

Supplementary File

Supplementary Table 1 The recruiting criteria for patients in this study.

Recruiting criteria	Content
The inclusion criteria	1) diagnosis of CNG according to Chinese Consensus on Chronic Gastritis, 2) aged between 35 and 70 years, 3) voluntary provision of written informed consent.
The exclusion criteria	1) Patients with gastric related surgery, 2) Patients with atrophic changes, intestinal metaplasia or suspected malignant changes in the gastric mucosa, 3) Comorbidities of other system diseases in heart, liver, lung, kidney or blood system, 4) Female patients is going to having a baby, pregnant or lactating, 5) Having life-threatening illness such as tumor and so on, 6) Patients received other kinds of medicine in the last 2 weeks before recruitment, 7) Judged as inappropriate to be enrolled in the trial by investigators.
The rejection criteria	1) Misdiagnosis, 2) Patients who do not follow the drug dosage taking, 3) Patients who cannot complete the follow-up.

Supplementary Table 2 The parameters for chromatography for evodiamine, rutaecarpine, limonin, 6-gingerol, and ginsenoside Rb1

Time (min)	A (C ₂ H ₃ N)	B (0.01% H ₃ PO ₄)
0	10	90
10	15	85
40	30	70
51	90	10
60	90	10
61	10	90
75	10	90

Note: Chromatographic column: Welch Ultimate AQ-C18 (4.6×250 mm, 5 μm), detection wavelength: 203 nm; flow rate: 1 ml/min, column temperature: 30 °C; injection volume: 10 μl.

Supplementary Table 3 The parameters for chromatography for dehydroevodiamine.

Time (min)	A (C ₂ H ₃ N)	B (0.01% H ₃ PO ₄)
0	10	90
10	15	85
40	30	70

Note: Chromatographic column: Welch Ultimate AQ-C18 (4.6×250 mm, 5 μm), detection wavelength: 203 nm; flow rate: 1 ml/min, column temperature: 30 °C; injection volume: 10 μl.

Supplementary Table 4 Score of endoscopy evaluation

Item	Grade	Score
Red plaques	No red plaques in gastric mucosa	0
	Red plaques with sporadic or interrupted linear type in gastric mucosa	1
	Intensive plaques or linear series type in gastric mucosa	2
	Red plaques with extensive and obvious fusion type in gastric mucosa	3
Erosion	No ruptured erosion	0
	Sporadic erosion in gastric mucosa	1
	Local, multiple erosion in gastric mucosa and no more than five area	2
	Extensive, multiple erosion in gastric mucosa and more than five area	3
Hemorrhage	No flattened hemorrhagic spots or plaques in gastric mucosa	0
	Local hemorrhagic spots or plaques in gastric mucosa	1
	Multiple sites of hemorrhagic spots or plaques in gastric mucosa	2
	Widespread hemorrhagic spots or plaques in gastric mucosa	3
Bile reflux	No bile flow back into stomach	0
	Mild yellow bile flow back into stomach or yellowish mucinous lake	1
	Middle yellow bile flow back into stomach	2
	Massive yellow bile flow back into stomach	3

Notes: This table referred the standard in Chinese Consensus on Chronic Gastritis and the literature of 'XX Zhang, WW Chen, B She, et al. The efficacy and safety of Jian-Wei-Qu-Tong Pills for the treatment of chronic non-atrophic gastritis (spleen and stomach qi deficiency with damp-heat stasis syndrome): study protocol for a phase II, randomized controlled trial. Trial. 2014, 15: 272'.

Supplementary Table 5 Grade of histopathological changes

Item	Grade	Score
Chronic inflammation	Normal mononuclear cells in gastric mucosa	0
	No more than 1/3 of chronic inflammatory cells localized in the mucosa	1
	More than 1/3 but no more than 2/3 of chronic inflammatory cells localized in the mucosa	2
	Dense accumulation of chronic inflammatory cells in the whole mucosa	3
Active chronic inflammation	Normal neutrophils in mucosal layer	0
	No more than 1/3 of neutrophils in lamina propria of the mucosa	1
	More than 1/3 but no more than 2/3 of neutrophils in the mucosal layer and in superficial, pit as well as glandular epithelial cells.	2
	Dense infiltration of neutrophils, abscess with moderate activity.	3

Notes: This table referred the standard in Chinese Consensus on Chronic Gastritis and the literature of 'XX Zhang, WW Chen, B She, et al. The efficacy and safety of Jian-Wei-Qu-Tong Pills for the treatment of chronic non-atrophic gastritis (spleen and stomach qi deficiency with damp-heat stasis syndrome): study protocol for a phase II, randomized controlled trial. Trial. 2014, 15: 272'.

Supplementary Table 6 The stabilization and control for representative compounds in

WZYD

Compounds	Content in sample(mg)	Content (mg/g)
Ginsenoside Rb1	0.7178	0.6766
Dehydroevodiamine	0.6773	0.6384
Limonin	2.8144	2.6529
6-Gingerol	0.1634	0.1540
Evodiamine	3.9623	3.7348
Rutaecarpine	0.8555	0.8064

Supplementary Table 7 Core metabolites identified as the biomarkers for the difference between WZYD B and WZYD A. (WZYD B, patients before WZYD treatment; WZYD A, patients after WZYD treatment; HP, healthy people)

Fomula	Compounds	Class I	Class II	Regulation
C22H32O3	16-HDoHE	FA	Oxidized lipids	up
C10H14N5O7P	3'-Adenylic acid	Nucleotide And Its metabolites	Nucleotide And Its metabolites	down
C8H8O4	3-Hydroxy-4-methoxybenzoic acid	Benzene and substituted derivatives	Benzene and substituted derivatives	up
C11H9NO4	8-Methoxyalkynurate	Organic acid And Its derivatives	Organic acid And Its derivatives	down
C32H58N2O7S	Chaps	Bile acids	Bile acids	up
C5H11O8P	D-Arabinose 5-phosphate	Carbohydrates and Its metabolites	Phosphate sugars	up
C5H6N2O4	L-Dihydroorotic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down
C9H19NO4	Pantothenol	CoEnzyme and vitamins	CoEnzyme and vitamins	up
C5H4N2O2	Pyrimidine-4-carboxylic acid sodium salt	Heterocyclic compounds	Heterocyclic compounds	up
C33H42N4O6	Urobilin	Tryptamines,Cholines,Pigments	Pigments	up

Supplementary Table 8 Differential metabolites among HP, WZYD B and WZYD A. (WZYD B, patients before WZYD treatment; WZYD A, patients after WZYD treatment; HP, healthy people)

Formula	Compounds	Class I	Class II	HP/WZYD B	HP/WZYD A	WZYD B/WZYD A
C10H16O4	(+)-Camphoric acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C6H11NO2	(+/-)-High-Proline	Amino acid and Its metabolites	Amino acid derivatives	down	FALSE	FALSE
C18H35NO	(E,Z)-2-Amino-3,14-octadecadien-1-ol	Alcohol and amines	Alcohols	FALSE	down	FALSE
C14H28O3	(R)-3-Hydroxymyristic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C9H10O3	(S)-2-Hydroxy-3-phenylpropanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C6H12O3	(S)-Leucic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C20H30O3	(±)12-HEPE	FA	Oxidized lipids	down	down	FALSE
C20H32O3	(±)12-HETE	FA	Oxidized lipids	down	down	FALSE
C20H30O3	(±)15-HEPE	FA	Oxidized lipids	down	down	FALSE
C20H32O3	(±)15-HETE	FA	Oxidized lipids	down	down	FALSE
C20H30O3	(±)18-HEPE	FA	Oxidized lipids	down	down	FALSE
C5H9NO2	1-Aminocyclobutanecarboxylic acid	Amino acid and Its metabolites	Amino acid derivatives	down	down	FALSE
C11H8O3	1-Hydroxy-2-Naphthoate	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C11H15N5	1-Methyladenosine	Nucleotide And Its	Nucleotide And Its	up	up	FALSE

O4		metabolites	metabolites			
		Benzene and substituted	Benzene and substituted			
C14H18O9	1-O-vanillyl- β -D-glucose	derivatives	derivatives	up	up	FALSE
C18H36O3	10-Hydroxystearic Acid	FA	Oxidized lipids	down	down	FALSE
C20H32O3	11,12-EET	FA	Oxidized lipids	down	down	FALSE
C22H32O3	11-HDoHE	FA	Oxidized lipids	down	down	FALSE
C18H34O4	12,13-DiHOME	FA	Oxidized lipids	down	FALSE	FALSE
C18H32O3	12,13-EpOME	FA	Oxidized lipids	down	down	FALSE
C12H24O3	12-Hydroxydodecanoic acid	FA	FFA	up	up	FALSE
C18H36O3	12-Hydroxyoctadecanoic acid	FA	FFA	down	down	FALSE
C22H32O3	14(S)-HDHA	FA	Oxidized lipids	down	down	FALSE
C20H28O3	15-deoxy- δ -12,14-PGJ2	FA	Oxidized lipids	up	up	FALSE
C22H29Cl		Hormones and hormone	Hormones and hormone			
O6	15S-Cloprostenol	related compounds	related compounds	up	up	FALSE
C22H32O3	16-HDoHE	FA	Oxidized lipids	down	FALSE	up
C10H12N4		Nucleotide And Its	Nucleotide And Its			
O4	2'-Deoxyinosine	metabolites	metabolites	up	up	FALSE
C11H15N5		Nucleotide And Its	Nucleotide And Its			
O4	2'-O-methyladenosine	metabolites	metabolites	down	down	FALSE
		Organic acid And Its	Organic acid And Its			
C7H14O2	2,2-Dimethylpentanoic acid	derivatives	derivatives	down	down	FALSE
	2,6,6-Trimethyl-2-cyclohexene-1,					
C9H12O2	4-dione	Aldehyde,Ketones,Esters	Ketones	up	up	FALSE
		Benzene and substituted				
C9H10O3	2-(4-hydroxyphenyl) propionate	derivatives	Phenolic acids	down	down	FALSE
C8H7NO3	2-(Formylamino)Benzoic Acid	Benzene and substituted	Phenolic acids	up	FALSE	FALSE

C7H8O2	2-Acetyl-5-methylfuran	derivatives Heterocyclic compounds	Heterocyclic compounds	up	up	FALSE
C8H6O3	2-Carboxybenzaldehyde	Benzene and substituted derivatives	Benzene and substituted derivatives	up	up	FALSE
C5H10O3	2-Hydroxy-2-Methyl Butyric acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H10O3	2-Hydroxy-3-Methyl Butanoic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H10O3S	2-Hydroxy-4-(methylthio)butyric acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C8H16O3	2-Hydroxycaprylic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C6H12O3	2-Hydroxyhexanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C6H12O3	2-Hydroxyisocaproic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H12O9P 2	2-Methyl-d-erythritol 2,4-cyclodiphosphate	Carbohydrates and Its metabolites	Phosphate sugars	down	down	FALSE
C6H10O4	2-Methylglutaric Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C7H14O2	2-Methylhexanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C4H7NO	2-Pyrrolidinone	Heterocyclic compounds	Heterocyclic compounds	up	up	FALSE
C6H10O7	2-keto-D-gluconic acid	Carbohydrates and Its metabolites	Sugar acids	down	down	FALSE
C10H14N5	3'-Adenylic acid	Nucleotide And Its	Nucleotide And Its	FALSE	down	down

O7P		metabolites	metabolites			
C12H16O5	3-(3,4,5-trimethoxyphenyl)propionic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C9H10O3	3-(3-Hydroxyphenyl)Propionate Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C4H10OS	3-(Methylthio)-1-propanol	Alcohol and amines	Alcohols	up	up	FALSE
C11H9NO2	3-Amino-2-menacarboxylic acid	Benzene and substituted derivatives	Phenolic acids	FALSE	down	FALSE
C7H7NO3	3-Amino-4-Hydroxybenzoic Acid	Benzene and substituted derivatives	Phenolic acids	up	up	FALSE
C7H7NO3	3-Amino-5-hydroxybenzoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C8H8O4	3-Hydroxy-4-methoxybenzoic acid	Benzene and substituted derivatives	Benzene and substituted derivatives	down	FALSE	up
C9H11NO3	3-Hydroxy-L-phenylalanine	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C14H28O3	3-Hydroxy-tetradecanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C7H7NO3	3-Hydroxyanthranilic Acid	Benzene and substituted derivatives	Phenolic acids	up	up	FALSE
C12H16N2O4	3-Hydroxycaprolactone	Aldehyde,Ketones,Esters	Esters	up	up	FALSE
C9H8O3	3-Hydroxycinnamic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H8O5	3-Hydroxyglutaric acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE

C9H9NO4	3-Hydroxyhippuric Acid	Amino acid and Its metabolites	Amino acid derivatives	up	FALSE	FALSE
C8H8O3	3-Hydroxyphenylacetic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C6H10O2	3-methyl-4-pentenoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C6H9N3O	4-Amino-5-hydroxymethyl-2-methylpyrimidine	Heterocyclic compounds	Heterocyclic compounds	up	up	FALSE
C10H20O2	4-Ethyl octanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H6O6	4-Hydroxy-2-Oxoglutaric Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C9H10O4	4-Hydroxy-3-methoxyphenylacetic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C7H8O2	4-Hydroxybenzyl alcohol	Benzene and substituted derivatives	Benzene and substituted derivatives	up	up	FALSE
C9H9NO4	4-Hydroxyhippurate	Amino acid and Its metabolites	Amino acid derivatives	up	FALSE	FALSE
C20H28O3	4-Hydroxyretinoic Acid	CoEnzyme and vitamins	CoEnzyme and vitamins	up	up	FALSE
C7H14O2	4-Methylhexanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C9H18O2	4-Methyloctanoic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C20H26O3	4-Oxoretinoic acid	Benzene and substituted derivatives	Benzene and substituted derivatives	FALSE	down	FALSE
C8H8O3	4-acetoxyphenol	Benzene and substituted	Phenolics	up	up	FALSE

C11H15N5 O3S	5'-Deoxy-5'-(Methylthio) Adenosine	derivatives Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C8H14N3O 7P	5-Aminoimidazole ribonucleotide	Nucleotide And Its metabolites	Nucleotide And Its metabolites	down	down	FALSE
C9H12N2O 6	5-Hydroxy-2'-deoxyuridine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C6H12O3	5-Hydroxyhexanoic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C8H7NO	5-Hydroxyindole	Heterocyclic compounds	Indole and Its derivatives	down	down	FALSE
C5H7N3O	5-Methylcytosine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C10H14N2 O6	5-Methyluridine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C6H7N3O	6-aminonicotinamide	Nucleotide And Its metabolites	Nucleotide And Its metabolites	down	FALSE	FALSE
C16H23N5 O5	7-(alpha-D-glucosyl)-N(6)-isopen tenyladenine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	down	FALSE	FALSE
C6H7N5O	7-Methylguanine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C11H9NO4	8-Methoxyalkynurate	Organic acid And Its derivatives	Organic acid And Its derivatives	FALSE	down	down
C20H36O5	8-isoprostaglandin F1 α	FA	Oxidized lipids	up	up	FALSE
C18H34O5	9(S),12(S),13(S)-TriHOME	FA	Oxidized lipids	down	down	FALSE
C18H34O4	9,10-DiHOME	FA	Oxidized lipids	down	down	FALSE
C18H32O3	9,10-EpOME	FA	Oxidized lipids	down	down	FALSE

C18H36O4	9,10-dihydroxystearic acid	FA	FFA	down	down	FALSE
C20H32O2	AA	FA	Oxidized lipids	down	down	FALSE
C20H30O2	Abietic acid	Others	Others	down	down	FALSE
C7H13NO3	Acetylvaline	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C6H10O4	Adipic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H14N4	Agmatine	Alcohol and amines	Polyamines	up	up	FALSE
C8H14N2O	Ala-Glu	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C9H19N3O	Ala-Lys	Amino acid and Its metabolites	Amino acid derivatives	down	down	FALSE
C8H14N2O	Ala-Pro	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C6H12N2O	Ala-Ser	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C19H26O2	Androstenedione	Hormones and hormone related compounds	Hormones and hormone related compounds	up	up	FALSE
C9H17N3O	Asn-Met	Amino acid and Its metabolites	Small Peptide	FALSE	up	FALSE
C13H16N2O5	Asp-Phe	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C9H16O4	Azelaic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C6H13NO4	Bicine	Organic acid And Its derivatives	Organic acid And Its derivatives	down	FALSE	FALSE

C33H34N4		Tryptamines,Cholines,Pigmen				
O6	Biliverdin	ts	Pigments	down	down	FALSE
C6H17N3	Caldine	Alcohol and amines	Amines	down	down	FALSE
C21H41NO						
5	Carnitine C14-OH	FA	CAR	down	down	FALSE
C21H41NO						
4	Carnitine C14:0	FA	CAR	down	down	FALSE
C21H37NO						
5	Carnitine C14:2-OH	FA	CAR	FALSE	down	FALSE
C21H35NO						
6	Carnitine C14:2:DC	FA	CAR	down	down	FALSE
C22H41NO						
6	Carnitine C15:DC	FA	CAR	down	down	FALSE
C23H45NO						
5	Carnitine C16-OH	FA	CAR	down	down	FALSE
C23H45NO						
4	Carnitine C16:0	FA	CAR	down	down	FALSE
C23H43NO						
4	Carnitine C16:1	FA	CAR	down	down	FALSE
C23H41NO						
4	Carnitine C16:2	FA	CAR	down	FALSE	FALSE
C25H49NO						
5	Carnitine C18-OH	FA	CAR	FALSE	down	FALSE
C25H47NO						
5	Carnitine C18:1-OH	FA	CAR	down	down	FALSE
C25H45NO	Carnitine C18:2	FA	CAR	down	down	FALSE

4						
C25H45NO						
5	Carnitine C18:2-OH	FA	CAR	down	down	FALSE
C25H43NO						
4	Carnitine C18:3	FA	CAR	down	down	FALSE
C27H49NO						
4	Carnitine C20:2	FA	CAR	down	down	FALSE
C9H17NO4	Carnitine C2:0	FA	CAR	down	down	FALSE
C13H23NO						
6	Carnitine C6:DC	FA	CAR	up	up	FALSE
C32H58N2						
O7S	Chaps	Bile acids	Bile acids	down	down	up
		Organic acid And Its derivatives	Organic acid And Its derivatives			
C6H8O7	Citric Acid			down	down	FALSE
C8H16N2O		Organic acid And Its derivatives	Organic acid And Its derivatives			
4	Cork-oximate			up	up	FALSE
C4H10N3O		Nucleotide And Its metabolites	Nucleotide And Its metabolites			
5P	Creatine phosphate			down	down	FALSE
C14H16N2		Amino acid and Its metabolites				
O4	Cyclo(Phe-Glu)		Small Peptide	down	FALSE	FALSE
		Nucleotide And Its metabolites	Nucleotide And Its metabolites			
C5H9N3O2	Cyclocreatine			up	up	FALSE
C8H14N2O		Amino acid and Its metabolites				
3S	Cys-Pro		Small Peptide	down	down	FALSE
C9H15N3O		Nucleotide And Its metabolites	Nucleotide And Its metabolites			
11P2	Cytidine 5'-diphosphate			down	down	FALSE

C12H22O11	D-(+)-sucrose	Carbohydrates and Its metabolites	Sugars	down	down	FALSE
C5H11O8P	D-Arabinose 5-phosphate	Carbohydrates and Its metabolites	Phosphate sugars	down	FALSE	up
C6H11Na2O9P	D-Fructose 6-Phosphate-Disodium Salt	Carbohydrates and Its metabolites	Phosphate sugars	down	down	FALSE
C6H10O7	D-Galacturonic Acid	Carbohydrates and Its metabolites	Sugar acids	down	down	FALSE
C6H12O7	D-Gluconic Acid	Carbohydrates and Its metabolites	Sugar acids	down	down	FALSE
C6H13NO6	D-Glucosaminic acid	Carbohydrates and Its metabolites	Sugar acids	FALSE	up	FALSE
C6H13O9P	D-Glucose 6-Phosphate	Carbohydrates and Its metabolites	Phosphate sugars	down	down	FALSE
C4H6O5	D-Malic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C6H13O9P	D-Mannose 6-phosphate	Carbohydrates and Its metabolites	Phosphate sugars	down	down	FALSE
C6H8O7	D-Saccharic Acid 1,4-lactone (hydrate)	Carbohydrates and Its metabolites	Sugars	down	down	FALSE
C12H22O11	D-cellobiose	Carbohydrates and Its metabolites	Sugars	up	up	FALSE
C22H32O2	DHA	FA	Oxidized lipids	down	FALSE	FALSE
C8H10O4	DL-3,4-Dihydroxyphenyl glycol	Benzene and substituted derivatives	Benzene and substituted derivatives	up	up	FALSE
C10H18N2	Dethiobiotin	CoEnzyme and vitamins	CoEnzyme and vitamins	up	up	FALSE

O3

		Benzene and substituted derivatives	Benzene and substituted derivatives			
C9H9NO4	Dopaquinone			up	up	FALSE
C20H30O2	EPA	FA	Oxidized lipids	down	down	FALSE
C10H20O2	FFA(10:0)	FA	FFA	down	down	FALSE
C12H24O2	FFA(12:0)	FA	FFA	down	down	FALSE
C14H28O2	FFA(14:0)	FA	FFA	down	down	FALSE
C18H28O2	FFA(18:4)	FA	FFA	FALSE	down	FALSE
C20H32O2	FFA(20:4)	FA	FFA	down	down	FALSE
C22H36O2	FFA(22:4)	FA	FFA	down	down	FALSE
C22H32O2	FFA(22:6)	FA	FFA	down	FALSE	FALSE
C22H30O2	FFA(22:7)	FA	FFA	down	down	FALSE
C9H18O2	FFA(9:0)	FA	FFA	down	down	FALSE
C9H14O3	Furfural diacetal	Others	Others	up	up	FALSE
C7H13N3O 4	Gln-Gly	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C11H20N2 O5	Glu-Ile	Amino acid and Its metabolites	Small Peptide	FALSE	up	FALSE
C10H18N2 O5S	Glu-Met	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C10H18N2 O5	Glu-Val	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C7H13N3O 4	Gly-Gln	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C8H17N3O 3	Gly-Lys	Amino acid and Its metabolites	Small Peptide	FALSE	down	FALSE

C11H14N2 O3	Gly-Phe	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C20H23N3 O4	Gly-Phe-Phe	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C25H44NO 7P	Glycerophospho-N-Arachidonoyl Ethanolamine	GP	LPE	up	up	FALSE
C10H13N5 O5	Guanosine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C9H10O4	Hydroxyphenyllactic acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C5H10N2O 3	Hydroxypiperazic acid	Heterocyclic compounds	Heterocyclic compounds	up	up	FALSE
CH4N2O2	Hydroxyurea	Others	Others	down	down	FALSE
C8H14N2O 5	Hyp-Ser	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C9H16N2O 5	Hyp-Thr	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C3H9N3O2 S	Hypotaurocyamine	Alcohol and amines	Polyamines	up	up	FALSE
C9H18N2O 3	Ile-Ala	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C11H20N2 O5	Ile-Glu	Amino acid and Its metabolites	Small Peptide	FALSE	up	FALSE
C12H20N4 O3	Ile-His	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C12H24N2	Ile-Ile	Amino acid and Its	Small Peptide	up	up	FALSE

O3		metabolites				
C12H24N2		Amino acid and Its				
O3	Ile-Leu	metabolites	Small Peptide	up	up	FALSE
C12H25N3		Amino acid and Its				
O3	Ile-Lys	metabolites	Small Peptide	down	down	FALSE
C9H7NO	Indole-3-Carboxaldehyde	Heterocyclic compounds	Indole and Its derivatives	FALSE	up	FALSE
C11H11NO						
3	Indole-3-lactic acid	Heterocyclic compounds	Indole and Its derivatives	FALSE	down	FALSE
C9H7NO	Indole-4-carboxaldehyde	Heterocyclic compounds	Indole and Its derivatives	FALSE	up	FALSE
C6H13O9P	Inositol 1-phosphate	Alcohol and amines	Alcohols	down	down	FALSE
		Organic acid And Its				
C2H6O4S	Isethionic acid	derivatives	Sulfonic acids	up	up	FALSE
		Organic acid And Its	Organic acid And Its			
C6H8O7	Isocitric acid	derivatives	derivatives	up	up	FALSE
C12H22O1						
1	Kojibiose	Others	Others	down	down	FALSE
C6H14N4O		Amino acid and Its				
2	L-Arginine	metabolites	Amino acids	up	up	FALSE
		Amino acid and Its				
C4H8N2O3	L-Asparagine Anhydrous	metabolites	Amino acids	up	up	FALSE
		Amino acid and Its				
C4H7NO4	L-Aspartic Acid	metabolites	Amino acids	FALSE	up	FALSE
C6H13N3O		Amino acid and Its				
3	L-Citrulline	metabolites	Amino acids	up	up	FALSE
		Amino acid and Its				
C3H7NO2S	L-Cysteine	metabolites	Amino acids	down	down	FALSE

C5H6N2O4	L-Dihydroorotic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	FALSE	down	down
C6H12O5	L-Fucose	Carbohydrates and Its metabolites	Sugars	up	up	FALSE
C5H10N2O3	L-Glutamine	Amino acid and Its metabolites	Amino acids	up	up	FALSE
C6H12O6	L-Gulose	Carbohydrates and Its metabolites	Carbohydrates and Its metabolites	down	down	FALSE
C7H16N4O2	L-Homoarginine	Amino acid and Its metabolites	Amino acids	down	down	FALSE
C5H9NO2	L-Proline	Amino acid and Its metabolites	Amino acids	down	down	FALSE
C7H14N2O3	L-Theanine	Amino acid and Its metabolites	Amino acids	down	down	FALSE
C9H11NO3	L-Tyrosine	Amino acid and Its metabolites	Amino acids	up	up	FALSE
C28H52NO7P	LPC(0:0/20:3)	GP	LPC	up	up	FALSE
C30H52NO7P	LPC(0:0/22:5)	GP	LPC	up	up	FALSE
C28H52NO7P	LPC(20:3/0:0)	GP	LPC	up	up	FALSE
C30H52NO7P	LPC(22:5/0:0)	GP	LPC	up	up	FALSE
C26H54NO6P	LPC(O-18:1/0:0)	GP	LPC	down	FALSE	FALSE

C21H42NO							
7P	LPE(0:0/16:1)	GP	LPE	up	up	FALSE	
C23H44NO							
7P	LPE(0:0/18:2)	GP	LPE	up	up	FALSE	
C25H46NO							
7P	LPE(0:0/20:3)	GP	LPE	up	up	FALSE	
C25H42NO							
7P	LPE(0:0/20:5)	GP	LPE	FALSE	up	FALSE	
C27H46NO							
7P	LPE(0:0/22:5)	GP	LPE	up	up	FALSE	
C27H44NO							
7P	LPE(0:0/22:6)	GP	LPE	up	up	FALSE	
C21H42NO							
7P	LPE(16:1/0:0)	GP	LPE	up	up	FALSE	
C25H46NO							
7P	LPE(20:3/0:0)	GP	LPE	up	up	FALSE	
C25H44NO							
7P	LPE(20:4/0:0)	GP	LPE	up	up	FALSE	
C25H42NO							
7P	LPE(20:5/0:0)	GP	LPE	FALSE	up	FALSE	
C27H46NO							
7P	LPE(22:5/0:0)	GP	LPE	up	up	FALSE	
C27H44NO							
7P	LPE(22:6/0:0)	GP	LPE	up	up	FALSE	
C30H30O7	LY223982	Benzene and substituted derivatives	Benzene and substituted derivatives	up	up	FALSE	

C9H18N2O 3	Leu-Ala	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C11H20N2 O5	Leu-Glu	Amino acid and Its metabolites	Small Peptide	FALSE	up	FALSE
C12H24N2 O3	Leu-Leu	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C15H22N2 O3	Leu-Phe	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C9H19N3O 3	Lys-Ala	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C8H17N3O 3	Lys-Gly	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C12H25N3 O3	Lys-Leu	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C15H23N3 O3	Lys-Phe	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C11H21N3 O3	Lys-Pro	Amino acid and Its metabolites	Small Peptide	FALSE	down	FALSE
C11H23N3 O3	Lys-Val	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C25H38O4	MG(0:0/22:6/0:0)	GL	MG	up	up	FALSE
C21H40O4	MG(18:1/0:0/0:0)	GL	MG	up	up	FALSE
C23H38O4	MG(20:4/0:0/0:0)	GL	MG	up	up	FALSE
C25H38O4	MG(22:6/0:0/0:0)	GL	MG	up	up	FALSE
C4H4O4	Maleic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE

C12H24O1			Carbohydrates and Its					
1	Maltitol		metabolites	Sugar alcohols	up	up	FALSE	
C13H16N2			Hormones and hormone	Hormones and hormone				
O2	Melatonin		related compounds	related compounds	up	up	FALSE	
C10H20N2			Amino acid and Its					
O3S	Met-Val		metabolites	Small Peptide	down	down	FALSE	
C11H11NO								
3	Methoxyindoleacetic Acid		Heterocyclic compounds	Indole and Its derivatives	FALSE	down	FALSE	
C11H11NO								
2	Methyl Indole-3-Acetate		Heterocyclic compounds	Indole and Its derivatives	FALSE	up	FALSE	
			Amino acid and Its					
C4H9NO2S	Methylcysteine		metabolites	Amino acids	down	down	FALSE	
C12H14O4	Monobutyl phthalate		Aldehyde,Ketones,Esters	Esters	down	down	FALSE	
			Benzene and substituted					
C11H14O4	Multifidol		derivatives	Phenolics	up	up	FALSE	
C11H12N2			Amino acid and Its					
O4	N'-Formylkynurenine		metabolites	Amino acid derivatives	up	up	FALSE	
C11H18N2	N(Alpha)-Acetyl-Epsilon-(2-Prop		Amino acid and Its					
O4	enal)Lysine		metabolites	Small Peptide	down	FALSE	FALSE	
	N,-N-diacetyl-O-methylhydroxyl							
C5H9NO3	amine		Alcohol and amines	Polyamines	up	up	FALSE	
C11H11NO			Benzene and substituted	Benzene and substituted				
3	N-(3-Hydroxypropyl)phthalimide		derivatives	derivatives	FALSE	down	FALSE	
			Amino acid and Its					
C8H15NO3	N-Acetyl-L-Leucine		metabolites	Amino acid derivatives	up	up	FALSE	
C11H13NO	N-Acetyl-L-Tyrosine		Amino acid and Its	Amino acid derivatives	up	up	FALSE	

4		metabolites				
C11H13NO		Amino acid and Its				
3	N-Acetyl-L-phenylalanine	metabolites	Amino acid derivatives	up	up	FALSE
C6H10N2O		Amino acid and Its				
4	N-Alpha-Acetyl-L-Asparagine	metabolites	Amino acid derivatives	FALSE	down	FALSE
C5H9N3O4		Amino acid and Its				
	N-Amidino-L-Aspartate	metabolites	Amino acid derivatives	up	up	FALSE
C4H9NO2		Amino acid and Its				
	N-Ethylglycine	metabolites	Amino acid derivatives	down	FALSE	FALSE
C5H9NO4		Amino acid and Its				
	N-Methyl-D-Aspartic Acid	metabolites	Amino acid derivatives	down	down	FALSE
C6H11NO4		Amino acid and Its				
	N-Methyl-L-Glutamate	metabolites	Amino acid derivatives	up	up	FALSE
C4H9NO2		Amino acid and Its				
	N-Methylalanine	metabolites	Amino acid derivatives	down	FALSE	FALSE
C14H25NO		Carbohydrates and Its	Carbohydrates and Its			
11	N-acetyl-D-Lactosamine	metabolites	metabolites	down	down	FALSE
C5H9NO3		Amino acid and Its				
	N-acetyl-beta-alanine	metabolites	Amino acid derivatives	up	up	FALSE
C7H14N2O		Amino acid and Its				
3	N-acetylorithine	metabolites	Amino acid derivatives	up	up	FALSE
C12H15NO		Amino acid and Its				
4	N-lactoyl-phenylalanine	metabolites	Amino acid derivatives	down	down	FALSE
C9H20N2O		Amino acid and Its				
2	N6,N6,N6-Trimethyl-L-lysine	metabolites	Amino acid derivatives	down	down	FALSE
C14H17N5		Nucleotide And Its	Nucleotide And Its	down	down	FALSE
	N6-Succinyl Adenosine					

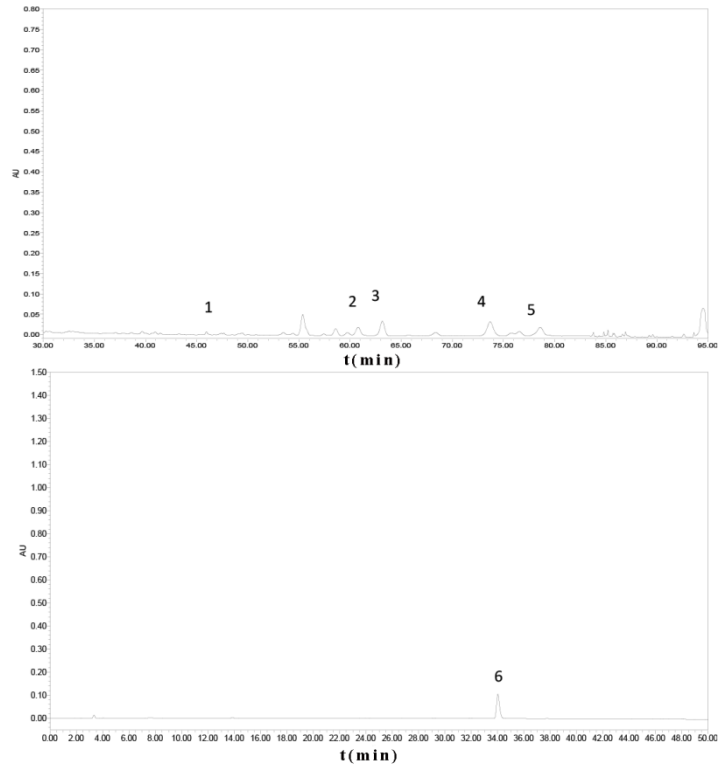
O8		metabolites	metabolites			
C11H15N5		Nucleotide And Its	Nucleotide And Its			
O4	N6-methyladenosine	metabolites	metabolites	up	up	FALSE
C6H6N2O	Nicotinamide	CoEnzyme and vitamins	CoEnzyme and vitamins	down	FALSE	FALSE
C5H9NO4	O-Acetyl-L-serine	Amino acid and Its metabolites	Amino acid derivatives	down	down	FALSE
C3H8NO6P	O-Phospho-L-Serine	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C18H35NO	Oleamide	Alcohol and amines	Amines	FALSE	down	FALSE
C5H4N2O4	Orotic Acid	CoEnzyme and vitamins	CoEnzyme and vitamins	down	down	FALSE
C28H56NO						
8P	PC(12:0/12:0)	GP	PC	up	up	FALSE
C18H37NO						
2	Palmitoylethanolamide (PEA)	Alcohol and amines	Amines	down	down	FALSE
C9H19NO4	Pantothenol	CoEnzyme and vitamins	CoEnzyme and vitamins	FALSE	FALSE	up
C18H27N3		Amino acid and Its				
O4	Phe-Ala-Leu	metabolites	Small Peptide	up	up	FALSE
C13H17N3		Amino acid and Its				
O4	Phe-Asn	metabolites	Small Peptide	up	up	FALSE
C11H14N2		Amino acid and Its				
O3	Phe-Gly	metabolites	Small Peptide	up	up	FALSE
C14H20N2		Amino acid and Its				
O3S	Phe-Met	metabolites	Small Peptide	up	up	FALSE
C18H20N2		Amino acid and Its				
O3	Phe-Phe	metabolites	Small Peptide	up	up	FALSE
C12H16N2	Phe-Ser	Amino acid and Its	Small Peptide	up	up	FALSE

O4		metabolites				
C20H21N3		Amino acid and Its				
O3	Phe-Trp	metabolites	Small Peptide	up	up	FALSE
C9H10O3	Phenyllactate(Pla)	Organic acid And Its	Organic acid And Its	down	down	FALSE
C6H11NO2	Piperidine acid	derivatives	derivatives	down	down	FALSE
C10H16N2		Organic acid And Its	Organic acid And Its	down	down	FALSE
O5	Pro-Glu	derivatives	derivatives	down	down	FALSE
C11H20N2		Amino acid and Its	Small Peptide	down	down	FALSE
O3	Pro-Leu	metabolites	Small Peptide	down	FALSE	FALSE
C8H14N2O		Amino acid and Its	Small Peptide	down	FALSE	FALSE
4	Pro-Ser	metabolites	Small Peptide	down	FALSE	FALSE
C10H18N2		Amino acid and Its	Small Peptide	down	down	FALSE
O3	Pro-Val	metabolites	Small Peptide	down	down	FALSE
C5H4N2O2	Pyrimidine-4-carboxylic acid sodium salt	Heterocyclic compounds	Heterocyclic compounds	down	FALSE	up
H4O7P2	Pyrophosphate	Organic acid And Its	Phosphoric acids	down	down	FALSE
C7H12O6	Quinic acid	derivatives	Organic acid And Its	down	down	FALSE
C4H5NO2S		derivatives	derivatives	down	down	FALSE
2	Raphanusamic acid	Organic acid And Its	Organic acid And Its	down	down	FALSE
C4H9NO3S	S-Methyl-L-Cysteine-S-oxide	derivatives	derivatives	down	down	FALSE
C7H15N3O	S-methyl-L-thiocitrulline	Amino acid and Its	Amino acid derivatives	up	up	FALSE
		metabolites	Amino acid derivatives	FALSE	up	FALSE

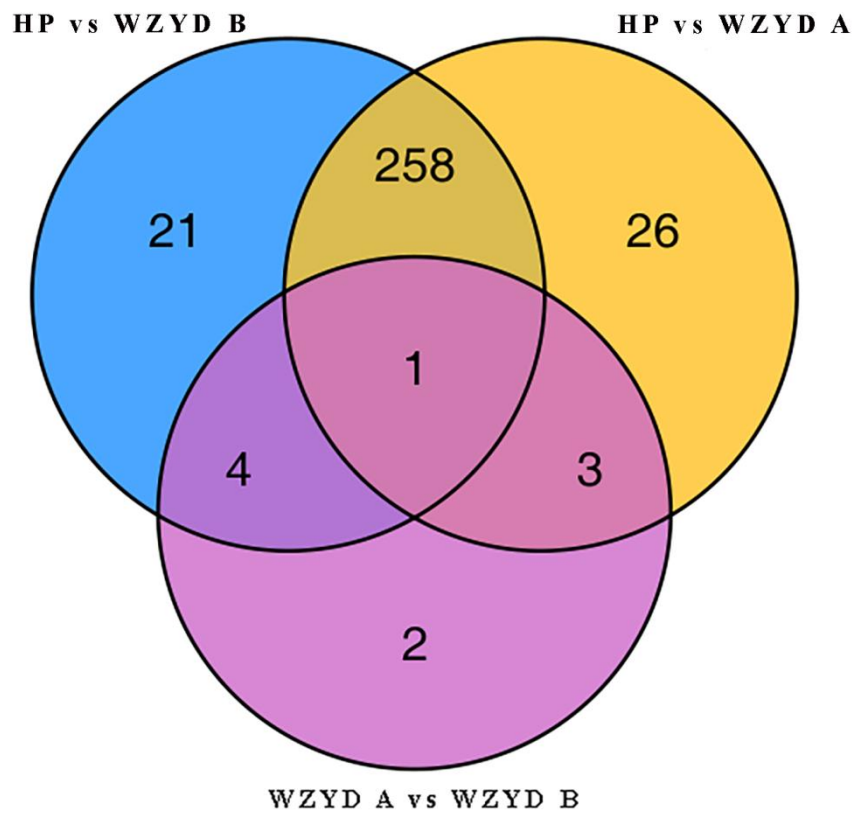
2S		metabolites				
C10H18O4	Sebacate	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C6H12N2O4	Ser-Ala	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C8H16N2O4	Ser-Val	Amino acid and Its metabolites	Small Peptide	FALSE	down	FALSE
C6H15O9P	Sorbitol 6-phosphate	Carbohydrates and Its metabolites	Phosphate sugars	down	down	FALSE
C23H50N2O5P	Sphingosyl-phosphocholine	SL	SM	down	down	FALSE
C4H6O4	Succinic Acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	FALSE	FALSE
C4H4O3	Succinic anhydride	Organic acid And Its derivatives	Organic acid And Its derivatives	up	up	FALSE
C8H6O4	Terephthalic Acid	Benzene and substituted derivatives	Phenolic acids	down	down	FALSE
C27H40O3	Testosterone	Hormones and hormone related compounds	Hormones and hormone related compounds	down	down	FALSE
C6H15O4P	Triethyl-phosphate	Organic acid And Its derivatives	Phosphoric acids	down	down	FALSE
C7H7NO2	Trigonelline	CoEnzyme and vitamins	CoEnzyme and vitamins	down	FALSE	FALSE
C9H10O3	Tropine	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C16H19N3O5	Trp-Glu	Amino acid and Its metabolites	Small Peptide	down	down	FALSE

C13H17N3 O5	Tyr-Asn	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C12H16N2 O5	Tyr-Ser	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
CH4N2O	Urea	Alcohol and amines	Amines	up	up	FALSE
C5H8N2O5	Ureidosuccinic acid	Amino acid and Its metabolites	Amino acid derivatives	up	up	FALSE
C5H4N4O3	Uric acid	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C9H12N2O 6	Uridine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C33H42N4 O6	Urobilin	Tryptamines,Cholines,Pigmen ts	Pigments	FALSE	FALSE	up
C8H16N2O 3	Val-Ala	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C9H18N2O 4	Val-Thr	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C5H4N4O2	Xanthine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	up	up	FALSE
C10H12N4 O6	Xanthosine	Nucleotide And Its metabolites	Nucleotide And Its metabolites	down	down	FALSE
C10H14N2 O6	cyclo(glu-glu)	Amino acid and Its metabolites	Small Peptide	up	up	FALSE
C8H14N2O 5	gamma-Glu-Ala	Amino acid and Its metabolites	Small Peptide	down	down	FALSE
C9H12N2O	B-Pseudouridine	Nucleotide And Its	Nucleotide And Its	up	up	FALSE

6		metabolites	metabolites			
C5H8O5	α -Hydroxyglutaric Acid (sodium salt)	Organic acid And Its derivatives	Organic acid And Its derivatives	down	down	FALSE
C10H18N2		Amino acid and Its metabolites				
O5S	γ -Glu-Met		Small Peptide	up	up	FALSE



Supplementary Figure 1 The stabilization and control for representative compounds in WZYD by UHPLC.(1 Ginsenoside Rb1; 2 Limonin; 3 6-Gingerol; 4 Evodiamine; 5rutaecarpine; 6 Dehydroevodiamine)



Supplementary Figure 2 Differential metabolites of Venn diagram.(WZYD B, patients before WZYD treatment; WZYD A, patients after WZYD treatment; HP, healthy people)