# Systems pharmacology exploration of botanic drug pairs reveals the mechanism for treating different diseases

Wei Zhou[a,b,c,d] , Jinan Wang[a], ZiyinWu[a], Chao Huang[a] , Aiping Lu[c,d], YonghuaWang[a,b,*]

[a] Key Laboratory of Xinjiang Endemic Phytomedicine Resources, Ministry of Education; Pharmacology Department, School of Pharmacy, Shihezi University, Shihezi, Xinjiang, China.

[b] Center of Bioinformatics, Northwest A & F University, Yangling 712100, Shaanxi, China.

[c] Institute of Arthritis Research, Shanghai Academy of Chinese Medical Sciences, Guanghua Integrative Medicine Hospital / Shanghai University of T.C.M, Shanghai 200052, China.

[d] Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing 100700, China.

*Corresponding author: YH Wang: dcpwyh@163.com. Tel. & Fax: +86-029-87092262.

## Supplementary table legends

**Table S1** The computational efficiency of algorithms used in our strategy.

**Table S2** 92 active compounds from three Danshen herb pairs and corresponding predicted OB, DL and DHL.

**Table S3** All compounds, targets and related diseases information of three Danshen herb pairs.

**Table S4** 70 active compounds in four herbs and the corresponding calculated OB, DL and HL.

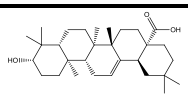
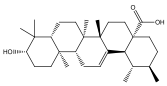
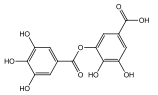
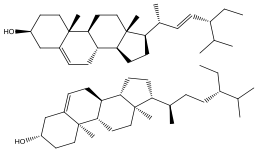
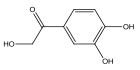
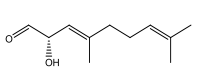
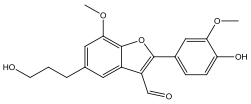
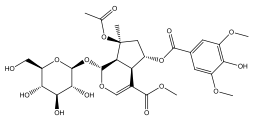
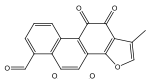
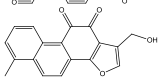
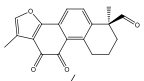
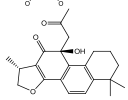
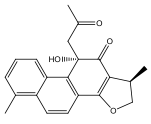
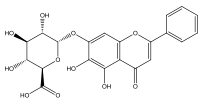
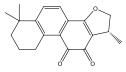
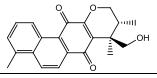
**Table S5** Enriched PCA-related molecular properties terms of three Danshen herb pairs.

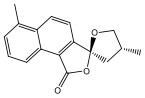
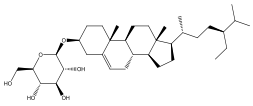
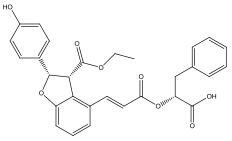
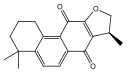
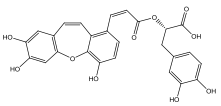
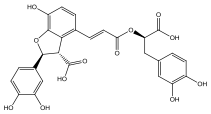
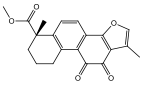
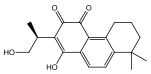
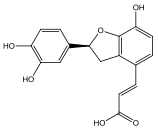
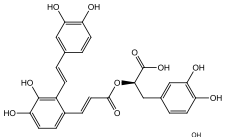
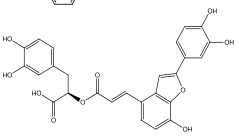
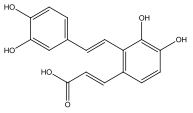
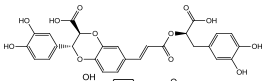
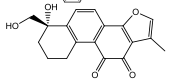
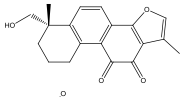
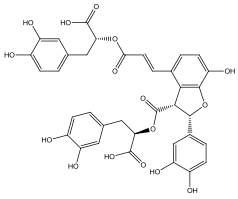
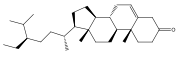
**Table S6** The information of compound-target-disease network in three Danshen herb pairs.

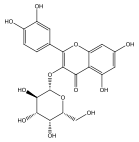
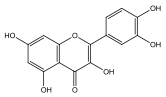
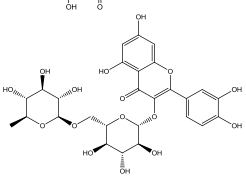
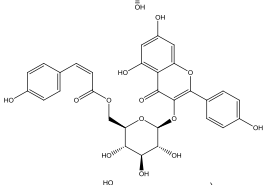
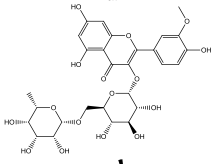
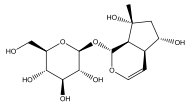
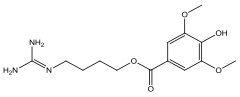
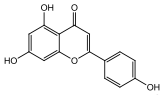
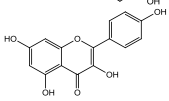
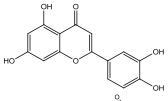
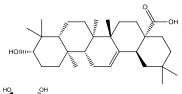
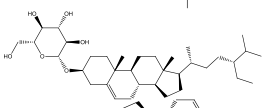
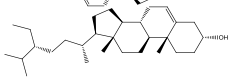
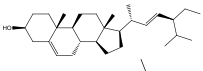
Table S1 The computational efficiency of algorithms used in our strategy.

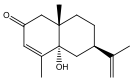
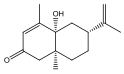
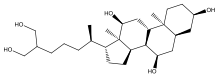
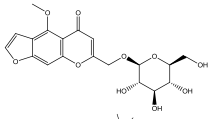
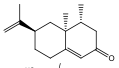
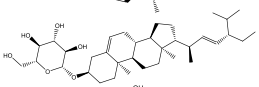
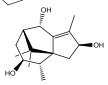
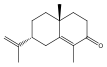
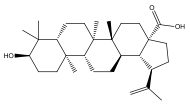
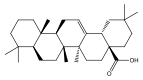
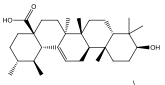
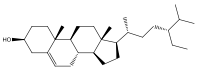
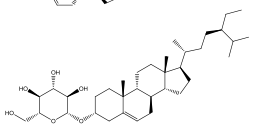
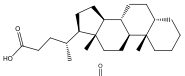
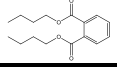
| Algorithm | Software/Language | CPU Type | CPU Time | Memory |
|---|---|---|---|---|
| OB | Matlab | 16 core 3.2G Hz | < 30 minutes | 8G |
| DL | Matlab | 16 core 3.2G Hz | < 5 minutes | 8G |
| HL | Matlab | 16 core 3.2G Hz | < 5 minutes | 8G |
| SVM/RF | Matlab | 16 core 3.2G Hz | < 4 hour | 8G |
| Docking | Autodock | 16 core 3.2G Hz | < 50 hour | 8G |
| MD | Amber 10 | 16 core 3.2G Hz | ～1 month | 32 * 16 node |

Table S4 70 active compounds in four herbs and the corresponding calculated OB, DL and HL.

| NO. | Compound | Structure | OB | DL | HL | Herbs |
|---|---|---|---|---|---|---|
| DS1 | oleanolic acid |  | 29.02 | 0.76 | 4.56 | *S.miltiorrhizae* |
| DS2 | ursolic acid |  | 16.77 | 0.75 | 4.73 | *S.miltiorrhizae* |
| DS3 | digallic acid |  | 61.85 | 0.26 | 5.29 | *S.miltiorrhizae* |
| DS4 | stigmasterol |  | 43.83 | 0.76 | 5.34 | *S.miltiorrhizae* |
| DS5 | gamma-sitosterol | | 36.91 | 0.75 | 5.07 | *S.miltiorrhizae* |
| DS11 | 1-(3,4-dihydroxyphenyl)-2-hydroxyethanone |  | 56.79 | 0.04 | 17.93 | *S.miltiorrhizae* |
| DS12 | 3,7-dimethylocta-2,6-dien-1-yl formate |  | 50.95 | 0.03 | 7.13 | *S.miltiorrhizae* |
| DS14 | 2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-3-benzofurancarboxaldehyde |  | 62.78 | 0.40 | 7.89 | *S.miltiorrhizae* |
| DS15 | 6-o-syringyl-8-o-acetyl shanzhiside methyl ester |  | 46.69 | 0.71 | 9.94 | *S.miltiorrhizae* |
| DS16 | formyltanshinone |  | 73.44 | 0.42 | 24.12 | *S.miltiorrhizae* |
| DS17 | przewaquinone B |  | 62.24 | 0.41 | 24.94 | *S.miltiorrhizae* |
| DS19 | tanshinaldehyde |  | 52.47 | 0.45 | 23.49 | *S.miltiorrhizae* |
| DS20 | tanshinol Ⅱ |  | 57.95 | 0.56 | 4.28 | *S.miltiorrhizae* |
| DS21 | tanshinol Ⅰ |  | 56.97 | 0.52 | 5.15 | *S.miltiorrhizae* |
| DS22 | baicalin |  | 10.21 | 0.75 | 15.46 | *S.miltiorrhizae* |
| DS23 | cryptotanshinone |  | 52.34 | 0.40 | 17.30 | *S.miltiorrhizae* |
| DS24 | dan-shexinkum d |  | 38.88 | 0.55 | 30.00 | *S.miltiorrhizae* |

| | | | | | | |
|---|---|---|---|---|---|---|
| DS25 | danshen spiroketal lactone |  | 50.43 | 0.31 | 15.19 | *S.miltiorrhizae* |
| DS26 | daucosterol |  | 36.91 | 0.63 | 9.46 | *S.miltiorrhizae* |
| DS28 | ethyl lithospermate |  | 26.37 | 0.82 | 15.32 | *S.miltiorrhizae* |
| DS29 | isocryptotanshinone |  | 54.98 | 0.39 | 31.92 | *S.miltiorrhizae* |
| DS30 | isosalvianolic acid c |  | 2.48 | 0.83 | 5.91 | *S.miltiorrhizae* |
| DS31 | lithospermic acid |  | 2.67 | 0.76 | 15.68 | *S.miltiorrhizae* |
| DS32 | methyltanshinonate |  | 19.19 | 0.55 | 24.11 | *S.miltiorrhizae* |
| DS33 | neocryptotanshinone |  | 52.49 | 0.32 | 14.46 | *S.miltiorrhizae* |
| DS34 | prolithospermic acid |  | 64.37 | 0.31 | 8.82 | *S.miltiorrhizae* |
| DS35 | salvianolic acid A |  | 2.96 | 0.70 | 5.21 | *S.miltiorrhizae* |
| DS36 | salvianolic acid C |  | 2.50 | 0.81 | 13.62 | *S.miltiorrhizae* |
| DS37 | (Z)-3-[2-[(E)-2-(3,4-dihydroxyphenyl)vinyl]-3,4-dihydroxy-phenyl]acrylic acid |  | 88.54 | 0.26 | 4.31 | *S.miltiorrhizae* |
| DS38 | salvianolic acid j |  | 43.38 | 0.72 | 5.77 | *S.miltiorrhizae* |
| DS39 | tanshindiol a |  | 75.39 | 0.46 | 23.45 | *S.miltiorrhizae* |
| DS40 | tanshinone Ⅱb |  | 65.26 | 0.45 | 23.48 | *S.miltiorrhizae* |
| DS41 | salvianolic acid B |  | 3.01 | 0.41 | 18.53 | *S.miltiorrhizae* |
| YMC1 | beta-sitosterone |  | 38.00 | 0.76 | 5.45 | *H. leonuri* |

| | | | | | | |
|---|---|---|---|---|---|---|
| YMC2 | (−)-alloaromad endrene |  | 54.04 | 0.10 | 12.06 | *H. leonuri* |
| YMC3 | quercetin-3-o-galactopyranoside |  | 56.53 | 0.77 | 17.47 | *H. leonuri* |
| YMC4 | quercitin |  | 46.43 | 0.77 | 14.40 | *H. leonuri* |
| YMC5 | rutin |  | 46.43 | 0.68 | 16.13 | *H. leonuri* |
| YMC6 | tiliroside |  | 1.94 | 0.66 | 16.51 | *H. leonuri* |
| YMC7 | Isorhamnetin-3-o-beta-d-rutinoside |  | 62.00 | 0.65 | 13.95 | *H. leonuri* |
| YMC8 | leonuridine |  | 106.15 | 0.33 | 6.42 | *H. leonuri* |
| YMC9 | leonurine |  | 19.12 | 0.20 | 4.71 | *H. leonuri* |
| YMC10 | apigenin |  | 69.81 | 0.21 | 16.62 | *H. leonuri* |
| YMC11 | kaempferol |  | 69.31 | 0.24 | 12.68 | *H. leonuri* |
| XF1 | luteolin |  | 36.16 | 0.78 | 15.94 | *C.rotundus* |
| XF4 | oleanolic acid |  | 29.02 | 0.76 | 4.56 | *C.rotundus* |
| XF5 | daucosterol |  | 36.91 | 0.62 | 10.12 | *C.rotundus* |
| XF6 | β-sitosterol |  | 36.91 | 0.75 | 5.37 | *C.rotundus* |
| XF7 | stigmasterol |  | 43.83 | 0.76 | 5.57 | *C.rotundus* |
| XF9 | isocurcumenol |  | 97.67 | 0.13 | 9.52 | *C.rotundus* |

| | | | | | | |
|---|---|---|---|---|---|---|
| XF11 | (4aS,6R,8aS)-4a-hydroxy-4,8a-dimethyl-6-prop-1-en-2-yl-5,6,7,8-tetrahydro-1H-naphthalen-2-one |  | 53.42 | 0.12 | 6.42 | *C.rotundus* |
| XF12 | beta-Rotunol |  | 59.69 | 0.12 | 6.63 | *C.rotundus* |
| XF14 | (-)-dehydroaromadendrene |  | 53.59 | 0.10 | 11.69 | *C.rotundus* |
| XF15 | 5beta-Cyprinol |  | 12.57 | 0.83 | 6.20 | *C.rotundus* |
| XF16 | guaidiol |  | 72.00 | 0.11 | 8.86 | *C.rotundus* |
| XF18 | khelloside |  | 74.96 | 0.72 | 14.34 | *C.rotundus* |
| XF19 | ledane |  | 52.82 | 0.10 | 11.80 | *C.rotundus* |
| XF20 | nootkatene |  | 33.13 | 0.71 | 7.07 | *C.rotundus* |
| XF21 | nootkatone |  | 33.04 | 0.75 | 4.39 | *C.rotundus* |
| XF23 | rotundenol |  | 74.95 | 0.84 | 7.51 | *C.rotundus* |
| XF24 | stigmasterol glucoside |  | 43.83 | 0.63 | 7.69 | *C.rotundus* |
| XF25 | sugetriol |  | 68.87 | 0.16 | 8.51 | *C.rotundus* |
| XF26 | alpha-cyperone |  | 35.37 | 0.10 | 5.49 | *C.rotundus* |
| ZL1 | epibetulinic acid |  | 15.66 | 0.78 | 8.62 | *E.japonicum* |
| ZL2 | oleanolic acid |  | 17.74 | 0.76 | 4.83 | *E.japonicum* |
| ZL3 | ursolic acid |  | 17.70 | 0.76 | 4.86 | *E.japonicum* |
| ZL4 | β-sitosterol |  | 36.91 | 0.75 | 5.36 | *E.japonicum* |
| ZL5 | daucosterol |  | 36.91 | 0.63 | 6.88 | *E.japonicum* |
| ZL6 | cholanic acid |  | 18.95 | 0.59 | 5.27 | *E.japonicum* |
| ZL7 | dibutyl phthalate |  | 64.54 | 0.13 | 5.41 | *E.japonicum* |