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A Systematic Review on Chemical Constituents of Suanzaoren Decoction, a Traditional Chinese Medicine Prescription

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Abstract

Traditional Chinese Medicine prescription Suanzaoren decoction (SZRD) is composed of Ziziphi Spinosae Semen, Chuanxiong Rhizoma, Anemarrhenae rhizoma, Poria and Licorice. It was used to treat central nervous system diseases such as insomnia and anxiety for thousands of years. This paper aims to systematically understand varieties and quantities of compounds and clarify chemical components of SZRD, subsequently to further provide the reference for phytochemistry and pharmacology researches of SZRD. Our results showed that SZRD contained 145 components, including flavonoids, triterpenoids, steroids, coumarins, phthalides, and volatile oils, etc., while five-single herbs contain 1104 components. Only in terms of compound number, there were 80 common components in SZRD and its five herbs, which accounted for 6.8% of total compounds in all 5 herbs and 55.2% of compounds in SZRD. The components of SZRD were not simply the sum of one in every single herb. It is necessary to perform parallel studies among SZRD and its herbs. This review discussed the problems that existed in the chemical research of SZRD and pointed out the direction for its further research.

Keywords

Traditional Chinese Medicine, Suanzaoren Decoction, Chemical Ingredient

1. Introduction

Suanzaoren decoction (SZRD), a classic Traditional Chinese Medicine (TCM) prescription, was first described in the book "*Jin Gui Yao Lue*" by Zhongjing

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Zhang in Han dynasty. SZRD is consists of five herbs, Suanzaoren (Ziziphi Spinosae Semen, *Ziziphus jujuba Mill. var. spinosa* (*Bunge*) *Hu ex H.F. Chou*), Chuanxiong (Chuanxiong Rhizoma, *Ligusticum chuanxiong Hort.*), Zhimu (Anemarrhenae rhizoma, *Anemarrhena asphodeloides Bge.*), Fuling (Poria, *Poria cocos* (*Schw.*) *Wolf*) and Gancao (Licorice, *Glycyrrhiza uralensis Fisch.*, *Glycyrrhiza inflata Bat. or Glycyrrhiza glabra L.*) at a ratio of 15:6:6:6:3. In the clinic of TCM, SZRD is the most common herbal formula prescribed by TCM doctors to treat central nervous system diseases such as insomnia [1] [2] [3], secondary insomnia [4] [5] [6] [7], anxiety [8], depression [9], menopausal syndrome [10] and other diseases [11] [12]. Clinical researches showed that the combination of SZRD and other drugs, including TCM and chemicals, can improve insomnia [13] [14] [15] [16], anxiety [16] [17] [18], depression [19] [20] and other diseases [21], enhance the efficiency of treatment, and reduce adverse reactions. Besides, SZRD has pharmacological characteristics of immune protective and sedative effects [22].

The clinical therapeutic effect and pharmacological function of SZRD originate in its chemical composition. A vast lot of chemical components in SZRD have been isolated and identified using high-performance liquid chromatography (HPLC) and mass spectrometry (MS) technology. In this paper, we investigated and analyzed chemical ingredients of SZRD and its five-single herbs on basis of literatures in the last 5 years and calculated the percentage based on compounds number of a certain class in the total number of compounds. We also focused on similarities and differences of ingredients between SZRD and its herbs.

2. Chemical Constituents of Five Herbs in Suanzaoren Decoction

2.1. Suanzaoren (Ziziphi Spinosae Semen, *Ziziphus jujuba* Mill. var. *spinosa* (Bunge) Hu ex H.F. Chou)

We used "Suanzaoren", "Zaoren", "Ziziphi Spinosae Semen", "Jujube", "*Ziziphus jujuba Mill. var. spinosa* (*Bunge*) *Hu ex* H. F. Chou" as key words to search chemical components of Ziziphi Spinosae Semen. We mainly focused on the literatures of the past five years, and tried to get more ingredients at the same time. Results showed mounts of literatures on ingredients of Ziziphi Spinosae Semen have been reported until now. The 36 chemical components in standard decoction of Ziziphi Spinosae Semen are isolated by using UPLC-Q/TOF-MS and UPLC-PDA system, including nucleosides, phenolic acids, alkaloids and flavonoids [23]. The 109 components are identified in Ziziphi Spinosae Semen by UPLC-Q/TOF-MS and principal component analysis (PCA), including 66 flavonoids, 15 triterpenoid saponin, 19 alkaloids, 8 terpenoid acids and 1 phenolic acid [24]. Research on components in crude and parched Ziziphi Spinosae Semen shows that 40 chemical ingredients (flavonoids, saponins, alkaloids and triterpenoids, etc.) are changed during stir-frying process and 19 key markers

can contribute to classification of crude and parched Ziziphi Spinosae Semen [25]. The sedative and hypnotic effects of Ziziphi Spinosae Semen were significantly enhanced after processing. These researches provided a rapid and effective approach to monitor quality consistency of Ziziphi Spinosae Semen.

We totally collected 175 compounds in Ziziphi Spinosae Semen [23]-[40], which were divided into 8 categories, including flavonoids (62 compounds), alkaloids (28 compounds), amino acids (6 compounds), nucleosides (4 compounds), phenolic acids (4 compounds), triterpenoids (61 compounds), volatile oils (9 compounds) and others (1 compound) (**Table 1**). Ziziphi Spinosae Semen has the highest proportion of flavonoids (36%), followed by triterpenes (35%), and the lowest proportion of phenolic acids (2%) and nucleotides (2%) (**Figure 1(a)**).

2.2. Chuanxiong (Chuanxiong Rhizoma, *Ligusticum chuanxiong Hort.*)

The chemical constituents of Chuanxiong Rhizoma are searched by using "Chuanxiong", "Chuanxiong Rhizoma", "*Ligusticum chuanxiong Hort.*", "*Ligusticum sinense Oliv*" and we focused on the literature of the past five years, including English and Chinese literature. The study indicated that 73 chemical compounds in the essential oil from Chuanxiong Rhizoma were detected and 33 compounds with main component Z-Ligustilide were identified by gas chromatgraphy-mass spectrometry (GC-MS) [41]. The other study showed that 30 chemical components in Chuanxiong Rhizoma were separated and identified by using ultra-performance liquid chromatography with electrospray ionization-time of flight mass spectrometry (UPLC-ESI-TOF/MS) technology, including 20 phthalides, 2 flavonoids, 1 alkaloid and 7 phenolic acids [42]. Research on components of dried rhizome from Chuanxiong Rhizoma showed that 10 phthalide derivatives were isolated by using HPLC technology and spectroscopic analyses and 6 of them were identified as ligusticoside A-F for the first time [43].

Chuanxiong Rhizoma contained 324 compounds, which could be divided into 10 categories [41]-[56], including volatile oils (162 compounds, 50%), phthalides (chemical classification instead of plastic pollution) (85 compounds, 26%), phenolic acids (20 compounds, 6%), polysaccharides (17 compounds, 5%), alkaloids (14 compounds, 4%), flavonoids (6 compounds, 2%), ceramides and cerebrosides (5 compounds, 2%), coumarins (3 compounds, 1%), triterpenoids (4 compounds, 1%) and others (8 compounds, 3%) (**Table 2**, **Figure 1(b)**).

2.3. Zhimu (Anemarrhenae rhizoma, *Anemarrhena asphodeloides Bge.*)

We used "Zhimu", "Anemarrhenae rhizoma", "*Anemarrhena asphodeloides Bge.*", "*Anemarrhena asphodeloides Bunge*" as key words to search chemical components of Anemarrhenae rhizoma, and the literatures were mainly in recent years which contained all the components as much as possible. It's reported that 32 chemical constituents were identified in Anemarrhenae rhizoma, which

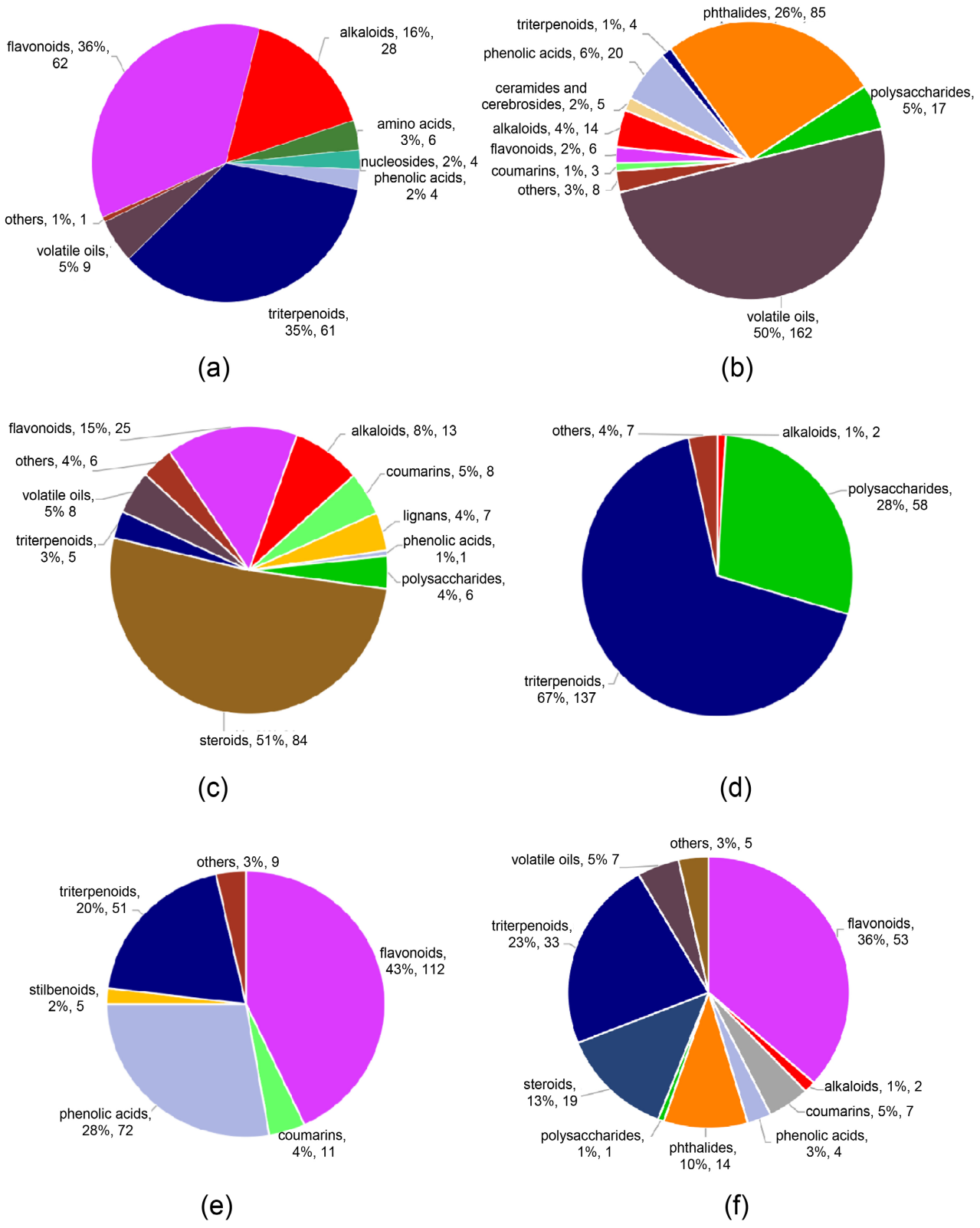

Figure 1. Chemical constituents in suanzaoren decoction and its herbs. (a) Constituents in Ziziphi Spinosae Semen; (b) Constituents in Chuanxiong Rhizoma; (c) Constituents in Anemarrhenae rhizome; (d) Constituents in Poria; (e) Constituents in Licorice; (f) Constituents in SZRD.

Table 1. Chemical constituents in Suanzaoren (Ziziphi Spinosae Semen, *Ziziphus jujuba Mill. var. spinosa* (*Bunge*) *Hu ex* H. F. Chou).

Class	Compound
Triterpenoids	24-hydroxyceanothic acid, 2-o-protocatechuoyl aliphitolic acid, 2α-hydroxypyracrenic acid, 3-ketoursolic acid, 5α,8α-epidioxy-(22e,4r)-ergosta-6,22-dien-3β-ol, acetyl jujuboside B, alhpitolic acid, betulic acid, betulin, betulinic acid, betutin, campesterol, ceanothenic acid, ceanothic acid, epiceanothic acid, jujuboside A, jujuboside A_1, jujuboside A_2, jujuboside B, jujuboside B_1, jujuboside c, jujuboside D, jujuboside E, jujuboside G, jujuboside h, jujuboside I, jujuboside II, jujuboside III, jujuboside IV, lupeol, methyl betulinate, projujuboside B, protojujuboside A, protojujuboside B, protojujuboside B_1, protojujuboside D, protojujuboside H, pseudolaroside B, stigmast-4-en-3-one, ursolic acid, 2α-hydroxyursolic acid, 3-o-cis-p-coumaroyl alphitolic acid, 3-o-cis-p-coumaroyl maslinic acid, 3-o-protocatechuoyl ceanothic acid, 3-o-trans-p-coumaroyl alphitolic acid, 3-o-trans-p-coumaroyl maslinic acid, Azukisaponin II, betulonic acid, cecropiacic acid, colubrinic acid, corosolic acid, hydroxyoleanonic acid lactone, isoceanothic acid, lulutonic acid, maslinic aicd, oleanolic acid, pomonic acid, zizyberanalic acid, zizyphus saponin I, zizyphus saponin II, zizyphus saponin III
Flavonoids	6-hydroxyflavone, 6'''-(-)-phaseoylspinosin, 6'''-(4'''-o-β-d-glucopyranosyl)-vanilloylspinosin, 6'''-(4''''-o-glu)-p-hydroxyben zoylspinosin, 6'''-diferuloylspinosin, 6'''-dihydrophaseoylspinosin, 6'''-ferulylspinosin, 6'''-pcoumaloylspinosin, 6'''-pcoumaroylspinosin, 6'''-phydroxybenzoylspinosin, 6'''-phydroxylbenzoyspinosin, 6'''-sinapoylspinosin, 6'''-vanilloylspinosin, 6"6'''-diferuloylisospinosin, acylated flavuone c-glycoside I, acylated flavuone c-glycoside II, acylated flavuone c-glycoside III, apigenin-6-c-[(6-o-phydroxybenzyol)-(β-d-glucopyranosyl(1→2)(β-d-glucopyranoside), isospinosin, isovitexin-2, isovitexin-2''-o-(6-feruloyl)-glucopyranoside, isovitexin-2''-o-d-glucopyranoside, isovitexin-2''-o-glucopyranoside, isovitexin-2''-o-β-d-glc, isovitexin-2''-o-β-d-glucopyranoside, puerarin, quercetin, rutin, spinorhamnoside, spinosina, vitexin-4''-o-glucoside, zivulgarin, 7-o-(6'''-o-feruloylglucosyl)-isocytisoside, catechin, 4-o-(6'''-o-feruloylglucosyl)-swertisin, 6''-feruloyl-6'''-vanillylspinosin, isoswertisin, ispinosin, kaemperol-3-o-rutinoside, kaempferol 3-o-α-l-rhamnopyranosyl-(1→2)-o-[o-α-l-rhamnopyranosyl-(1→6)]-β-d-glucopyranoside, kaempferol-3-o-β-d-xylopyranosyl-(1→2)-[α-l-rhamnopyranosyl-(1→6)]-β-d-glucopyrano-side), kaempferol-3-rutinoside, 2''-o-glucoylisoswertisin, 6'',6'''-diferuloylspinosin, apigenin-6-c-d-glucopyranoside, 2''-b-o-glucopyranosyl swertisin, swertish, isopinosina, epicatechin, 4-(2-methoxy-phenyl)-l-[2-(n-2''-pyridinyl)-p-iodobenza-mido]-ethyl-piperazine, camelliaside B, catechine, nervilifordin J, 6'''-feruloylspinosin, glucosylvitexin, nicotiflorin, saponarin, spinosin, swertisin, isoquercitrin, isovitexin, vicenin II
Alkaloids	amphibine, coclaurine K, lysicamine, nornuciferine I_a, nornuciferine I_b, nuciferine e, sanjoinine A, sanjoinine B, sanjoinine C, sanjoinine D, sanjoinine e, sanjoinine F, sanjoinine G_1, sanjoinine G_2, sanjoinine I_a (nornuciferine), sanjoinine I_b (norisocorydine), zizyphusine, 5-hydroxy-6-methoxynoraporphine, n-methylasimilobine, 6-(2',3'-dihydroxyl-4'-hydroxymethyl-tetrahydro-furan-1'-yl)-cyclopentene[c]pyrrole-1,3-diol, jubanine C, jubanine F, jujube cyclic peptide, juzirine, nummularine B, adenosine, magnoflorine, tryptophan
Amino Acids	aminocaproic acid, citric acid, cycol(arginine–proline), glutamic acid dipeptide, phenylalanine, 6-glu-coclaurine
Nucleosides	cyclic adenosine monophosphate, cyclic guanosine monophosphate, guanosine hydrate, uridine monophosphate
Phenolic Acids	hydroxybenzoic acid, linoleic acid, protocatechuic acid, oleic acid
Volatile Oils	9,12-octadecadienoic acid, 9-octadecenoic acid, arachidic acid, docosanoic acid, lauric acid, myristic acid, palmitic acid, palmitoleic acid, stearic acid
Others	ebelin lactone

Table 2. Chemical constituents in Chuanxiong (Chuanxiong Rhizoma, *Ligusticum chuanxiong Hort.*).

Class	Compound
Volatile Oils	bornyl acetate, caryophyllene, germacrene D, germacrene d-4-ol, methyl-eugenol, p-cymen-8-ol, sabinene, terpinen-4-ol, tetradecanoic acid, *α*-cadinol, *α*-copaene, *α*-farnesene, *α*-phellandrene, *α*-pinene, *α*-selinene, *α*-terpinen, *α*-terpinene, *α*-terpineol, *α*-terpinolene, *α*-terprinene, *α*-thujene, *β*-chamigrene, *β*-elemene, *β*-farnesene, *β*-germacrene, *β*-linalool, *β*-myrcene, *β*-ocimenen, *β*-phellandrene, *β*-pinene, *β*-selinene, *γ*-cadinene, *γ*-gurjunene, *γ*-muurolene, *γ*-selinene, *γ*-terpinene, θ-cadinene, τ-muurolol, τ-terpinen, (+)-*β*-linalool, (1s,5s)-(-)-2(10)-pinene, 2-methoxy-4-vinylphenol, butanal, cubebene, dodecanoic acid, methyl ester hexadecanoic, n-hexadecanoic acid, n-hexadecanoic acid methyl ester, octadecanoic acid, pentadecanoic acid, pentadecanoic acid ethyl ester, spathulenol, cis,cis-linoleic acid, (E)-2-hexenal, (E)-3-decen-2-ol, (N)-(-)-p-menth-1-en-4-ol, 1n-a-pinene, limonene, n-tridecane, o-cymene, n-hexacosane, p-eugenol , p-limonene, p-menth-1-en-8-ol, p-mentha-1,4(8)-diene, p-mentha-1,4-dien-7-ol, l-(+)-ascorbic acid 2,6-dihexadecanoate, n-eicosane, carotol, cedrol, cis-3-hexen-1-ol, cis-*β*-terpineol, (-)-calamenene, (-)-spathulenol, epiglobulol, igusticoside A, igusticoside b, linoleic acid ethyl ester, linoleic acid methyl ester, (E)-2-methoxy-4-(3-(methylsulfonyl)prop-1-en-1-yl)phenol, (S)-3-ethyl-4-methylpentanol, [(Z)-1,2-diphenyleth-1enyl]-trimethylsilan, 1,1-dimthyl-1,2,3,5,7,8,9,9a-octahydro-benzocyclohepten-6-one, 1,2,3,4,4a,7-hexahydro-1,6-dimethyl-4-(1,-methylethyl)-naphthalene, 1,3,5-dodecatriene, 1,3-cyclohexadiene-5-pentyl, 1,4-cyclohexadiene-1,2-dicarboxylic anhydride, 1,5,5-trimethyl-6-methylene-cyclohexene, 1,5-copaenol, 1,7,7-trimethyl-bicyclo[2.2.1]hept-2-yl, 1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-cyclohexane, 1-hexadecanol, 1-lsopropyl-4-methylbicyclo[3.1.0]hex-2-ene, 1-methoxy adamantane, 1-methyl-4-(1-methylethenyl)-benzene, 1-methyl-4-(methylethyl)-(E)-2-cyclohexenol, 1-phenyl-1-pentanone, 2,4-decadienal, 2,5,5,8a-tetramethyl-3,5,6,7,8,8a-hexahydro-1(2h)-naphthalenone, 2,5-dimethyl-3-hexyne-2,5-diol, 2,6,10-trimethyltetradecane, 2-chloro-1-(2,4-dimethylphenyl)-2-methyl-1-propanone, 2-lsopropenyl-4a,8-dimethyl-1,2,3,4,4a,5,6,7,-octahydronaphthalene, 2-octyl-phenol, 2-pentadecanone-6,10,14-trimethyl , 3,7-dihydro-7-(2-hydroxyethyl)-1,3-dimethyl-1h-purine-2,6-dione, 3-ethyl-4-methylpentan-1-ol, 3-hydroxy-4-methoxypropiophenone, 4(10)-thujene, 4-[*β*-d-apiofuranosyl-(1→6)-*β*-d-glucopyranosyloxy]-3-methoxypropio-phenone, 4-hydroxy-2-methylacetophenone, 4-isopropylidene-1-winyl-o-menth-8-ene, 5-pentylcyclohexa-1,3-diene, 6-butyl-1,4-cycloheptadiene, 8-propoxycedrane, 9,12-octadecadienal, a-caryophyllene, angelicide, ansaspirolide, cis,trans-4-methyl-3-oxabicyclo[4.4.0]decane, cis-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol, cis-3-buty-4-vinyl-cyclopentene, copaene, cubebol, cubenene, di-epi-1,10-cubenol, diepi-*α*-cedrene epoxide, diethyl phthalate, dodecamenthylcyclohexasiloxane, dodecanal, ethyl hexadecanoate, ethyl linoleate, heneicosane, humulane-1,6-dien-3-ol, llavandulyl propionate, methyl benzoylformate, neophytadiene, nonadecanol, pentadecyl alcohol, phthalic anhydride, phytol, squalene, tetradecanmethyl-cycloheptasiloxane, trans-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol, trans-p-menth-1-en-3-ol, trans-sedanolide, trans-*α*-bergamotene, tropone, valerophenone, viridiflorol, 1-hydroxy-1-(3-methoxy-4-hydroxyphenyl)-ethane, 3-methoxy-4-hydroxystyrene, coniferyl ferulate, sedanonic acid, 5-hydroxymethyl-6-endo-3-ethoxy-4-hydroxyphenyl-8-oxa-bicyclo[3.2.1]-oct-3-one, succinic acid, ligubenzocycloheptanone A, (S)-2-(2-carboxyl-2-hydro-xyethylthio)-ferulic acid, caffeic acid, ferulic acid, butylidenephthalide, dicaffeoylquinic acid
Alkaloids	1-acetyl-*β*-carboline, 1-*β*-ethylacrylate-7-aldehydo-*β*-carboline, 2,3-diphenyl-1,3,4-oxadiazol-3-ium-5-olaten-pentyl-4,5-dihydrophthalide, adenine, adenosine, choline, cyclotetradecane, ligustrazine, l-isobutyl-l-valine anhydride, l-valine-l-valine anhydride, pelolyrine, tetramethylpyrazine, trimethylamine, uracil

Continued

Ceramides and Cerebrosides	(2N)-2-hydroxy-n-[(2s,3s,4n,8e)-1,3,4-trihydroxypentadec-8-en-2-yl]heptacosanamide, (2N)-2-hydroxy-n-[(2s,3s,4s,8e)-1,3,4-trihydroxyicos-8-en-2-yl]tetracosanamide, (2N)-2-hydroxy-n-(3s,4s,5s)-4-hydroxy-5-[(4e)-undec-4-en-1-yl]tetrahydrofuran-3-yl heptacosanamide, (2N)-n-[(2n,3s,4n,8e)-1-(*β*-d-glucopyranosyloxy)-3,4-dihydroxyoctadec-8-en-2-yl]-2-hydroxyhexadecanamide, (2N)-n-[(2s,3n,4e,8e)-1-(*β*-d-glucopyranosyloxy)-3-hydroxydodeca-4,8-dien-2-yl]-2-hydroxydocosanamide
Coumarins	5,7,8-trimethyl-dihydrocoumarin, scopoletin, cnidioside A
Flavonoids	apigenin, apigenin-7-o-*β*-d-glueuronide, daidzein, astragalin, 2-(1-oxopentyl)-benzoic acid methyl ester
Phenolic Acids	icariside F_2, ligusticumacid A, ligusticumacid B, ligusticumacid C, ligusticumacid d, ligusticumacid e, ligusticumacid F, 5-hydroxymethyl-6-endo-3-methoxy-4-hydroxyphenyl-8-oxa-bicyclo (3.2.1)-oct-3-one, chrysophanol, folic acid, gallic acid, palmitinic acid, p-hydroxybenzoic acid, sinapic acid, vanillin, chlorogenic acid, vanillic acid, linoleic acid, protocatechuic acid, oleic acid
Phthalides	levistilide A, ligustilide, 3-butylene-4,5-dihydroxyph-thailde, senkyunolide Q, senkyunolide R, senkyunolide S, e-senkyunolide E, ligusticoside A, z-ligustilide , z-senkyunolide E, (z,z')-6,8',7,3'-diligustilide, 3-butylidene-6-hydroxy-5,6-dihydrophthalide, 3-carboxyethyl-phthalide, 4,5-dihydro-3-butylidenephthalide, 3,6,8,3a-diligustilide, 3,8-dihydrodiligustilide, 3-butylidenephthalide, 3-hydroxy-4,5,6,7-tetrahydro-6,7-dihydroxy-3-butylphthalide, 4,5-dihydro-3-butylphthalide, 4,7-dihydroxy-3-butylphthalide, 4-hydroxy-3-butylphthalide, butylphthalide, chuanxiongins A, chuanxiongins B, chuanxiongins C, chuanxiongins d, chuanxiongins E, chuanxiongins F, chuanxiongnolide A, chuanxiongnolide B, chuanxiongnolide R_1, chuanxiongnolide R_2, hexahydro-3-butylphthalide, levistolide A, neocnidilide, senkyunolide B, senkyunolide C, senkyunolide E, senkyunolide G, senkyunolide K, senkyunolide l, senkyunolide M, senkyunolide N, senkyunolide O, senkyunolide P, tokinolide B, wallichilide, z,z'-3,3',8,8'-diligustilide, z'-3,8-dihydro-6,6',7,3'a-diligustilide, z-6,7-epoxyligustilide, z-butylidenephthalide, z-ligustilide dimer e-232, 3-butylidene-7-hydroxyphthalide, 3-carboxyrthyl-phthalide, 6-hydroxy-senkyunolide B, celephthalide A, chuanxiongoside A, chuanxiongoside B, (3'z)-(3s,8n,3a's,6'n)-4,5-dehydro-3.3a',8.6'-diligustilide, (3'z)-(3s,8s,3a's,6'n)-4,5-dehydro-3.3a',8.6'-diligustilide, thiosenkyunolide C, trans-neocridilide, chuanxiongdiolide A, chuanxiongdiolide B, chuanxiongdiolide L_1, chuanxiongdiolide L_2, chuanxiongdiolide L_3, chuanxiongdiolide L_4, chuanxiongdiolide L_5, chuanxiongdiolide R_1, chuanxiongdiolide R_2, chuanxiongdiolide R_3, igustilide, 3-butyl-4-hydroxyphthalide, 3-butylphthalide, e-ligustilide, riligustilide, senkyunolide A, senkyunolide D, senkyunolide F, senkyunolide h, senkyunolide I, senkyunolide J, z,z'-6,8',7,3'-diligustilide, cnidilide
Polysaccharides	LCA, LCB, LCC, LCX0, LCX1, LCX2, LCP-1, LCP-2, LCP-3, LCP-4, Arabinose, galactose, galacturonic acid, glucose, glucuronic acid, nhamnose, mannose
Triterpenoids	progesterone, xiongterpene, Globulol, ergosterol peroxide
Others	(-)-alloaromadendrane-4*β*,10*α*,13,15-tetrol, 3-o-*β*-d-apiofuranosyl-(1→6)-*β*-d-glucopyranoside, 4-pentylcyclohex-3-ene-1*α*,2*β*-diol, campest-4-en-3-one, monopalmitin, *β*-d-apiofuranosyl-(1→6)-*β*-d-glucopyranosyl-3,4-dimethoxy-benzoate, aurantiamide acetate, lignoceric acid

contained 18 steroids, 6 flavonoids, 4 phenylpropanoids, 2 alkaloids, and 2 benzophenones using UPLC-Q-TOF/MS combination with characteristic fragments filter and neutral loss filter method [57]. The study on chemical constitutions of crude Anemarrhenae rhizoma (CAR) and salt-processed Anemarrhenae rhizoma (SAR) showed that a total of 24 components as main contributors had significant difference, and 7 main constituents were simultaneously determined by

ultra-high-performance liquid chromatography-quadrupole mass spectrometry (UHPLC-MS), timosaponin N, timosaponin E_1, timosaponin BII, timosaponin BIII, anemarrhenasaponin I, timosaponin AII and timosaponin AIII [58].

We sorted out 163 components of Anemarrhenae rhizoma [57]-[76], which were classified into 10 categories, including steroids (84 compounds, 51%), flavonoids (25 compounds, 15%), alkaloids (13 compounds, 8%), coumarins (8 compounds, 5%), volatile oils (8 compounds, 5%), triterpenoids (5 compounds, 3%), polysaccharides (6 compounds, 4%), lignans (7 compounds, 4%), phenolic acids (1 compound, 1%) and others (6 compounds, 4%) (**Figure 1(c)**, **Table 3**).

2.4. Fuling (Poria, Poria Cocos (Schw.) Wolf.)

We used key words "Fuling", "Poria", "*Poria cocos* (*Schw.*) *Wolf.*", "*Wolfiporia extensa* (*Peck*) *Ginns*" to find the ingredients in Poria, and selected literatures in the past five years. We found many methods have been developed for analysis and quality control of Poria. For instance, qualitative and quantitative methods to analyze carbohydrates (polysaccharides, oligosaccharides and monosaccharides) in three different parts (epidermis, middle and inner) of Poria by high performance gel permeation chromatography coupled with charged aerosol detector (HPGPC-CAD), altra-performance liquid chromatography coupled with triple quadrupole mass spectrometry (UHPLC-QqQ-MS/MS), PCA and orthogonal partial least squared discriminant analysis (OPLS-DA) [77]. It is an efficient dereplication strategy to identify triterpene acid analogues in Poria based on ultra-performance liquid chromatography with electrospray ionisation quadrupole time-of-flight tandem mass spectrometry (UPLC-ESI-QTOF-MS/MS), and 62 triterpene acids were characterized [78]. A method based on UHPLC-MS combined metabolomics approach is established to explain the distribution of triterpene compounds in four parts, which are Poriae Cutis (PC), Rubra Poria (RP), White Poria (WP) and Poria cum Radix Pini (PRP) and 51 triterpene compounds are tentatively identified in Poria. The PC and PRP show a quite clear discrimination by the PCA and OPLS-DA, and 12 differential compounds are found [79].

The four classes of chemical components in Poria included 204 compounds [77]-[96], containing triterpenoids (137 compounds, 67%), polysaccharides (58 compounds, 28%), alkaloids (2 compounds, 1%) and others (7 compounds, 4%) (**Table 4**, **Figure 1(d)**).

2.5. Gancao (Licorice, *Glycyrrhiza uralensis Fisch.*, *Glycyrrhiza inflata Bat.* or *Glycyrrhiza Glabra L.*)

We used key words "Gancao", "Zhigancao", "Licorice", "*Glycorrhizae Radix et Rizoma*", "*Glycorrhiza urensis Fisch.*", "*Glycorrhiza inflata Bat.*", "*Glycorrhiza glabra L.*" to find the ingredients in Licorice, and we were mainly based on the literature of the past five years and delete the literature with duplicate components.

Table 3. Chemical constituents in Zhimu (Anemarrhenae rhizoma, *Anemarrhena asphodeloides Bge*.).

Class	Compound
Steroids	(25R)-26-o-β-d-glucopyranosyl-5α-furostane-20(22)-en-3β,26-diol-3-o-β-d-glucopyranosyl-(1→2)-β-d-glucopyranosyl-(1→4)-β-d-galactopyranoside, (25S)-26-o-β-d-glucopyranosyl-22-hydroxy-5β-furostane-3β,26-diol, 3-o-β-d-glucopyranosyl-(1→2)-o-β-d-galactopyranoside, (25S)-officinalisnin-I, 20(22)-en-5β-furost-3β,15α-diol-3-o-β-d-glucopyranosyl-(1→2)-β-d-galactopyranoside, 21-formyl sarsasapogenin, 21-hydroxysarsasapogenin, 25(27)-ene-anemarrhenasaponin I, 25(27)-ene-Gurilioside H, 25(27)-ene-timosaponin AII, 25(27)-ene-timosaponin AIII, 25(27)-ene-timosaponin N, 25R-timosaponin AIII, 25R-timosaponin BII, 25R-timosaponin BIII, 25R-timosaponin D, 25R-timosaponin E, 25S-karatavioside C, 2-hydroxyl-timosaponin AIII, 3,4-dihydroxyallylbenzene-3-o-α-L-rhamnopyranosyl(1→6)-β-d-glucopyranoside, anemarnoside A, anemarnoside B, anemarrhena S_1, anemarrhena S_2, anemarrhena S_3, anemarrhena S_4, anemarrhena S_5, anemarrhena saponin III, anemarrhenasaponin F, anemarrhenasaponin I, anemarrhenasaponin Ia, anemarrhenasaponin II, anemarsaponin B II, asparagoside G, curilioside H, degalactotigonin, desgalactotigonin, dimethisterone, diuranthoside A, f-gitonin, filicinoside-A, hostaplantagineoside C, karatavioside C, macrostemonoside F, macrostemonoside J, officinalisinin-I, petunioside N, purpureagitoside, sarsasapogenin, smilageninoside, solanigroside F, spicatoside B, timopregnane A, timosaponin AI, timosaponin AII, timosaponin AIII, timosaponin AIV, timosaponin B, timosaponin B I, timosaponin B II, timosaponin B III, timosaponin B IV, timosaponin C, timosaponin D, timosaponin E, timosaponin E_1, timosaponin F, timosaponin G, timosaponin H_1, timosaponin I_1, timosaponin I_2, timosaponin L, timosaponin N, timosaponin P, timosaponin Q, timosaponin U, timosaponin V, timosaponin W, timosaponin E_1, tomatoside A, tuberoside G, uttroside B, xilingsaponin B, zimoside A
Alkaloids	adenosine, coumaroyl tyramine, cyclo dileucyl, cyclo hetaleucyl, cyclo hexaleucyl, cyclo nonaleucyl, cyclo octaleucyl, cyclo pentaleucyl, cyclo tetraleucyl, cyclo trileucyl, n-cis-feruloyl tyramine, n-trans-feruloyltyramine, tryptophan
Polysaccharides	d-galactose, d-galacturonic acid, d-glucose, d-mannose, l-arabinose, l-rhamnose
Phenolic Acids	oleic acid
Flavonois	(2,6-dihydroxy-3-(((1s,4s,6r)-4-hydroxy3,7-dioxabicyclo[4.1.0]heptan-4-yl)methyl)-4-methoxyphenyl)(4-hydroxyphenyl)methanone, (2s)-7,4′-dihydroxy-5-methoxyflavone, (4-hydroxyphenyl)(2,3,4-trihydroxyphenyl)methanone, (s)-5-(2,4-dihydroxy-3-(4-hydroxybenzoyl)-6-methoxyphenyl)pyrrolidin-2-one, 2,4',6-trihydroxy-4-methoxy benzophenone, 2,6,4'-trihydroxy-4-methoxy Benzophenone, 2',4',4-trihydroxy chalcone, 2'-o-methylisoliquiritigenin, 2'-o-methylphloretin, 4',6-dihydroxy-4-methoxybenzophenone-2-o-(2''),3-c-(1'')-1''-desoxy-α-l-fructofuranoside, anemarchalconyn, e-4'-demethyl-6-methyleucomin, E-5,7-dihydroxy-3-(4'-hydroxybenzylidene)chroman-4-one, foliamangiferoside A, iriflophene, iriflophenone, iriflpohenone-3-c-β-d-glucoside, isomangiferin, isosakuranetin, isovitexin, mangiferin, mangiferoxanthone A, methyl 2-(2,4-dihydroxy-3-(4-hydroxybenzoyl)-6-methoxyphenyl) acetate, neomangiferin, vitexin
Triterpenoids	platycodin D, platycodin D_2, platycodin D_3, platycoside A, polygalacin D_2
Volatile Oils	dihydroxy-octadecadienoic acid, dihydroxy-octadecaenoic acid, dihydroxy-octadecatrienoic acid, hydroxy-octadecadienoic acid, hydroxy-octadecatrienoic acid, inolenic acid, tearic acid, trihydroxy-octadecaenoic acid
Coumarins	cis-hinokiresinol, hinokiresinol, methoxy-cis-hinokiresinol, monomethyl-cis-hinokiresinol, oxy-hinokiresinol, trans-hinokiresinol, broussonin A, broussonin B
Lignans	3''-hydroxy-4''-methoxy-4''-dehydroxynyasol, 3''-methoxynyasol, 4-hydroxy acetophenone, 4-hydroxybenzaldehyde, 4'-o-methylnyasol, anemarcoumarin A, nyasol,
Others	(s)-5-(2-hydroxy-5-(3-(4-hydroxy phenyl) propyl)-4-methoxy phenyl) pyrrolidin-2-one, aneglycoside A, aneglycoside B, aneglycoside C, phytosphingosine, α-d-Glucose monoallyl ether

Table 4. Chemical constituents in Fuling (Poria, *Poria cocos* (*Schw.*) *Wolf*).

Class	Compound
Polysaccharides	ab-PCM3-I-S1, ab-PCM3-I-S2, ab-PCM3-I-S3, ab-PCM3-I-S4, ab-PCM3-I-S5, ac-PCM2, ac-PCM3-I-S1, ac-PCM3-I-S2, ac-PCM3-I-S3, ac-PCM3-I-S4, ac-PCM3-I-S5, arabinose, carboxymethylated P. cocos polysaccharides, carboxymethylpachymaram, CMP, CS-PCS3-II, fucose, galactose, galacturonic acid, glucose, glucuronic acid, mannose, oxidized P. cocos polysaccharides, pachyman, PC-II, PCP3-I, PCP3-II, PCP4-I, PCP4-II, PCP-E, PCP-H, PCP-M, PCPS, PCP-U, PCS1, PCS2, PCS3-I, PCS3-II, PCS4-I, PCS4-II, PCSC, PCWPS, PCWPW, Pi-PCM, Pi-PCM0, Pi-PCM1, Pi-PCM2, Pi-PCM3-I, poria cocos polysaccharide-1(PCP-1), PPSW-1, rhamnose, rib, ribose, sum, wc-PCM0, wc-PCM1, wc-PCM2, xylose
Triterpenoids	11*β*-ethoxydaedaleanic acid A, 15*α*-hydroxy-3-oxolanosta-8,24-dien-21-oic acid, 15*α*-hydroxydehydrotrametenolic acid, 15*α*-hydroxydehydrotumulosic acid, 15*α*-hydroxyeburiconic acid, 16-deoxyporicoic acid B, 16-hydroxy-3,24-dioxolanosta-7,9-dien-21-oic acid, 16-o-acetyl pachymic acid, 16*α*,25-dihydroxy dehydroeburiconic acid, 16*α*,25-dihydroxyeburiconic acid, 16*α*,27-dihydroxydehydrotrametenoic acid, 16*α*,29-dihydroxy eburiconic acid, 16*α*-acetoxy-26,27-dimethoxyl-lanosta-8,24-dien-21-oic acid, 16*α*-acetoxy-lanosta-7,9,24-dien-21-oic acid, 16*α*-acetoxy-lanosta-8,24-dien-21-oic acid, 16*α*-acetoxypolyporenic acid C, 16*α*-acetyloxy-24-methylene-3-oxolanosta-7,9-dien-21-oic acid, 16*α*-acetyloxye buriconic acid, 16*α*-hydroxy-3-oxolanosta-8,24-dien-21-oic acid, 16*α*-hydroxydehydrotrametenonic aicd, 16*α*-hydroxy eburiconic acid, 16*α*-hydroxy-lanosta-7,9,24-trien-21-oic acid, 16*α*-hydroxy-lanosta-8,24-dien-21-oic acid, 16*α*-hydroxy trametenolic acid, 16,29-dihydroxy-3,4-seco-lanosta-4(28),8,24(31)-trien-3,21-dioic acid, 2'-3'-dihydrosorbicillin, 25,26-dihydroxy dehydropachymic acid, 25-hydroxy-3-epidehydrotumulosic acid, 25-hydroxy-3-epitumulosic acid, 25-hydroxy pachymic acid, 25-hydroxy polyporenic acid C, 25-hydroxyporicoic acid C, 25-hydroxyporicoic acid H, 25-methoxy-29-hydroxy poricoic acid HM, 25-methoxy poricoic acid A, 25*α*-hydroxytumulosic acid, 26-hydroxyporicoic acid DM, 26-hydroxy poricoic acid G, 29-hydroxydehydropachymic acid, 29-hydroxydehydrotumulosic acid, 3-(2-hydroxy acetoxy)-5*α*,8*α*-peroxydehydrotumulosic acid, 3,4-seco-lanosta-4,7,9,24-tetraen-3,21-dioic acid, 31-hydyoxyl-16-o-acetylpachymic acid, 3-acetyloxy-16*α*-hydroxy trametenolic acid, 3-epi-(3'-hydroxy-3'-methylglutaryloxyl)-dehydrotumulosic acid, 3-epi-dehydropachymic acid, 3-epi-dehydrotumulosic acid, 3-epi-pachymic acid, 3-o-acetyl-16*α*,26-dihydroxytrametenolic acid, 3-o-acetyl-16*α*-hydroxydehydrotrametenolic acid, 3-o-acetyl-16*α*-hydroxytrametenolic acid, 3-o-acetyl-dehydroeburicoic acid, 3-oxo-16*α*-hydroxy-lanosta-7,9(11),24-trien-21-oic acid, 3-oxo-6,16*α*-dihydroxy-lanosta-7,9(11),24(31)-trien-21-oic acid, 3-oxo-lanosta-7,9(11),24(31)-trien-21-oic acid, 3-oxo-lanosta-7,9(11),24-trien-21-oic acid, 3*α*,16*α*,25-Trihydroxylanosta-8,24-dien-21-oic acid, 3*β*,15*α*-Bis(acetyloxy)-24-methylenelanost-8-en-21-oic acid, 3*β*,15*α*-dihydroxy-24-oxolanosta-8-en-21-oic acid, 3*β*,15*α*-dihydroxy lanosta-7,9(11),24-triene-21-oic acid, 3*β*,16*α*-bis(acetyloxy)-29-hydroxylanosta-8,24-dien-21-oic acid, 3*β*,16*α*-dihydroxy-24-hydroxy methyl lanosta-7,9-dien-21-oic acid, 3*β*,16*α*-dihydroxy lanosta-7,9(11),24(31)-trien-21-oic acid, 3*β*,16*α*-dihydroxylanosta-7,9(11),24-trien-21-oic acid, 3*β*,26-dihydroxy-lanosta-7,9,24-trien-21-oic acid, 3*β*-acetoxy-16*α*,26-dihydroxylanosta-8,24-dien-21-oic acid, 3*β*-acetoxy-lanosta-7,9(11),24-trien-21-oic acid, 3*β*-acetyloxy-16*α*-hydroxy-24-oxolanost-7,9(11)-dien-21-oic acid, 3*β*-acetyloxy-16*α*-hydroxy-24-oxolanost-8-en-21-oic acid, 3*β*-hydroxy-16*α*-acetoxylanosta-7,9(11),24-trien-21-oic acid, 3*β*-p-hydroxybenzoyldehydrotumulosic acid, 3*α*-hydroxyl-26-methoxyl-8,24(31)-diene-21-oic acid, 3*β*-acetoxy-16*α*-hydroxy-lanosta-8,24-diene-21-oic acid, 5*α*,8*α*-Peroxydehydrotumulosic acid, 6,16*α*-dihydroxydehydroeburiconic acid, 6,16*α*-dihydroxydehydrotrametenonic acid, 6-hydroxy polyporenic acid C, 6*α*-hydroxydehydropachymic acid, 6*α*-hydroxy-polyporenic acid C, 9,11-dehydroergosterol peroxide, 6-hydroxy-3*β*,16*α*-diacetoxy-lanosta-7,9,24-tetraen-21-oic acid, acetoxyeburicoic acid, acetyl-eburicoic acid, ceanphytamic acid A, ceanphytamic acid B, daedaleanic acid A, daedaleanic acid B, dehydroeburic acid, dehydroeburicoic acid, dehydroeburicoic acid monoacetate, dehydroeburiconic acid, dehydropachymic acid, dehydrosulphurenic acid, dehydrotrametenolic acid, dehydrotrametenonic acid, dehydrotumulosic acid, dehypachymic acid, deyhdrotarmetenolic acid, eburicoic acid, eburicoic acid acetate, ergosterol

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	peroxide, harzianone, hederagenin, hispindic acid B, lanosta-7,9,24-trien-21-oic acid, lanosta-8,24-dien-21-oic acid, me trametenolate, oleanic acid, pachymic acid, pinicolic acid, pinicolic acid A, pinicolic acid E, polyporenic acid C, poriacosone A, poriacosone B, poricoic acid A, poricoic acid AE, poricoic acid AM, poricoic acid B, poricoic acid C, poricoic acid CE, poricoic acid CM, poricoic acid D, poricoic acid DM, poricoic acid E, poricoic acid F, poricoic acid G, poricoic acid GE, poricoic acid GM, poricoic acid h, poricoic acid HE, poricoic acid HM, poricoic B, pregna-7-en-3α,11α,15α,20-quadriol, trametenolic acid, tumulosic acid, ursolic acid
Alkaloids	adenosine, thymine
Others	(3S,6S)-3-[(1R)-1-hydroxyethyl]-6-(phenylmethyl)-2,5-piperazinedione, (5-formylfuran-2-yl) methyl 2-(4-hydroxyphenyl) acetate, (5-formylfuran-2-yl) methyl 2-hydroxy propanoate, 5-hydroxy methylfurfural, sohiracillinone, sohirnone A, sorbicillin

Many methods have been developed for the analysis and the quality control of Licorice. The 58 phenolic acids including 11 new compounds (glycybridins A-K) were isolated from Licorice using nuclear magnetic resonance (NMR) and MS analyses combination with experimental and computed electronic circular dichroism data [97]. The 8 triterpenoids including glyuralsaponin A-G were separated from Licorice root by using ultraviolet (UV), infrared (IR), NMR spectrum and other technologies [98]. In addition, 122 chemical ingredients including glycyuralin A-F from the roots and stems of Licorice were isolated and identified adopting a combined strategy using NMR and MS spectroscopic data measurement [99].

We totally collected 260 components of Licorice [97]-[109], which were classified into 6 categories, including flavonoids (112 compounds, 43%), triterpenoids (51 compounds, 20%), phenolic acids (72 compounds, 28%), coumarins (11 compounds, 4%), stilbenoids (5 compounds, 2%) and others (9 compounds, 3%) (**Figure 1(e)**, **Table 5**).

3. The Chemical Constituents in Suanzaoren Decoction

We used "Suanzaoren decoction", "Suan-Zao-Ren decoction", "Suan-Zao-Ren-Tang", "Zizyphus Combination", "Suanzaoren Formulae", "Suan Zao Ren Tang", "Ziziphus spinose decoction", "Suanzaoren prescription" as key words to search chemical components in SZRD, and classified them according to their chemical structure. Results showed that only five literatures on the ingredients of SZRD were reported. For example, 101 constituents are identified in Suan-Zao-Ren granule using UHPLC-Q-TOF-MS coupled with multiple data processing approaches [110]. These 48 components were characterized in SZRD using liquid chromatography time-of-flight mass spectrometry (LC-Q/TOF-MS) and liquid chromatography coupled with ion trap mass spectrometry (LC-IT-MS) technology and 31 compounds were identified for the first time [111]. The 22 chemical compounds were isolated in SZRD by using ultra-performance liquid chromatography coupled with electrospray ionization/quadrupole-time-of-flight mass spectrometry (UPLC-ESI-Q-TOF-MS)

Table 5. Chemical constituents in Gancao (Licorice, *Glycyrrhiza uralensis Fisch.*, *Glycyrrhiza inflata Bat. or Glycyrrhiza glabra L.*).

Class	Compound
Flavonoids	7,4'-dihydroxyflavone 7-O-glucopyranoside, apigenin 6-C-rhamnopyranoside-8-C-[6'''-(3-hydroxy-3-methylglutaroyl)]-glucopyranoside, daidzin, glucoliguiritin apioside, glycyroside, isoliquiritigenin 4,4'-di-O-glucopyranoside, isoliquiritin, isoschaftoside, isoviolanthin, liquiritigenin 7,4'-di-O-glucopyranoside, liquiritin, liquiritin apioside, neoisoliquiritin, neoliquiritin, schaftoside, soliquiritin apioside, sophoraflavone B, syringic acid 4-O-glucopyranoside, vicenin II, (2R,3R)-3,4',7-trihydroxy-3'-prenylflavane, (2s)-abyssinone I, 2,3-dehydrokievitone, 3,4-didehydroglabridin, 3'-hydroxy-4'-O-methylglabridin, 3-hydroxyglabrol, 4'-O-methylglabridin, 5,8-dihydroxy-flavone-7-O-beta-D-glucuronide, 5-hydroxy-8-methoxyl-flavone-7-O-beta-D-glucuronide, 6-prenylnaringenin, 7,2'-dihydroxy-4'-methoxy-8-(3-methyl-2-butenyl) isoflavanone, 8-prenyl-phaseollinisoflavan, abyssinone II, chalcones isoliquiritin, derrone, echinatin, euchrenone A_5, flavanone, flavonol, formononetin, galbrene, genistein, glabranin, glabrene, glabridin, glabroisoflavanone A, glabroisoflavanone B, glabrol, glabrone, glisoflavanone, glucoliquiritin apioside, glychionide A, glychionide B, glycyrrhisoflflavone, glyinflanin H, glyzarin, hispaglabridin A, hispaglabridin B, isobavachalcone, isoflavan, isoflavanone, isoflavone, isolicoflavonol, isoliquiritigenin, isoliquiritin apioside, isoononin, isoquercitrin, isotrifoliol, isoviolantin, kanzonol B, kanzonol C, kanzonol U, kanzonol W, kanzonol X, kanzonol Y, kanzonol Z, kumatakenin, licochalcone A, licochalcone B, licochalcone C, licochalcone D, licochalcone E, licoflavanone, licoflavonol, licoflflavone A, licoflflavone B, licoflflavone C, licoisoflavones A, licoisoflavones B, licoisoflflavone A, licorice glycoside A, licorice glycoside B, licorice glycoside C_1, licorice glycoside C_2, licorice glycoside D_1, licorice glycoside D_2, licuraside, liquiritigenin, lupiwighteone, mangiferin, medicarpin, naringenin, ononin, paratocarpins B, parvisoflavones A, pinocembrin, prunetin, retrochalcones, rhamnoliquiritin, shinflavanone, shinpterocarpin, violantin, wighteone
Triterpenoids	12-acetoxyganoderic acid F, 18β-glycyrrhetinic acid, 22β-acetoxylglycyrrhizin, 24-hydroxy-licorice saponin A3, 3β-O-[β-D-glucuronopyranosyl-(1→2)-β-D-glucuronopyranosyl]-24-hydroxylglabrolide, glabrolide, glycyrrhetic acid, glycyrrhetic acid-3-O-mono-β-d-glucuronide, glycyrrhizic acid, glyuralsaponin A, glyuralsaponin B, glyuralsaponin C, glyuralsaponin D, glyuralsaponin E, glyuralsaponin F, glyuralsaponin G, glyuralsaponin H, isoglycyrrhizin, licorice saponin A_3, licorice saponin B_2, licorice saponin C_2, licorice saponin E, licorice saponin E_2, licorice saponin G_2, licorice saponin N_4, squasapogenol GP-B_2, uralsaponin B, uralsaponin F, yunganoside K_2, 22β-acetoxyglycyrrhizin, 22β-acetoxyl-glycyrrhaldehyde, 3-O-glucuronopyranosyl-glycyrrhetinic acid, 3β-O-[glucuronopyranosyl-(1→2)-glucuronopyranosyl]-olean-9,12-diene-30-oic-acid, araboglycyrrhizin, glycyrrhetinic acid, glycyrrhizin, licorice-saponin H_2, licorice-saponin J_2, uralsaponin C, uralsaponin M, uralsaponin N, uralsaponin P, uralsaponin Q, uralsaponin R, uralsaponin S, uralsaponin T, uralsaponin U, uralsaponin V, uralsaponin W, uralsaponin X, uralsaponin Y
Phenolic acids	11b-hydroxy-11b,1-dihydromedicarpin, 1-methoxyphaseollin, 2'-hydroxyisolupalbigenin, 2-one-4-methoxy-pyran, 3-methoxy-9-hydroxy-pterocarpan, 5,7,4'-trihydroxy-3'(3-methylbut-2-enyl)-3-methoxy flavone, 6,8-diprenylgenistein, 6-C-prenylorobol, 7-methoxy-2',4'-dihydroxy isoflavone, 7-O-methylluteone, abiochanin A, allolicoisoflavone B, angustone A, daidzein, dehydroglyasperin C, dehydroglyasperin D, gancaonin I, gancaonin L, genkwanin, glicophenone, glicoricone, glyasperin C, glyasperin D, glycybridins A, glycybridins B, glycybridins C, glycybridins D, glycybridins E, glycybridins F, glycybridins G, glycybridins H, glycybridins I, glycybridins J, glycybridins K, glycyfuranocoumarin A, glycyfuranocoumarin B, glycyfuranocoumarin C, glycyfuranocoumarone A, glycyrol, glycyrrhiza-isoflavone C, glycyuralin A, glycyuralin B, glycyuralin C, glycyuralin D, glycyuralin E, glycyuralin F, glyurallin A, hirtellanine I, homobutein, isoangustone A, isoderrone, isoglabrone, isoglycycoumarin, isoglycyrol, isolupalbigenin, kaempferol, kaempferol 3-O-methyl ether, kumatakenin B, licoarylcoumarin, licocoumarone, licoflavone A, licoisoflavanone, licoisoflavone A, licoisoflavone B, licoricidin, licoricone, luteone, phaseollin, pratensein, semilicoisoflavone B, topazolin, uralenol

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Stilbenoids	dihydro-3,3',4'-trihydroxy-5-O-isopentenyl-6-isopentenylstilbene, dihydro-3,3'-dihydroxy-5β-d-O-glucopyranosyloxy-4'-methoxystilbene, dihydro-3,5,3'-trihydroxy-4'-methoxystilbene, dihydro-3,5-dihydroxy-4'-acetoxy-5'-isopentenylstilbene, dihydrostilbenes
Coumarins	glabrocoumarin, glabrocoumarone A, glabrocoumarone B, glycocoumarin, glycycoumarin, glycyrin, herniarin, licofuranocoumarin, licopyranocoumarin, liqcoumarin, umbelliferone
Others	[6",6"-dimethyl pyrano (2",3":4,5)]-3'-γ,γ-dimethylallyl-2',3,4'-trihydroxychalcone, 1",2"-dehydrocyclokievitone, 2'-O-demethybidwillol, dehydroglyceollin I, erybacin, licoagrocarpin, licoagrochalcone A, xambioona, gup-II

method with MassLynx™ MassFragment [112]. There were 13 active marker compounds (neomangiferin, mangiferin, spinosin, liquiritin apioside, liquiritin, 6'''-feruloylspinosin, senkyunolide I, timosaponin BII, isoliquiritoside, timosaponin C, jujuboside A, jujuboside B, and timosaponin AIII) were separated in diverse SZRD including lab-prepared Suanzaoren oral liquid, Suanzaoren mixture, and clinical Suanzaoren granules using high-performance liquid chromatography with diode array detection and evaporative light scattering detection (HPLC-DAD-ELSD) [113]. In addition, 11 chemical components (neomangiferin, mangiferin, spinosin, liquiritin apioside, liquiritin, fumalic acid, 6'''-feruloylspinosin, senkyunolide I, isoliquiritin, glycyrrhizic acid and senkyunolide A) of SZRD in different batches, including SZRD extracts, lab-made SZRD granules and clinical medicine, were determined by HPLC-PDA, which indicated that HPLC-PDA method would be helpful to improve quality evaluation and quality control in productive processes [114]. The 8 compounds (jujuboside, spinosin, ferulic acid, senkyunolide I, sarsasapogenin, mangiferin, liquiritoside and glycyrrhizic acid) were considered chemical quality control standard of SZRD [115].

We totally collected 145 compounds of SZRD in all [110] [111] [112] [113] [114], which were divided into 10 categories, including flavonoids (53 compounds, 36%), alkaloids (2 compounds, 1%), coumarins (7 compounds, 5%), phenolic acids (4 compounds, 3%), phthalide (14 compounds, 10%), triterpenoids (33 compounds, 23%), steroids (19 compounds, 13%), volatile oils (7 compounds, 5%), polysaccharide (1 compound, 1%) and others (5 compounds, 3%) (**Figure 1(f)**, **Table 6**). Flavonoids, one of the main active ingredients found at present, contained the largest number of ingredients in SZRD [116].

4. Comparative Analysis of Chemical Constituents in Herbs and Suanzaoren Decoction

4.1. Comparative Analysis of Chemical Constituents in Herbs

We obtained a total of 1104 chemical components without duplication in 5 herbs (**Figure 2(a)**). Adenosine existed in Ziziphi Spinosae Semen, Chuanxiong Rhizoma, Poria and Anemarrhenae rhizoma. Oleic acid existed in Anemarrhenae

Table 6. Chemical constituents in suanzaoren decoction.

Class	Compound
Flavonoids	(3R)-Vestitol, 5,7-Dihydroxyflavanone, 6''-Feruloyspinosin, 6''''-(4''''-O-β-D-glucopyranosyl)vanilloyl spinosin, 6,8-di-C-glucosyl-2(R)-naringenin, 6,8-di-Cglucosyl-2(s)naringenin, 6'''-Feruloylspinosin, 6''''-dihydrophaseoylspinosin, 6''-feroylspinol, choerospondin, echinatin, formononetin, gancaonin A, gancaonin H, glabrene, glabrol, glucoliquiritin, glucosylvitexin, glyinflanin A, isoliquiritigenin, isoliquiritin, isolquiritigenin, isoshaftoside, isoviolanthin, isovitexin, kanzonol F, kanzonol H, kumatakenin, licochalcone A, licochalcone B, licoleafol, licorice glycoside A, licorice glycoside D_1, licorice glycoside D_2, licorice glycoside E, licoricidin, licorisoflavan A, liquiritigenin, liquiritin, liquiritin apioside, lupiwighteone, mangiferin, neolicuroside, neomangiferin, nicotiflorin, ononin, pinocembrin, saponarin, schaftoside, shaftoside, spinosin, swertisin, vicenin II
Triterpenoids	16-Deoxyporicoic acid B, 16α-Hydroxytrametenolic acid, 22-Acetoxyglycyrrhizin, 3β,16α-Dihydroxylanosta-7,9(11),24-trien-21-oic acid, apioglycyrrhizin, betulinic acid, dehydrotrametenolic acid, dehydrotrametenonic acid, dibutyluralsaponin A, glabric acid, glycyrrhetic acid, glycyrrhizic acid, glycyrrhizin, isoliquiritoside, jujuboside A, jujuboside B, liangwanoside I, licorice saponin H_2, licorice saponin J, licorice saponin K_2, licorice saponine A_3, licorice saponine G_2, licoricesaponin B_2, oleanolic acid, pachymic acid, polyporenic acid C, poricoic acid A, poricoic acid B, uralsaponin A, uralsaponin B, yunganoside J_1, yunganoside K_2, yunganoside L_1
Coumarins	glycycoumarin, glycyrin, glycyrol, hedysarimcoumestan, inflacoumarin A, isoglycyrol, neoglycyrol
Steroids	(25s)-26-O-β-D-Glucopyranosyl-22-hydroxy-5β-furostane-3β, 26-diol3-O-β-D-Glucopyranosyl-(1-2)-O-β-D-galactopyranoside, (25s)-26-O-β-D-Glucopyranosyl-22-hydroxy-5β-furostanolalkenyl-3β, 26-diol3-O-β-D-glucopyranosyl-(1-2)-O-β-D-galactopyranoside, anemarsaponin B, anemarsaponin C, anemarsaponin E, anemarsaponin F, anemarrhena saponin II, anemarrhena saponin I, diosgenin, sarsasapogenin, timosaponin AI, timosaponin AIII, timosaponin AIV, timosaponin B II, timosaponin C, timosaponin E1, timosaponin E, timosaponin N, xilingsaponin B
Phenylpropanoids	timobiose
Phenolic Acids	chlorogenic acid, vanillic acid, neochlorogenic acid, ryptochlorogenic acid
Phthalide	3-Butyl-4-hydroxyphthalide, 3-Butylphthalide, cnidilide, E-butylidenephthalide, E-ligustilide, riligustilide, senkyunolide A, senkyunolide D, senkyunolide F, senkyunolide H, senkyunolide I, senkyunolide J, Z,Z'-6,8',7,3'-diligustilide, Z-ligustilide
Alkaloids	amphibine D, magnoflorine
Volatile oils	butylidenephthalide, caffeic acid, dicaffeoylquinic acid, ferulic acid, fumalic acid, neochlorogenic acid, palmitic acid, yptochlorogenic acid
Others	3β-30-hydroxy-11,30-dioxoolean-12-en-3-yl-2-O-a-L-arabinopyrano-syl-b-Dglucopyranosiduronic acid, emodin, liguiritigenin-7-O-β-D-apiofuransyl-40-O-3-D-glucose, ligustilide dimer, unganoside K_2

rhizoma, Chuanxiong Rhizoma and Ziziphi Spinosae Semen.

There are 8 common components presenting in Chuanxiong Rhizoma and Poria, which are galacturonic acid, mannose, arabinose, ergosterol peroxide, rhamnose, galactose, glucuronic acid, and glucose. Ziziphi Spinosae Semen and Chuanxiong Rhizoma contain linoleic acid and protocatechuic acid. Ziziphi Spinosae Semen and Anemarrhenae rhizoma contain tryptophan and isovitexin.

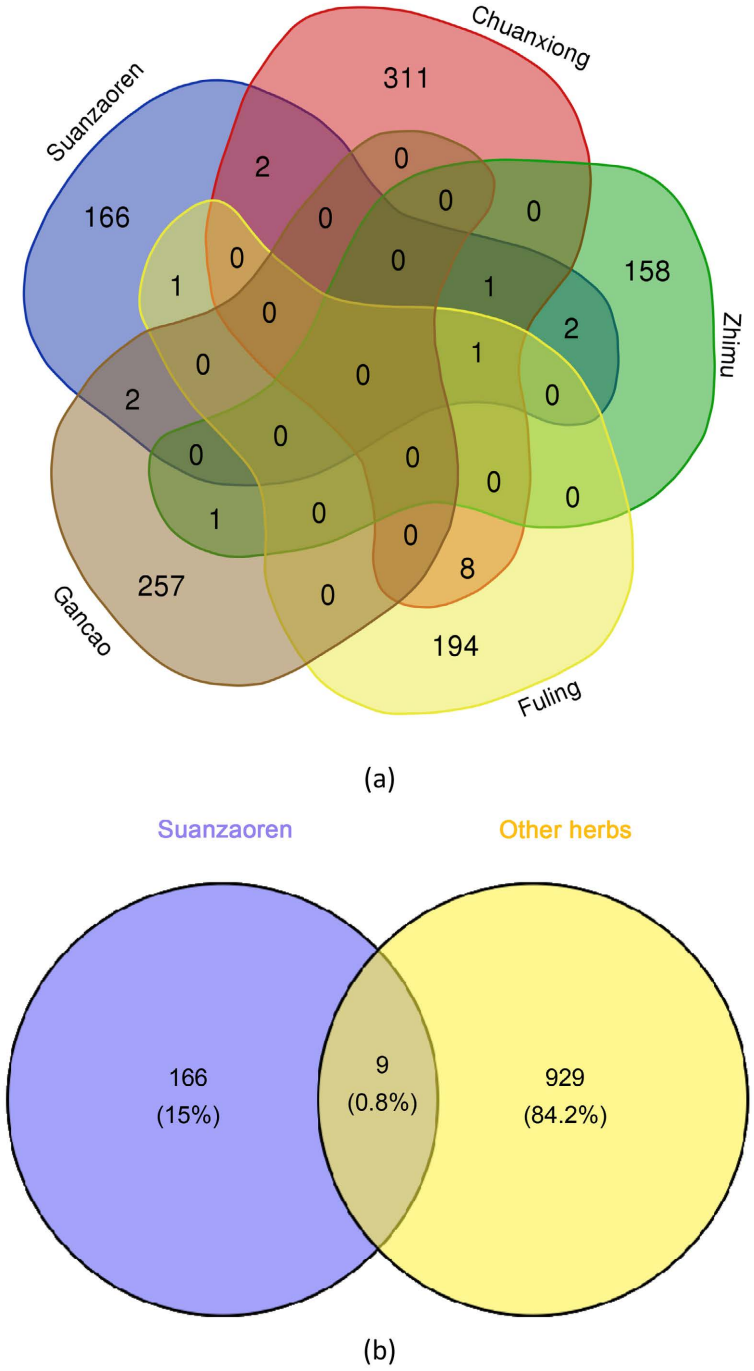

Figure 2. Chemical compounds in five-single herbs of Suanzaoren decoction. (a) Intersection of compounds in five-single herbs; (b) Intersection of compounds between Ziziphi Spinosae Semen and other four herbs.

Ziziphi Spinosae Semen and Licorice include isoquercitrin and vicenin II. Ziziphi Spinosae Semen and Poria contain ursolic acid. Anemarrhenae rhizoma and Licorice contain only one component mangiferin (**Figure 2(a)**).

In SZRD, Ziziphi Spinosae Semen seed is "Jun" (the monarch). There are 175 chemical compounds in Ziziphi Spinosae Semen seed, accounting for 15.8% in

all 5 herbs (Figure 2(b)). When compared with total compounds in the other four herbs, there are 9 common compounds with 0.8% of total compounds in all 5 herbs, including adenosine, tryptophan, isoquercitrin, isovitexin, vicenin II, linoleic acid, oleic acid, protocatechuic acid and ursolic acid (Figure 2(b)).

4.2. Comparative Analysis of Chemical Constituents between Suanzaoren Decoction and Herbs

4.2.1. Ingredients between Suanzaoren Decoction and Herbs

After comparing 145 compounds in SZRD with 1104 in 5 herbs, We found there were 80 common components which accounted for 6.8% of total compounds in all herbs and 55.2% of compounds in SZRD (Figure 3(a)), containing 7 categories, including 27 flavonoids, 17 triterpenoids, 12 steroids, 5 volatile oils, 4 coumarins, 14 phenolic acids and 1 alkaloid (Figure 3(b)) and found that 14 compounds came from Ziziphi Spinosae Semen, 18 from Chuanxiong Rhizoma, 15 from Anemarrhenae rhizoma, 9 from Poria and 27 from Licorice.

In addition, 65 compounds in SZRD are not contained in Ziziphi Spinosae Semen, Anemarrhenae rhizoma, Chuanxiong Rhizoma, Poria and Licorice (Figure 3(c)). These distinctive compounds account for 5.6% of total compounds in all herbs and 44.8% of SZRD compounds (Figure 3(a)), and include alkaloids (1 compound), coumarins (3 compounds), flavonoids (25 compounds), phenolic acids (1 compound), phthalides (2 compounds), polysaccharides (1 compound), steroids (7 compounds), triterpenoids (17 compounds), volatile oils (3 compounds) and others (5 compounds). The number of flavonoids is the highest among SZRD, followed by triterpenoids, suggesting ingredients of SZRD are not simply the sum of the single ingredients and new compounds will produce after decocting SZRD.

The amounts of volatile oils, alkaloids and polysaccharides are decreased while the number of flavonoids is increased in SZRD compared with 5 single herbs (Figure 4(a) and Figure 4(b)). In general, there are many water-soluble compounds in SZRD, such as flavonoids, triterpenoids, accounting for 59.31%. However, triterpenoids, flavonoids and volatile oils account for 22.95%, 18.24% and 15.93% respectively in 5 single herbs. Amino acids, ceramides and cerebrosides, lignans, nucleotides, steroids and stilbenides are not found in SZRD. We inferred it might due to the extraction of SZRD just exists in aqueous decoction, the proportion of components with larger polarity is significantly increased, while the proportion of components with weak polarity is relatively low. On the other hand, it may because the lack of literature on the components of SZRD, and the literatures are just for the analysis of specific components and lack researches on specific components.

4.2.2. Ingredients between Suanzaoren Decoction and Ziziphi Spinosae Semen

We compared 145 compounds contained in SZRD with 175 in Ziziphi Spinosae Semen, the monarch of SZRD (Figure 4(c)). There are 14 common components,

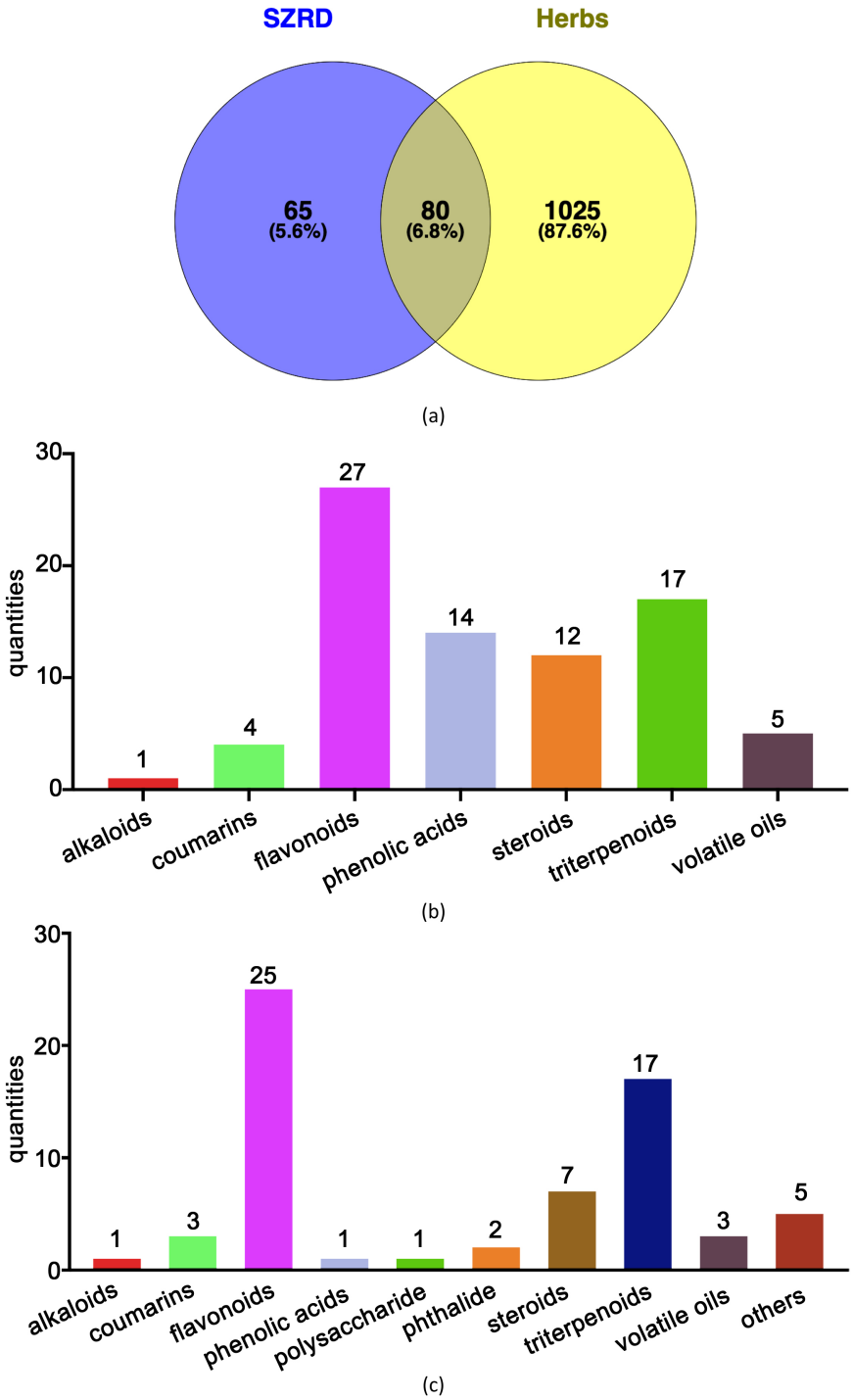

Figure 3. Chemical compounds in suanzaoren decoction and its herbs. (a) Intersection of compounds in SZRD and its herbs; (b) Classification of same compounds of SZRD and its herbs; (c) Classification of different compounds of SZRD and its herbs.

accounting for 9.7% in SZRD, which are flavonoids (6'''-Feruloylspinosin, glucosylvitexin, isovitexin, nicotiflorin, saponarin, spinosin, wertisin, vicenin II), triterpenoids (betulinic acid, jujuboside A, jujuboside B, oleanolic acid), alkaloid (magnoflorine) and volatile oil (palmitic acid), while it has 131 different

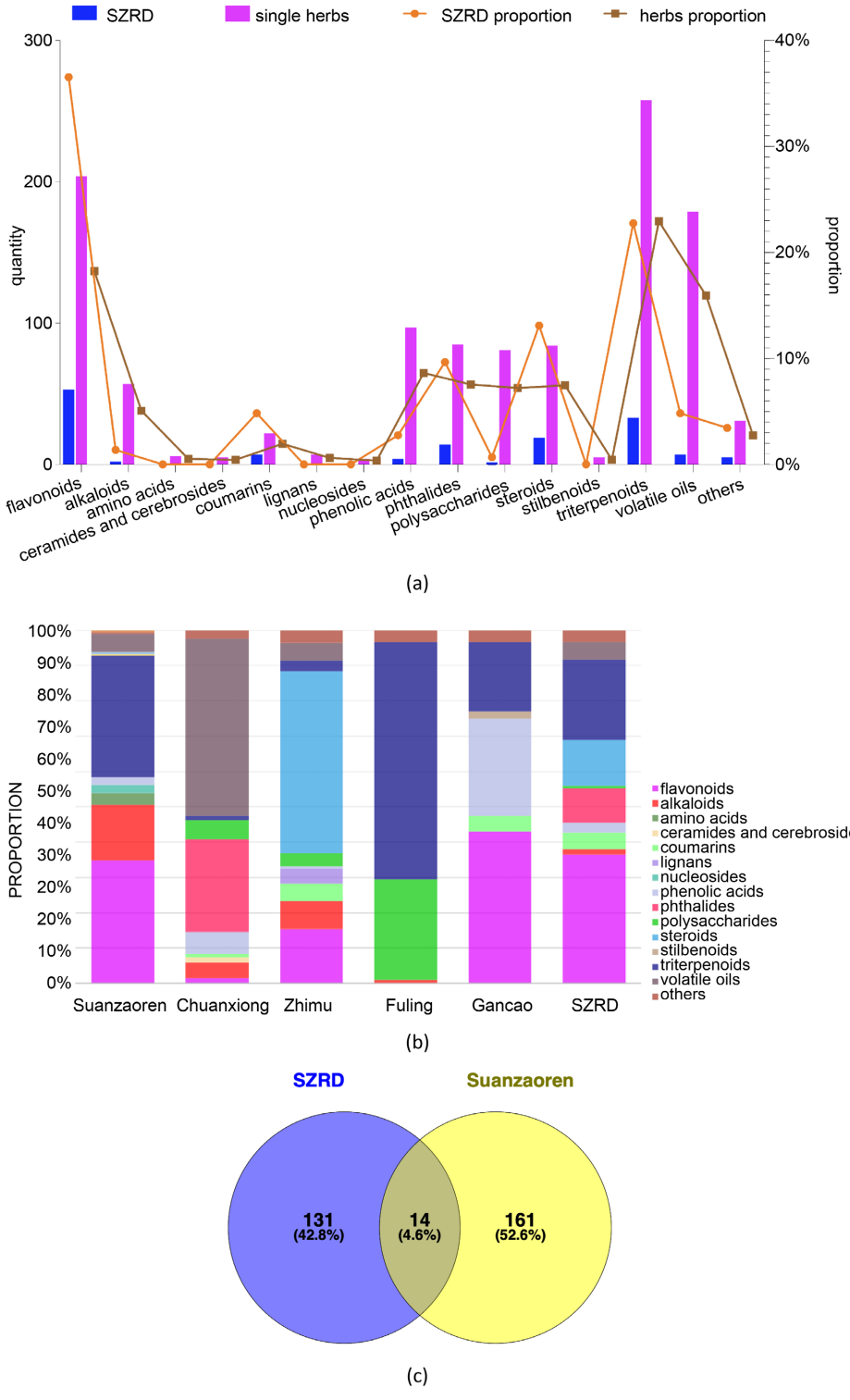

Figure 4. Chemical compounds in suanzaoren decoction and five-single herbs. (a) Proportion and quantity of various ingredients in total ingredients of herbs and SZRD. The column chart shows the quantity of various ingredients in the total compounds of herbs or the prescription, while line chart shows the proportion of various ingredients in the total compounds of herbs or the prescription. The left ordinate indicates quantity and the right ordinate indicates proportion. (b) Proportion of various ingredients in herbs and SZRD. (c) Intersection compounds of SZRD and Ziziphi Spinosae Semen.

compounds (90.3%) (Figure 4(c)), including flavonoids (45 compounds), alkaloid (1 compound), coumarins (7 compounds), phenolic acids (4 compounds), phthalides (14 compounds), triterpenoids (29 compounds), steroids (19 compounds), volatile oils (6 compounds), polysaccharide (1 compound) and others (5 compounds) (Figure 4(a) and Figure 4(b)).

5. Summary and Perspectives

In SZRD, Ziziphi Spinosae Semen is the monarch drug, Chuanxiong Rhizoma and Poria are minister drugs, Anemarrhenae rhizoma is an adjuvant, Licorice is conductant drug, which can reconcil various drugs. Totally, we collected 145 and 1104 chemical ingredients in SZRD and its five-single herbs respectively and found 80 common ingredients between SZRD and five-single herbs, while 65 different compounds only in SZRD. Taken together, our study elucidated that components of SZRD were not simply the sum of one in every single herb. Based on the analysis of the relationship of ingredients between five-single herbs and the whole prescription, we found that the problems existed in the chemical research of SZRD and possible further research direction.

5.1. What Has Already Been Shown to Be Not Promising

1) As the chemical profile of the decoction is dependent on the quality of the plant materials, each compound probably was a wide range of concentrations. Therefore, we highlighted names, numbers and variabilities of compounds in the five herbs and SZRD, nothing is said about the quantities or actual concentrations of these compounds in this review.

2) As different methods have been used, it will be difficult to compare the results of the various studies. There was an effect of the experimental conditions on the overall extracted chemical profile of the decoction. It may be different conditions and time of soaking and decocting, different extraction solvents, different apparatus and parameters to identify SZRD and five-single herbs. That means this number of compounds is very much based on the sensitivity and selectivity of the methods of analysis. For example, the compounds mentioned represent a wide range of polarities, and many of them from five-single herbs will probably not being extraction extracted in SZRD.

3) The variability in the raw materials had an effect on the plant materials on the overall extracted chemical profile of the decoction. For example, the different local growing environments of plants.

4) The different understanding of researchers on the compounds, and global chemical components had an effect on compound being obtained and identified in herbs.

5) It is unbalanced at present of the studies among Ziziphi Spinosae Semen, Chuanxiong Rhizoma, Anemarrhenae rhizoma, Poria, Licorice and SZRD, that mean there were more compounds in herbs with many reports than that with few reports. It was lack of global chemical components for each herb and SZRD.

5.2. What Looks Promising

1) As SZRD is composed of Ziziphi Spinosae Semen, Chuanxiong Rhizoma, Anemarrhenae rhizoma, Poria, Licorice, it is necessary to perform parallel studies among SZRD and its herbs.

2) As pharmacological activity has a dose-response curve, moreover synergy and antagonistic effect may occur between compounds in certain ratios, it is the biological activity of the individual compounds and their concentration that determine the activity of the final preparation. Therefore, it is necessary to study phytochemistry and pharmacological activities at the same time.

3) What is needed is to integrate the data on activity of extracts and pure compounds with the data on traditional use and the data on the chemistry.

5.3. The Limitations of This Article

1) Compounds collection of SZRD and five-single herbs were mainly based on the literature in the past five years, but few had been reported more than five years.

2) This paper did not carry out a classification analysis for non-English name compounds.

3) For the chemical composition of SZRD and its five-single herbs, we just simply classified them based on their chemical structures while not carrying out subcategory analysis.

Although these results are exploratory and need to be interpreted with caution, our study provides important information that may help offer subsequent studies to determine the compounds and explore pharmacology research about SZRD. This review may provide the reference for phytochemistry and pharmacology researches of SZRD, and also point out the direction for its further research.

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Consent for Publication

All authors have given consent for publication.

Competing interests

The authors declare that they have no competing interests.

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