

Supplementary Information

Herb-target interaction network analysis helps to disclose molecular mechanism of traditional Chinese medicine

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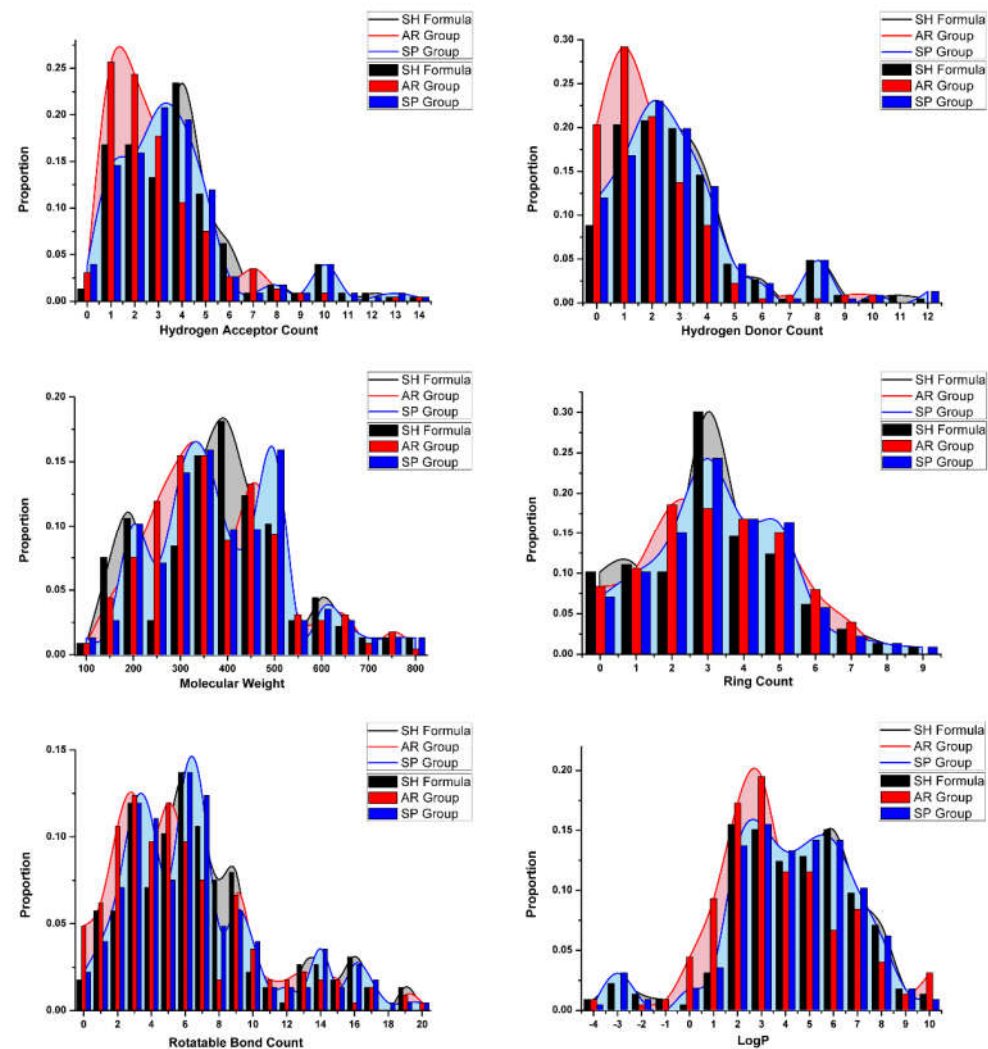
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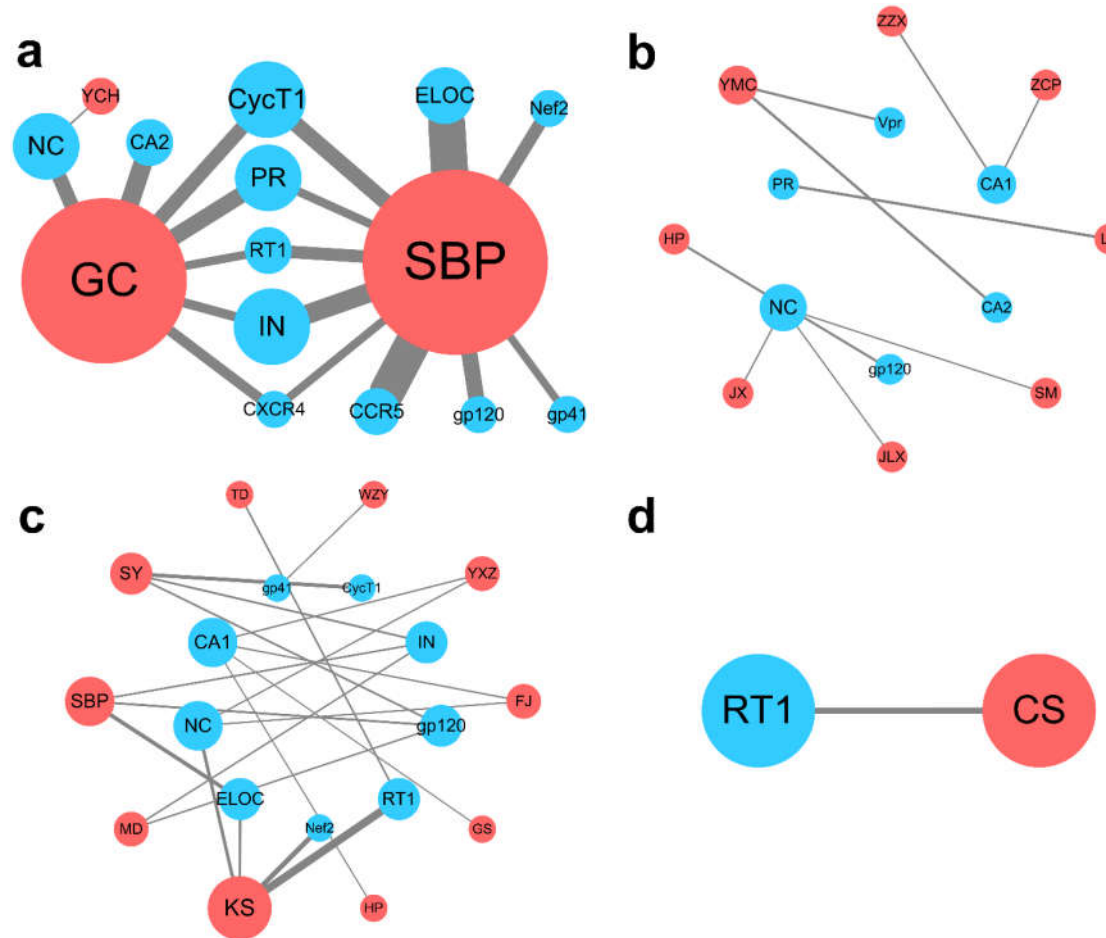
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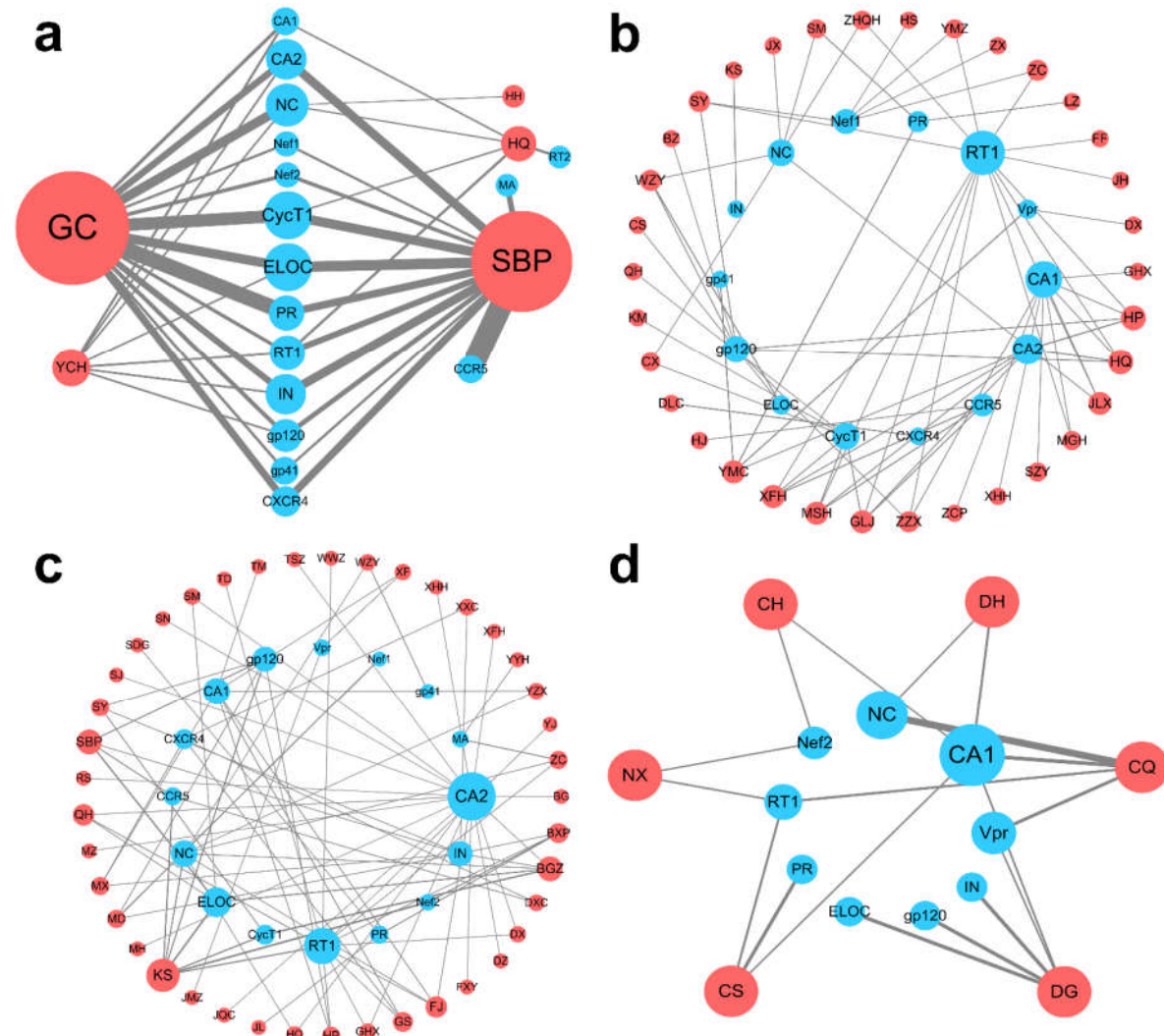
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Supplementary Figure S1. Chemical property distributions of SH formula (black histogram and grey area), AR group (red histogram and pink area) and SP group (blue histogram and cyan area).

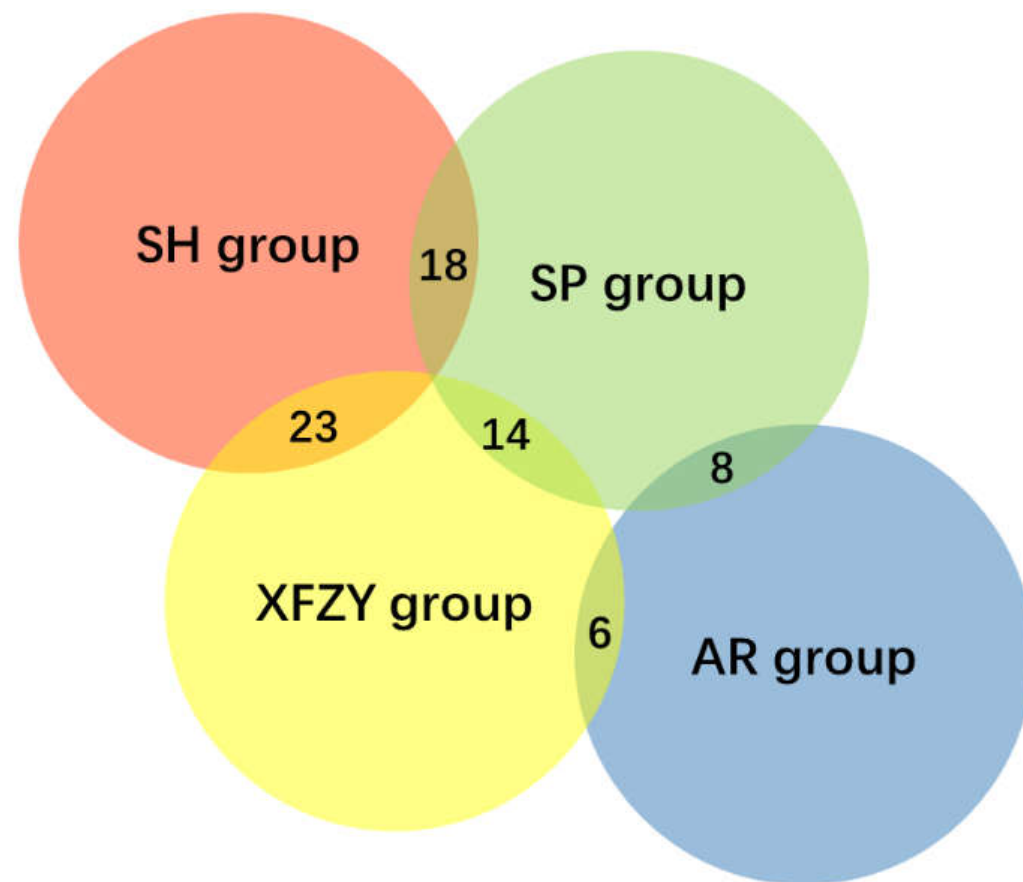


Supplementary Figure S2. Herb-target network of HIV-1 related proteins and SH formula (a), AR group (b), SP group (c) and XFZY group (d). The cutoff is set as top 30% by all four software. GC, SBP, YCH, and CS represents *Glycyrrhiza uralensis*, *Morus alba*, *Artemisia capillaries* and *Paeonia rubra*, respectively. Node sizes of herbs and targets are weighted by active compound numbers, edge sizes are weighted by HTFs.



Supplementary Figure S3. Herb-target network of HIV-1 related proteins and SH formula (a), AR group (b), SP group (c) and XFZY group (d). The cutoff is set as top 50% by all four software. GC, HH, HQ, SBP, YCH, CH, CQ, CS, DG, DH, NX represents *Glycyrrhiza uralensis*, *Carthamus tinctorius*, *Astragalus membranaceus*, *Morus alba*, *Artemisia*

capillaries, *Bupleurum chinense*, *Ligusticum wallichii*, *Paeonia rubra*, *Angelica sinensis*, *Rehmannia glutinosa* and *Achyranthes bidentata* respectively. Node sizes of herbs and targets are weighted by active compound numbers, edge sizes are weighted by HTFs.



Supplementary Figure S4. Overlap compounds between SH formula and control groups.

Supplementary Table S1. HTF of active herbs in SH formula against 17 viral proteins.

Herb	PR	RT1	RT2	IN	NC	CA1	CA2	MA	Nef1	Nef2	Vpr	gp120	gp41	CCR5	CXCR4	CycT1	ELOC
<i>Glycyrrhiza uralensis</i>	107.65	33.83	0.00	83.80	62.67	24.70	41.27	0.00	0.00	0.00	0.00	16.60	11.85	0.00	65.20	79.03	0.00
<i>Carthamus tinctorius</i>	0.00	0.00	0.00	0.00	1.46	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
<i>Astragalus membranaceus</i>	0.00	8.62	0.00	0.00	0.00	5.92	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.21	0.00
<i>Morus alba</i>	75.02	78.98	0.00	133.87	0.00	0.00	69.70	0.00	0.00	61.82	0.00	44.15	17.66	248.05	75.35	77.22	136.78
<i>Artemisia capillaries</i>	0.00	0.00	0.00	0.00	10.10	13.35	9.08	0.00	0.00	0.00	0.00	8.57	0.00	0.00	0.00	0.00	11.85

Supplementary Table S13. Number of potential inhibitors in each group to 17 viral proteins (top 50% cutoff).

Group	PR	RT1	RT2	IN	NC	CA1	CA2	MA	Nef1	Nef2	Vpr	gp120	gp41	CCR5	CXCR4	CycT1	ELOC	Total
SH formula	6	6	1	8	9	3	8	1	2	2	0	5	3	3	4	11	11	83
AR group	3	15	0	1	6	11	8	0	5	0	2	6	1	4	1	6	2	71
SP group	3	14	0	7	8	8	21	2	1	2	2	7	1	3	4	4	10	97
XFZY group	1	3	0	1	7	11	0	0	0	2	5	1	0	0	0	0	1	32

Supplementary Table S14. HTF of active herbs in SH group against 17 viral proteins (top 50% cutoff).

Herb	PR	RT1	RT2	IN	NC	CA1	CA2	MA	Nef1	Nef2	Vpr	gp120	gp41	CCR5	CXCR4	CycT1	ELOC
<i>Glycyrrhiza uralensis</i>	193.70	32.99	0.00	72.63	115.18	32.11	77.65	0.00	20.34	37.38	0.00	42.42	23.34	0.00	84.76	153.75	111.89
<i>Carthamus tinctorius</i>	0.00	0.00	0.00	0.00	1.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
<i>Astragalus membranaceus</i>	0.00	21.36	22.10	0.00	6.41	9.87	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	8.68	0.00
<i>Morus alba</i>	88.66	70.00	0.00	105.47	0.00	0.00	105.69	62.79	19.63	36.53	0.00	52.17	20.86	293.15	89.05	112.62	127.62
<i>Artemisia capillaries</i>	0.00	14.46	0.00	12.58	10.60	18.69	12.72	0.00	0.00	0.00	0.00	11.99	0.00	0.00	0.00	0.00	11.06

Supplementary Table S18. The Latin name, Chinese name and compound number of TCMHD herbs.

Latin name	Chinese name	Compound number	Latin Name	Chinese Name	Compound number
<i>Artemisia argyi</i>	aiye	34	<i>Gentiana scabra</i>	longdan	8
<i>Ferula assafoetida</i>	awei	17	<i>Aloe barbadensis</i>	luhui	31
<i>Croton tiglium</i>	badou	33	<i>Apocynum venetum</i>	luobumaye	9
<i>Stemona tuberosa</i>	baibu	23	<i>Trachelospermum jasminoides</i>	luoshiteng	10
<i>Ginkgo biloba</i>	baiguo	35	<i>Portulaca oleracea</i>	machixian	7
<i>Bletilla striata</i>	baiji	25	<i>Ephedra sinica</i>	mahuang	21
<i>Chelidonium majus</i>	baiqucai	28	<i>Ophiopogon japonicus</i>	maidong	32
<i>Paeonia lactiflora</i>	baishao	33	<i>Hordeum vulgare</i>	maiya	11
<i>Pulsatilla chinensis</i>	baitouweng	14	<i>Vitex trifolia</i>	manjingzi	29
<i>Cynanchum atratum</i>	baiwei	10	<i>Rhododendron dauricum</i>	manshanhong	19
<i>Dictamnus dasycarpus</i>	baixianpi	22	<i>Strychnos nuxvomica</i>	maqianzi	28
<i>Angelica dahurica</i>	baizhi	36	<i>Rosa rugosa</i>	meiguihua	47
<i>Atractylodes macrocephala</i>	baizhu	10	<i>Prunus mume</i>	meihua	3
<i>Illicium verum</i>	bajiaohuixiang	17	<i>Dryopteris crassirhizoma</i>	mianmaguanzhong	12
<i>Morinda officinalis</i>	bajitian	10	<i>Commiphora myrrha</i>	moyao	11
<i>Isatis indigotica</i>	banlangen	21	<i>Paeonia suffruticosa</i>	mudanpi	7
<i>Pinellia ternata</i>	banxia	14	<i>Oroxylum indicum</i>	muhudie	4
<i>Syringa reticulata</i>	baomazipi	8	<i>Vitex negundo</i>	mujingye	12
<i>Menispermum dauricum</i>	beidougen	35	<i>Akebia quinata</i>	mutong	10
<i>Glehnia littoralis</i>	beishashen	41	<i>Aucklandia lappa</i>	muxiang	53
<i>Piper longum</i>	biba	12	<i>Equisetum hiemale</i>	muzei	15
<i>Areca catechu</i>	binlang	23	<i>Daucus carota</i>	nanheshi	15
<i>Mentha haplocalyx</i>	bohe	11	<i>Schisandra sphenanthera</i>	nanwuweizi	12
<i>Psoralea corylifolia</i>	buguzhi	29	<i>Rhododendron molle</i>	naoyanghua	16
<i>Atractylodes lancea</i>	cangzhu	29	<i>Arctium lappa</i>	niubangzi	10
<i>Platycladus orientalis</i>	cebaiye	19	<i>Achyranthes bidentata</i>	niuxi	12

<i>Bupleurum chinense</i>	chaihu	49	<i>Ligustrum lucidum</i>	nvzhenzi	20
<i>Citrus reticulata</i>	chenpi	41	<i>Eupatorium fortunei</i>	peilan	27
<i>Aquilaria sinensis</i>	chenxiang	28	<i>Fritillaria ussuriensis</i>	pingbeimu	10
<i>Plantago asiatica</i>	cheqiancao	12	<i>Eriobotrya japonica</i>	pipaye	19
<i>Paeonia lactiflora</i>	chishao	9	<i>Taraxacum officinale</i>	pugongying	26
<i>Vigna angularis</i>	chixiaodou	5	<i>Typha angustata</i>	puhuang	17
<i>Dioscorea nipponica</i>	chuanshanlong	7	<i>Notopterygium incisum</i>	qianghuo	44
<i>Aconitum carmichaeli</i>	chuanwu	25	<i>Peucedanum praeruptorum</i>	qianhu	25
<i>Andrographis paniculata</i>	chuanxinlian	24	<i>Euphorbia lathyris</i>	qianjinzi	10
<i>Ligusticum chuanxiong</i>	chuanxiong	58	<i>Pharbitis nil</i>	qianniuzi	12
<i>Ailanthus altissima</i>	chunpi	15	<i>Sinomenium acutum</i>	qingfengteng	13
<i>Acanthopanax senticosus</i>	ciwujia	17	<i>Artemisia annua</i>	qinghao	104
<i>Rheum officinale</i>	dahuang	31	<i>Gentiana macrophylla</i>	qinjiao	13
<i>Angelica sinensis</i>	danggui	51	<i>Dianthus superbus</i>	qumai	8
<i>Codonopsis pilosula</i>	dangshen	57	<i>Lonicera japonica</i>	rendongteng	3
<i>Salvia miltiorrhiza</i>	danshen	65	<i>Panax ginseng</i>	renshen	78
<i>Oryza sativa</i>	daoya	20	<i>Cistanche deserticola</i>	roucongong	27
<i>Isatis indigotica</i>	daqingye	15	<i>Myristica fragrans</i>	roudoukou	11
<i>Allium sativum</i>	dasuan	30	<i>Cinnamomum cassia</i>	rougui	11
<i>Sargentodoxa cuneata</i>	daxueteng	6	<i>Boswellia carterii</i>	ruxiang	14
<i>Gleditsia sinensis</i>	dazaojiao	4	<i>Saururus chinensis</i>	sanbaicao	19
<i>Ziziphus jujuba</i>	dazao	34	<i>Morus alba (cortex)</i>	sangbaipi	47
<i>Juncus effuses</i>	dengxincao	13	<i>Morus alba (mulberry)</i>	sangshen	10
<i>Kadsura interior</i>	dianjixueteng	17	<i>Morus alba (folium)</i>	sangye	42
<i>Rehmannia glutinosa</i>	dihuang	67	<i>Morus alba (ramulus)</i>	sangzhi	16
<i>Eugenia caryophyllata</i>	dingxiang	19	<i>Panax notoginseng</i>	sanqi	51
<i>Sanguisorba officinalis</i>	diyu	31	<i>Hippophae rhamnoides</i>	shaji	48
<i>Cordyceps sinensis</i>	dongchongxiacao	19	<i>Sophora tonkinensis</i>	shandougen	20

<i>Rabdosia rubescens</i>	donglingcao	31	<i>Phytolacca acinosa</i>	shanglu	11
<i>Amomum kravanh</i>	doukou	7	<i>Kaempferia galanga</i>	shannai	9
<i>Angelica pubescens</i>	duhuo	41	<i>Dioscorea opposita</i>	shanyao	21
<i>Eucommia ulmoides</i>	duzhong	34	<i>Crataegus pinnatifida</i>	shanzha	18
<i>Saposhnikovia divaricata</i>	fangfeng	24	<i>Cornus officinalis</i>	shanzhuyu	30
<i>Stephania tetrandra</i>	fangji	17	<i>Astragalus complanatus</i>	shayuanzi	5
<i>Cassia acutifolia</i>	fanxieye	8	<i>Cnidium monnieri</i>	shechuangzi	20
<i>Dioscorea hypoglauca</i>	fenbixie	10	<i>Belamcanda chinensis</i>	shegan	16
<i>Apis mellifera</i>	fengjiao	10	<i>Zingiber officinale</i>	shengjiang	77
<i>Poria cocos</i>	fuling	33	<i>Cimicifuga foetida</i>	shengma	10
<i>Aconitum carmichaeli</i>	fuzi	39	<i>Lycopodium japonicum</i>	shenjincao	17
<i>Glycyrrhiza uralensis</i>	gancao	84	<i>Dendrobium nobile</i>	shihu	20
<i>Zingiber officinale</i>	ganjiang	29	<i>Punica granatum</i>	shiliupi	11
<i>Nardostachys chinensis</i>	gansong	29	<i>Silybum marianum</i>	shuifeiji	13
<i>Euphorbia kansui</i>	gansui	42	<i>Luffa cylindrica</i>	sigualuo	9
<i>Ligusticum sinense</i>	gaoben	11	<i>Ziziphus jujuba</i>	suanzaoren	21
<i>Alpinia officinarum</i>	gaoliangjiang	22	<i>Caesalpinia sappan</i>	sumu	28
<i>Pueraria lobata</i>	gegen	20	<i>Aesculus chinensis</i>	suoluozi	10
<i>Lycium chinense</i>	gouqizi	41	<i>Santalum album</i>	tanxiang	24
<i>Uncaria rhynchophylla</i>	gouteng	31	<i>Asparagus cochinchinensis</i>	tiandong	14
<i>Trichosanthes kirilowii</i>	gualou	30	<i>Trichosanthes kirilowii</i>	tianhuafen	9
<i>Pogostemon cablin</i>	guanghuoxiang	23	<i>Gastrodia elata</i>	tianma	18
<i>Phellodendron amurense</i>	guanhuangbai	22	<i>Cinnamomum camphora</i>	tianranbingpian	12
<i>Hypericum perforatum</i>	guanyejinsitao	10	<i>Hyoscyamus niger</i>	tianxianzi	24
<i>Cinnamomum cassia</i>	guizhi	10	<i>Tetrapanax papyriferus</i>	tongcao	14
<i>Piper kadsura</i>	haifengteng	30	<i>Bolbostemma paniculatum</i>	tubeimu	12
<i>Eclipta prostrata</i>	hanmolian	11	<i>Smilax glabra</i>	tufuling	9
<i>Albizia julibrissin</i>	hehuanpi	22	<i>Pseudolarix amabilis</i>	tujingpi	24

<i>Glycine max</i>	heidou	21	<i>Cuscuta australis</i>	tusizi	8
<i>Carpesium abrotanoides</i>	heshi	7	<i>Vaccaria segetalis</i>	wangbuliuxing	11
<i>Polygonum multiflorum</i>	heshouwu	13	<i>Claviceps purpurea</i>	weilingxian	8
<i>Juglans regia</i>	hetaoren	26	<i>Schisandra chinensis</i>	wuweizi	68
<i>Nelumbo nucifera</i>	heye	13	<i>Lindera aggregata</i>	wuyao	17
<i>Terminalia chebula</i>	hezi	13	<i>Evodia rutaecarpa</i>	wuzhuyu	47
<i>Alpinia galanga</i>	hongdoukou	13	<i>Prunella vulgaris</i>	xiakucao	32
<i>Carthamus tinctorius</i>	honghua	32	<i>Cyperus rotundus</i>	xiangfu	18
<i>Magnolia officinalis</i>	houpu	44	<i>Periploca sepium</i>	xiangjiapi	36
<i>Sophora japonica</i>	huaihua	7	<i>Citrus medica</i>	xiangyuan	8
<i>Zanthoxylum bungeanum</i>	huajiao	11	<i>Curculigo orchioides</i>	xianmao	17
<i>Coptis chinensis</i>	huanglian	12	<i>Foeniculum vulgare</i>	xiaohuixiang	11
<i>Scutellaria baicalensis</i>	huangqin	44	<i>Podophyllum emodii</i>	xiaoyelian	15
<i>Astragalus membranaceus</i>	huangqi	16	<i>Rubia cordifolia</i>	xicao	42
<i>Fritillaria hupehensis</i>	hubeibeimu	10	<i>Allium macrostemon</i>	xiebai	19
<i>Picrorhiza scrophulariaeflora</i>	huhuaglian	12	<i>Crocus sativus</i>	xihonghua	42
<i>Piper nigrum</i>	hujiao	55	<i>Magnolia denudata</i>	xinyi	13
<i>Viscum coloratum</i>	hujisheng	5	<i>Siegesbeckia orientalis</i>	xixiancao	27
<i>Trigonella foenumgraecum</i>	huluba	40	<i>Asarum sieboldii</i>	xixin	22
<i>Cannabis sativa</i>	huomaren	9	<i>Panax quinquefolium</i>	xiyangshen	25
<i>Polygonum cuspidatum</i>	huzhang	25	<i>Inula britannica</i>	xuanfuhua	15
<i>Dalbergia odorifera</i>	jiangxiang	34	<i>Dipsacus asperoides</i>	xuduan	12
<i>Platycodon grandiflorum</i>	jiegang	12	<i>Brucea javanica</i>	yadanzi	58
<i>Brassica juncea</i>	jiezi	16	<i>Cissampelos pareira</i>	yahunu	16
<i>Celosia cristata</i>	jiguanhua	10	<i>Corydalis yanhusuo</i>	yanhusuo	31
<i>Abrus cantoniensis</i>	jigucao	11	<i>Chrysanthemum indicum</i>	yejuhua	9
<i>Tribulus terrestris</i>	jili	15	<i>Eupatorium lindleyanum</i>	yemazhui	20
<i>Inula japonica</i>	jinfecao	23	<i>Stauntonia chinensis</i>	yemugua	6

<i>Schizonepeta tenuifolia</i>	jingjie	22	<i>Leonurus artemisia</i>	yimucao	30
<i>Ajuga decumbens</i>	jinguciao	21	<i>Stellaria dichotoma</i>	yinchaihu	14
<i>Conyza blinii</i>	jinlongdancao	8	<i>Artemisia capillaries</i>	yinchen	54
<i>Lysimachia christinae</i>	jinqiancao	3	<i>Papaver somniferum</i>	yingsuke	13
<i>Psammosilene tunicoides</i>	jintiesuo	8	<i>Ginkgo biloba</i>	yinxingye	20
<i>Rosa laevigata</i>	jinyingzi	12	<i>Epimedium brevicornum</i>	yinyanghuo	14
<i>Lonicera japonica</i>	jinyinhua	32	<i>Solidago decurrens</i>	yizhihuanghua	8
<i>Murraya paniculata</i>	jiulixiang	60	<i>Alpinia oxyphylla</i>	yizhi	26
<i>Centella asiatica</i>	jixuecao	7	<i>Daphne genkwa</i>	yuanhua	11
<i>Selaginella tamariscina</i>	juanbai	12	<i>Polygala tenuifolia</i>	yuanzhi	29
<i>Cassia tora</i>	juemingzi	15	<i>Phyllanthus emblica</i>	yuganzi	44
<i>Chrysanthemum morifolium</i>	juhua	10	<i>Curcuma longa</i>	yujin	22
<i>Cichorium intybus</i>	juju	11	<i>Houttuynia cordata</i>	yuxingcao	23
<i>Tussilago farfara</i>	kuandonghua	18	<i>Echinops grijsii</i>	yuzhouloulou	9
<i>Corydalis bungeana</i>	kudiding	11	<i>Acorus calamus</i>	zangcangpu	28
<i>Melia azedarach</i>	kulianpi	31	<i>Alisma orientale</i>	zexie	29
<i>Picrasma quassioides</i>	kumu	76	<i>Fritillaria thunbergii</i>	zhebeimu	31
<i>Sophora flavescens</i>	kushen	74	<i>Anemarrhena asphodeloides</i>	zhimu	23
<i>Prunus armeniaca</i>	kuxingren	22	<i>Citrus aurantium</i>	zhishi	12
<i>Picria felterrae</i>	kuxuanshen	9	<i>Valeriana jatamansii</i>	zhizhuxiang	17
<i>Capsicum annuum</i>	lajiao	33	<i>Gardenia jasminoides</i>	zhizi	27
<i>Zanthoxylum nitidum</i>	liangmianzhen	12	<i>Panax pseudoginseng</i>	zhujieshen	6
<i>Forsythia suspensa</i>	lianqiao	27	<i>Arnebia euchroma</i>	zicao	28
<i>Nelumbo nucifera (plumule)</i>	lianxixin	9	<i>Peucedanum decursivum</i>	zihuaqianhu	17
<i>Nelumbo nucifera (seed)</i>	lianzi	10	<i>Perilla frutescens</i>	zisuye	10
<i>Ganoderma lucidum</i>	lingzhi	102	<i>Aster tataricus</i>	ziwan	17