

Supplementary Materials

Supplementary Materials show the ESI-MS spectra and the proposed fragmentation pathway of the 13 components in HLS and disease and compound network pharmacological screening results. Figure S1: The ESI-MS spectra and the proposed fragmentation pathway of chlorogenic acid. Figure S2: The ESI-MS spectra and the proposed fragmentation pathway of typhaneoside. Figure S3: The ESI-MS spectra and the proposed fragmentation pathway of isorhamnetin-3-O-neohesperidoside. Figure S4: The ESI-MS spectra and the proposed fragmentation pathway of cynaroside. Figure S5: The ESI-MS spectra and the proposed fragmentation pathway of notoginsenoside R₁. Figure S6: The ESI-MS spectra and the proposed fragmentation pathway of ginsenoside Rg₁. Figure S7: The ESI-MS spectra and the proposed fragmentation pathway of baicalin. Figure S8: The ESI-MS spectra and the proposed fragmentation pathway of berberine hydrochloride. Figure S9: The ESI-MS spectra and the proposed fragmentation pathway of ginsenoside Rb₁. Figure S10: The ESI-MS spectra and the proposed fragmentation pathway of dehydrocostus lactone. Figure S11: The ESI-MS spectra and the proposed fragmentation pathway of dioscin. Figure S12: The ESI-MS spectra and the proposed fragmentation pathway of imperatorin. Figure S13: The ESI-MS spectra and the proposed fragmentation pathway of costunolide. Table S1: Target of 13 components from two database. Table S2: Target of disease from two database.

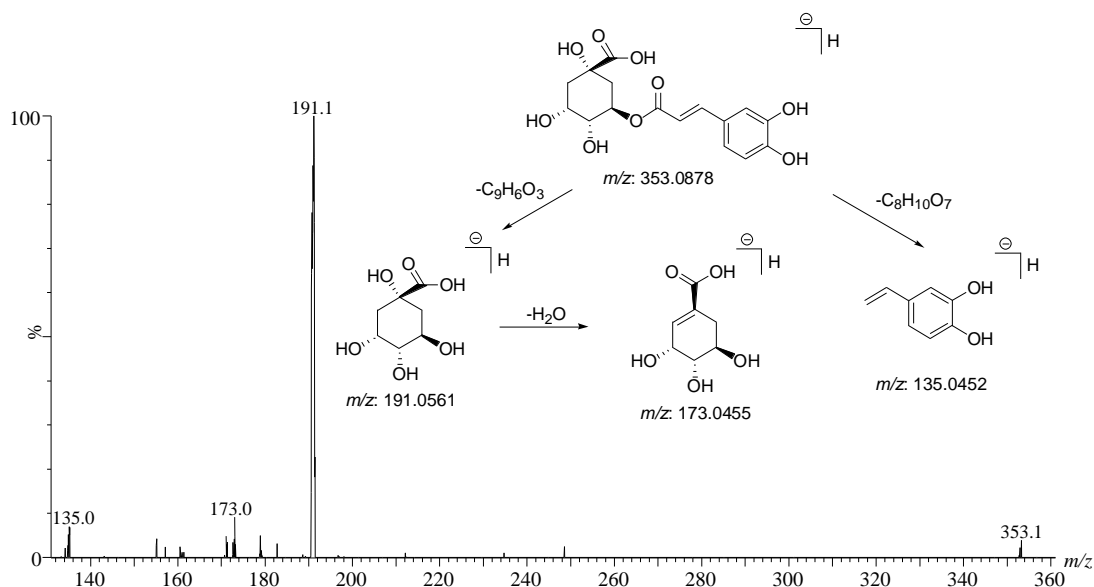


Figure S1: The ESI-MS spectra and the proposed fragmentation pathway of Chlorogenic acid

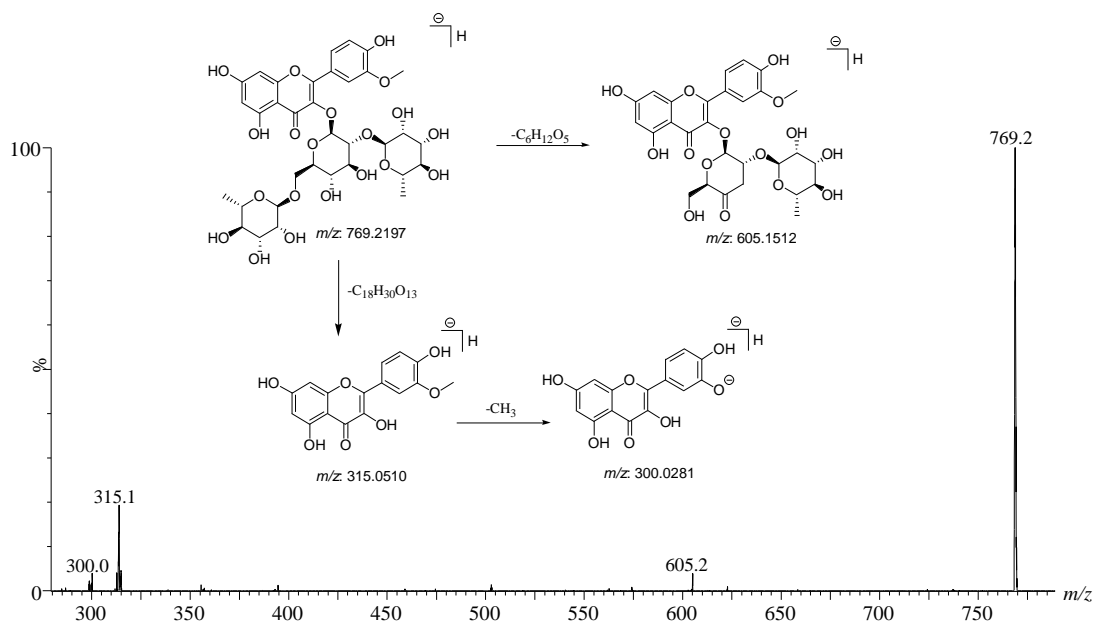


Figure S2: The ESI-MS spectra and the proposed fragmentation pathway of typhaneoside

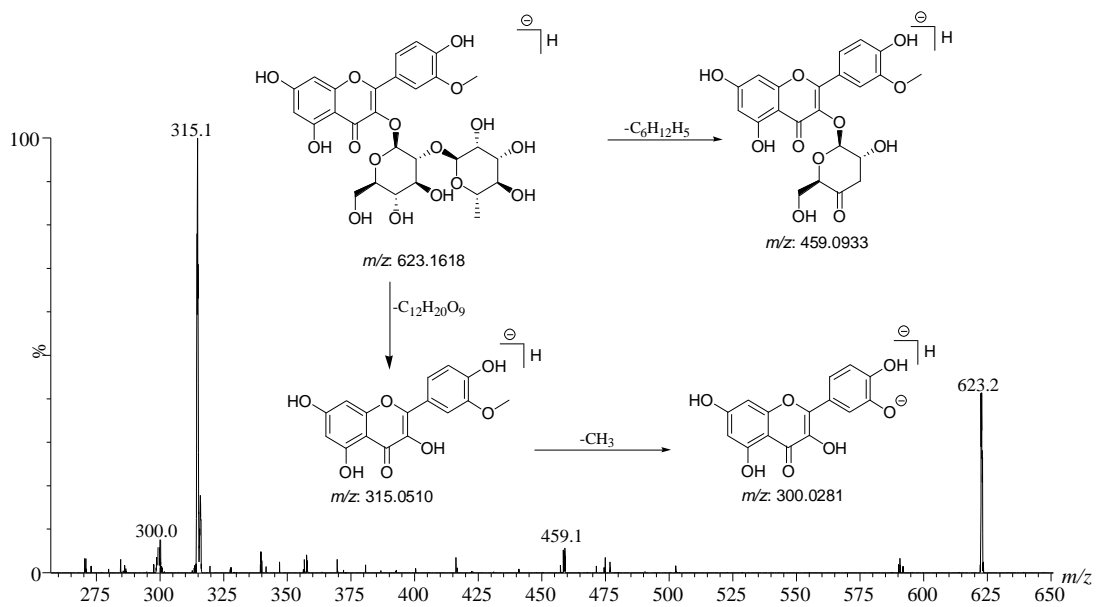


Figure S3: The ESI-MS spectra and the proposed fragmentation pathway of isorhamnetin-3-*O*-neohesperidoside

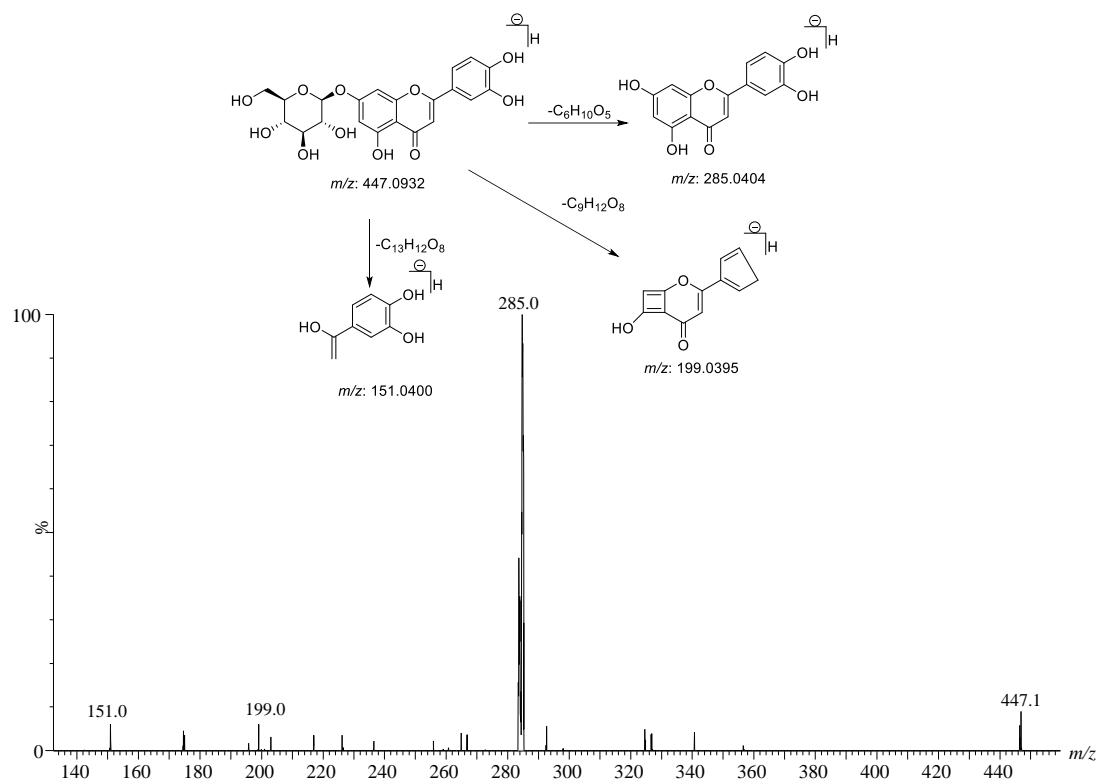


Figure S4: The ESI-MS spectra and the proposed fragmentation pathway of cynaroside

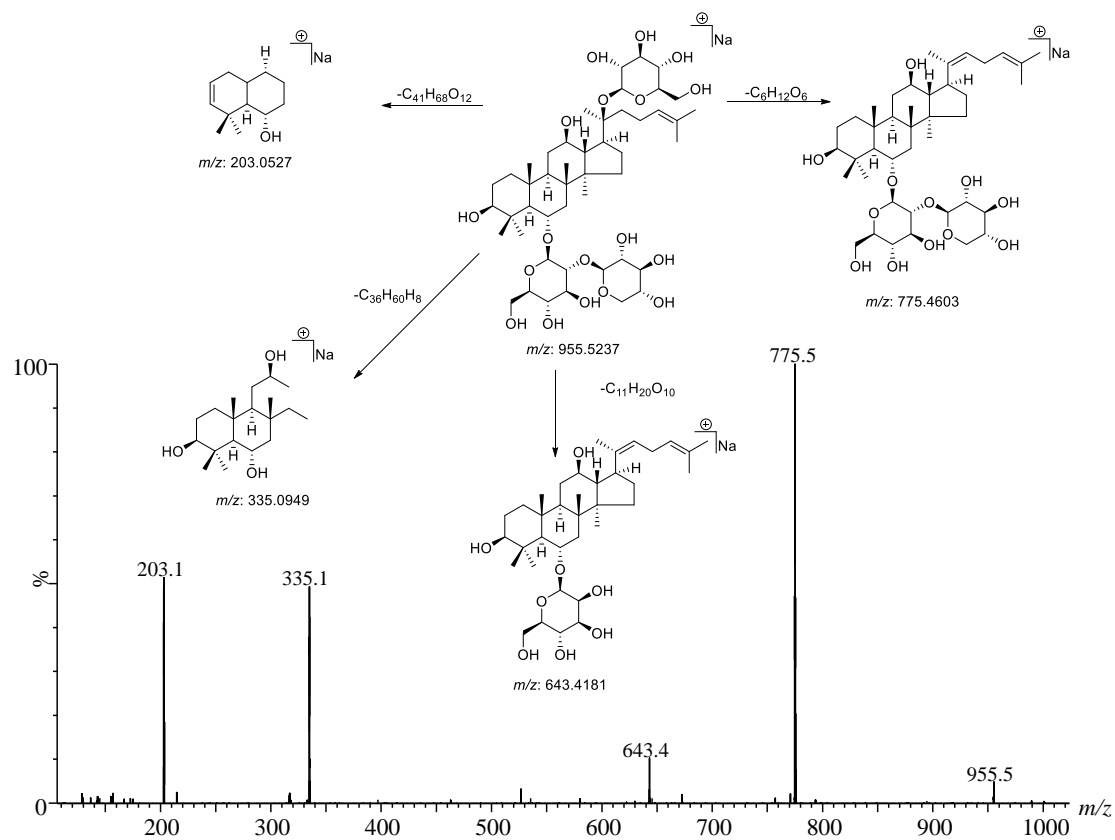


Figure S5: The ESI-MS spectra and the proposed fragmentation pathway of notoginsenoside R₁

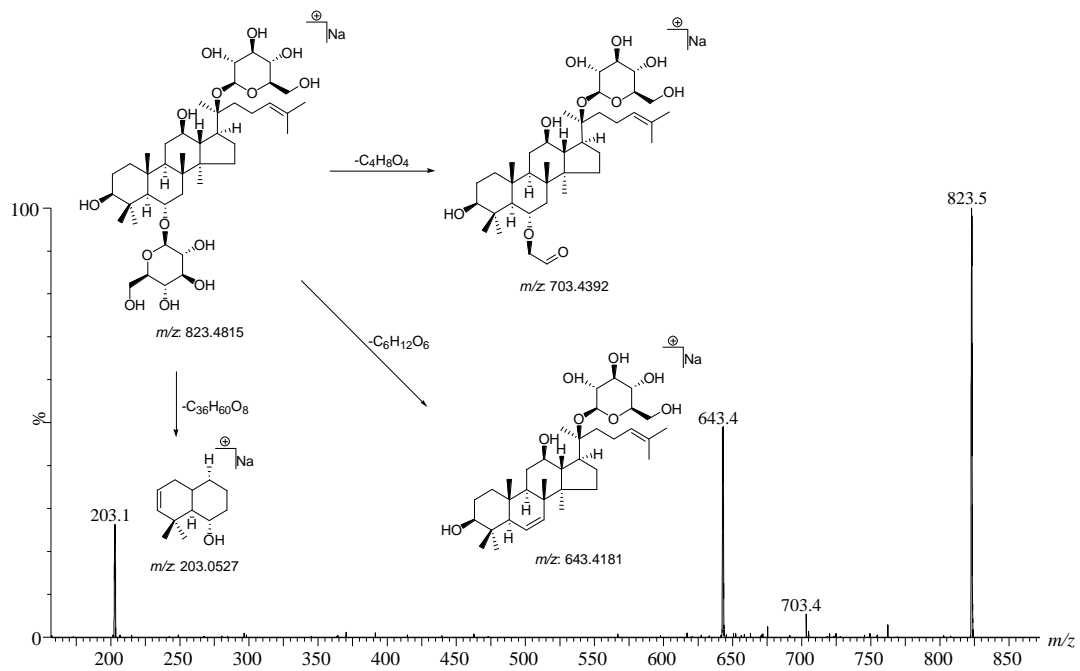


Figure S6: The ESI-MS spectra and the proposed fragmentation pathway of ginsenoside Rg₁

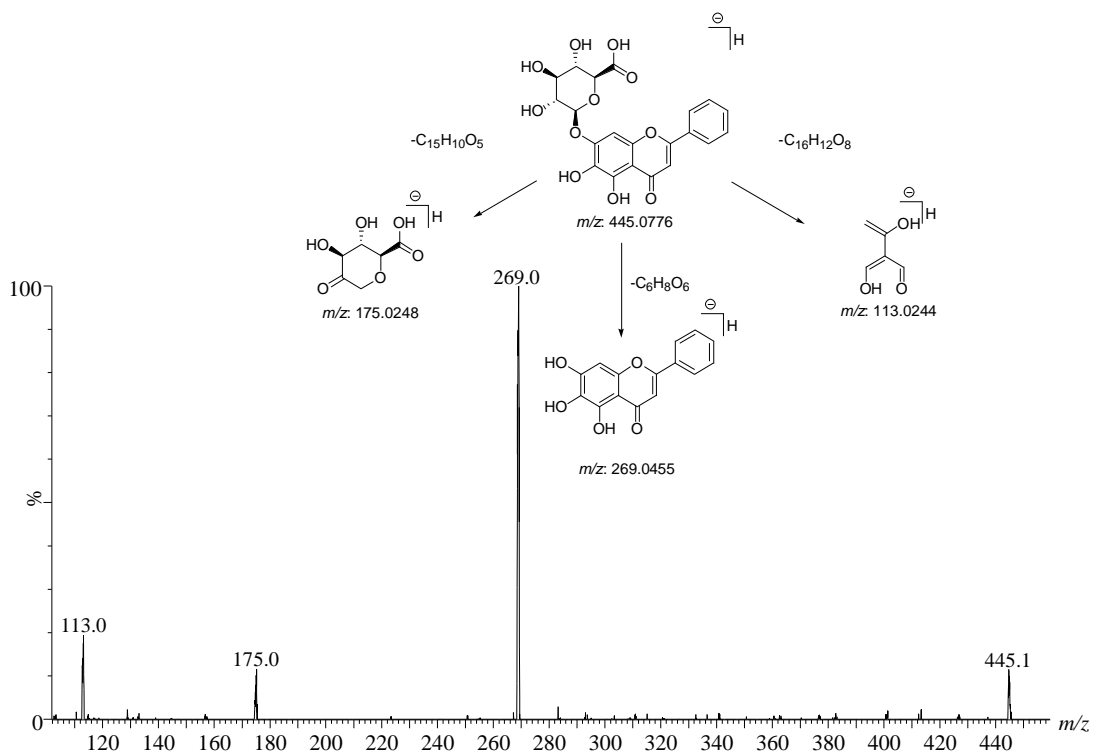


Figure S7: The ESI-MS spectra and the proposed fragmentation pathway of baicalin

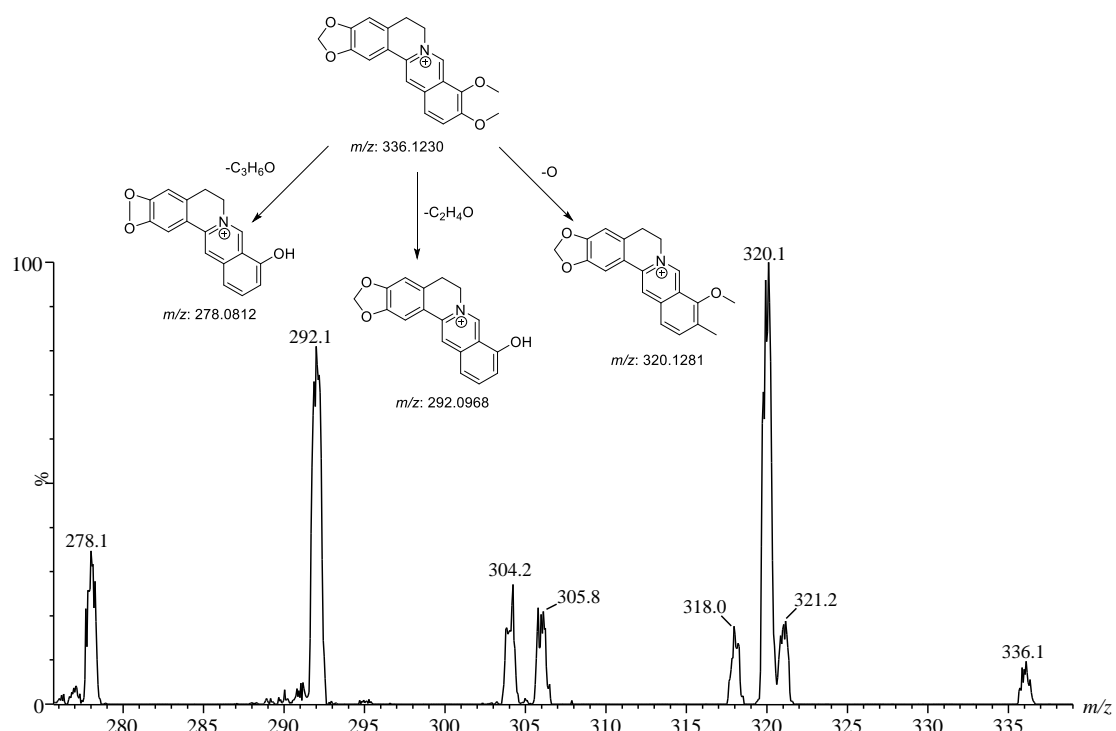


Figure S8: The ESI-MS spectra and the proposed fragmentation pathway of berberine hydrochloride

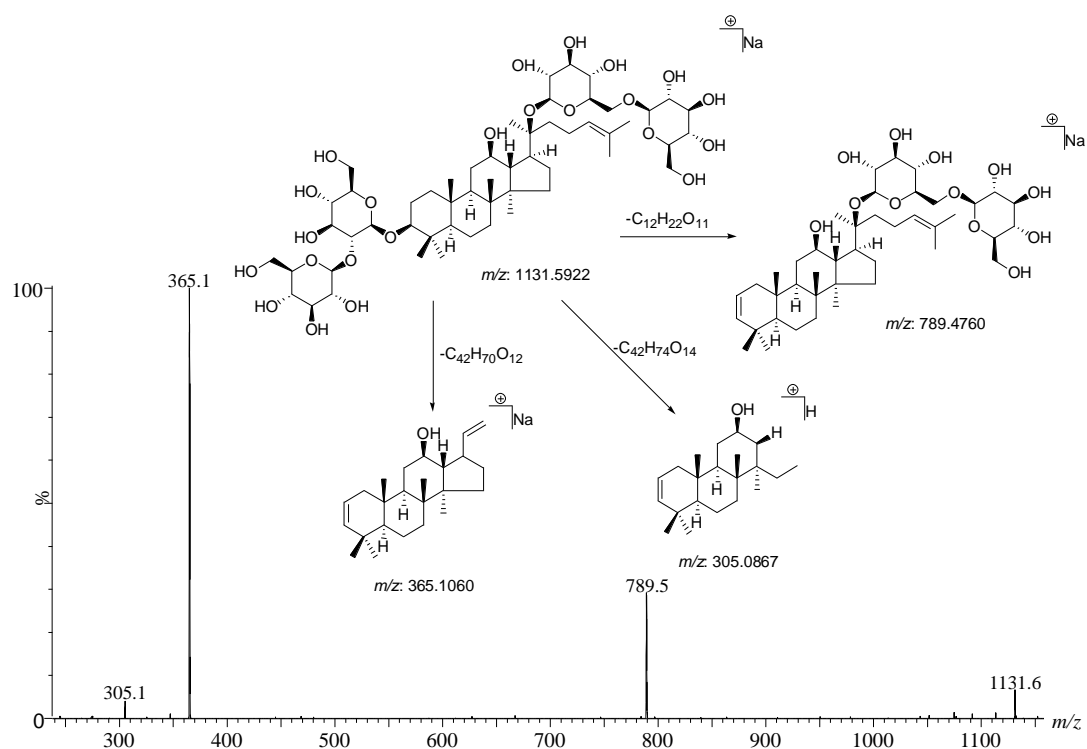


Figure S9: The ESI-MS spectra and the proposed fragmentation pathway of ginsenoside Rb₁

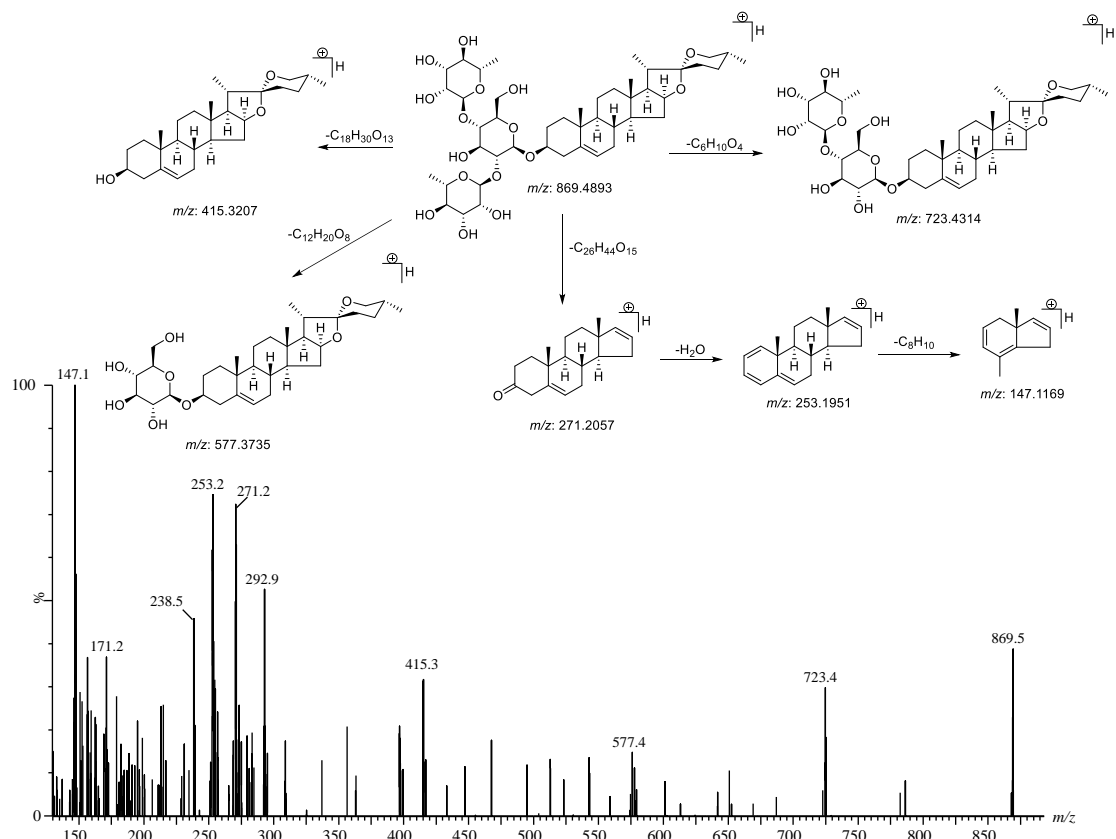


Figure S10: The ESI-MS spectra and the proposed fragmentation pathway of dehydrocostus lactone

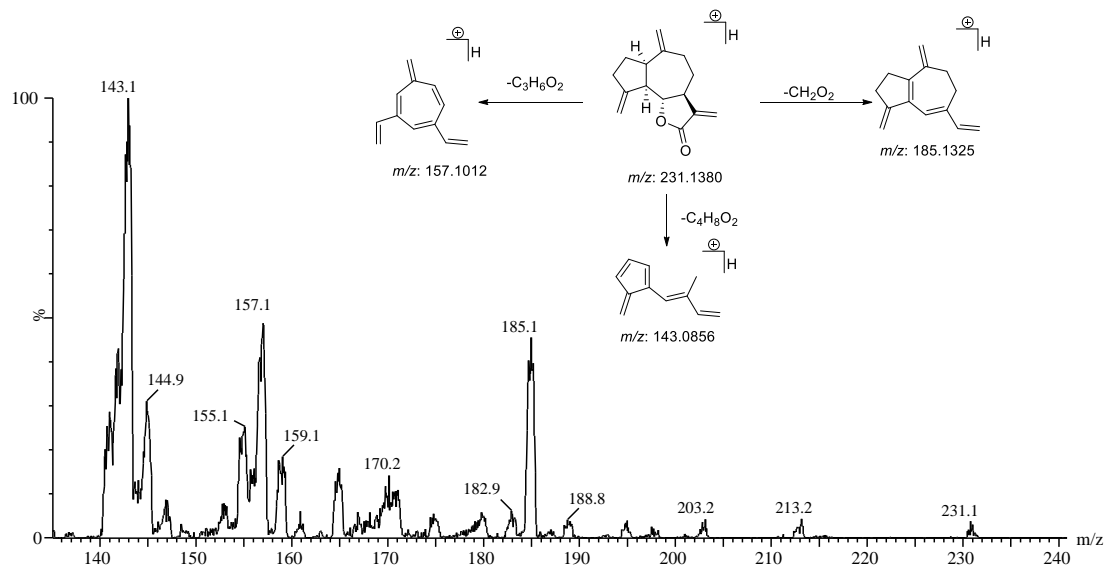


Figure S11: The ESI-MS spectra and the proposed fragmentation pathway of dioscin

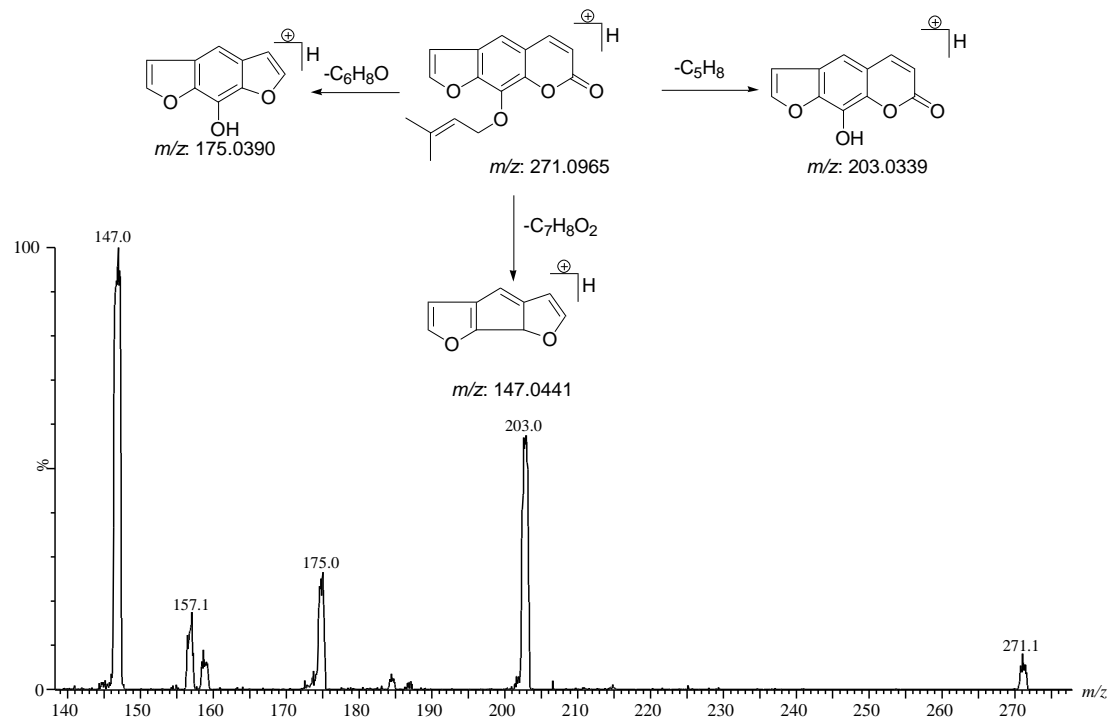


Figure S12: The ESI-MS spectra and the proposed fragmentation pathway of imperitorin

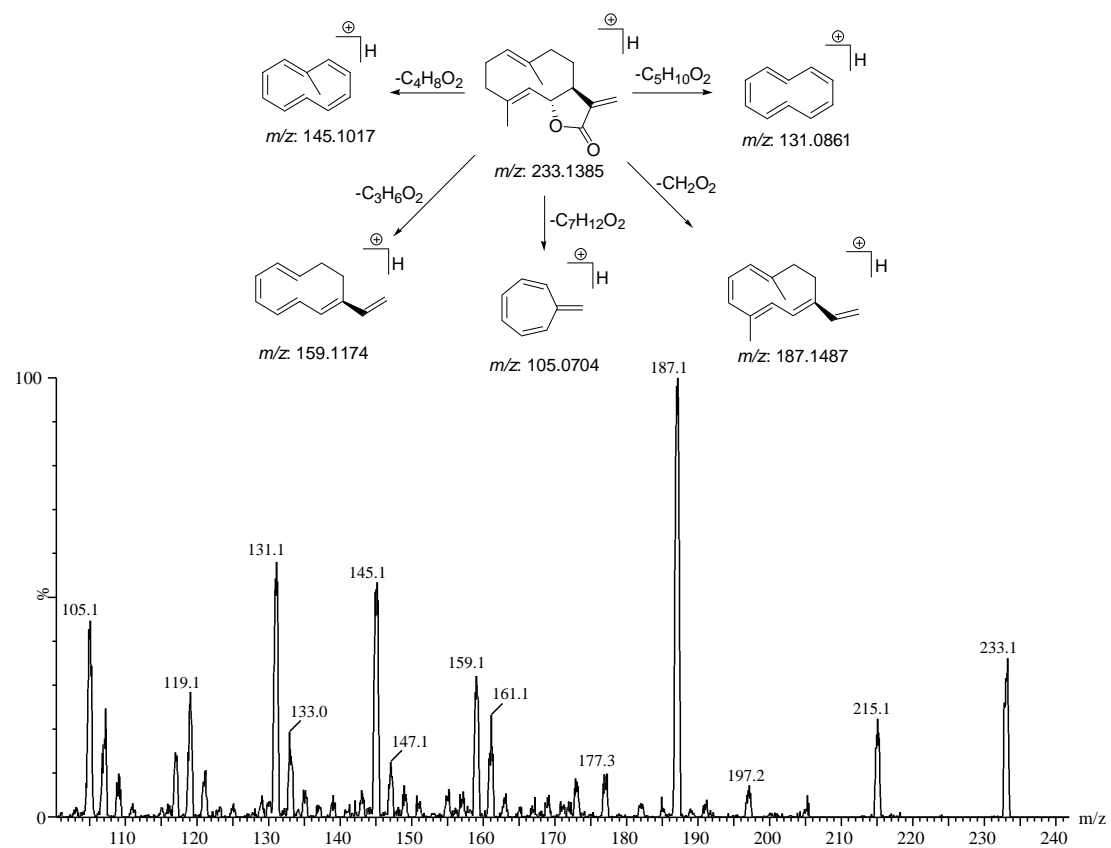


Figure S13: The ESI-MS spectra and the proposed fragmentation pathway of costunolide

Table S1: Target of 13 components from two database

| Compounds | Swiss Target Prediction database | SEA database |
|-------------------|---|--|
| Chlorogenic acid | AKR1B1, AKR1B10, MMP13, MMP2, APP, MMP12, SLC37A4, CA2, CA1, CA12, CA9, PYGL, PRKCD, PRKCA, NEU4, BACE1, CASP3, PDE4D, PDE9A, PDE1B, KDR, ENGASE, CA5B, ABCB1, NEU3, NEU2, ELANE, OGA, TREH, CASP6, CASP7, CASP8, CASP1, CASP2, ECE1, EGLN1, ADAMTS5, FTO, YARS, DNMT3B, SELL, SELP, NAALAD2, SLC13A5, HPRT1, ADORA3, MGAM, MAPK8, SI, PTPN22, FOLH1, AHCY, MGLL, ITGAL, ACLY, CFTR, MME, GSR, PIK3CG, AMPD3, PTGS1, MAPK1, AKR1C4, ADA, MMP16, GRIK2, GRIK3, MMP14, MMP8, CA14, ENPEP, ALOX5, IGF1R, INSR, GRK6, IKBKB, SRC, POLB, PIN1, HK2, HK1, ACE, CDK2, IGFBP3, GNPAT, ACP1, KDM4D, KDM4C, MMP1, FPGS, PYGM, AMY2A, MMP9, GPR35, KMT2A, DOT1L, SUV39H1, DNMT1, INMT, SMYD2, CXCL12, NR0B2, MYOC, NFKB1, MAPT, GLO1, CA6, CBS, CA5A, HSPE1, HSPD1, TTR, CA7, PTPN11, RELA, IKBKG, NFE2L2, ICAM1, ITGB2 | CXCL12, NR0B2, MYOC, AKR1B10, APP, NFKB1, MAPT, SLC37A4, GLO1, CA6, CA5B, CBS, , CA5A, HSPE1, HSPD1, TTR, AKR1B1, CA7, PTPN11, RELA, IKBKG, NFE2L2 |
| Typhaneoside | AKR1B1, NMUR2, ADRA2A, ADRA2C, ACHE, NOX4, RPS6KA3, NQO2, PTGS2, CA7, CA12, CA4, CD38, CA2, PDE5A, XDH, TNF, IL2, ALOX5, TERT, ABCG2, CYP1B1, ADORA1, PLG, ABCC1, SRC, APP, ALDH2, MCL1, CA1, CA9, CA13, EGFR, SQLE, SERPINE1, MAPT, KDM4E, GPR35, AVPR2, TOP2A, MAOA, IGF1R, FLT3, CYP19A1, INSR, F2, PIM1, AURKB, DRD4, GLO1, MYLK, MPO, PIK3R1, DAPK1, PYGL, SYK, GSK3B, PTK2, HSD17B2, KDR, MMP13, MMP3, CA3, ALOX15, PLK1, CA6, CDK1, MMP9, PIK3CG, MMP2, PKN1, CA14, CSNK2A1, ALOX12, MET, NEK2, CXCR1, CAMK2B, ALK, AKT1, NEK6, PLA2G1B, CA5A, AXL, APEX1, NUA1, AKR1C2, AKR1C1, AKR1C3, AKR1C4, AKR1A1, , SIGMAR1, DRD2, F10, AMY1A, OPRD1, OPRM1, CDK5R1, CCNB3, P4HB, CD22, ELAVL3, AMY2A, TYR, CBS, MPG, KCND3, , ALDH1B1, ALDH1A2, FGF1, CYP2C8, CBR1, FGF2, ELAVL1, PTPRS, ALPI, ERAP1, TDP1, CDK5, CCNB1, CCNB2 | P4HB, CD22, ELAVL3, NMUR2, AMY2A, TYR, CBS, MPG, RPS6KA3, KCND3, ALDH1B1, ALDH1A2, CA7, FGF1, CYP2C8, CBR1, FGF2, ELAVL1, PTPRS, ALPI, ERAP1, TDP1 |
| Isorhamnetin-3-O- | NMUR2, ADRA2A, ADRA2C, ACHE, AKR1B1, CA7, CA12, CA4, NOX4, CA2, RPS6KA3, | P4HB, CD22, SLC28A3, ELAVL3, AMY2A, TYR, |

| | | |
|--------------------------------|---|---|
| neohesperidoside | <p>PTGS2, NQO2, XDH, CD38, PDE5A, NF, IL2, ADORA1, ALOX5, TERT, ABCG2, ADORA3, CYP1B1, PLG, TDP1, KCNA3, SQLE, PRKCD, PRKCA, PRKCB, PRKCE, PRKCH, TP53, SERPINE1, VCP, SLC29A1, TNNC1, ADRB1, ITGA3, ITGB1, KCNH2, CCR, TRAP1, HSP90AA1, HSP90AB1, APP, CHEK2, CHEK1, MCL1, ALDH2, CA13, EGFR, ADORA2A, MAPT, KDM4E, GPR35, AVPR2, TOP2A, MAOA, IGF1R, FLT3, CYP19A1, NSR, F2, PIM1, AURKB, DRD4, GLO1, MYLK, MPO, PIK3R1, DAPK1, PYGL, SYK, GSK3B, PTK2, HSD17B2, KDR, MMP13, MMP3, CA3, ALOX15, PLK1, CA6, CDK1, MMP9, PIK3CG, MMP2, PKN1, CA14, CSNK2A1, ALOX12, MET, NEK2, CXCR1, CAMK2B, ALK, AKT1, NEK6, P4HB, CD22, SLC28A3, ELAVL3, AMY2A, TYR, AMY1A, FGF1, MAG, FGF2, LGALS4, LGALS8, CBS, MPG, VEGFA, SLC5A1, SLC5A2, KCND3, ALDH1B1, ALDH1A2, SLC5A4, SELL, ALPI, CYP2C8, CBR1, LGALS3, CA9, IL6, SELP, ELAVL1, LGALS9, ERAP1, PTPRS, ABCC1, ITGA4, TNNT2, TNNT2</p> | <p>AMY1A, FGF1, MAG, FGF2, LGALS4, LGALS8, CBS, MPG, VEGFA, RPS6KA3, SLC5A1, SLC5A2, ABCG2, KCND3, CA7, ALDH1B1, ALDH1A2, ALOX5, NOX4, AKR1B1, SLC5A4, SELL, ALPI, CYP2C8, CBR1, LGALS3, GLO1, CA9, IL6, SELP, ELAVL1, LGALS9, ERAP1, PTPRS, ABCC1,</p> |
| Cynaroside | <p>TNF, IL2, AKR1B1, ADORA1, CA7, CA12, XDH, RPS6KA3, ALDH2, EGFR, CD38, CA2, CA4, NOX4, ADRA2C, PTGS2, SLC29A1, CA1, ALOX5, PDE5A, PLG, ACHE, F10, NQO2, NMUR2, ADRA2A, ABCB1, PRKCG, PRKCD, PRKCA, PRKCB, PRKCZ, PRKCE, PRKCH, PRKACA, ABCC1, CYP1B1, OPRD1, KDM5A, ABCG2, SIGMAR1, DRD2, KISS1R, CA13, SQLE, PLA2G2A, TP53, CDK5R1, MAOA, FLT3, CCNB3, GLO1, APP, SYK, GSK3B, PARP1, TTR, MMP9, MMP2, MMP12, AKR1B10, TNKS2, TNKS, ARG1, ADORA3, ADORA2A, TERT, ITGAV, PTPRS, TNNC1, CA9, ITGA2B, ITGB1, PIM1, KIT, KCNA3, F7, SERPINE1, BCL2L1, BCL2, MAPT, KDM4E, GPR35, AVPR2, TOP2A, IGF1R, INSR, AURKB, DRD4, MYLK, MPO, PIK3R1, DAPK1, PYGL, SRC, PTK2, HSD17B2, KDR, MMP13, CREB1, SLC5A2, SLC28A3, P4HB, TYR, SLC5A1, ELAVL3, CBS, SLC5A11, PGF, AMY1A, B4GALT1, KCND3, FGF1, ALDH1B1, VEGFA, ALDH1A2, HRAS, SLC5A4, FGF2, ST6GAL1, ALPI, CYP1A1, GRK6, CYP2C8, ERAP1, CALM1, NEK6, IL6, ELAVL1, GSTO1, CA3, MNAT1, CA5A, KDM4A, TNNT2, TNNT2, ITGB3, ITGA5, ITGB6, CDK5, CCNB1, CCNB2, CDK1</p> | <p>TNF, CREB1, SLC5A2, SLC28A3, P4HB, TYR, SLC5A1, ELAVL3, CYP1B1, CBS, SLC5A11, PGF, AMY1A, B4GALT1, KCND3, FGF1, VEGFA, ALDH1A2, NMUR2, HRAS, SLC5A4, FGF2, AKR1B1, ST6GAL1, RPS6KA3, ALPI, CA4, CA7, CYP1A1, CA12, ABCB1, GRK6, ALOX5, CYP2C8, ERAP1, ABCG2, CALM1, NEK6, IL6, KDM4E, ELAVL1, GSTO1, TERT, CA3, MNAT1, CA5A, KDM4A, TNNT2, TNNT2</p> |
| Notoginsenoside R ₁ | STAT3, PTAFR, IL2, VEGFA, FGF1, FGF2, HPSE, RORC, ATP1A1, PSEN2, HSP90AA1, | / |

Ginsenoside Rg₁

LGALS4, LGALS3, LGALS8, BCL2L1, CDK1, HSD11B2, HSD11B1, HTR2B, ADRA2A, ADRA2C, ADRA2B, DRD1, DRD2, ADRA1D, HTR2A, HTR2C, ADRA1A, DRD3, CYP2D6, HTR6, HTR1B, SLC5A2, SLC5A1, PPM1B, PPP1CC, PPP2CA, PPP2R5A, HDAC6, F11, F7, PTPRA, AR, NR3C1, MMP9, MMP12, MMP8, TOP1, OPRD1, ITGAV, NTSR2, MET, NTSR1, ITGA2B, PTPN1, ADORA1, ALDH2, CDK2, HLA-A, F9, TYMS, SRC, GRB2, CAPN1, CTSB, BACE1, ITGB5, LIPC, ADORA2A, ITGA4, SLC37A4, LIPG, CASP3, SLC28A2, ADRB2, MAPK1, P2RY12, JAK3, AGTR1, LCK, TNK2, F10, PTPRC, KDR, TRPV1, METAP2, PLG, PRSS1, ROCK2, PRSS3, MTOR, CCNA2, PIK3CG, PIK3CA, SCARB1, PPARG, PPARA, C3AR1, GLI1, PFKFB3, F3, CCNA1, PSENE1, NCSTN, APH1A, PSEN1, APH1B, ITGB3, STAT3, IL2, PTAFR, BCL2L1, VEGFA, FGF1, FGF2, HPSE, ATP1A1, HSP90AA1, TYMS, ITGAV, ITGA2B, REN, TACR2, AKT2, RPS6KA1, ROCK1, AKT1, LGALS4, LGALS3, LGALS8, PSEN2, HSD11B2, HSD11B1, OPRD1, S1PR1, PTPRA, IGF1R, EGFR, MMP1, MMP12, MAPK8, MAPK9, SYK, MAP2K1, GRB2, PTPN1, CAPN1, BCL2A1, MTOR, F10, LNPEP, SLC5A2, SLC5A1, DPP4, SLC37A4, LTBR, PIK3CA, RORC, EPHX2, ADK, XIAP, BACE1, CSF1R, ADRB2, PPARA, NTRK1, NTRK2, PLG, PRSS1, ROCK2, HDAC3, HDAC6, DHODH, HDAC8, HDAC1, ITGB1, ITGB5, MMP9, KMT5A, F3, CASP3, PPARG, CTSD, MMP13, MMP2, HCAR2, ITGA4, C3AR1, ANPEP, PTGDR2, PPIA, ADORA1, CDK2, PTPRF, CCR5, SELP, CDK1, PDE2A, CASP1, AGTR1, SRC, F11, F7, HTR2B, ITGB3, NCSTN, APH1A, PSEN1, APH1B, PSENE1, ITGA5, ITGB6

Baicalin

AKR1B1, ADORA1, TNF, IL2, XDH, PTGS2, RPS6KA3, EGFR, ACHE, NQO2, NMUR2, ADRA2A, ADRA2C, NOX4, ALDH2, CA2, CA12, FDFT1, MAPK14, IMPDH2, NEU2, POLA1, CA13, ASNS, HPRT1, CD38, P2RY1, FPGS, MGAM, ALOX5, GAA, FGF2, CA1, CA9, HK2, HK1, POLD1, EGLN1, POLB, POLG, KDM5A, TYMS, P2RY4, P2RY2, P2RY6, KCNA3, CASP3, ITPR1, NEU4, MAG, FOLR1, GART, SELP, MMP16, MMP1, MMP14, MMP8, FOLH1, EIF4E, NPC1L1, AMY2A, KDM4D, KDM4C, ABCB1, CASP6, CASP7, CASP8, CASP1, CASP2, DNMT1, F10, DNMT3B, ANPEP, ERAP2, DHFR, PTPN22, YARS, SQLE, ADCY10, CA7, CA4,

CREB1, PTPRS, MRP3, P4HB, CYP1B1, AMY1A, CYP1A1, PGF, ABCB1, KCND3, TNKS, SIGMAR1, CBS, CALM1, ALDH1B1, ALDH1A2, NMUR2, FGF2, AKR1B1, ABCG2, GRK6, ODC1, AKR1B10, NR4A2, ALPI, , SLCO1B1, NOX4, ST6GAL1, KDM4E, ABCC1, TNKS2

| | | |
|-----------------------------|--|---|
| | CAPN1, ITGAV, NEU3, PIK3CA, ATIC, CMA1, IDO1, SIGMAR1, DRD2, ENPEP, LAP3, P2RY11, NAALAD2, ERAP1, ITGB1, ADORA2B, HDAC3, HDAC6, HDAC2, CREB1, PTPRS, MRP3, P4HB, CYP1B1, AMY1A, CYP1A1, PGF, KCND3, TNKS, CBS, CALM1, ALDH1B1, ALDH1A2, ABCG2, GRK6, ODC1, AKR1B10, NR4A2, ALPI, SLCO1B1, ST6GAL1, KDM4E, ABCC1, TNKS2, ITGB3, ITGA4 | |
| Berberine hydrochloride | / | RAC1, RGS17, CDC42, F3, TOP2B, CYP1B1, P2RX7, IL2 |
| Ginsenoside Rb ₁ | STAT3, PTAFR, IL2, VEGFA, FGF1, FGF2, HPSE, RORC, PSEN2, HSP90AA1, LGALS4, LGALS3, LGALS8, BCL2L1, CDK1, HSD11B2, HSD11B1, ATP1A1, KDR, HTR2B, ADRA2A, ADRA2C, ADRA2B, DRD1, DRD2, ADRA1D, HTR2A, HTR2C, ADRA1A, DRD3, CYP2D6, HTR6, HTR1B, PPM1B, PTPN1, PPP1CC, PPP2CA, PPP2R5A, F2, AR, NR3C1, TRPV1, METAP2, HLA-A, GLI1, PTPA, TYMS, PRKCA, SLC6A2, TLR9, JUN, ERBB2, IGF1R, EGFR, MMP13, MMP2, MMP8, VDR, AURKB, AURKA, RAP1A, PDE4D, GLRA1, GLRA2, NTSR2, SORT1, NTSR1, PFKFB3, MET, ADORA1, OPRD1, FDFT1, CCKAR, CCKBR, PRKCD, PRKCB, PRKCE, PRKCH, PRKCQ, MLNR, CA2, CA1, CA12, CA9, PTGS2, F2RL1, SSTR5, SSTR2, SSTR4, SSTR1, SSTR3, PPM1A, CNR1, CES2, ENPP2, LPAR2, LPAR3, LPAR1, TTL, TBXA2R, AMY2A, F3, PRKAA2, PRKAG1, PRKAB1, PSENEN, NCSTN, APH1A, PSEN1, APH1B, CYP19A1, PTGS2, F2, PRSS1, CTSC, HSD11B1, KCNK2, CYP11B2, PARP1, POLB, CYP11B1, FLT3, LRRK2, GSK3B, CYP17A1, TBXAS1, CTSK, DRD4, PRKDC, AR, EPHX1, XPO1, ADRA2C, MAPK14, CYP2A6, MPO, MAOB, HSD17B3, PDE7A, SRD5A1, ADH1A, TYMS, CTSL, CTSB, FNTA, PABPC1, PIK3CD, ADH1C, MTNR1A, MTNR1B, CA3, CA12, CA14, CA13, CA5B, IDO1, CA5A, TNKS2, EPHX2, NQO2, CHRNA4, PTGS1, BRD9, CHRNA3, MGLL, CTRB1, P2RX7, SLC6A4, HMOX1, ALDH2, ELANE, ALDH1A1, ALDH3A1, GABRB3, GRM5, QPCT, CTSC, KAT2B, DRD2, GABRA2, CTSH, CTSE, CTSS, CTSV, HTR7, GRM4, ABCC9, KCNJ11, PIM1, PGGT1B, MST1R, KCNJ5, MET, PGR, CEL, ACE, TNKS, HMGCR, ABCB1, GABRA1, EGFR, PDGFRA, KIF11, GABRA5, KCNA5, GPR55, BRD4, TAAR1, | AMY2A, F3, PRKAA2, PRKAG1, PRKAB1 |
| Dehydrocostus lactone | | UBE2D3, RELA |

| | | |
|-------------|--|---|
| Dioscin | <p>UBE2D3, RELA, KCNJ3, PDGFRB, GABRG2, CHRNB2, PIK3R1, FNTB, CHRNB4, GABRA3 IL2, STAT3, PTAFR, PTPN1, ATP1A1, PPM1B, PPP1CC, PPP2CA, PPP2R5A, HSD11B2, HSD11B1, VEGFA, FGF1, FGF2, HPSE, F2, TYMS, PTPRA, GLI1, HSP90AA1, PSEN2, CDK1, PTPN11, PFKFB3, BACE1, NPC1L1, TTL, JUN, PDCD4, TBXAS1, LGALS4, LGALS8, ADORA1, ELANE, PTPN22, RAP1A, PDE4D, GPR55, GPR34, BCL2L1, HTR2B, ADRA2A, ADRA2C, ADRA2B, DRD1, ADRA1D, HTR2A, HTR2C, DRD3, CYP2D6, HTR6, ADRA1A, HTR1B, PDGFRB, FLT3, AURKB, MET, AURKC, AURKA, P2RY10, ITGB1, CASP3, DHFR, OPRD1, REN, S1PR3, S1PR1, LTB4R, CSF1R, ITGAV, NTRK1, MDH1, NTRK2, MDH2, RORC, MMP13, MMP2, MMP8, PRKCA, NPR1, NPR3, SERPINE1, C3AR1, CAPN1, METAP2, TK2, POLA1, AKR1B1, GLS, ADAMTS4, MMP3, MMP7, PTPRS, ABCB1, ABCG2, ADORA2A, ADORA3, GSK3B, FPGS, AMY2A, CRYAB, DHCR24, CYP17A1, NPC1, AMY1A, YWHAZ, ABCC4, NR1H3, SRD5A2, EBP, P4HB, SREBF2, ITGB3, ITGA5, ITGA4, PSEN1, APH1B, PSENE1, NCSTN, APH1A</p> | <p>AMY2A, CRYAB, DHCR24, CYP17A1, NPC1, AMY1A, YWHAZ, ABCC4, NR1H3, SRD5A2, EBP, P4HB, SREBF2</p> |
| Imperatorin | <p>MAOA, ACHE, KCNA3, BACE1, CYP1A2, GABRB3, GABRA2, CYP19A1, MAPK14, NOS2, ADORA1, PDE10A, ADORA2B, NTRK1, HDAC3, ADRA2A, ADRA2C, HDAC2, ADRA2B, ADRA1B, JAK2, HDAC1, CSNK1D, FNTA, PGGT1B, PTGER1, CCNE2, TAAR1, MTOR, PIK3CD, PIK3CB, GRM5, PIK3CG, MCHR1, PIK3CA, PDE5A, PRKDC, HSF1, GYS1, BRS3, TGFB1, PTK2B, MAOB, FAAH, CLK4, GSK3A, DYRK1A, PDE8B, PGR, MAPKAPK2, MAPK8, CSNK1G1, CCR2, ADRA1A, PPOX, PIM1, CA9, PTGER4, PTGER2, PTGER3, HCRTR2, HCRTR1, BCHE, CNR1, PTGS1, PTGS2, CNR2, MAP2K1, SRD5A1, FLT3, JAK1, TYK2, NAAA, CA12, PTAFR, HRH3, EPHX1, TK1, SLC1A3, SIRT2, HCAR2, P2RX7, TLR9, GABRA1, KCNH2, PTPN1, GABRA5, DUT, PIP4K2C, PRKCG, CDK2, PIM2, CDC7, HTR2B, ELANE, HTR7, CDC25B, GABRA3, GABRG2, FNTB, CCNE1</p> | / |
| Costunolide | <p>CYP19A1, AR, FNTA, IL1B, TTL, HMGCR, PGR, PDE4D, PTPN1, GSK3B, TYMS, PARP1, PTGS2, PCSK7, ATP12A, POLA1, POLB, CYP11B1, CYP11B2, FLT3, ADH1A, TBXAS1, CDC25C, PDCD4, MPO, EPHX1, PRKDC, CA3, PRKCA, LRRK2, SRD5A1, KCNK2, CTSK,</p> | / |

IMPDH2, HSD11B2, PRKCE, HSD11B1, PABPC1, ADH1C, MTNR1A, MTNR1B, MAOB, CTSL, CTSB, ACHE, PRKCD, CA2, CYP17A1, ADRA2C, GABRB3, PDE7A, GLI2, GLI1, MAOA, ABCB1, EPHX2, MAPK14, KAT2B, F2, PRSS1, CDC25B, DRD4, SIRT2, XPO1, PPARA, PPARD, EDNRA, NQO2, KIF11, IKBKB, BCL2L1, DNNT, RPS6KA5, ITGAL, TBXA2R, IARS, CHRNA3, BRD9, CEL, ACE, TNKS2, TNKS, AHR, ALOX15, KCNJ5, ALOX12, HSD17B3, TAS2R31, JAK3, MMP13, JAK1, JAK2, MMP1, PLA2G1B, PPARG, ELANE, PTPRC, PTPRF, CYP2A6, TDO2, CHRN4, GABRA5, GABRG2, FNTB, KCNJ3

Table S2: Target of disease from two database

| Disease | OMIM database | DisGeNET database |
|---------------------------|--|---|
| Fracture traumatic injury | BCC1, BMND3, CMM, DEL1p36, ZBTB40IT1, ISG15, AGRN, TNFRSF18, B3GALT6, SCNN1D, TAS1R3, ATAD3A, GNB1, CFAP74, GABRD, PRKCZ, SKI, DYT13, RER1, PEX10, PLCH2, TNFRSF14, TP73, SMIM1, NPHP4, ICMT, TNFRSF25, CAMTA1, SCZD12, PER3, TNFRSF9, DJ1, MIG6, SLC45A1, CA6, MIR34A, PIK3CD, NMNAT1, KIF1B, DFFA, TARDBP, MTOR, ANGPTL7, UBIAD1, FBXO6, MTHFR, NPPA, PLOD1, MFN2, TNFRSF1B, VPS13D, GBD2, PDPN, PRDM2, EFHD2, CTRC, CASP9, SPEN, CLCNKA, EPHA2, RNU1A, MFAP2, ATP13A2, SDHB, PADI3, PADI4, PADI6, PAX7, TAS1R2, PLA2G2E, PLA2G2A, PLA2G5, PLA2G2D, CAMK2N1, MUL1, PINK1, DDOST, ECE1, ALPL, HSPG2, ZBTB40, C1QA, C1QC, C1QB, EPHB2, KDM1A, HNRPR, ID3, RPL11, GALE, HMGCL, FUCA1, SRSF10, IL22RA1, CLIC4, RUNX3, RHD, RHCE, LDLRAP1, SELENON, SLC30A2, TRIM63, UBXN11, RPS6KA1, ARID1A, SFN, NR0B2, SLC9A1, TMEM222, SYTL1, FCN3, GPR3, AHDC1, FGR, G1P3, SMPDL3B, EYA3, CHC1, YTHDF2, OPRD1, MECR, MATN1, SDC3, FABP3, KHDRBS1, CCDC28B, LCK, HDAC1, TSSK3, YARS1, FNDC5, HPCA, AK2, AZIN2, GJB4, GJB3, GJA4, NCDN, CLSPN, AGO1, ADPRHL2, COL8A2, TRAPPC3, CSF3R, GRIK3, SNIP1, DNALI1, RSPO1, YRDC, POU3F1, AKIRIN1, MACF1, BMP8B, PPT1, ZMPSTE24, COL9A2, KCNQ4, CTPS1, FOXO6, HIVEP3, PPCS, P3H1, SLC2A1, | G1P2, CMS8, AITR, SEMDJL1, T1R3, HAYOS, MRD42, KIAA1751, GEFSP5, PKC2, SGS, NALD, PLCL4, HVEM, CILD47, VEL, SLSN4, TNFRSF12, KIAA0833, FASPS3, ILA, PARK7, RALT, DNB5, MIRN34A, APDS, NMNAT, CMT2A, DFF1, TDP43, FRAP1, CDT6, TERE1, FBX6, PND, LH1, KIAA0214, TNFR2, SCAR4, TI1A, RIZ, SWS1, CLCR, APAF3, MINT, ECK, RNU1, MAGP, PARK9, SDH2, UHS1, PADI5, OZEMA16, RMS2, T1R2, PLA2B, FRFB, SPLASH, MULAN, PARK6, OST, HOPS, PLC, KIAA0478, C1QD1, C1QG, C1QD2, EPHT3, LSD1, HNRNPR, DBA7, FUSIP1, IL22R1, MTCLIC, CBFA3, HDFNRH, RHNA, ARH, SEPN1, ZNT2, RNF28, SOC, RSK1, C1orf4, SHP, NHE1, C1orf160, SLP1, HAKA1, XIGIS, SRC2, IFI616, ASML3B, RCC1, NRBF1, CRTM, SYND3, SAM68, MGC1203, IMD22, RPD3L1, STK22C, YARS, FRCP2, DYT2, ODC1L, CX30.3, CX31, CX37, KIAA0607, EIF2C1, |

CFAP57, CDC20, ELOVL1, ARTN, RNF220, TMEM53, PTCH2, EIF2B3, UROD, ZSWIM5, MUTYH, TOE1, TESK2, MMACHC, PRDX1, NASP, POMGNT1, RAD54L, BMND14, PAINQTL1, UQCRH, MKNK1, CYP4A11, TAL1, STIL, FOXE3, TRABD2B, PARK10, DMRTA2, RAB3B, ORC1, PRPF38A, TUT4, SCP2, CPT2, MAGOH, GLIS1, VWF, PRDX6, MMP12, NMNAT3, KLK6, NEK1, S1PR1, ASIC1, PDGFRB, TYRO3, MYLK, HMGB1, EPHA4, KCNA2, KCNB1, PRKCG, PRKCA, PRKCB, PRKCD, PRKCE, PRKCI, PRKCQ, KCNA1, KCNA10, KCNA3, KCNA4, KCNA5, KCNA6, KCNB2, KCNC1, KCNC2, KCNC3, KCNC4, KCNQ1, KCNQ2, KCNQ3, KCNQ5, KCNAB1, KCNAB2, KCNV1, KCNV2, KCNH1, KCNH2, KCNH3, KCNH4, KCNH5, KCNH6, KCNH7, KCNH8, KCNG1, KCNG2, KCNG3, KCNG4, KCNS1, KCNS3, MXRA8, HPCAL4, EDN2, AKR1A1, CTH, TNNT3, NEXN, F3, VUR1, CELSR2, MYBPHL, SORT1, ADORA3, SLC16A1, PTPN22, NGF, REG4, NOTCH2, TXNIP, ECM1, CTSK, FLG2, PKLR, YY1AP1, BDET, NTRK1, AIM2, CRP, ATP1A2, FCGR2A, FCGR2B, DDR2, RGS5, CREG1, ATP1B1, F5, SELP, FASLG, LAMC2, HMCN1, CELIAC7, MGR6, PRG4, PTGS2, PLA2G4A, KCNT2, CFH, CFHR3, CFHR1, INAVA, PKP1, TNNT2, ADORA1, CHI3L1, REN, DSTYK, MAPKAPK2, IL10, CD55, LAMB3, HSD11B1, HHAT, PACC1, PROX1, SLC30A10, EPHX1, AGT, EGLN1, GGPS1, LYST, ACTN2, FH, NLRP3, HYT3, VSNL1, SDC1, MPV17, EIF2B4, XDH, MCFD2, TTC7A, CALM2, RTN4, LGALS1, DYSF, DCTN1, TACR1, SFTP, CELIAC8, COPD, ANKRD23, SEMA4C, IL1R1, MERTK, IL1A, IL1B, IL37, IL1RN, PROC, ACMSD, CXCR4, HNMT, SYNTH, ACVR1, ITGB6, GCG, IFIH1, FIGN, SCN2A, SCN9A, GAD1, PDE1A, ITGAV, TFPI, COL3A1, STAT1, CASP10, CASP8, CTLA4, IDH1, CPS1, FN1, IGFBP5, CXCR2, PNKD, SPEG, SLC4A3, PI7, COL4A4, COL4A3, CHRNG, INPP5D, ATG16L1, UGT1A1, TRPM8, ACKR3, LRRFIP1, PDCD1, BHLHE40, SCLC1, PLCD1, MYD88, SCN10A, SCN11A, RPSA, TRAK1, CELIAC9, CDCP1, TMEM158, CCR1, CCR3, TREX1, COL7A1, DAG1, ARMET, TLR9, WNT5A, FLNB, ACOX2, MITF, ROBO1, CHMP2B, PROS1, DCBLD2, CBLB, DUBR, RETNLB, DPPA2, GSK3B, FSTL1, HCFP1, CSTA, RAB7, ATP2C1, PCCB, COPB2, PLSCR1, AGTR1, CELIAC10, P2RY14, P2RY12, MLM, C1DELp36

ARH3, FECD1, BET3, GCSFR, GLUR7, NEDHCS, P28, FLJ40906, IRIP, ACF7, OP2, CLN1, FACE1, EDM2, DFNA2A, CTPS, KRC, CMD2C, LEPRE1, GLUT1, WDR65, OZEMA14, SSC1, HLD23, NET4, VWM3, KIAA1511, MYH, PCH7, PRXI, MEB, HR54, MC3DN11, MNK1, TCL5, SIL, FKHL12, TIKI2, AAOPD, ORC1L, PRP38A, ZCCHC11, IIAE4, DNS, IMD38, ALGAZ, IFI15, PBD6B, GTR, EDSSPD2, CILD49, EJM7, PHRINL, MDS, C1orf222, EIG10, LARD, ATFB6, EDSKCL1, HMSN6A, PBD6A, IMD109, TR2, IMD14B, LCA9, NBLST1, DR3, CECBA, CD137, IDDNPF, ROCHIS, SHILCA, IMD14A, PNAT1, CMT2A1, ALS10, SKS, SCCD, FBG2, ATRST2, ANP, LLH, CMT2A2A, TNFBR, CTPA, ARCC2, T1A2, GP36, OTS8, AGGRUS, CMT2A2B, SHARP, HIAA0929, CTPP1, RATARS, MAGP1, KRPPD, SDHIP, CTRCT6, PAD, MC2DN4, CMYP19, SPG78, PGL4, PLA2L, HPPA, SJA, MOM1, C1orf166, CDG1R, OST48, HPPO, SJS1, TNSALP, SJS, CAPB, CPRF, C1QD3, HPPI, DRT, AOF2, NEDDFSB, ERK, BHC110, PCBC, KIAA0601, BDPLT22, TASR, TASR1, TASR2, PEBP2A3, HPPC, FHCB1, CMYP3, FHCB2, SELN, TNZD, SMRZ, FHCL4, AML2, B120, SMARCF1, MURF1, APNH, NEDMOSBA, JFC1, MRD14, CSS2, MRD25, LIKNS, DYTOABG, CMP, SDCN, STK22D, CMTDIC, KIAA1945, EKVP2, DFNA2B, EKVP1, NEDIES, EIF2C, GERP95, CONDSIAS, PPCD2, NEDLBAS, SCN7, SPGF83, GAMOS10, KIAA1251, LIS9, MADB, STE24, STL5, RSDM1, IMD24, GROS1, HTLV, OI8, DYT18, IKSHD, PED, GLUT1DS,

CTDI, EIG12, DYT9, SDCHCN, LGMDR15, RP76, MDDGC3,
PAGA, NKEFA, MDDGA3, HRAD54, CTRCT34, ASGD2,
AAT11, SCL, MCPH7, ASMD, MDDGB3, KIAA0191, ARMD1,
FASL, JEB3A, ARMD4, CFHL3, CFHL1, AHUS1, DUSTYPK,
RCM3, APT1LG1, LAMB2T, FIBL6, ALPS1B, JEB3B, MSF,
ASRT7, GURDP, DEE57, HUS, HLF4, HFL1, IBD29, LVNC6,
CMD1D, CAKUT1, YKL40, ADTKD4, RIP5, SPG23, GVHDS,
CROM, JEB1B, HSD11L, SKI1, ZMYND6, SM20, HMNDYT1,
ECYT3, PYPAF1, HIFPH2, MDHLO, DFNA34, CMH23,
MCUL1, FCU, KEFH, HLP3, CMYP8, FMRD, FCAS1,
NALP3, MPD6, C1orf12, CHAPLE, JEB1A, CORTRD2,
NNMS, THPH4, IMD95, WHIMS1, SGMRT1, FOP, FIL1Z,
DIRA, THPH3, IBD31, NPY3R, BFIS3, HSAN2D, EA9, ALK2,
DEE11, SFNP, AGS7, BFNIS, BFIC3, PN1, DEE89, WHIMS2,
KIPP1184, SQT7, PMGEDSV, IMD31A, ALPS2, ALPS2B,
CELIAC3, IMD31B, ALPS5, IMD31C, PDC, IL8R2,
TAHCCP2, CNM5, AE3, SERPINE2, BFH1, ATS3, BRP17,
FPD1, DYT8, IBD10, GNT1, BFH2, CMKOR1, TRIP, GPR159,
FLAP1, RDC1, BILIQTL1, IMD68, FEPS3, LAMBR,
KIAA1042, ICAS, DEE68, IMNEPD2, YRS, YTS, TYRRS,
CMD1CC, ASP3, HLP4, ALR, CCDD, NELIN, TFA, MEGF3,
EGFL2, LDLCQ6, NT3, HHF7, MCT1, PEP, NGFB, FARIMPD,
AGS2, VDUP1, URBWD, HCCA2, IFPS, PK1, YAP, DEE98,
TRKA, MHP2, CD32, FHM2, IGFR2, NTRKR3, TKT, WRCN,
RPRGL1, THPH2, GRMP, TNFSF6, LAMNB2, FBLN6, HAPO,
FHM3, CACP, SZP, PLA2G4, SLICK, HF1, FHR3, FHR1,

C1orf106, EDSFS, CMH2, RDC7, GP39, RTD, KIAA0472, MK2, CSIF, DAF, AI1A, HSD11, MART2, TMEM206, HALAH, ZNT10, GIDID, SERPINA8, PHD2, GGPPS1, CHS1, CMD1AA, HLRCC, CIAS1, MINAT, VILIP, KIAA1140, MTDPS6, VWM4, XAN1, PKCE, F5F8D2, TTC7, LQT15, NOGO, CMT2EE, LGMDR2, HMN7B, TAC1R, SFTB3, NK1R, SMDP1, DARP, SEMAF, IL1RA, RP38, IL1H4, MMD1, IL1F7, MVCD4, PC, KIAA1739, D2S201E, MRT51, IL1RP1, ACVRLK2, AI1H, SMDCF, MDA5, GFND2, SCN2A1, NENA, SCP, FNZ, VNRA, LACI, EDSVASC, CANDF7, MCH4, MCH5, IDDM12, LETS, PHN, FN, IBP5, IL8RB, R1, APEG1, SLC2C, ATS2, ACHRG, SHIP, APG16L, UGT1, TRPP8, CXCR7, GCF2, SLEB2, HLHB2, DEC1, NDNC3, MYD88D, FEPS2, HSAN7, LAMR1, OIP106, STRA13, SIMA135, RIS1, CMKBR1, CKR3, AGS1, NDNC8, DAG, ARP, CRV, HERNS, SCT, BRCACOX, WS2A, DUTT1, DMT1, THPH5, ESDN, RVCLS, DUM, RELMB, PESCRG1, NORS, FRP, MBS2, STFA, CMT2B, BCPM, NYS8, MCPH19, MMTRA1B, AGTR1A, AREI, BPR105, P2Y12, LINC0883, FIZZ2, ECAT15-2, MIR198, PSS4, STF1, PSN, HHD, OPDD, AT2R1, KIAA0001, BDPLT8, CKR1, CMKBR3, HM145, MDDGA9, MDDGC9, LGMDR16, AOI, CBAS6, CMM8, SAX3, VPS2B, THPH6, COMMAD, CPHD8, FTDALS7, LRS1, PTPN8, HSAN5, GRNG, HJCYS, MCT1D, LYP, CMH20, PSS6
