |
| PRA              | Mairin   | 456.78 | 55.38 | 0.73   | 0.78 |
| PRA              | Kaempferol   | 286.25 | 41.88 | 0.26   | 0.24 |
| PRA              | (+)-Catechin   | 290.29 | 54.83 | -0.03  | 0.24 |
| PRA              | 11 $\alpha$ ,12 $\alpha$ -epoxy-3 $\beta$ -23-dihydroxy-30-norolean-20-en-28,12 $\beta$ -olide | 470.71 | 64.77 | 0.09   | 0.38 |
| PRA              | Paeoniflorigenone  | 318.35 | 87.59 | -0.09  | 0.37 |
| PRA              | Palbinone  | 358.52 | 43.56 | 0.00   | 0.53 |
| PRA              | Paeoniflorin   | 480.51 | 53.87 | -1.47  | 0.79 |

|     |                 |        |       |       |      |
|-----|-----------------|--------|-------|-------|------|
| PRA | Paeoniflorin_qt | 318.35 | 68.18 | -0.34 | 0.40 |
| CR  | Mandenol        | 308.56 | 42.00 | 1.46  | 0.19 |
| CR  | Myricanone      | 356.45 | 40.60 | 0.67  | 0.51 |
| CR  | Perlolyrine     | 264.30 | 65.95 | 0.88  | 0.27 |
| CR  | Senkyunone      | 326.52 | 47.66 | 1.15  | 0.24 |
| CR  | Wallichilide    | 412.57 | 42.31 | 0.82  | 0.71 |

---

AGR: *Angelicae Gigantis Radix*, RRP: *Rehmanniae Radix Preparata*, PRA: *Paeoniae Radix Alba*, CR: *Cnidii Rhizoma*, MW: molecular weight, OB: oral bioavailability, Caco-2: Caco-2 cell permeability, DL: drug-likeness score.

**Supplementary Table S3. List of the targets of active chemical compounds in SMT.**

| Herbal medicines | Compound            | Targets   |
|------------------|---------------------|---|
| AGR              | Marmesin            | ADRB2*, AR*, CDK2*, CHEK1*, CHRM1, CHRM2, DPP4*, ESR1*, F2*, HSP90AA1*, LACTB*, LTA4H, PIK3CG*, PIM1*, PRKACA*, PTGS1*, PTGS2*, PTPN1, RXRA*, SLC6A4*   |
| AGR              | Decursin            | ACHE*, ADRB2*, ANGPT2*, AR*, CA2*, CALM1*, CDK2*, CHRM1, CHRM3*, CTNNB1*, DAPK3, DPP4*, ESR1*, F2*, HSP90AA1*, KLK3*, MMP9*, PARP1*, PDE3A*, PIM1*, PTGS2*, PTPN1, SCN5A*   |
| AGR/PRA          | $\beta$ -Sitosterol | ADRA1A, ADRA1B*, ADRB2*, BAX*, BCL2*, CASP3*, CASP8*, CASP9*, CHRM1, CHRM2, CHRM3*, CHRM4, CHRNA2, CHRNA7, CYP17A1*, DRD1*, GABRA1, GABRA2, GABRA3, GABRA5, GPBAR1, HSP90AA1*, HTR2A*, ICAM1*, JUN*, KCNH2*, MAP2*, NCOA2*, NPC1L1*, OPRM1*, PARP1*, PDE3A*, PGR*, PIK3CG*, PON1*, PRKACA*, PRKCA*, PTGS1*, PTGS2*, SCN5A*, SLC6A4*, TGFB1*   |
| RRP              | Stigmasterol        | ABCA1*, ABCG5*, ABCG8*, ADH1C*, ADRA1A, ADRA1B*, ADRA2A, ADRB1, ADRB2*, AKR1B1, CDCA8, CHRM1, CHRM2, CHRM3*, CHRNA7, CTRB1, CXCL8*, CYP17A1*, GABRA1, GABRA3, HTR2A*, IGHG1*, IL10*, LTA4H, LTF*, MAOA*, MAOB*, NCOA1, MDM2*, MEX3D, MTOR*, NCOA2*, NPC1L1*, NR1D2, NR3C2*, PGR*, PLAU*, PRKACA*, PTGS1*, PTGS2*, RAC1*, RUVBL1*, RXRA*, SCN5A*, SLC6A2*, SLC6A3*, SLC01B1*, TNF*, TNNC1, USF1* |
| RRP/PRA/CR       | Sitosterol          | ABCB11*, ABCG5*, ABCG8*, APOE*, CASP3*, CYP17A1*, CYP7A1*, DHCR24, DRAP1, GPBAR1, ICAM1*, NCOA2*, NPC1L1*, NR3C2*, PGR*, RANBP2, SREBF1, SREBF2   |
| PRA              | Mairin              | AKR1B10*, FOLH1*, GPBAR1, MDM2*, MEX3D, MMAB*, MTOR*, PGR*, POLB*, RAC1*, RNF31*, RPS3*, SAE1, UBA2   |

|     |                   |   |
|-----|-------------------|---|
| PRA | Kaempferol        | ABCB1*, ABCC1*, ABCG2*, ACHE*, ADRA1B*, AHR, AHSA1, AKR1B1, AKR1C3*, AKT1*, ALOX5*, AR*, BAX*, BCHE*, BCL2*, CA12, CA2*, CA7, CALM1*, CASP3*, CDK1*, CHRM1, CHRM2, C1SD1*, CTDSP1, CYP1A1*, CYP1A2*, CYP1B1*, CYP2D6*, CYP3A4*, DAPK1*, DIO1, DPP4*, EGFR*, ESR1*, ESRRA, F2*, F7*, FLT3*, GABRA1, GABRA2, GSTM1*, GSTM2*, GSTP1*, HAS2, HCK*, HMOX1*, HSD17B1, HSD17B2, HSP90AA1*, ICAM1*, IKBKB*, INSR*, JUN*, MAPK8*, MMP1*, MPO*, NCOA2*, NOS2*, NOS3*, NOX4, NR1I2*, NR1I3*, P4HB*, PGR*, PIK3CG*, PIM1*, PPARG*, PPP3CA, PRKACA*, PRSS1*, PSMD3*, PTGS1*, PTGS2*, PTPRS, RELA*, RPS6KA3, SELE*, SLC2A1*, SLC2A4*, SLC6A2*, SLPI*, STAT1*, TNF*, TOP2A*, TOP2B, TYR*, UGT1A3*, UGT1A7*, UGT1A8*, UGT1A9*, UGT3A1, VCAM1*, XDH* |
| PRA | (+)-Catechin      | ALPL*, APOB*, BACE1*, CA1*, CA12, CA2*, CA3*, CA4*, CA5A, CA5B, CA6, CA7, CA9*, CALM1*, CAT*, CSF2*, DNMT1*, ESR1*, FUT4*, HAS2, HMOX1*, HSP90AA1*, LACTB*, NCOA2*, PGD*, PGF*, PON1*, PRKACA*, PTGS1*, PTGS2*, RXRA*, SLC22A11, SLC47A1  |
| PRA | Paeoniflorigenone | DRAP1, ECH1, FKBP4, GABRA1, HOXB1, NR1D2, RUVBL1*, SULT2A1  |
| PRA | Palbinone         | ARHGEF7, MMAB*, NR3C2*, PGR*  |
| PRA | Paeoniflorin      | BLVRA, CDY2A, CDY2B, F13A1*, FLI1*, HNRNPR, MAGEA4*, MORF4L18*, SEC23A*   |
| CR  | Mandenol          | ACBD7, FAAH, GPR174*, GPR34, LPAR1, LPAR2*, LPAR3, LPAR4, LPAR6, NCOA2*, OXER1, P2RY10, PRKCA*, PTGS1*, PTGS2*, TGFA*   |
| CR  | Myricanone        | ADRB2*, AR*, CCNA2*, CDK2*, CHEK1*, DPP4*, ESR1*, ESR2*, F2*, F7*, GSK3B*, HSP90AA1*, IGHG1*, KCNH2*, KDR*, MAPK14*, NCOA1, NOS2*, PDE3A*, PIM1*, PPARG*, PTGS1*, PTGS2*, RXRA*, SCN5A*   |
| CR  | Perlolirine       | AMD1*, F2*, PRKACA*, PTGS2*, PTPRN*, RPS3*, RXRA*, S100A8*  |
| CR  | Senkyunone        | NR1D2   |



|    |              |   |
|----|--------------|---|
| CR | Wallichilide | BLVRA, HOXB13, NCOA2*, NR3C1*, NR3C2*, PRPS1, PTGS2*, STARD3, VRK2* |
|----|--------------|---|

---

AGR: *Angelicae Gigantis Radix*, RRP: *Rehmanniae Radix Preparata*, PRA: *Paeoniae Radix Alba*, CR: *Cnidii Rhizoma*.

\*, Targets associated with myelosuppression.