

Network-pharmacology-based validation of TAMS/CXCL-1 as key mediator of XIAOPI formula preventing breast cancer development and metastasis

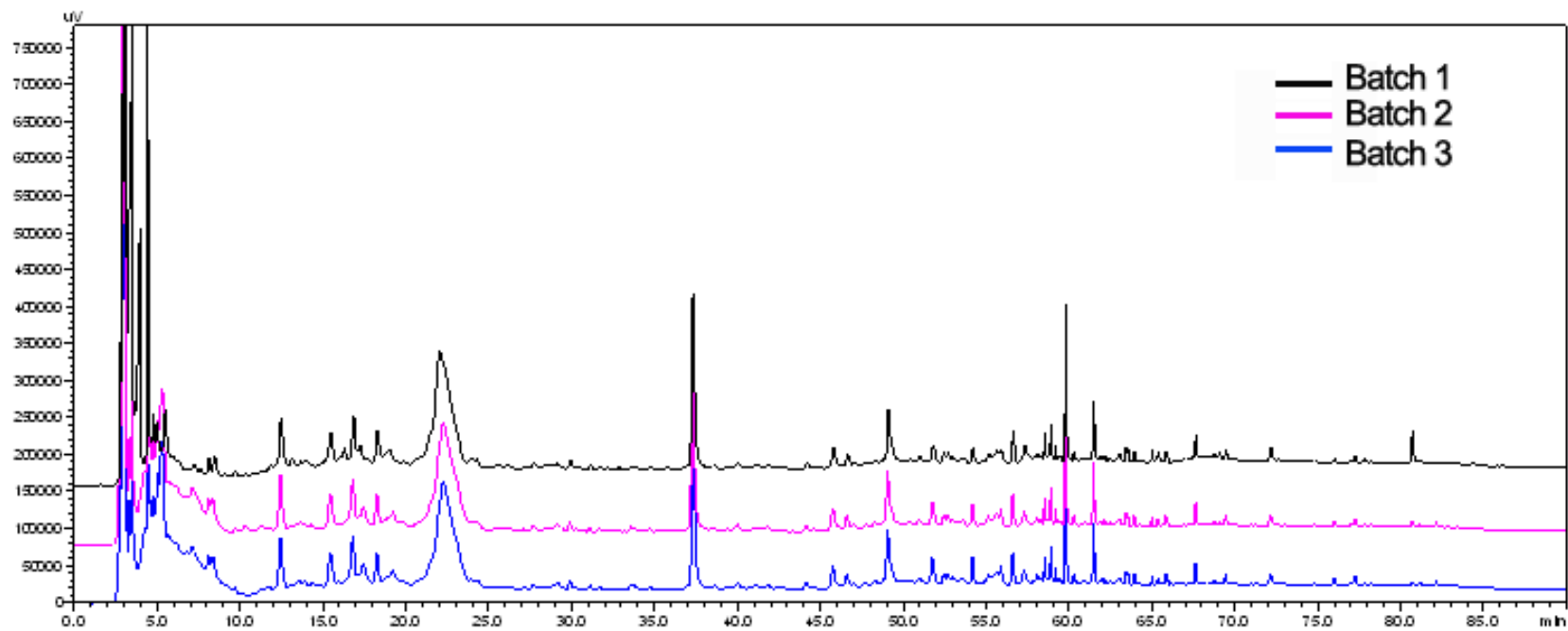
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Supplementary Figure 1

Supplementary Figure 1 Chemical fingerprints remains consistent between 3 batches of XIOPI formula.

	A	B	C	D	E	F	G	H	I	J	K	L
1	POS	POS	NEG	NEG	6Ckine	CTACK	Eotaxin-1	G-CSF	GM-CSF	IL-2	IL-3	IL-4
2	POS	POS	NEG	NEG	6Ckine	CTACK	Eotaxin-1	G-CSF	GM-CSF	IL-2	IL-3	IL-4
3	IL-5	IL-6	IL-9	IL-10	IL12p40/70	IL-12p70	IL-13	IL-17	IFN gamma	KC	Leptin	MCP-1
4	IL-5	IL-6	IL-9	IL-10	IL12p40/70	IL-12p70	IL-13	IL-17	IFN gamma	KC	Leptin	MCP-1
5	MCP-5	MIP-1 alpha	MIP-2	MIP-2 beta	RANTES	SCF	sTNFRI	TARC	TIMP-1	TNF alpha	THPO	VEGF
6	MCP-5	MIP-1 alpha	MIP-2	MIP-2 beta	RANTES	SCF	sTNFRI	TARC	TIMP-1	TNF alpha	THPO	VEGF
7	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	POS
8	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	BLANK	POS

Supplementary Figure 2 Cytokine layout of the mouse cytokine antibody array C2 kits.

Supplementary Table 1: The putative major ingredients and targets of 10 herbs in XIAOPI formula

Latin name	Chinese Name	Number of Screening ingredients	Major ingredients	Number of Targets
Epimedium Brevicornum	 淫羊藿	23	24-epicampesterol Linoleyl acetate poriferast-5-en-3beta-ol DFV Chryseriol 8-Isopentenyl-kaempferol sitosterol kaempferol olivil Anhydroicaritin C-Homoerythrinan, 1,6-didehydro- 3,15,16-trimethoxy-, (3.beta.)- Yinyanghuo A Yinyanghuo C Yinyanghuo E 6-hydroxy-11,12-dimethoxy-2,2-dimethyl-1,8-dioxo -2,3,4,8-tetrahydro-1H-isochromeno[3,4-h] isoquinolin-2-ium 8-(3-methylbut-2-enyl)-2-phenyl-chromone	246

			Anhydroicaritin-3-O-alpha-L-rhamnoside 1,2-bis(4-hydroxy-3-methoxyphenyl)propan-1,3-diol Icariin Icariside A7 luteolin Magnograndiolide quercetin	
Cistanche Deserticola		6	beta-sitosterol Marckine arachidonate quercetin suchilactone Yangambin	198
Ligustrum Lucidum		9	beta-sitosterol kaempferol taxifolin Lucidumoside D Lucidumoside D_qt eriodictyol Olitoriside_qt luteolin quercetin	215
			1,2,5,6-tetrahydrotanshinone Poriferasterol poriferast-5-en-3beta-ol isoimperatorin	

Salvia
Miltiorrhiza








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sugiol
Dehydrotanshinone II A
5,6-dihydroxy-7-isopropyl-1,1
-dimethyl-2,3-dihydrophenanthren-4-one
2-isopropyl-8-methylphenanthrene-3,4-dione
3 α -hydroxytanshinone II a
4-methylenemiltirone
formyltanshinone
Methylenetanshinquinone
przewaquinone c
sclareol
tanshinaldehyde
Danshenol B
Salvilenone
cryptotanshinone
dan-shexinkum d
danshenspiroketallactone
deoxyneocryptotanshinone
dihydrotanshinlactone
dihydrotanshinone I
epidanshenspiroketallactone
C09092
isocryptotanshi-none
Isotanshinone II
manool
miltionone II

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			<p>miltipolone</p> <p>Miltirone</p> <p>neocryptotanshinone ii</p> <p>1-methyl-8,9-dihydro-7H-naphtho[5,6-g]benzofuran-6,10,11-trione</p> <p>salvilenone I</p> <p>salviolone</p> <p>tanshinone iia</p> <p>(6S)-6-(hydroxymethyl)-1,6-dimethyl-8,9-dihydro-7H-naphtho[8,7-g]benzofuran-10,11-dione</p> <p>tanshinone VI</p>	
<p>Curcuma Aromatica</p>	 <p>郁金</p>	3	<p>beta-sitosterol</p> <p>Sitosterol</p> <p>Naringenin</p>	69
<p>Rhizoma Curcumae</p>	 <p>莪术</p>	3	<p>hederagenin</p> <p>Germacron</p> <p>curzerene</p> <p>galeopsin</p> <p>ZINC04073977</p> <p>preleoheterin</p>	32

Leonurus heterophyllus	 益母草	8	iso-preleoheterin quercetin arachidonic acid isorhamnetin kaempferol	223
Radix Polygoni Multiflori Preparata	 何首乌	6	questin rhein emodin polygodial chrysazin resveratrol aluminum	358
Crassostrea Gigas	 牡蛎	5	calcium sulphate calcium phosphate silicon calcium carbonate	149
Carapax Trionycis	 鳖甲	4	gondoic acid Vaccenic acid 8-Octadecenoic acid oleic acid	182

Supplementary Table 2 The targeting genes of XIAOPI formula related to breast cancer

*COL1A1 POSTN EGFR SPARC FN1 TF CXCL10 MMP2 STAT1 CCNA2 NCOA3 IFI27 E2F1 PLAT JUN TGFA CAV1 HSPA5 BIRC5 BMP2 FAP PCNA FOS TGFB2 PDGFB INSR
TNFRSF10B CDK2 NCOA1 GSTP1 CTSK PIK3CB CA2 CHEK1 NR1I2 TOP2A GSTM1 PPARA CAT CD80 EGR1 PARP1 IL2RA EDNRA CCNE1 VEGFA CDK1 PDGFRB BCL2
GNAS MMP1 CCNB1 RAD51HIF1A G6PD PTGS1 MAP2K1 CXCL1 ROCK1 FGF1 SPP1 PLAU VCAM1 BRCA2 ERCC1 PTGS2 CDKN2A EGF TNS1 PRKAA1 TNFRSF10A IRS1
MAPK14 CCNE2 GDF15 PTK2 CLDN4 CD28 SLC6A3 CFLAR BRCA1*
