

Table S1. Information for candidate active compounds of *Brucea javanica* (L.) Merr.

ID	PubChem CID	Name	Candidate Target genes
Y1	985	Palmitic acid	ABAT(0.81), ABL1(1.0), ACADSB(0.81), ACOX1(0.8), ACSL3(0.86), ACSL4(0.86), ADH5(1.0), ALDH5A1(0.81), ARF1(1.0), ARF6(1.0), BEVgp1(1.0), C8G(1.0), CALM1(1.0), CNR1(0.83), CNR2(0.83), cumD(0.85), cyp102A1(0.95), CYP2C8(1.0), cypC(0.95), ECI2(1.0), ELOVL4(0.86), fabB(1.0), fabF(1.0), fabH(1.0), fadR(1.0), FADS1(0.86), FADS2(0.86), FFAR1(0.86), fhuA(1.0), FKBP1A(1.0), FURIN(1.0), gag(1.0), gag-pol(1.0), GLTP(1.0), GM2A(1.0), GUCA1A(1.0), HAO1(0.8), HDAC2(0.81), HDAC9(0.81), HNF4A(1.0), HNF4G(1.0), INS(1.0), LALBA(1.0), LIP3(1.0), lipB(1.0), lpxC(1.0), LTB4R(0.8), LTB4R2(0.8), LTF(1.0), luxF(1.0), LY96(1.0), mdlB(0.8), NCOA1(1.0), nef(1.0), NR1H4(0.95), nrdB(1.0), OGDH(0.8095), pab(1.0), PAEP(1.0), PKIA(1.0), PLA2G1B(1.0), PLA2G2A(1.0), PLA2G2D(1.0), PLA2G2E(1.0), PMP2(1.0), PPARA(1.0), PPARD(0.95), PPARG(1.0), PPA_RS05235(0.95), PPP3CA(1.0), PPP3R1(1.0), PPT1(1.0), PRKACA(1.0), PTGS1(0.95), PTGS2(0.95), pvdQ(1.0), PVgp1(1.0), PVR(1.0), RCVRN(1.0), RHO(1.0), Rv1372(1.0), RXRA(0.95), RXRB(0.81), RXRG(0.81), S100B(0.86), SCN10A(0.81), SCN11A(0.81), SCN1A(0.81), SCN1B(0.81), SCN2A(0.81), SCN2B(0.81), SCN3A(0.81), SCN3B(0.81), SCN4A(0.81), SCN4B(0.81), SCN5A(0.81), SCN7A(0.81), SCN8A(0.81), SCN9A(0.81), SEC14L2(1.0), SLC8A1(0.86), SEREBF1(0.81), tcp14(1.0), tesA(1.0), TLR4(1.0), TM1468(1.0), tonB(1.0), TRAPPC3(1.0), TRPV1(0.86), VLDLR(1.0), ANXA1(0.81), ATP1A1(0.84), ATP1A2(0.82), ATP1A3(0.82), CASP3(0.83), GABRB3(0.86), GLRA3(0.86), HSD11B1(0.83), HSD11B2(0.81), HSD3B1(0.81), LPL(0.83), NFKB1(0.83), NFKB2(0.83), NR3C1(0.81), PPP1CC(0.80), SLCO1B3(0.91), TNF(0.8333), VDR(0.81), YWHAE(0.81)
Y3	-	Aglycone Of Yadanzioides D	ATP1A1(0.81), TRPV1(0.80)
Y4	-	Simaroubolide	ATP1A1(0.8077), PPP1CC(0.8077)
Y5	3084828	Bruceantarin	ATP1A1(0.81), TRPV1(0.807)
Y6	5281305	Bruceantinol	ATP1A1(0.85), CASP3(0.81), GABRB3(0.84), GLRA3(0.84), HSD11B1(0.81), LPL(0.81), NFKB1(0.81), NFKB2(0.82), PPP1CC(0.82), TNF(0.82), TRPV1(0.81)
Y7	101600137	Bruceene	ATP1A(0.81), PPP1CC(0.83)
Y8	161496	Bruceine B	ATP1A1(0.87), GABRB3(0.82), GLRA3(0.82), PPP1CC(0.83), TRPV1(0.82)
Y9	441788	Bruceine D	ATP1A1(0.83), PPP1CC(0.81)

Y1 0	-	Bruceine E 2-B-D-Glucopyranoside	ATP1A1(0.87), ATP1A2(0.85), ATP1A3(0.85), PPP1CC(0.8), SLCO1B3(0.84)
Y1 1	102059835	Bruceine G	ATP1A1 (0.83), PPP1CC (0.83)
Y1 2	21126551	Bruceine I	ATP1A1(0.84), ATP1A2(0.82), ATP1A3(0.8246), GABRB3(0.86) , GLRA3(0.86), NR3C1(0.80), PPP1CC (0.84), SLCO1B3(0.81)
Y1 3	441789	Bruceoside A	ATP1A1(0.83), ATP1A2(0.81), ATP1A3(0.81), GABRB3(0.84), GLRA3 (0.84), SLCO1B3(0.82)
Y1 4	73122	Bruceoside C	ATP1A1(0.84), ATP1A2(0.83), ATP1A3(0.83), GABRB3(0.86), GLRA3 (0.86), SLCO1B3(0.84)
Y1 5	442510	Cleomiscosin A	AHR(0.88), AKR1C3(0.83), ALDH2(0.83), AR(0.80), AURKB(0.88), CBR1(0.83) acrB(0.83), ADH1C(0.83), AKR1C2(0.83), aldA(0.83), cat(0.84), cat3(0.84), cbh(0.83), CES1(0.83), COX4I1(0.83), COX5A(0.83), COX5B(0.83), COX6A2(0.83), COX6B1(0.83), COX6C(0.83), COX7A1(0.83), COX7B(0.83), COX7C(0.83), COX8A(0.83), ctaC(0.83), ctaD(0.83), DKFZp686P18130(0.83), EFTUD1(0.83), ESRRG(0.83), FABP6(0.83), FECH(0.83), fusA(0.84), gag-pol(0.80), GPBAR1(0.83), GSTP1(0.83), HSD11B1(0.80), ksi(0.83), MT-CO1(0.83), MT-CO2(0.8333), MT-CO3(0.83), NR1H4(0.83), NR1I2(0.83), PLA2G1B (0.83), ppcA(0.83)
Y1 6	101109523	Isofouquierone Peroxide	ATP1A1(0.83) , ATP1A2(0.81), ATP1A3(0.81), GABRB3(0.84), GLRA3(0.84), SLCO1B3(0.82)
Y1 7	11169907	Javanicoside B	ATP1A1(0.81), GABRB3(0.86), GLRA3(0.86), SLCO1B3 (0.81)
Y1 8	-	Javanicoside D	ATP1A1(0.84), ATP1A2(0.83), ATP1A3(0.83), GABRB3(0.86), GLRA3(0.86), SLCO1B3 (0.81)
Y1 9	11445415	Javanicoside F	acrB(0.85), ADH1C(0.85), AKR1C1(0.80), AKR1C2(0.85), aldA(0.85), ALOX5(0.83), ANXA1(0.83), AR(0.83), casp8(0.82), cat(0.91) , cat3(0.91), cbh(0.85), CES1(0.85), CLEC4E(0.80), COX4I1(0.85), COX5A(0.85), COX5B(0.85), COX6A2(0.85), COX6B1(0.85), COX6C(0.85), COX7A1(0.85), COX7B(0.85), COX7C(0.85), COX8A(0.85), ctaC(0.85), ctaD(0.85), DKFZp686P18130(0.85), EFTUD1(0.85), ESR1(0.83), ESRRG(0.85), FABP6(0.85), FECH(0.85) , fusA(0.91), gag-pol(0.86) , GPBAR1(0.85), GSTP1(0.85), HMGCR(0.82), HOXA10(0.82) , HSD11B1(0.95), HSD11B2(0.86) , HSD3B1(0.83), IGHG2(0.86), ITGAL(0.81) , ITGB2(0.81), ksi(0.85), LSS(0.83), MT-CO1(0.85), MT-CO2(0.85), MT-CO3(0.85), mvaA(0.82), NCOA2(0.80), ncsA(0.84), NFkB1(0.81), NFkB2(0.81), NPPB(0.83), NR1H4(0.85), NR1I2(0.85), NR1I3(0.80), NR3C1(0.83), NR3C2(0.80), PGR(0.80), PLA2G1B(0.85), ppcA
Y2 0	193076	Macedonic Acid	

			(0.85), PRLR(0.80), PTGS1(0.83), RORA(0.80) , SULT2B1(0.80), VDR(0.83)
			ANXA1(0.80), AR(0.83), ATP1A1(0.81), cat(0.83), cat3(0.83), fus A(0.83), gag-
Y2 1	-	Semialatic Acid	pol(0.83), HSD11B2(0.80), HSD3B1(0.80), IL1B(0.83),IL6(0.83), NFKB1(0.83), NFKB2(0.83), NR3C1(0.81), PPP1CC(0.88), SLCO1B3(0.81), TNF(0.83), VDR (0.80), YWHAE (0.82)
Y2 2	10409280	Yadanziolide C	ATP1A1(0.83 , PPP1CC (0.81)
Y2 3	72952	Yadanzioside B	ATP1A1(0.86), ATP1A2(0.84), ATP1A3(0.84), GABRB3(0.88), G LRA3(0.88), SLCO1B3 (0.86), YWHAE (0.8)
Y2 4	-	Yadanzioside D	ATP1A1(0.84), ATP1A2(0.82), ATP1A3(0.82), GABRB3(0.83), G LRA3(0.83), SLCO1B3(0.81)
Y2 5	3000798	Yadanzioside F	ATP1A1(0.82), ATP1A2(0.81), ATP1A3(0.81), GABRB3(0.81), G LRA3(0.81)
Y2 6	101659162	Yadanzioside H	ATP1A1(0.84), ATP1A2(0.83), ATP1A3(0.83), GABRB3(0.86), G LRA3(0.86), SLCO1B3(0.84)
Y2 7	101659163	Yadanzioside J	ATP1A1(0.84), ATP1A2(0.83), ATP1A3(0.83), GABRB3(0.83), G LRA3(0.83), SLCO1B3(0.84)
Y2 8	21636149	Yadanzioside L	ATP1A1(0.86), ATP1A2(0.84), ATP1A3(0.84), GABRB3(0.88), G LA3 (0.88), SLCO1B3 (0.86), YWHAE (0.80)
Y2 9	101659164	Yadanzioside N	ATP1A1(0.83), ATP1A2(0.81), ATP1A3(0.810), GABRB3(0.84), GLRA3(0.84), SLCO1B3(0.82)
Y3 0	11765370	Yadanzioside P	ATP1A1(0.86), ATP1A2(0.84), ATP1A3(0.84), GABRB3(0.88), G LRA3(0.88), SLCO1B3(0.86), YWHAE (0.80)

Table S2. Information for candidate active compounds of *Curcuma phaeocaulis* val.

ID	PubChem CID	Name	Candidate Target genes
E1	64685	Isoborneol	AKR1D1(0.81), AR(0.84), CACNA1C(0.86), CACNA1D(0.86), C ACNA1F(0.86), CACNA1S(0.86), CACNB1(0.86), CACNB2(0.86) , CACNB3(0.86), CACNB4(0.86), camC(0.83), ESR1(0.81), ESR2(0.81), fabG3(0.81), GABRA1(0.84), GABRA2(0.84), GABRA3(0.84), GABRA4(0.8438), GABRA5(0.84), GABRA6(0.84), GABRB1(0.84), GABRB2(0.84), GABRB3(0.84), GABRD(0.84), GABRE(0.84), GABRG1(0.84), GABRG2(0.84), GABRG3(0.84), GABRP(0.84), GABRQ(0.84), HSD17B1(0.81), HSD17B11(0.81), IGHG2(0.81), LSS(0.80), NR1I3(0.81), NR3C2(0.81), OPRK1(0.86), SULT2A1(0.81), TRPA1(0.86) , TRPM8(0.86), TRPV3 (0.86), VDR(0.82)
E2	11230	Terpinen-4-ol	VDR(0.84)
E3	6448	Bornyl acetate	AR(0.84), camC(0.86), ESR1(0.84) , HSD17B1(0.84), NR3C2(0.84), TRPA1(0.86), TRPM8(0.86), TRPV1(0.86), TRPV3(0.86)

E4	68071	Pinocembrin	ACTB(0.83), AHR(0.83), AKR1C1(1.0), AKT1(0.89), ATP5A1(0.83), ATP5B(0.83), ATP5C1(0.83), CBR1(0.83), CDK6(0.8), CEBPB(0.83), CSNK2A1(0.83), CSNK2B(0.8333), CYP19A1(1.0), CYP1B1(1.0), EIF3F(0.83), ESR1(1.0), ESR2(1.0), ESRRA(0.89), ESRRB(0.89), fabZ(0.89), GPER(0.89), HCK(0.83), HIBCH(0.83), HSP90AA1(0.83), HSPA2(0.83), IGHG1(0.83), JAK1(0.83), KANSL3(1.0), MTTP(0.84), NCOA1(0.89),NCOA2(0.89), NQO2(0.83), NR1I2(0.89), PIK3CG(0.83), PIM1(0.83), PTK2B(0.89), RUVBL2(0.83), SF3B3(0.83), SHBG(1.0), SOAT1(0.84), SOAT2(0.84), STK17B(0.83), TOP2A(0.89), ttgR(1.0), UBA1 (0.83), UGT3A1(0.86)
E5	454	Octanal	ACOT13(0.87), DBI(1.0), RHO(1.0)
E6	8163	2-Undecanone	ACOT13(1.0), DBI(0.87), RHO(0.87)
E7	887	Methanol	MB(1.0)
E8	557157	Bicyclo[3.3.1]nonan-2-ol	ADH1B(0.84)
E9	62367	Sabinene Hydrate	NR1I3 (0.81)
E10	5352470	Humulene epoxide	LCN9 (0.8)
E11	189061	Procurcumenol	AKR1C1(0.84), AKR1C2(0.84), AR(0.86), choB(0.81), ESR1(0.86), ESR2(0.81), GABRA1(0.81), GABRA2(0.81), GABRA3(0.81), GABRA4(0.81), GABRA5(0.81), GABRA6(0.81), GABRB1(0.81), GABRB2(0.81), GABRB3(0.81), GABRD(0.81), GABRE(0.81), GABRG1(0.81), GABRG2(0.81), GABRG3(0.81), GABRP(0.81), GABRQ(0.81), GRIN1(0.81), GRIN2A(0.81), GRIN2B(0.81), GRIN2C(0.81), GRIN2D(0.81), GRIN3A(0.81), GRIN3B(0.81), HSD17B1(0.81), ksi(0.81), LSS(0.82), NCOA2(0.84), NPPB(0.82), NR1I2(0.84), NR1I3(0.81), NR3C2(0.84), PGR(0.84), PPARA(0.81), SIGMAR1(0.81), SULT2A1(0.81),SULT2B1(0.84), VDR (0.83)
E12	568123	2,4-Dimethyl-4-octanol (3Z,7Z)-3,7,10,10-	LCN9(0.84)
E13	5318105	Tetramethyl-12-Oxa-Bicyclo[9.1.0]Deca-3,7-Diene	LCN9(0.80)
E14	561925	3-Ethyl-3-hydroxy-10,13-dimethyl-2,4,5,6,7,8,9,11,12,14,15,16-dodecahydro-1H-cyclopenta[a]phenanthren-17-one	acrB(0.86), ADH1C(0.86), AKR1C1(0.81), AKR1C2(0.86), AKR1D1(0.91), aldA(0.86), AR(0.94), BCL2(0.83), cbh(0.86), CES1(0.86),COX4I1(0.86), COX5A(0.86), COX5B(0.86), COX6A2(0.86), COX6B1(0.86), COX6C(0.86), COX7A1(0.86), COX7B(0.86), COX7C(0.86), COX8A(0.86), ctaC(0.86), ctaD(0.86),DKFZp686P18130(0.86), EFTUD1(0.86), ESR1(0.91), ESR2(0.85), ESRRG(0.86), fabG3(0.91), FABP6(0.86), FECH(0.86), G6PD(0.81), GABRA1(0.94), GABRA2(0.94), GABRA3(0.94), GABRA4(0.94), GABRA5(0.94)

			.94) , GABRA6(0.94), GABRB1(0.94) , GABRB2(0.94), GABRB3(0.94) , GABRD(0.94), GABRE(0.94) , GABRG1(0.94), GABRG2(0.94) , GABRG3(0.94), GABRP(0.94) , GABRQ(0.94), GPBAR1(0.86) , GSTP1(0.86), HSD17B1(0.91), HSD17B11(0.91) , IGHG2(0.91) , ksi(0.86) , MT-CO1(0.86), MT-CO2(0.86) , MT-CO3(0.86), NCOA2(0.82) , NR1H4(0.89), NR1I2(0.86) , NR3C1(0.82), NR3C2(0.91) , PGR(0.81), PLA2G1B(0.86) , ppcA(0.86), SULT2A1(0.91), SULT2B1(0.81) AKR1C1(0.83), AKR1C2(0.83), AR(0.86), choB(0.81), CLEC4E(0.89), ESR1(0.86), ESR2(0.81), GABRA1(0.81), GABRA2(0.81), GABRA3(0.81), GABRA4(0.81), GABRA5(0.81), GABRA6(0.81) , GABRB1(0.81), GABRB2(0.81), GABRB3(0.81), GABRD(0.81), GABRE(0.81), GABRG1(0.81), GABRG2(0.81), GABRG3(0.81), GABRP(0.81), GABRQ(0.81), GRIN1(0.81), GRIN2A(0.81), GRIN2B(0.81), GRIN2C(0.81), GRIN2D(0.81) , GRIN3A(0.81), GRIN3B(0.81), HOXA10(0.80), HSD17B1(0.81), ksi(0.81), LSS(0.91), NCOA2(0.83), NPPB(0.82), NR1I2(0.83), NR1I3(0.89), NR3C2(0.83), PGR(0.83), PPARA(0.81), RORA(0.89), SIGMAR1(0.81) , SULT2A1(0.81) , SULT2B1 (0.83), VDR (0.94)
E15	11770062	Cubenol	
E16	5463721	(3Z,7E)-1,5,5,8-Tetramethyl-12-oxabicyclo[9.1.0]dodeca-3,7-diene	LCN9 (0.8)
E17	11776892	Aerugidiol	AR(0.88), CYP27B1(0.81) , HOXA10(0.86), HSD11B2(0.81), NCOA1(0.83), NPPB(0.88), RXRA(0.81), VDR(0.88)
E18	9992974	(4Ar,5R,5As,6Ar)-6A-Hydroxy-3,5A-Dimethyl-5-(3-Oxobutyl)-4,4A,5,5A,6,6A-Hexahydro-2H-Cyclopropa[F][1]Benzofuran-2-One	AR(0.8), IGHG2(0.83), ncsA(0.80), NR3C2(0.80), PGR (0.80)
E19	7649	Ethyl 3-phenylprop-2-enoate	nprS (0.8)
E20	14543198	Isoprocucumenol	AKR1C1(0.82), AKR1C2(0.82), AR(0.84), ESR1(0.84), NCOA2(0.82), NPPB(0.8), NR1I2(0.82), NR3C2(0.82) , PGR(0.82), SULT2B1(0.82) , VDR(0.85)
E21	10069916	(2,4-Dihydroxy-6-Methoxyphenyl)(3-Methyl-2-(3-Methylbut-2-	PLA2G2E (0.88)

Enyl)-6-
Phenylcyclohex-
3-
Enyl)Methanone

Table S3. Information for candidate active compounds of *Arnebia euchroma*.

ID	PubChem CID	Chemical Component	Candidate Target genes
Z1	689043	Caffeic Acid	CTRB1(0.83), dhbE(0.87), hutH(1.0), LCN2(0.87), MIF(1.0), mn dD(0.8), nahD(0.91), pac(0.8), pcaG(0.8), pcaH(0.8), pyp(1.0), xy nY(0.83), xynZ(0.83)
Z2	9967285	Acetylalkannin	PLA2G2E (0.83)
Z3	5317332	Alkannin Angelate	PLA2G2E (0.81), snoaL (0.81) CYC1(0.84), dsbB(0.84), MT- CYB(0.84), NDUFV3(0.84), petA(0.84), petB(0.84), petC(0.84), p ufC(0.84), pufL(0.84), pufM(0.84), puhA(0.84), sdhA(0.84), SDH A(0.84), sdhB(0.84),sdhC(0.84), sdhD(0.84), sqr(0.84), UQCR10(0.84), UQCR11(0.84), UQCRB(0.84), UQCRC1(0.84), UQCRC2(0.84), UQCRFS1(0.84),UQCRH(0.84),UQCRQ (0.84)
Z4	6505036	Arnebifuranone	
Z5	442720	Alkannin beta, beta- dimethylacrylate	PLA2G2E (0.80), snoaL(0.81)
Z6	5320238	Eicosyl Caffeate	ESR1(0.81), lpxC (0.8)
Z7	5318685	Isovalerylshikonin	snoaL(0.8)
Z8	-	1-Methyl- Acetylshikonin	PLA2G2E (0.83)
Z9	5320237	Octadecanyl Caffeate	ESR1 (0.81), lpxC (0.80)
Z10	5320239	Tetracosyl Caffeate	ESR1 (0.81), lpxC (0.80)

Table S4. Threshold setup

Parameters/Thresholds	Description
Threshold of Tanimoto score	0.8, which can guarantee a high similarity between the compound and the known drug.
Threshold of PPI scores	0.9, which is the highest confidence.
Threshold of degree and BC	Degree ≥ 6 and BC ≥ 0.036 , respectively represent the upper quarter.
Threshold of FDR for GO	10^{-10}
Threshold of FDR for KEGG	10^{-5}

Table S5. GO biological process enrichment analysis.

GO-term	Description	Count in gene set	FDR
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GO:0014070	response to organic cyclic compound	51/873	1.33E-32
GO:1901700	response to oxygen-containing compound	60/1427	2.00E-32
GO:0033993	response to lipid	48/825	1.17E-30
GO:0010033	response to organic substance	74/2815	1.43E-29
GO:0071407	cellular response to organic cyclic compound	39/505	1.75E-28
GO:0009719	response to endogenous stimulus	54/1353	1.08E-27
GO:0009725	response to hormone	45/854	5.50E-27
GO:0071495	cellular response to endogenous stimulus	46/1106	1.56E-23
GO:0065008	regulation of biological quality	74/3559	2.41E-23
GO:0042221	response to chemical	79/4153	2.64E-23
GO:0071396	cellular response to lipid	34/486	2.64E-23
GO:0070887	cellular response to chemical stimulus	65/2672	4.39E-23
GO:0071310	cellular response to organic substance	60/2219	4.78E-23
GO:0048545	response to steroid hormone	29/324	2.09E-22
GO:0032870	cellular response to hormone stimulus	33/585	6.28E-20
GO:0009636	response to toxic substance	30/468	2.14E-19
GO:0009893	positive regulation of metabolic process	66/3280	3.95E-19
GO:0048518	positive regulation of biological process	83/5459	1.07E-18
GO:0031325	positive regulation of cellular metabolic process	63/3060	1.90E-18
GO:0048522	positive regulation of cellular process	78/4898	4.55E-18
GO:0051049	regulation of transport	48/1732	7.56E-18
GO:0051173	positive regulation of nitrogen compound metabolic process	61/2946	8.24E-18
GO:1901701	cellular response to oxygen-containing compound	36/896	1.68E-17
GO:0071383	cellular response to steroid hormone stimulus	21/197	2.47E-17
GO:0050896	response to stimulus	96/7824	2.65E-17
GO:0010941	regulation of cell death	46/1638	3.10E-17
GO:0010243	response to organonitrogen compound	35/876	6.22E-17
GO:0042493	response to drug	35/900	1.37E-16
GO:0032879	regulation of localization	55/2524	1.49E-16
GO:0032501	multicellular organismal process	86/6507	7.06E-16
GO:0030522	intracellular receptor signaling pathway	19/173	7.07E-16
GO:0051716	cellular response to stimulus	84/6212	7.31E-16
GO:0007154	cell communication	77/5219	7.86E-16
GO:0023052	signaling	76/5108	1.02E-15
GO:0051239	regulation of multicellular organismal process	56/2788	1.96E-15
GO:0009605	response to external stimulus	46/1857	2.71E-15
GO:2000377	regulation of reactive oxygen species metabolic process	18/169	7.56E-15
GO:0009755	hormone-mediated signaling pathway	18/171	8.91E-15
GO:0042981	regulation of apoptotic process	41/1501	9.85E-15
GO:0010817	regulation of hormone levels	26/511	1.34E-14
GO:0032768	regulation of monooxygenase activity	13/56	2.06E-14

GO:0010604	positive regulation of macromolecule metabolic process	57/3081	2.89E-14
GO:0043401	steroid hormone mediated signaling pathway	16/131	5.14E-14
GO:0046677	response to antibiotic	21/305	5.14E-14
GO:0031328	positive regulation of cellular biosynthetic process	44/1846	5.71E-14
GO:0032101	regulation of response to external stimulus	29/732	8.59E-14
GO:0043269	regulation of ion transport	27/618	9.76E-14
GO:0007165	signal transduction	70/4738	9.77E-14
GO:0008202	steroid metabolic process	19/248	2.00E-13
GO:0042592	homeostatic process	39/1491	2.17E-13
GO:1903428	positive regulation of reactive oxygen species biosynthetic process	12/51	2.17E-13
GO:2000379	positive regulation of reactive oxygen species metabolic process	14/94	2.59E-13
GO:0048523	negative regulation of cellular process	67/4454	2.84E-13
GO:0050727	regulation of inflammatory response	21/338	2.84E-13
GO:0009628	response to abiotic stimulus	33/1052	3.50E-13
GO:0048583	regulation of response to stimulus	62/3882	4.72E-13
GO:0006811	ion transport	36/1292	4.87E-13
GO:1903426	regulation of reactive oxygen species biosynthetic process	13/77	5.54E-13
GO:0065009	regulation of molecular function	57/3322	5.94E-13
GO:0048519	negative regulation of biological process	70/4953	8.60E-13
GO:0051050	positive regulation of transport	30/892	1.26E-12
GO:0019216	regulation of lipid metabolic process	21/373	1.54E-12
GO:0048584	positive regulation of response to stimulus	44/2054	1.77E-12
GO:0051234	establishment of localization	64/4248	1.77E-12
GO:0006810	transport	63/4130	1.85E-12
GO:0062012	regulation of small molecule metabolic process	20/332	1.92E-12
GO:0006954	inflammatory response	23/482	2.05E-12
GO:0071417	cellular response to organonitrogen compound	23/485	2.29E-12
GO:0010646	regulation of cell communication	56/3327	2.40E-12
GO:0055114	oxidation-reduction process	30/923	2.62E-12
GO:0010647	positive regulation of cell communication	39/1631	2.72E-12
GO:0010942	positive regulation of cell death	26/663	2.72E-12
GO:0023056	positive regulation of signaling	39/1638	3.03E-12
GO:0051179	localization	71/5233	3.22E-12
GO:0023051	regulation of signaling	56/3360	3.39E-12
GO:0003008	system process	41/1827	3.61E-12
GO:0031347	regulation of defense response	26/676	3.86E-12
GO:0032502	developmental process	72/5401	4.11E-12
GO:0006950	response to stress	55/3267	4.14E-12
GO:0045944	positive regulation of transcription by RNA polymerase II	32/1104	5.73E-12

GO:0042127	regulation of cell population proliferation	38/1594	6.16E-12
GO:0042391	regulation of membrane potential	21/408	6.16E-12
GO:0097305	response to alcohol	17/233	8.25E-12
GO:0080134	regulation of response to stress	34/1299	1.32E-11
GO:0051240	positive regulation of multicellular organismal process	37/1551	1.35E-11
GO:0048878	chemical homeostasis	30/995	1.40E-11
GO:0002682	regulation of immune system process	35/1391	1.58E-11
GO:0043066	negative regulation of apoptotic process	28/859	1.61E-11
GO:0006952	defense response	33/1234	1.73E-11
GO:0050793	regulation of developmental process	46/2416	1.75E-11
GO:0051704	multi-organism process	44/2222	1.90E-11
GO:0045429	positive regulation of nitric oxide biosynthetic process	10/42	2.42E-11
GO:1904407	positive regulation of nitric oxide metabolic process	10/42	2.42E-11
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	39/1770	2.61E-11
GO:0009892	negative regulation of metabolic process	49/2762	2.63E-11
GO:0032496	response to lipopolysaccharide	18/298	2.71E-11
GO:0060548	negative regulation of cell death	29/953	2.71E-11
GO:0044237	cellular metabolic process	92/8797	2.88E-11
GO:0031324	negative regulation of cellular metabolic process	46/2463	3.13E-11
GO:0048856	anatomical structure development	68/5085	3.21E-11
GO:0031323	regulation of cellular metabolic process	75/6082	3.56E-11
GO:0044092	negative regulation of molecular function	31/1119	3.76E-11
GO:0009410	response to xenobiotic stimulus	17/262	3.91E-11
GO:0080090	regulation of primary metabolic process	74/5982	5.19E-11
GO:0034762	regulation of transmembrane transport	22/524	5.78E-11
GO:0010557	positive regulation of macromolecule biosynthetic process	38/1758	8.97E-11
GO:0071704	organic substance metabolic process	93/9135	8.97E-11
GO:0009967	positive regulation of signal transduction	35/1493	9.18E-11
GO:0050790	regulation of catalytic activity	43/2249	1.04E-10
GO:0019222	regulation of metabolic process	77/6516	1.08E-10
GO:0006367	transcription initiation from RNA polymerase II promoter	14/162	1.14E-10
GO:0062013	positive regulation of small molecule metabolic process	13/129	1.16E-10
GO:0044281	small molecule metabolic process	38/1779	1.20E-10
GO:0002376	immune system process	44/2370	1.33E-10
GO:1902533	positive regulation of intracellular signal transduction	28/959	1.59E-10
GO:0006629	lipid metabolic process	31/1192	1.63E-10
GO:0003006	developmental process involved in reproduction	23/622	1.83E-10
GO:0007584	response to nutrient	15/208	1.94E-10

GO:0051091	positive regulation of DNA-binding transcription factor activity	16/250	1.99E-10
GO:0051707	response to other organism	26/835	2.54E-10
GO:0051090	regulation of DNA-binding transcription factor activity	19/403	2.87E-10
GO:0065007	biological regulation	105/11740	3.58E-10
GO:0044238	primary metabolic process	90/8808	3.83E-10
GO:0060135	maternal process involved in female pregnancy	10/60	4.03E-10
GO:0009987	cellular process	116/14652	4.27E-10
GO:0051247	positive regulation of protein metabolic process	35/1587	4.27E-10
GO:0006796	phosphate-containing compound metabolic process	40/2065	4.76E-10
GO:0008152	metabolic process	94/9569	4.90E-10
GO:0007275	multicellular organism development	63/4726	4.91E-10
GO:1901615	organic hydroxyl compound metabolic process	19/420	5.31E-10
GO:0045595	regulation of cell differentiation	36/1695	5.47E-10
GO:0048513	animal organ development	48/2926	6.16E-10
GO:0045893	positive regulation of transcription, DNA-templated	33/1435	6.17E-10
GO:0043065	positive regulation of apoptotic process	22/604	6.44E-10
GO:0051172	negative regulation of nitrogen compound metabolic process	42/2307	7.92E-10
GO:0048731	system development	58/4144	8.45E-10
GO:0051094	positive regulation of developmental process	31/1286	8.90E-10
GO:0051924	regulation of calcium ion transport	15/236	8.90E-10
GO:0050999	regulation of nitric-oxide synthase activity	9/45	9.19E-10
GO:0009617	response to bacterium	21/555	9.40E-10

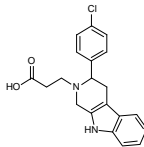
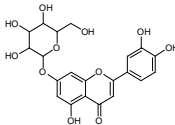
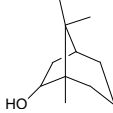
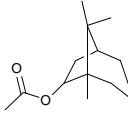
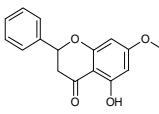
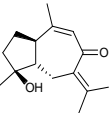
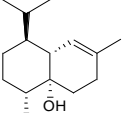
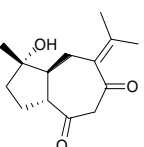
Table S6. KEGG pathway enrichment analysis.

Pathway	Description	Count in gene set	FDR
hsa04932	Non-alcoholic fatty liver disease (NAFLD)	17/149	4.49E-14
hsa05010	Alzheimer's disease	17/168	1.41E-13
hsa05152	Tuberculosis	16/172	2.30E-12
hsa05200	Pathways in cancer	23/515	7.92E-12
hsa05134	Legionellosis	11/54	8.06E-12
hsa04915	Estrogen signaling pathway	12/133	3.13E-09
hsa04919	Thyroid hormone signaling pathway	11/115	9.61E-09
hsa05016	Huntington's disease	13/193	1.10E-08
hsa04657	IL-17 signaling pathway	10/92	1.59E-08
hsa04913	Ovarian steroidogenesis	8/49	4.37E-08
hsa05014	Amyotrophic lateral sclerosis (ALS)	8/50	4.59E-08
hsa05161	Hepatitis B	11/142	4.59E-08
hsa05167	Kaposi's sarcoma-associated herpesvirus infection	12/183	4.59E-08
hsa05145	Toxoplasmosis	10/109	4.68E-08
hsa04024	cAMP signaling pathway	12/195	7.16E-08

hsa05169	Epstein-Barr virus infection	12/194	7.16E-08
hsa00140	Steroid hormone biosynthesis	8/58	8.54E-08
hsa04064	NF-kappa B signaling pathway	9/93	1.52E-07
hsa05162	Measles	10/133	2.05E-07
hsa04659	Th17 cell differentiation	9/102	2.88E-07
hsa05012	Parkinson's disease	10/142	3.33E-07
hsa05133	Pertussis	8/74	3.78E-07
hsa04668	TNF signaling pathway	9/108	3.98E-07
hsa04022	cGMP-PKG signaling pathway	10/160	8.41E-07
hsa05164	Influenza A	10/168	1.24E-06
hsa05222	Small cell lung cancer	8/92	1.53E-06
hsa05146	Amoebiasis	8/94	1.71E-06
hsa05418	Fluid shear stress and atherosclerosis	9/133	1.74E-06
hsa04714	Thermogenesis	11/228	1.86E-06
hsa04720	Long-term potentiation	7/64	1.92E-06
hsa05168	Herpes simplex infection	10/181	1.93E-06
hsa05031	Amphetamine addiction	7/65	1.98E-06
hsa05203	Viral carcinogenesis	10/183	2.00E-06
hsa04151	PI3K-Akt signaling pathway	13/348	2.04E-06
hsa04261	Adrenergic signaling in cardiomyocytes	9/139	2.04E-06
hsa05140	Leishmaniasis	7/70	2.80E-06
hsa04015	Rap1 signaling pathway	10/203	4.42E-06
hsa04260	Cardiac muscle contraction	7/76	4.45E-06
hsa05204	Chemical carcinogenesis	7/76	4.45E-06
hsa05144	Malaria	6/47	4.72E-06
hsa04114	Oocyte meiosis	8/116	5.08E-06
hsa04621	NOD-like receptor signaling pathway	9/166	6.78E-06
hsa04380	Osteoclast differentiation	8/124	7.78E-06
hsa04014	Ras signaling pathway	10/228	1.02E-05
hsa01100	Metabolic pathways	23/1250	1.05E-05
hsa04010	MAPK signaling pathway	11/293	1.25E-05
hsa04213	Longevity regulating pathway - multiple species	6/61	1.63E-05
hsa05215	Prostate cancer	7/97	1.63E-05
hsa04933	AGE-RAGE signaling pathway in diabetic complications	7/98	1.69E-05
hsa05034	Alcoholism	8/142	1.74E-05
hsa05142	Chagas disease (American trypanosomiasis)	7/101	1.93E-05
hsa05166	HTLV-I infection	10/250	1.93E-05
hsa04620	Toll-like receptor signaling pathway	7/102	2.01E-05
hsa05165	Human papillomavirus infection	11/317	2.21E-05
hsa04921	Oxytocin signaling pathway	8/149	2.22E-05
hsa04931	Insulin resistance	7/107	2.56E-05
hsa04917	Prolactin signaling pathway	6/69	2.60E-05
hsa04920	Adipocytokine signaling pathway	6/69	2.60E-05
hsa00980	Metabolism of xenobiotics by cytochrome P450	6/70	2.72E-05

hsa01524	Platinum drug resistance	6/70	2.72E-05
hsa04976	Bile secretion	6/71	2.84E-05
hsa05033	Nicotine addiction	5/40	2.90E-05
hsa04080	Neuroactive ligand-receptor interaction	10/272	3.20E-05
hsa05202	Transcriptional misregulation in cancer	8/169	4.61E-05
hsa04961	Endocrine and other factor-regulated calcium reabsorption	5/47	5.70E-05
hsa04911	Insulin secretion	6/84	6.46E-05
hsa05323	Rheumatoid arthritis	6/84	6.46E-05
hsa05030	Cocaine addiction	5/49	6.56E-05
hsa00190	Oxidative phosphorylation	7/131	7.27E-05
hsa04211	Longevity regulating pathway	6/88	7.81E-05
hsa04210	Apoptosis	7/135	8.50E-05
hsa04923	Regulation of lipolysis in adipocytes	5/53	8.81E-05

Table S7. The results of molecular docking of potential compounds in the sites of proteins (PDB ID: 5AAU, 2AZ5, 3OCB and 4KIK) performed using Autodock Vina.

Target	Ligand	Structure	ΔG (kcal/mol)	Ref.
ESR1	XBR		-7.9	[1]
	Y20		-8.2	
	E1		-5.5	
	E3		-6.5	
	E4		-8.6	
	E11		-7.9	
	E15		-7.8	
	E20		-7.7	

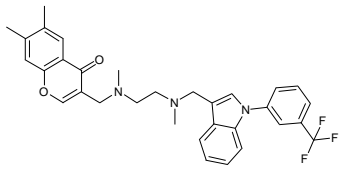
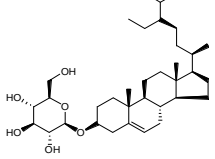
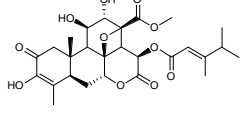
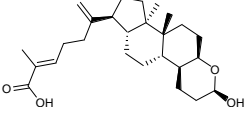
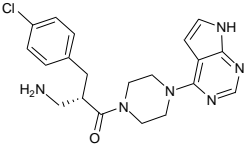
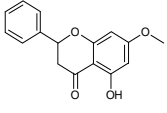
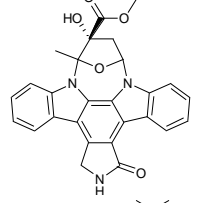
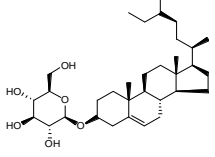
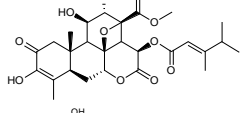
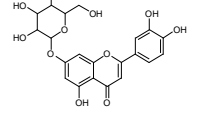
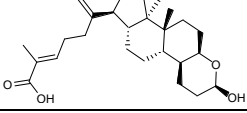
TNF	307		-7.9	[2]
	Y2		-8.3	
	Y6		-7.0	
	Y21		-8.4	
AKT1	XM1		-8.9	[3]
	E4		-8.2	
NFKB1	Compound 5		-8.8	[4]
	Y2		-9.2	
	Y6		-7.8	
	Y20		-8.7	
	Y21		-7.4	

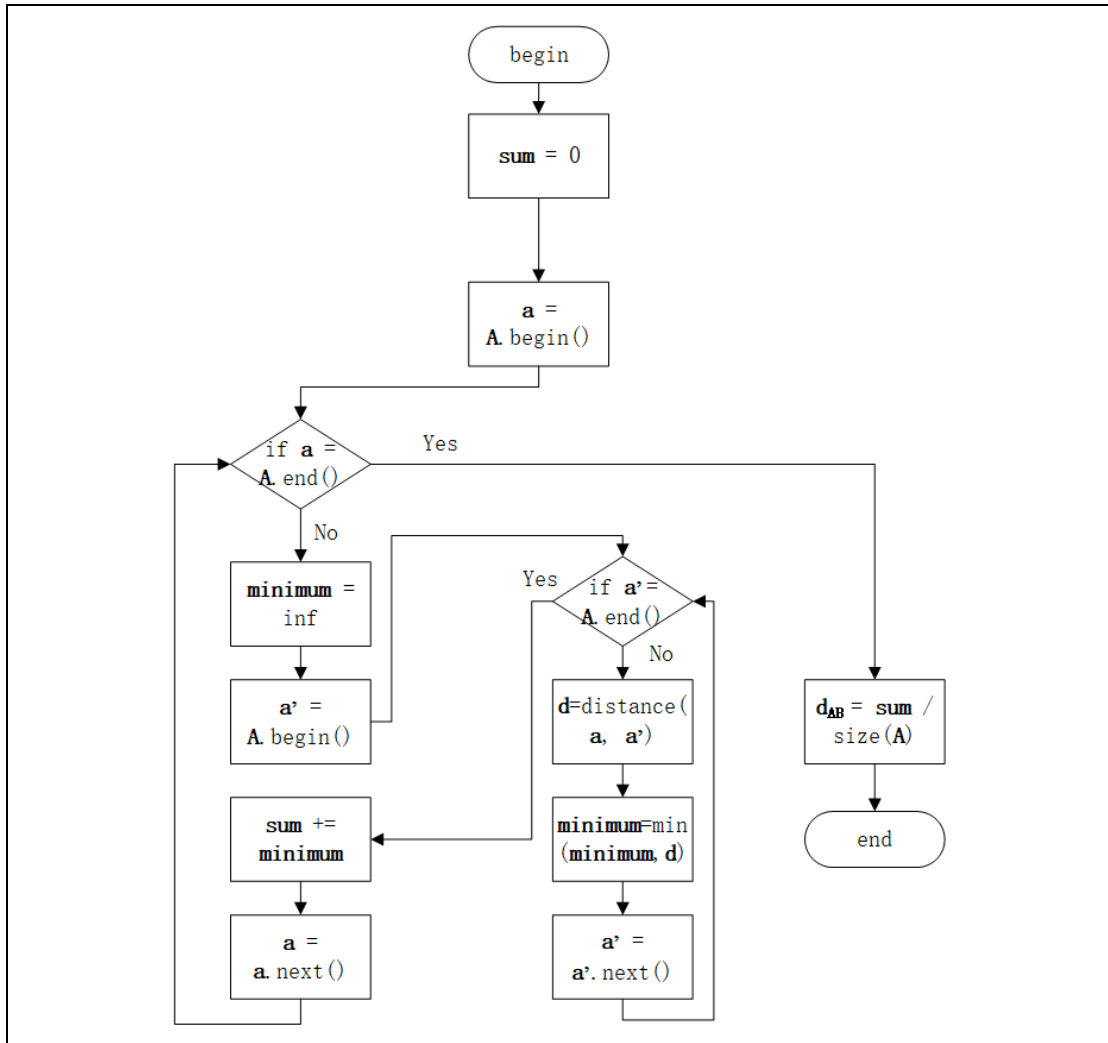
Table S8. pseudocode to compute $\langle d_{AB} \rangle$, $\langle d_{AA} \rangle$

Input: network G, node set A, node set B

Output: d_{AB}

```
1  sum = 0
2  for a in A:
3      minimum = ∞
4      for b in B:
5          d = distance(G, a, b)
6          minimum = min(minimum, d)
7          sum += minimum
8  for b in B:
9      minimum = ∞
10     for a in A:
11         d = distance(G, a, b)
12         minimum = min(minimum, d)
13         sum += minimum
14  dAB = sum / (size(A)+size(B))
```

Flowchart

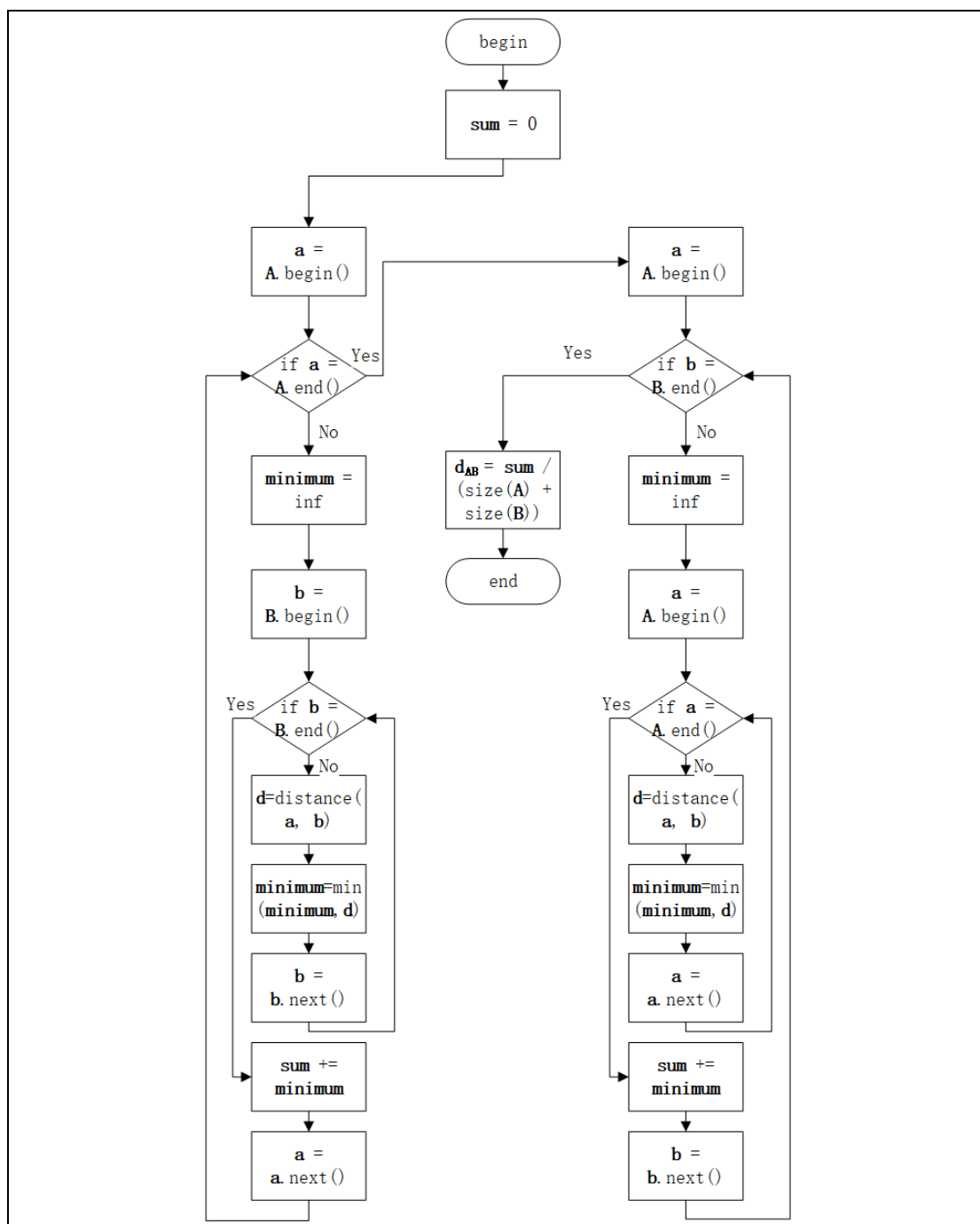


Input: network G, node set A

Output: d_{AA}

- 1 `sum = 0`
- 2 **for** a **in** A:
- 3 `minimum = ∞`
- 4 **for** a' **in** A:
- 5 **if** a != a':
- 6 `d = distance(G, a, a')`
- 7 `minimum = min(minimum, d)`
- 8 `sum += minimum`
- 9 `dAA = sum / (size(A))`

Flowchart



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