

Table SI. Significant active components of the Erjing pill that meet the absorption, distribution, metabolism, excretion and toxicity conditions (n=65).

No.	Name	Database
GQZ004	Lauric acid	TCMSP
GQZ008	Nicotinic acid	TCMSP
GQZ011	Physcion	TCMSP
GQZ013	Dibutylphthalate	TCMSP
GQZ017	Paeonol	TCMSP
GQZ035	Atropine	TCMSP
GQZ039	Solavetivone	TCMSP
GQZ044	Atropine	TCMSP
GQZ048	Ethyl anisate	TCMSP
GQZ049	3-Hydroxy- β -ionone	Chinese chemistry database
GQZ054	6-Methoxy-7-hydroxycoumarin	Chinese chemistry database
GQZ072	Atropine	Chinese chemistry database
GQZ073	Baogongteng B	Chinese chemistry database
GQZ089	Hyoscyamine	Chinese chemistry database
GQZ090	Isoleucine	Chinese chemistry database
GQZ095	Leucine	Chinese chemistry database
GQZ100	Niacin nicotinic acid	Chinese chemistry database
GQZ102	Phenylalanine	Chinese chemistry database
GQZ105	Safranal	Chinese chemistry database
GQZ106	Scopoletin	Chinese chemistry database
GQZ108	Solavetivone	Chinese chemistry database
GQZ111	Tryptophane	Chinese chemistry database
GQZ112	Tyrosine	Chinese chemistry database
GQZ113	Valine	Chinese chemistry database
GQZ116	β -Ionone	Chinese chemistry database
GQZ118	(-)-4'-O-Methyl-nyasol	TCM-Database@Taiwan
GQZ129	Atropine	TCM-Database@Taiwan
GQZ134	Cinnamic alcohol	TCM-Database@Taiwan
GQZ142	Glycitein	TCM-Database@Taiwan
GQZ149	Safrole	TCM-Database@Taiwan
GQZ157	Zederone	TCM-Database@Taiwan
HJ001	Apigenin	TCMSP
HJ006	(+)-Syringaresinol	TCMSP
HJ007	Diosgenin	TCMSP
HJ008	HMF	TCMSP
HJ009	Isoliquiritigenin	TCMSP
HJ010	Salicylic acid	TCMSP
HJ013	4',5-Dihydroxyflavone	TCMSP
HJ014	2',7-Dihydroxy-3',4'-Dimethoxyisoflavane	TCMSP
HJ015	4-Methylolfurfural	TCMSP
HJ019	Sibiricoside A _{qt}	TCMSP
HJ021	Sibiricoside B _{qt}	TCMSP
HJ024	Zhonghualiaoine 1	TCMSP
HJ030	Neosibiricoside D	Ref. (45)
HJ031	(25S)-Pratioside D1	Ref. (23)
HJ037	Huangjingenin	Ref. (46)
HJ041	Huangjinoside F	Ref. (46)
HJ057	Spirost-5-en-12-one-3-O- β -D-glucopyranosyl-(1 $\rightarrow$ 2)-[β -D-xylopyranosyl-(1 $\rightarrow$ 3)]- β -D-glucopyranosyl-(1 $\rightarrow$ 4)- β -D-galactopyranoside	Ref. (47)
HJ065	(25R)-Spirost-5-en-3 β ,17 α -diol-3-O- β -D-glucopyranosyl-(1 $\rightarrow$ 3)-[α -L-rhamnopyranosyl-(1 $\rightarrow$ 2)]- β -D-glucopyranoside	Ref. (48)
HJ069	Dioscin	Ref. (49)
HJ107	Neoliquiritin	Ref. (50)
HJ108	Liquiritigenin	Ref. (45)
HJ110	Neoisoliquiritin	Ref. (51)
HJ111	4',7-Dihydroxy-3'-methoxy isoflavone	Ref. (46)
HJ113	2',7-Dihydroxy-3',4'dimethoxyisoflavone	Ref. (46)
HJ114	(6aR,11aR)-10-Hydroxy-3,9-Dimethoxysaltanane	Ref. (46)

Table SI. Continued.

No.	Name	Database
HJ115	Polygonatine A	Ref. (52)
HJ116	Polygonatine B	Ref. (52)
HJ117	Kinganone	Ref. (53)
HJ132	5-Hydroxymethylfurfural	Isolated at laboratory
HJ133	Medioresinol	Isolated at laboratory
HJ134	2-(Hydroxyphenyl)-ethanol	Isolated at laboratory
HJ135	(25R)-3- β -Hydroxyspirost-5-en-12-one	Isolated at laboratory
HJ136	Polygonatine C	Isolated at laboratory
HJ137	3- β -hydroxyspirost-5,25-diene-12-one	Isolated at laboratory

TCMSP, Traditional Chinese Medicine Systems Pharmacology. YW performed the isolations within our group.

Table SII. Potential targets of Erjing pill in the treatment of Alzheimer's disease.

Uniprot ID	Gene symbol	Description
Q9Y5N1	HRH3	Histamine H3 receptor
Q9BXC0	HCAR1	Hydroxycarboxylic acid receptor 1
Q96JD6	AKR1E2	1,5-anhydro-D-fructose reductase
Q92843	BCL2L2	Bcl-2-like protein 2
Q92731	ESR2	Estrogen receptor beta
Q16850	CYP51A1	Lanosterol 14-alpha demethylase
Q16790	CA9	Carbonic anhydrase 9
Q16665	HIF1A	Hypoxia-inducible factor 1-alpha
Q15303	ERBB4	Receptor tyrosine-protein kinase erbB-4
Q14765	STAT4	Signal transducer and activator of transcription 4
Q13627	DYRK1A	Dual specificity tyrosine-phosphorylation-regulated kinase 1A
Q07817	BCL2L1	Bcl-2-like protein 1
Q06481	APLP2	Amyloid-like protein 2
Q05655	PRKCD	Protein kinase C delta type
Q04864	REL	Proto-oncogene c-Rel
Q04206	RELA	Transcription factor p65
Q01959	SLC6A3	Sodium-dependent dopamine transporter
P68400	CSNK2A1	Casein kinase II subunit alpha
P55055	NR1H2	Oxysterols receptor LXR-beta
P51681	CCR5	C-C chemokine receptor type 5
P49841	GSK3B	Glycogen synthase kinase-3 beta
P49840	GSK3A	Glycogen synthase kinase-3 alpha
P49286	MTNR1B	Melatonin receptor type 1B
P48039	MTNR1A	Melatonin receptor type 1A
P45983	MAPK8	Mitogen-activated protein kinase 8
P43004	SLC1A2	Excitatory amino acid transporter 2
P43003	SLC1A3	Excitatory amino acid transporter 1
P42224	STAT1	Signal transducer and activator of transcription 1-alpha/beta
P41597	CCR2	C-C chemokine receptor type 2
P41145	OPRK1	Kappa-type opioid receptor
P41143	OPRD1	Delta-type opioid receptor
P40763	STAT3	Signal transducer and activator of transcription 3
P35462	DRD3	D(3) dopamine receptor
P35354	PTGS2	Prostaglandin G/H synthase 2
P35228	NOS2	Nitric oxide synthase, inducible
P31645	SLC6A4	Sodium-dependent serotonin transporter
P30542	ADORA1	Adenosine receptor A1
P29475	NOS1	Nitric oxide synthase, brain
P29474	NOS3	Nitric oxide synthase, endothelial
P29274	ADORA2A	Adenosine receptor A2a
P28845	HSD11B1	Corticosteroid 11-beta-dehydrogenase isozyme 1
P28335	HTR2C	5-hydroxytryptamine receptor 2C
P28223	HTR2A	5-hydroxytryptamine receptor 2A
P28222	HTR1B	5-hydroxytryptamine receptor 1B
P27986	PIK3R1	Phosphatidylinositol 3-kinase regulatory subunit alpha
P27361	MAPK3	Mitogen-activated protein kinase 3
P27338	MAOB	Amine oxidase [flavin-containing] B
P25105	PTAFR	Platelet-activating factor receptor
P25101	EDNRA	Endothelin-1 receptor
P25100	ADRA1D	Alpha-1D adrenergic receptor
P24941	CDK2	Cyclin-dependent kinase 2
P24530	EDNRB	Endothelin receptor type B
P23975	SLC6A2	Sodium-dependent noradrenaline transporter
P23219	PTGS1	Prostaglandin G/H synthase 1
P22607	FGFR3	Fibroblast growth factor receptor 3
P22309	UGT1A1	UDP-glucuronosyltransferase 1-1
P22303	ACHE	Acetylcholinesterase
P21964	COMT	Catechol O-methyltransferase
P21917	DRD4	D(4) dopamine receptor

Table SII. Continued.

Uniprot ID	Gene symbol	Description
P21802	FGFR2	Fibroblast growth factor receptor 2
P21397	MAOA	Amine oxidase [flavin-containing] A
P20309	CHRM3	Muscarinic acetylcholine receptor M3
P20160	AZU1	Azurocidin
P18825	ADRA2C	Alpha-2C adrenergic receptor
P18507	GABRG2	Gamma-aminobutyric acid receptor subunit gamma-2
P17752	TPH1	Tryptophan 5-hydroxylase 1
P17516	AKR1C4	Aldo-keto reductase family 1 member C4
P17252	PRKCA	Protein kinase C alpha type
P16050	ALOX15	Arachidonate 15-lipoxygenase
P15559	NQO1	NAD(P)H dehydrogenase
P14902	IDO1	Indoleamine 2,3-dioxygenase 1
P14780	MMP9	Matrix metalloproteinase-9
P14416	DRD2	D(2) dopamine receptor
P14410	SI	Sucrase-isomaltase, intestinal
P14061	HSD17B1	Estradiol 17-beta-dehydrogenase 1
P12931	SRC	Proto-oncogene tyrosine-protein kinase Src
P12821	ACE	Angiotensin-converting enzyme
P11802	CDK4	Cyclin-dependent kinase 4
P11511	CYP19A1	Aromatase (EC 1.14.14.14)
P11473	VDR	Vitamin D3 receptor
P11362	FGFR1	Fibroblast growth factor receptor 1
P11309	PIM1	Serine/threonine-protein kinase pim-1
P11229	CHRM1	Muscarinic acetylcholine receptor M1
P10721	KIT	Mast/stem cell growth factor receptor Kit
P10636	MAPT	Microtubule-associated protein tau
P10415	BCL2	Apoptosis regulator Bcl-2
P10275	AR	Androgen receptor
P09917	ALOX5	Arachidonate 5-lipoxygenase
P09238	MMP10	Stromelysin-2
P08913	ADRA2A	Alpha-2A adrenergic receptor
P08908	HTR1A	5-hydroxytryptamine receptor 1A
P08631	HCK	Tyrosine-protein kinase HCK
P08581	MET	Hepatocyte growth factor receptor
P08254	MMP3	Stromelysin-1
P08253	MMP2	72 kDa type IV collagenase
P08246	ELANE	Neutrophil elastase
P08235	NR3C2	Mineralocorticoid receptor
P08172	CHRM2	Muscarinic acetylcholine receptor M2
P07451	CA3	Carbonic anhydrase 3
P07333	CSF1R	Macrophage colony-stimulating factor 1 receptor
P07101	TH	Tyrosine 3-monooxygenase
P06493	CDK1	Cyclin-dependent kinase 1
P06401	PGR	Progesterone receptor
P06276	BCHE	Cholinesterase
P06241	FYN	Tyrosine-protein kinase Fyn
P06239	LCK	Tyrosine-protein kinase Lck
P05771	PRKCB	Protein kinase C beta type
P05413	FABP3	Fatty acid-binding protein
P05186	ALPL	Alkaline phosphatase
P05093	CYP17A1	Steroid 17-alpha-hydroxylase
P05067	APP	Amyloid-beta A4 protein
P04278	SHBG	Sex hormone-binding globulin
P04150	NR3C1	Glucocorticoid receptor
P04066	FUCA1	Tissue alpha-L-fucosidase
P04062	GBA	Glucosylceramidase
P04035	HMGCR	3-hydroxy-3-methylglutaryl-coenzyme A reductase
P03956	MMP1	Interstitial collagenase
P03372	ESR1	Estrogen receptor

Table SII. Continued.

Uniprot ID	Gene symbol	Description
P00918	CA2	Carbonic anhydrase 2
P00915	CA1	Carbonic anhydrase 1
P00734	F2	Prothrombin
P00533	EGFR	Epidermal growth factor receptor
O60502	OGA	Protein O-GlcNAcase
O60218	AKR1B10	Aldo-keto reductase family 1 member B10
O43451	MGAM	Maltase-glucoamylase, intestinal
O14746	TERT	Telomerase reverse transcriptase
O00341	SLC1A7	Excitatory amino acid transporter 5

Table SIII. Top 10 genes related to five drugs from Gene Cards.

Drug name gene symbol	Relevance score
Donepezil	
ACHE	24.96
BCHE	13.77
APOE	12.76
CYP2D6	12.07
CHAT	9.04
APP	8.38
HTR2A	8.03
CYP3A4	7.53
CHRNA7	7.49
ABCB1	7.17
Galanthamine	
ACHE	13.95
BCHE	6.98
CYP2D6	5.00
APP	4.53
APOE	4.53
CHRNA4	3.96
CHRNA1	3.96
CHRNA2	3.96
CHRNA4	3.96
CHRNAE	3.96
Memantine	
ACHE	18.02
SLC22A2	15.06
GRIN2A	13.69
GRIN2B	13.17
APP	12.34
GRIN3A	11.16
MAPT	10.72
GRIN2D	10.13
ITIH4	10.03
CHRNA7	9.94
Rivastigmine	
ACHE	31.34
BCHE	25.71
APOE	13.81
CHAT	9.40
CHRNA7	9.31
CYP2D6	6.29
CYP3A4	6.29
SNAP25	2.89
SYP	2.89
IL10	2.82
Tacrine	
ACHE	29.93
BCHE	19.06
APP	13.62
APOE	12.21
CYP1A2	11.82
CHRM2	11.21
GPT	9.90
HNMT	8.89
CES1	8.63
MAPT	6.65

Table SIV. Docking score of 20 active components of *Erjing pill* and five control drugs.

Gene symbol small ligand	-cdocker energy
ACHE	
Rivastigmine	31.6986
Donepezil	25.2326
Tacrine	12.9288
Memantine	-3.2311
Gаланthamine	-28.9404
Polygonatine C	32.7512
2-(hydroxyphenyl)-ethanol	28.9543
5-hydroxymethylfurfural	25.4161
Kinganone	26.0632
Polygonatine A	26.8097
4-methylolfurfural	25.7515
4',5-Dihydroxyflavone	27.1523
HMF	28.8662
Apigenin	28.4536
Tyrosine	36.3527
Tryptophane	31.7370
Scopoletin	25.3608
Phenylalanine	29.2932
Leucine	28.1188
Isoleucine	25.7381
Baogongteng B	25.3608
6-methoxy-7-hydroxycoumarin	25.3608
Paeonol	25.5645
DBP	36.5189
Lauric acid	36.3968
BCHE	
Rivastigmine	28.7144
Tacrine	13.1051
Donepezil	12.6115
Memantine	0.4101
Gаланthamine	-14.5444
Polygonatine C	31.5178
2-(hydroxyphenyl)-ethanol	20.1236
5-hydroxymethylfurfural	20.5290
Kinganone	35.0817
Polygonatine A	16.5374
4-methylolfurfural	21.5816
4',5-Dihydroxyflavone	27.5608
HMF	23.5676
Apigenin	29.5767
Tyrosine	28.4149
Tryptophane	26.6987
Scopoletin	21.1919
Phenylalanine	26.2464
Leucine	21.6184
Isoleucine	22.7218
Baogongteng B	21.1919
6-methoxy-7-hydroxycoumarin	21.1919
Paeonol	19.6241
DBP	39.1575
Lauric acid	34.9687
APP	
Rivastigmine	31.0080
Tacrine	15.3489
Donepezil	12.7089
Memantine	-0.3712
Gаланthamine	-12.6602

Table SIV. Continued.

Gene symbol small ligand	-cdocker energy
Polygonatine C	31.0518
2-(hydroxyphenyl)-ethanol	23.3275
5-hydroxymethylfurfural	23.4178
Kinganone	42.6019
Polygonatine A	21.2442
4-methylolfurfural	23.7867
4',5-Dihydroxyflavone	28.8783
HMF	23.1469
Apigenin	33.4602
Tyrosine	31.6215
Tryptophane	29.2848
Scopoletin	20.8463
Phenylalanine	28.7645
Leucine	24.8503
Isoleucine	24.4198
Baogongteng B	20.8463
6-methoxy-7-hydroxycoumarin	20.8463
Paeonol	22.4596
DBP	37.5333
Lauric acid	36.1272
CHRM2	
Rivastigmine	36.5990
Tacrine	17.3629
Memantine	1.9253
Gаланthamine	-15.8278
Donepezil	-30.8953
Polygonatine C	34.0670
2-(hydroxyphenyl)-ethanol	21.4558
5-hydroxymethylfurfural	21.8403
Kinganone	33.4390
Polygonatine A	21.3999
4-methylolfurfural	21.6481
4',5-Dihydroxyflavone	25.9610
HMF	21.8566
Apigenin	25.6367
Tyrosine	28.8663
Tryptophane	28.9274
Scopoletin	23.2735
Phenylalanine	28.1534
Leucine	24.3766
Isoleucine	24.5597
Baogongteng B	23.2735
6-methoxy-7-hydroxycoumarin	23.2735
Paeonol	20.3232
DBP	36.5498
Lauric acid	37.3710
HTR2A	
Rivastigmine	25.3694
Tacrine	10.8328
Donepezil	2.3936
Memantine	-2.1427
Gаланthamine	-17.5362
Polygonatine C	23.7606
2-(hydroxyphenyl)-ethanol	16.5336
5-hydroxymethylfurfural	16.9804
Kinganone	27.6125
Polygonatine A	17.4480
4-methylolfurfural	17.3144
4',5-Dihydroxyflavone	20.6368

Table SIV. Continued.

Gene symbol small ligand	-cdocker energy
HMF	18.1174
Apigenin	25.2624
Tyrosine	23.4665
Tryptophane	19.7616
Scopoletin	15.9838
Phenylalanine	20.9866
Leucine	19.3125
Isoleucine	18.4317
Baogongteng B	15.9838
6-methoxy-7-hydroxycoumarin	15.9838
Paeonol	17.0100
DBP	28.5204
Lauric acid	27.3757
MAPT	
Rivastigmine	29.0070
Tacrine	11.9481
Memantine	-3.9305
Galanthamine	-16.5837
Polygonatine C	31.0493
2-(hydroxyphenyl)-ethanol	22.5335
5-hydroxymethylfurfural	21.7747
Kinganone	34.2625
Polygonatine A	18.0596
4-methylolfurfural	24.5261
4',5-Dihydroxyflavone	23.6590
HMF	21.1399
Apigenin	24.1273
Tyrosine	26.9016
Tryptophane	25.2548
Scopoletin	21.1696
Phenylalanine	25.3989
Leucine	24.1991
Isoleucine	20.9481
Baogongteng B	21.1696
6-methoxy-7-hydroxycoumarin	21.1696
Paeonol	18.5150
DBP	40.9866
Lauric acid	30.4694

ACHE, acetylcholinesterase; BCHE, butyrylcholinesterase; APP, amyloid protein precursor; HTR2A, 5-hydroxytryptamine receptor 2A; CHRM2, muscarinic acetylcholine receptor M2; MAPT, microtubule-associated protein tau.