Heliyon 9 (2023) e13692

Contents lists available at ScienceDirect

Heliyon



journal homepage: www.cell.com/heliyon

Research article

CelPress

Compound-level identification of sasang constitution type-specific personalized herbal medicine using data science approach



Sa-Yoon Park^{a, #}, Young Woo Kim^{b, c, #}, Yu Rim Song^c, Seon Been Bak^c, Young Pyo Jang^d, Il-Kon Kim^b, Ji-Hwan Kim^{e, **}, Chang-Eop Kim^{a, *}

^a Department of Physiology, College of Korean Medicine, Gachon University, Seongnam, 13120, Republic of Korea

^b Department of Computer Science and Engineering, Kyungpook National University, Daegu, 41566, Republic of Korea

^c School of Korean Medicine, Dongguk University, Gyeongju, 38066, Republic of Korea

^d College of Pharmacy, Kyung Hee University, Seoul, 02447, South Korea

e Department of Sasang Constitutional Medicine, Gil Hospital of Korean Medicine, Gachon University, Incheon, 21565, Republic of Korea

ARTICLE INFO

Keywords: Personalized herbal medicine Sasang constitutional medicine Chemical characteristics Compound information

ABSTRACT

Introduction: Sasang Constitutional Medicine (SCM) is a type of traditional Korean medicine where patients are classified as one of four Sasang constitution types (Sasang type) and medications consisting of medicinal herbs are prescribed according to the Sasang type. Despite the importance of personalized medicine, the operation mechanism is largely unknown. To gain a better understanding, we investigated the compound information that composes Sasang type-specific personalized herbal medicines on both multivariate and univariate levels.

Methods: Five machine learning classifiers including extremely randomized trees (ERT) were trained to investigate whether the Sasang type can be explained by compound information at the multivariate level. Hierarchical clustering was conducted to determine whether compounds are processed distributedly or specifically. Taxonomic and biosynthetic analyses were conducted on these compounds. A univariate level statistical test was conducted to provide more robust Sasang type-specific compound information.

Results: Using the trained ERT classifier, sixty important compounds were extracted. The sixty compounds were clustered into three groups, corresponding to each Sasang type-prominent compounds, suggesting that most compounds have specific preference for the Sasang type. Structural and biosynthetic characteristics of these Sasang type-prominent compounds were determined based on taxonomy and pathway analyses. Fourteen compounds showed statistically significant relevance with the Sasang type. Additionally, we predicted the Sasang type of unknown herbs, which were confirmed by their biological effects in functional assays.

Conclusion: This study investigated the personalized herbal medicines of the SCM using compound information. This study provided information on the chemical characteristics of the compounds that are essential for classifying the Sasang type of medicinal herbs, as well as predictions regarding the Sasang type of the commonly used but unidentified medicinal herbs.

* Corresponding author.

** Corresponding author.

E-mail addresses: jani77@gachon.ac.kr (J.-H. Kim), eopchang@gachon.ac.kr (C.-E. Kim).

 $^{\#}$ Park SY and Kim YW equally contributed to this work.

https://doi.org/10.1016/j.heliyon.2023.e13692

Received 12 August 2022; Received in revised form 1 February 2023; Accepted 7 February 2023

Available online 13 February 2023

2405-8440/© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1SEInduceBathanReconse Reads Allow3SEIARBathanArara Teratur Traub.3SEMEQChrapt ConstructionArara Teratur Traub.3SEMEQChrapt ConstructionChrapt Construction5SEMEQChrapt ConstructionChrapt Construction6SEMERConstructionChrapt Construction7SEATADathanArcea Catechi L7SEATADathanArcea Catechi L7SEATADathanArcea Catechi L7SEATADathanArcea Catechi L7SEATADathanArcea Catechi L7SEHAGacalasArcea Catechi L7SEHAGacalasArcea Catechi L7SEHAGacalasArcea Catechi L7SEHAGacalasArcea Catechi L7SEHAGacalasArcea Catechi L7SEHAGacalasAplalas Olifarials Reads HI Nick7SEHAGacalasAplalas Olifarials Reads HI Nick7SEHAGacalasAplalas Olifarials Reads HI Nick7SEHAReadsHI7SEHAReadsArcea Catechi L7SEHAReadsHI7SEHAReadsHI7SEHAReadsHI7HAHA		Sasang type	Chinese name	Pronunciation	English name
2 SE HI Barbia Attractyolock Macrocypical Kolds. 3 SE HE Barbia Attractyolock Macrocypical Kolds. 4 SE HE Conzolation Chrans Macrocypical Kolds. 5 SE HE Conzolation Chrans Macrocypical Kolds. 6 SE ME Conzolation Attractory Macrocypical Kolds. 7 SE ME Data Attractory Macrocypical Kolds. 9 SE Attractory Macrocypical Kolds. Attractory Macrocypical Kolds. 9 SE Attractory Macrocypical Kolds. Attractory Macrocypical Kolds. 9 SE Attractory Macrocypical Kolds. Attractory Macrocypical Kolds. 10 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 11 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 12 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 13 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 14 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 15 SE HE Conzolation Kolds. Attractory Macrocypical Kolds. 16 HE	1	SE	白芍藥	Baishao	Paeoniae Radix Alba
3SE¥ZBanciaArm Tentumbunb.6SEKapelCharapiCitura Reiculata7SEKapelConglanMilistant Bulbas7SEKapelDaugguiAracc actechu7SEKapelDaugguiAracc actechu7SEKapelDaugguiAracc actechu9SEKapelDaugguiAracc actechu9SEKapelDaugguiAracc actechu9SEKapelDaugguiAracca actechu9SEKapelDaugguiAracca actechu9SEKapelDaugguiAracca actechu10SEKapelDaugguiDaugguiDauggui11SESESEGaungiangDaugheris Rinzona12SEKapelGaungiangDaugheris RinzonaDaugei13SESEBAGaungiangDaugai Aracca Actechu14SESESEGaungiangDaugai Aracca15SERAGaungiangDaugai Aracca16SESEBAGaungiangDaugai Aracca17SERAGaungiangDaugai Aracca18SERAGaungiangDaugai Aracca19SERAGaungiangDaugai Aracca19SERAGaungiangDaugai Aracca19SERAGaungiangDaugai Aracca19SERAGaungiang<	2	SE	白朮	Baizhu	Atractylodes Macrocephala Koidz.
4SEHRChanarkongChanarkongChanarkongKhaoma6SEXE1CongolaAlli Fistolas Blobno7SEXE1CongolaAngelices Neuella La8SEXE4DanagaAngelices Neuella La9SEXE4DanaAljubac Fractural10SEXE4DanaAljubac Fractural11SEChiffParalAngelices Neuella Radis Radis12SEKE4GanipariaZargibas Bhaires Radis13SEKE4GanipariaZargibas Bhaires Radis14SEBEGanipariaZargibas Bhaires Radis15SEKE4GanipariaMagnola Officiarum Nitrione16SEBEGanipariaMagnola Officiarum Nitrione17SEFishGanipariaMagnola Officiarum Nitrione18SEBEGanipariaMagnola Officiarum Nitrione19SEKE4NagnolaCanaanconi Canadis19SEBENagnolaCanaanconi Canadis19SEKE4NagnolaCanaanconi Canadis19SEBENagnolaCanaanconi Canadis19SEKE4NagnolaCanaanconi Canadis19SEKE4NagnolaCanaanconi Canadis19SEKE4NagnolaCanaanconi Canadis19SEKE4NagnolaCanaanconi Canadis19SEKE4Nagnola <td< td=""><td>3</td><td>SE</td><td>半夏</td><td>Banxia</td><td>Arum Ternatum Thunb.</td></td<>	3	SE	半夏	Banxia	Arum Ternatum Thunb.
5SEHIMChanatong Maxima6SEHEAConghaiMitristudes Bulbos7SEKBDatagaiAreas Catechi I.8SEHEADatagaiAreas Catechi I.9SEKBDatagaiAreas Catechi I.9SEKBDatagaiAreas Catechi I.10SEKBDatagaiAreas Catechi I.11SEHFFullControl12SEHFGalazagianAreas Catechi13SEHEGalazagianAreas Catechi14SEHEGalazagianAreas Catechi15SEHEGalazagianProportional Bulba Practicas16SEHEGalazagianProportional Bulba17SEHEHIMHujaoProportional Bulba18SEHIMHujaoProportional BulbaBruba19SETERonguiGingaila Officialis BubbaBruba19SETENaguiaCategolia Officialis BubbaBruba20SETERonguiCategolia Officialis BubbaBruba21SETENaguiaProportional Unide22SETENaguiaAreas Catechi23SETENaguiaProportional Catechi24SETENaguiaProportional Unide25SETENaguiaProportional Catechi26SETE <t< td=""><td>4</td><td>SE</td><td>陳皮</td><td>Chenpi</td><td>Citrus Reticulata</td></t<>	4	SE	陳皮	Chenpi	Citrus Reticulata
6 SE XLIP Autopi 7 SE XLIP Autopi 8 SE XLIP Danggi Angelica Sinesis Ada'. 9 SE XLIP Dataon Missishi Pulbas. 10 SE XLIP Dataon Missishi Pulbas. 11 SE TAR Dataon Missishi Pulbas. 12 SE TAR Dataon Missishi Pulbas. 13 SE RE Ganjang. Diplace Officials Relationers. 14 SE RE Ganjang. Diplace Officiant. 15 SE RE Ganadamilant. Companies. 16 SE RE Ganadamilant. Companies. 17 SE RE RE Ganadamilant. 18 SE RE Re Re 19 SE RE Re Re 21 SE RE Re Re 22 SE RE Re Re 23 SE RE Re Re 24 SE RE Re Re 25 SE RE Re Re 26 RE RE	5	SE	川芎	Chuanxiong	Chuanxiong Rhizoma
7 SE 'Aby Danggui Applicas Neersis Raits 9 SE 'Aby Danagani Applicas Neersis Raits 9 SE 'AB Dataon Allifisatif Bulles 9 SE 'AB Dataon Julies Firstuss 11 SE 'AB Dataon Julies Firstuss 12 SE 'AB Gancroo Lororice 13 SE CB Gancroo Lororice 14 SE BB Ganlang Alphate Officinarum Rhizone 15 SE BB Ganlang Pappers Factors 16 SE BB Ganlang Pappers Factors 17 SE BB Ganlang Pappers Factors 18 SE HB Haina Papers Factors 19 SE HB Haina Papers Factors 20 SE AS Rade Nangain Canagan 21 SE AS Nangain Nangain And Stators 22 SE AS Nangain Canagan Canagan Canagan 23 SE AS Nangain Nangain And Stators 24 SE SE <	6	SE	葱白	Congbai	Allii Fistulost Bulbus
8SEXBDarageniAngelox Sinesis Radix10SEXFADaraonJujbae Protectos11SEMTADaraoJujbae Protectos12SEKFAGanicoLoorie13SERERealGanicosLoorie14SERERealGanicosLoorie15SEREGanicosCingiberis Ithizona16SERERealGanizosPoposteono Cablin (Riones) Bench.17SERFAGanizosPoposteono Cablin (Riones) Bench.18SEREGanizosPoposteono Cablin (Riones) Bench.19SERFAHoupoMagnolizo Officinais Red E: Wils19SEREMagnolizo Officinais Red E: Wils10SERERedOrageni21SEREMagnolizo Officinais Red E: Wils22SERERedOrageni23SERENegliaro,Zarujber Officinai Ronze24SERERealNegliaro,Zarujber Officinai Ronze25SERERENegliaro,Zarujber Officinai Ronze26SERERENegliaro,Zarujber Officinai Ronze27SERERENegliaro,Parato Cinage, C. A. Mey.28SERERENegliaro,Parato Cinage, C. A. Mey.29SERERENingliaro,Parato Cinage, C. A. Mey.29 <td>7</td> <td>SE</td> <td>大腹皮</td> <td>Dafupi</td> <td>Areca Catechu L.</td>	7	SE	大腹皮	Dafupi	Areca Catechu L.
98E大蒜DaxaoAllif Sativi Bubus118E大猪DaxaoJujaba Fractus118E日子PuziAconti Lacells Radix Preparata128F日本GancaoLicorice138ERafiGanlangZingbiers Missionan148ERafiGanlangilangAlplaiae Officianus Rhizome158ERafiGanlangilangAlplaiae Officianus Rhizome168EBigGuinghuxshangPagestemochbin (Blanco) Benth.168EBigHujaoMagnalia Officianis Redi Et Wils178EBigOingalCirin Riccianis Periodical	8	SE	當歸	Danggui	Angelicae Sinensis Radix
10 NB 大市 Dorace Jujubae Process 11 SE 竹子 Fuel Acontit Laterails Radix Preparata 12 SE 七葉 Ganicao Lacorie 13 SE 七葉 Ganicao Lacorie 14 SE 日葉 Ganicao Alpiales Officanau Rubizona 15 SE 七葉 Ganicao Papate Officanau Rubizona 16 SE 日葉 Ganicao Papate Officanau Rubizona 17 SE 月葉 月本 Houpa Magaolia Officianis Rubit Et Wis 18 SE 月本 Houpa Magaolia Officianis Rubit Et Wis 19 SE 月末 Rubitona Papate Secord Carlos (Rubicona) 20 SE 月末 Rubitona Papate Secord Rubitona 21 SE 日葉 Rubitona Papate Secord Rubitona 22 SE 日葉 Rubitona Papate Secord Rubitona 23 SE 日常 Nuchan Autentitona 24 SE 日常 Cargan Autentitona 25 SE 日常 Cargan Autentitona 26 SE 日常 Cargan Autentitona 27	9	SE	大蒜	Dasuan	Allii Sativi Bulbus
11NE(1子ProiA contil activate12SE日年GancianLicorice13SERatGanlingZingbiers (Bikconan14SFRatRatGanlingAlphiae Officinarus Rhizome15SERatRatGanlingPaptisenon Rhizome16SERatRatGuinantoni Ramulas17SEBPHuinaoPaperis Fractus18SEBRHuinaoPaperis Fractus19SEBRRathenPanas Ginseng C.A. May.21SEEffRathenPanas Ginseng C.A. May.22SEEffShenglingCingiber Officinals Retro (Fractus)23SEBRNanguiaComparison Correc24SEBRYingsukePaperoris Percitas25SEBRYingsukePaperoris Percitas26SEBRZindsienMartini27SEBRChainAtomiai Senen28SEBRZindsienMartini29SEBRYingsukePaperofis Percitas29SEBRDialoMartini29SEBRDialoMartini20SEBRDialoMartini21SEBRDialoMartini22SFBRBRMartini23SEBRDialoMartini24SEBRDialoMartin	10	SE	大棗	Dazao	Jujubae Fructus
12SE <td>11</td> <td>SE</td> <td>付子</td> <td>Fuzi</td> <td>Aconiti Lateralis Radix Praeparata</td>	11	SE	付子	Fuzi	Aconiti Lateralis Radix Praeparata
13SRÉEGanjangAppinse Officamen Rhizome15SRƧGuanghuoxtangAppinse Officamen Rhizome15SRƧGuanghuoxtangPeperis Parcine16SRƧGuanghuoxtangOrganome17SRØrNoupuMonto Officinalis Relot Et Wils18SRØrNoupuOrganome19SRÅgRessOrganome20SRÆRessParas Ginenge C. A. Mey.21SREffNonguiCanactome22SREffNonguiCanactome23SREffNonguiOrgen Farcine24SREffNanouNongui25SREffNanouOrgen Farcine26SREffNanouAppinse Protectos27SREffNanouAppinse Protectos28SRØffNanouAppinse Protectos29SREffNanouAppinse Protectos29SRØffNanouAppinse Protectos20SRØffNanouAppinse Protectos21SRØffNanouAppinse Protectos22SRØffNanouAppinse Protectos23SRØffNanouAppinse24SRØffNanouAppinse25SRØffNanouAppinse26SRØffNanouAppinse27 </td <td>12</td> <td>SE</td> <td>甘草</td> <td>Gancao</td> <td>Licorice</td>	12	SE	甘草	Gancao	Licorice
14SEBEGalangjiangApintome15SEBFAGuaphinovarangPeopstemon Cabiling Halanco Bench16SEBFAHujaoMagnolla Officialls Reld Et Wils18SEBRAHujaoPerstemon Ramulus19SEBRAMagnolla Officialls Reld Et Wils19SEBRAMagnolla Officialls Reld Et Wils20SEABANenshenPara Carlow Price21SECBANenshenConstannoul Cortex22SECBAStannoul CortexConstannoul Cortex23SEBAGWinnyaEvolue Processo24SECBAVingsukeParentishis Scopariae Horba25SEBAVingsukeApriniae Oraphylate Fractus26SEBAVingsukeApriniae Oraphylate Fractus27SEBACaragahaArractylodes Lancae (Thush.)De28SEBACaragahaArractylodes Lancae (Thush.)De29SEBAStannouArractylodes Lancae (Thush.)De31SEBAChannaArractylodes Lancae (Thush.)De32SYBADataArractylodes Lancae (Thush.)De33SYBADataArractylodes Lancae (Thush.)De34SYBADataArractylodes Lancae (Thush.)De35SYBADataArractylodes Lancae (Thush.)De36SYBADataArractylodes Lancae (Thush.)De37	13	SE	乾薑	Ganjiang	Zingiberis Rhizoma
15F.S.E.S.E.S.U.Guaghioxi.angPoinamoin Reanuals17S.R.J.M.HoupuCinamoin ReanualsHoupu17.1S.R.J.M.HoupuMegnein Criticalis Relat IV IVIs17.2S.R.T.R.OinspiCiralis Relat IV IVIs17.3S.R.T.R.OinspiCiralis Relat IV IVIs17.4S.R.T.R.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex27.4S.R.T.S.Nanoni Cortex28.4S.R.T.S.Nanoni Cortex29.4S.R.T.S.Nanoni Cortex29.4S.R.T.S.Nanoni Cortex29.4S.R.T.S.Nanoni Cortex29.4S.R.T.S.Nanoni Cortex29.4S.R.T.S.Nanoni Cortex29.5S.G.T.S.Nanoni Cortex29.6S.R.T.S.Nanoni Cortex29.7S.G.T.S.Nanoni Cortex29.8S.R.T.S.Nanoni Cortex29.9S.R.T.S.Nanoni Cortex29.1S.R.T.S.Nanoni Cortex29.1S.R.T.S.Nanoni Cortex <td>14</td> <td>SE</td> <td>良薑</td> <td>Gaoliangjiang</td> <td>Alpiniae Officinarum Rhizome</td>	14	SE	良薑	Gaoliangjiang	Alpiniae Officinarum Rhizome
16SE長枝GuizhGuizhGuizhGuizh17SE房林HoupuMagnola Officialis Rebel z Wils18SE舟根QiagiCitri Reticulate Petracynum Virde19SE舟皮QiagiCitri Reticulate Petracynum Virde20SE人参RenshenParat Ginearge C.A. Mey.21SE管柱RoguiCinnanomin Grots22SE生業ShengiangZinanomi Gorts23SE失業WilnyuEvdate Petracynum Virde24SE香付子XiangfuCinnanomi Corts25SE西藤YingskeParetris Petracynum26SE数BTArteniza Scoparia Herba27SE基管仁YingskePaperis Pericarpium28SEHTCangehuArtenizioa Arteniza Maranturus29SE五市CangehuArtenizioa Artenizioa Maranturus30SFJEJEStance (Thunh)Dc.31SEJEJEStance33SYJEDatunMath Burgehu34SYJEChalnuRadis Ance (Thunh)Dc.35SYJEDiguyiLyi Cortex36SYJEGanauiKansu Kalisi37SYJEGanauiKansu Kalisi38SYBAPanageingSpoinaevine Asiai39SYJEGanauiKansu Kalisi39SYBAFugenaKali	15	SE	藿香	Guanghuoxiang	Pogostemon Cablin (Blanco) Benth.
17SE厚林HoupuMegnala Officinalis Rede Iz Wils18SE青政QiagpiCirclinalis Rede Iz Wils19SE青政QiagpiCirclinalis Rede Iz Wils10SE人琴ReshenPanax Cinsengi C.A. Mey.21SEEXSegimaCinamamoni Cortes22SE里花SegimaSingher Officiale Rosco23SE奥茱萸WuzhuyuEvaluation Cortes24SE雪原YinchenArtensisiae Scopariae Herba25SE雪原YinchenArtensisiae Scopariae Herba26SE雪原YingsukePaperis Pericarpium27SE雪花ZinskinCangzhuAttractyodes Lancea (Thumb)Dc.28SE青花CangzhuAttractyodes Lancea (Thumb)Dc.29SE黃花SharenAmonum Aurantizuum H.T. Tsai ES. W.Zbao30SE黄花BioheMethae Herba31SESY東前子Cheqianzi34SY東前子CheqianziPaperia Corces (Schw.) Vol.35SY大香FulngParcia Corces (Schw.) Vol.36SY大香FulngSoposhiko'voice Radix37SY大香GansaiKushen38SY大香FulngParcia Corces (Schw.) Vol.39SY黄花GansaiCansia Radix Ragelicae Bisernate31SY黄花GansaiCansia Radix34SY黄花GansaiCansi	16	SE	桂枝	Guizhi	Cinnamomi Ramulus
18SE胡根HujãoPhujãoPhujão19SE内表Qiepi ACitri Reticulate Petracipum Wide20SE人夢RenshenParac Ginseng C. A. Mey.21SE官桂Rongui ACinnamom Grato22SE生薑ShengjiangZingber Officinale Roscoe23SE貴村子NingfuCypert Nitiona24SE曹村子NingfuCypert Nitiona25SE薗藤YingkePapeveris Petrasias26SE蟹菜YingkePapeveris Petrasias27SE茴香CangzhuAuranti Forcurs Immatrus28SE葡萄花HangqiHedysarun Militigum Maxin.29SE蒼花HangqiHedysarun Militigum Maxin.30SE黃花HangqiHedysarun Militigum Maxin.31SE砂仁SharenAnonum Aurantiacum H. T. Tsai E.S. W. Zhao33SY柴胡BohoMenthe Herba34SY柴胡DigupiUrantagini Semen35SY地母皮DigupiUrantagini Semen36SY大田Palanzaini SemenSemen37SY地母皮DigupiUrantagini Semen38SY世景FalangSponthioviae Badra39SY大石GoagiaMibi Fructus40SY菅子HangainCarlis Akbale41SYBATGoagiaLycii Fructus42SY竹子Goagia </td <td>17</td> <td>SE</td> <td>厚朴</td> <td>Houpu</td> <td>Magnolia Officinalis Rehd Et Wils</td>	17	SE	厚朴	Houpu	Magnolia Officinalis Rehd Et Wils
19SE売皮○jingpiClinitatice Pericarplum Virde20SE七著RonshenPanax Ginsery C.A. Mey.21SE管柱RonguiGinamomi Cortes22SE生業ShenplinayZingber Officinale Rosco23SE東菜菜WuzhuyuEvodiae Fructus24SE香付子KunguíCypert Nitionale Rosco25SE夏陽YinchenAtratisiae Scopariae Herba26SE夏陽YinchenAtratisiae Scopariae Herba27SE基智仁YinchenAtratisiae Scopariae Herba28SE東菜ZhishiAtratisioe Instrutus29SE古菜CangahuAtratisioe Instrutus30SE東菜HuangqiHerba31SEサピSharenAnomum Atraneticeum H.T. Tsal ES. W. Zho32SY東荷DuhoRadix Angelicae Bierata33SY東荷DuhoRadix Angelicae Bierata34SY東前子CheqianziHuingpin Seenen35SY大管DuhoRadix Angelicae Bierata36SY東前子GoagiaLubi Fructus37SY大管GananiKanenekae38SY大管GananiKanenekae39SY東前子GoagiaLubi Fructus34SY東第GananiCanshik Angelicae Bierata36SY大管GananiKanenekae37SY大Ganani <t< td=""><td>18</td><td>SE</td><td>胡椒</td><td>Hujiao</td><td>Piperis Fructus</td></t<>	18	SE	胡椒	Hujiao	Piperis Fructus
20SE人蔘RemoteParax Ginseng C. A. Mey.21SE管挂RonguinCinnamoni Cortex22SE生薑ShengiangZingher Officinale Roscoe23SE慶二各行/2XiangfuCyperl Rhizoma24SE國陳YinchenAremisiae Scopariae Herba25SE國陳YinchenApproximate Herba26SE國陳YinchenApproximate Scopariae Herba27SE基督仁YinchenApproximate Scopariae Herba28SE費素Transike Scopariae Herba29SE营酒CangahuAtractylodes Lancea (Thumb.)Dc.29SE营酒BoheMethate Herba31SEBCSharenAnomum Aurantiaeum H. T. Tsai E.S. W. Zhao32SY弊荷BoheMethate Herba33SY弊荷ChaihuRadix Supleuri34SY弊前子CheqinaziPlantaginis Semen35SY物母zDipupiPlantaginis Semen36SY幣酒FundingSepashnkoviae Radix37SY防氟GansuiKasui Radix38SY國紀子GonaziIncit Fractus39SY博士GonaziLancierae Laponicae Hos41SY竹屬GansuiKasui Radix42SY爾名GonaziLancierae Laponicae Hos43SY國紀子GonaziLancierae Laponicae Hos44SY曹素	19	SE	青皮	Qingpi	Citri Reticulatae Pericarpium Viride
11SE管植KongjiangCinnamoni Corte22SE生薯SkongjiangZingler Officinale Rosce23SE香竹子XiangfuEvodiae Fructus24SE香竹子XiangfuOperi Rhizona25SE萬根YinchenArtenisiae Scoparlae Herba26SE萬葉YingukePapaveris Pericarphum27SE基智仁YinhAlpinae Oxphyliae Fructus28SE硯石CangzhuAtractifoke Lancea Thumb,Dc.29SE黃花HuangqiHedysarum Multijugum Maxim.30SE黃花BohenAnomun Auraniacum H. T. Tsai El.S. W. Zhao31SE黃花CheqinariHoatspleruri33SY東菊BoheMenthae Herba34SY東朝子CheqinariHoatspleruri35SY東荷DuhuoRadix Angelicae Biseratae36SY菊活DuhuoRadix Angelicae Biseratae37SY博石FuegralNoticitae Radix38SY黄花GougiaiLycii Furctus44SY蕾鼠JinyinhuaLonierre Japonicae Flos45SY黄紀MatopCoursian Angelicae Biseratae46SY黄銀JinyinhuaLonierre Japonicae Flos47SY竹石MatopCoursian Course48SY大KJinyinhuaLonierre Japonicae Flos49SY大BaJinyinhuaSchizoneptea Herba4	20	SE	人蔘	Renshen	Panax Ginseng C. A. Mey.
12SE生薑大語NampianeIngiber Officinale Roscoe23SE慶祝與WukuyuEvodiae Froctus24SE國旗YinchenArtenisise Scopariae Herba25SE國旗YingsukePapaveris Pericarpium26SE國黨級YingsukePapaveris Pericarpium27SE台首YinhiAlpiniae Coxybijlae Fructus28SE伊賀XishiAtractylodes Lances (Thumb,Dc.29SE蒼花HanagqiHedysarmu Multiligum Maxim.30SE黄花BahenMoranu Aurantacau H.T. Tsai Et S. W. Zhao31SE砂仁SharenMomum Aurantacau H.T. Tsai Et S. W. Zhao32SY博奇BoheMether Herba33SY単前子CheqianziPlantaginis Senen34SY博奇DuhuoRadix Angelice Biseratae35SY横音DuhuoRadix Angelice Biseratae36SY横音GansaiRuki Fructus37SY横音GougialLyni Fructus38SY横客GougialLyni Fructus40SY黄素GansaiRuki Fructus41SY竹衣MachJingithaCortex Motian42SY竹子MachLingitoCortex Motian43SY金銀形JingithaCortex Motian44SY竹TJingithaCortex Motian45SY陳君MidanjCortex Motian <t< td=""><td>21</td><td>SE</td><td>官桂</td><td>Rougui</td><td>Cinnanmomi Cortex</td></t<>	21	SE	官桂	Rougui	Cinnanmomi Cortex
23SE展発WazhumEvo diae Fructus24SE商所YinchenArtensiae Scopariae Herba25SE國那YinchenArtensiae Scopariae Herba26SE國那YingukePapaveris Pericarpium27SE基督仁YinhAlphiae Oxyphyliae Fructus28SE서景CangzhuArtaruti Fructus Inmaturus29SE董九CangzhuArtaruti Fructus Inmaturus30SE黄九BahenMonum Artarutiscum H. T. Tsai Et S. V. Zhao31SE黄九ChahuRadix Bupleuri33SY博希BoheMenthae Herba34SY博希DahonRadix Angelicae Biserate35SY博希DuhonRadix Angelicae Biserate36SY博希PulangParataginis Semen37SY博希PulangParataginis Semen38SY博希BuhonRadix Angelicae Biserate39SY博希GangaiSaposhnikoviae Radix41SY博名GangaiKubher42SY博子FupenziKubher43SY曼素Saposhnikoviae Radix44SY金麗花JingiheCanisai Radix45SY曼素JingihanCanceraa Ingonicae Flos44SY曼素JingihanParataginis Sehe Eructus45SYJingiJingihanParataginis Sehe46SYJingiJingihan <td>22</td> <td>SE</td> <td>生薑</td> <td>Shengjiang</td> <td>Zingiber Officinale Roscoe</td>	22	SE	生薑	Shengjiang	Zingiber Officinale Roscoe
24SE哲好子XiangfuCyperi Rhizoma25SE茵藤YinchenArtarisias Coopriate Herba26SE黃紫松YingsukePapaveris Pericarpium27SE盖智仁YinduAlphine Oxyphyline Fructus28SE盖智仁YinduAlphine Oxyphyline Fructus29SE蒼朮CangzhuArtarctylodes Lancea (Thunb.)Dc.30SE蒼朮CangzhuAttarctylodes Lancea (Thunb.)Dc.31SE砂仁SharenAnonuum Aurantiacum H. T. Tsai Et S. W. Zhao32SY樊衛BobeMenthe Herba33SY樊衛ChalhuBadis Bupleuri34SY雙菊DihuoRadis Sugnes35SY樊衛DuhuoRadis Sugnes36SY雙高PangfengSapohnikoviae Radis37SY鬱蒼FulingPoria Cocos (Schw.) Wolf.38SY在茶FulingPoria Cocos (Schw.) Wolf.39SY橫蒼JinglieSachangkicea Biserate41SY台花JinglieSchizonepeten Herba42SY萬濟JinglieSchizonepeten Herba43SY台花JinglieSchizonepeten Herba44SY全羅JinglieSchizonepeten Herba45SY建厚JingliaCortex Mutan46SY樊丹YinglieSharchury47SY地積QianghunNorterey Tinkizona Et Radix48	23	SE	吳茱萸	Wuzhuyu	Evodiae Fructus
25SE菌療YinchenAremisiae Scopariae Herba26SE醫療处YingsukePapaveris Pericarpium27SE益智仁YingiukApiniae Oxyphyliae Fuctus28SE#KYingiukAurantii Fuctus Inmaturus29SE蓋木CangzhuAurantii Fuctus Inmaturus30SE黄花HuangaiHedyarum Multijugum Maxim.31SE黄花BoheMenthae Herba32SY弊着BoheMenthae Herba33SY弊着BoheMenthae Herba34SY車前子CheqianziPiantaginis Semen35SY地橡皮DigupiLycii Cortex36SY樹素子PilongPoriaccores (Schw.) Wolf.37SY防风PangfengSaposhnikoviae Radix38SY國素子PilongPoriaccores (Schw.) Wolf.39SY樹花子GouqiziLycii Fuctus41SY樹花子GouqiziLycii Fuctus42SY樹花子MudapiCortex Moutan43SY台素MudapiCortex Moutan44SY大道MitoguNotan45SY台素MudapiCortex Moutan46SYHitagMudapiCortex Moutan47SY竹素MudapiCortex Moutan48SYHitagQianghuNotan49SYHitagQianghuNotan51SYHitag<	24	SE	香付子	Xiangfu	Cyperi Rhizoma
26SE異報緊張YingsukePapaveris Pericarpium27SE益智仁YinhiAlpinae Oxyphyliae Process28SE서寬ZhishiAurantii Fructus Immaturus29SE蒼朮CangzhuAtractylodes Lancea (Thunb.)Dc.20SE蒼朮CangzhuAtractylodes Lancea (Thunb.)Dc.30SE黃朮CangzhuAtractylodes Lancea (Thunb.)Dc.31SE砂仁SharenAmomun Aurantiacum H.T. Tsai Ef. S.W. Zhao32SY柴胡ChalhuRadix Supleuri33SY柴胡ChaqianzPalataginis Semen34SY柴胡DigupiLycii Cortex35SY地骨皮DigupiSaposhnikoviae Radix36SY横方FungenzPalataginis Semen37SY防氮PangtengSaposhnikoviae Radix38SY茯苓FuignNoific39SY茯苓FuignNoific40SY甘遂GansuiKansui Radix41SY黃铊JingihuSophorae Flavescentis Radix42SY荊芥JingihuConciera Jonanciae Plos43SY美華KushenSophorae Flavescentis Radix44SY黃铊JingihuContex Moutan45SY美華KushenContex Moutan46SYXingMidongCatlis Atebliee47SY美華KushenParcetan Radix48SY	25	SE	茵蔯	Yinchen	Artemisiae Scopariae Herba
27SE結智仁YinhiAlpiniae Oxynlyliae Fucus28SE石北CangzhuAtractylodes Lancea (Thunb.)Dc.30SE黃戎HuangqiHedysarum Multijugum Maxim.31SE黃戎HuangqiHedysarum Multijugum Maxim.32SY殤荷BoheMenthae Herba33SY寒村BoheMenthae Herba34SY專前子CheqinaziPlantaginis Semen35SY雙方DuhuoRadix Angelicae Biseratae36SY雙方PulnaPantaginis Semen37SY防風FangfengSaposhnkoviae Kadix38SY雙活PulnaPantaginis Semen39SY酸石PulnaPunctus34SY大茶PulnaPantaginis Semen35SY大花PulnaPantaginis Semen36SY雙活PulnaPantaginis Semen37SY勝石DuhuoRadix Angelicae Biseratae38SY大茶PulnaPantaginis Semen39SY大花PulnaPantaginis Semen40SY大茶BaleJinginhuRadix Angelicae Biseratae41SY大香PulnaPunctus42SY快行JinginhuLoncerata Japonicae Flos43SY金銀MataginiCortex Moutan44SY金銀MataginiCortex Moutan45SY大通MataginiPunctus <t< td=""><td>26</td><td>SE</td><td>鸎粟殻</td><td>Yingsuke</td><td>Papaveris Pericarpium</td></t<>	26	SE	鸎粟殻	Yingsuke	Papaveris Pericarpium
28SE枳實ZhishiArractylodes Lancea (Thumb.)Dc.29SE蒼丸Cang2uArractylodes Lancea (Thumb.)Dc.30SE浸丸HuangqiHedysarum Multiguum Maxim.31SE沙仁SharenMontum Arrattiacum H. T. Tsai Et S. W. Zhao32SY夢荷BoheMenthae Herba33SY柴胡CheqianziPlantaginis Semen34SY鄭前子CheqianziPlantaginis Semen35SY地骨皮DigupiLycil Cortex36SY獨活DuhuoRadt: Angelicae Biserate37SY樹石FangfengSaposhnikoviae Radtx38SY夜客PulngPoria Cocos (Schw.) Wolf.39SY横名FuperatiRubi Fructus40SY樹石GonquiziLyci Fructus41SY枸杞子GouquiziLyci Fructus42SY榆杞子JingineSchizonepetae Herba43SY金銀花JingineSchizonepetae Herba44SY生夢子MudanpiConcerae Japonicae Iso45SY検刀皮MudanpiConcerae Maxima46SY大河大通Muton47SY朱石QianhuangCaulis Akebiae48SY女河大通MutonCorrus Mutan49SY朱石QianhuangCorrus Mutan51SY東爾子NiubagziCructus Arctii52SY大通MadQi	27	SE	益智仁	Yizhi	Alpiniae Oxyphyliae Fructus
P2SE青朮CargzhuAractylodes Lancea (Thumb.)Dc.30SE黃芪HuangqiHedysarum Multilugum Maxim.31SE砂仁SharenAnomum Arartiacum H. T. Tsai Et S. W. Zhao32SY薄荷BoheMenthae Herba33SY煤材内向heMenthae Herba34SY摩前子CheqinaziPlantaginis Semen35SY地向皮DuhuoRadix Angelicae Biseratae36SY懶活DuhuoRadix Angelicae Biseratae37SY防風FugenziSaposhnikoviae Radix38SY使茶FugenziRubi Fructus39SY酸盘子FugenziRubi Fructus40SY甘遂GouqiziLycii Fructus41SY枸杞子GouqiziLycii Fructus42SY荊芥JingiheCancerae Japonicae Flos44SY差極MutongCortex Moutan45SY建超MutongCalis Akebiae46SY大通子NiubangziFructus Arctii47SY東超MutongCortex Moutan48SY大通NiubangziPructus Arctii50SY東超MutongCortex Moutan51SY東銀ShazhuyuCorrus Moutan52SY東超JanghuoNotopertayi Rhzoma Et Radix53SY東銀KushenAisma Orientale (Sam.) Juz.54SY東超JanghuoCorrus Mout	28	SE	枳實	Zhishi	Aurantii Fructus Immaturus
30SE英氏HaargqiHeadysarum Multigum Maxim.31SE砂仁SharenAmonum Aurantiacum H. T. Tsai Et S. W. Zhao32SY湾荷BoheMenthae Herba33SY柴胡ChalhuRadix Bupleuri34SY車前子CheqianziPlantaginis Semen35SY地骨皮DjupiLycit Cortex36SY地骨皮DuhuoRadix Angelicae Biseratae37SY砂石PlangfengSaposhnikoviae Radix38SYグ香FulingPorta Cocco (Schw.) Wolf.39SY電石GansuiKansui Radix41SY樹石GouqiziLycit Fructus42SY南芥JingileSchizonepetae Herba43SY金銀花JingileSchizonepetae Herba44SY古婆SaposCortex Moutan45SY連翹LianqiaoCortex Moutan46SY中男子NiubargaiCrutus47SY大道MudanpiCortex Moutan48SY中男子NiubargaiPructus50SY地資SharenCorres Moutan51SY山茱萸SharenPructus52SY地資SharenPructus53SY夏SharenSindihuang54SY東爾LianqiaoCortex Moutan55SY地資SharenSindihuang56SY地資SharenSind	29	SE	蒼朮	Cangzhu	Atractylodes Lancea (Thunb.)Dc.
11医防仁SharenAnomum Auranitacum H. T. Tsai Et S. W. Zhao32SY薄荷BoheMenthae Herba33SY柴胡ChaihuRadix Bupleuri34SY퇙前子CheqianziPlantaginis Semen35SY地骨皮DiguipiLycii Cortex36SY地合皮DuhuoRadix Angelicae Biseratae37SY防風PangfengSposhnikoviae Radix38SY夜茶FulingPoria Cocco (Schw.) Wolf.39SY酸盆子FupenziRubi Fructus41SY村紀子GoaqiziLycii Fructus42SY南ガJingileSchizoneptae Herba43SY金銀花JinyihuaLonicera Japonicae Flos44SY並翹MudapiCortex Moutan45SY地角MudapiCortex Moutan46SY地局QianhuPeucedani Radix47SY林通QianhuPeucedani Radix48SY共房ShadhuyaCortex Moutan51SY東倉ShadhuyaCortex Roti53SY東倉XanshenFigwort Rot54SY東倉ShadhuyaCortex Roti55SY東倉ShadhugaShadhuga56SY東倉ShadhugaAliana Orientale (Sam.) Juz.57SY東倉ZezieAliana Orientale (Sam.) Juz.56SY山崎子ZhinuAnemarhenae Rhizoma57	30	SE	黃芪	Huangqi	Hedysarum Multijugum Maxim.
32SY矮荷BoheMenthae Herba33SY埃荷ChaihuRadix Bupleuri34SY町前子CheqianzlPlantaginis Semen35SY地骨皮DigupiLycii Cortex36SY地骨及DigupiLycii Cortex37SY防風PangfengSaposhnikoviae Radix38SYK%FulingPoria Coces (Schw.) Wolf.39SY覆蓋子PupenziRubi Fructus40SY層基子GougiziLycii Fructus41SY枸杞子GougiziSchizonepta Herba42SY菊芥JinginhuaConcerte Japonicae Flos43SY金銀花JinginhuaSophorae Flavescentis Radix44SY地村子MudapiCortex Moutan45SY連翹MutongCaulis Ackbiae46SY地村安MutongCaulis Ackbiae47SY地石QianhuPucuedani Radix48SY与子QianhuNotopterytii Nizona Et Radix50SY地菜QianhuRomaniae Radix Praeparata51SY如子ZexieAmeanrine Radix Praeparata52SY如母ZexieAmeanrine Radix Praeparata53SYU母菜ZhinuAmeanrinea Rhizona54SYJuftCardia Achizona55SYJuftZexie56SYJuftChinu57JuftJuftCardia Fructus	31	SE	砂仁	Sharen	Amomum Aurantiacum H. T. Tsai Et S. W. Zhao
33SY柴胡ChahuRadix Bupleuri34SY車前子CheqianziPlantaginis Semen35SY地骨皮DigupiLycii Cotex36SY陽活DuhuoRadix Angelicae Biseratae37SY防風FagfengSaposhnikoviae Radix38SY夜等FulingPoria Cocos (Schw.) Wolf.39SY酸盘子FupenziRaubi Fructus40SY甘遂GansuiKansui Radix41SY樹杞子GouqiziLycii Fructus42SY葡ガJingileSchizoneptae Herba43SY金銀花JingileSophorae Flavescentis Radix44SY音夢KushenSophorae Flavescentis Radix45SY連組LianqiaoCortex Moutan46SY地月皮MutongCortex Moutan47SY梅見QianhuPeucedani Radix48SY牛蒡子NibangziFructus Arctii49SY山茱萸ShazhuyuCornes Officialis Sieb. Et Zucc.51SY山茱萸ShudhuangRehmaniae Radix Praeparta53SY太多XashuAnemarthenae Rhizoma54SY山田子ZiziaGardeniae Fructus55SY山田子ZiziaGardeniae Fructus56SY山田子ZiziaGardeniae Fructus57SY山田子ZiziaGardeniae Fructus58SY山田子ZiziaGardeniae Fructus<	32	SY	薄荷	Bohe	Menthae Herba
34SY車前子CheqianziPlantaginis Semen35SY地骨皮DigupiLycii Cortex36SY獨活DuhuoRaitx Angelicae Biseratae37SY房面PenagfengSaposhnikoviae Radix38SY夜笨FulingPoria Coccos (Schw.) Wolf.39SY覆盆子PupenziRubi Fructus40SY覆盆子GouqiziLycii Fructus41SY枸杞子GouqiziLycii Fructus42SY南芥JingiheSchizonepetae Herba43SY查銀花NushenSophorae Flavescentis Radix44SY苦麥KushenSophorae Flavescentis Radix45SY黄檀MudapiCortex Moutan46SY校乃使MudapiCortex Moutan47SY木通MutongCulis Akebiae48SY大通QianhuPucedani Radix50SY大活QianghuoNotopterysii Rhizoma Et Radix51SY女参XuanshenFigwort Root52SY女参XuanshenFigwort Root53SY女参XuanshenFigwort Root54SY黄稲HuangboPolyporus Unbellatus (Pers)Fr.55SY黄稲HuangboPolyporus Unbellatus (Pers)Fr.56SY黃稲MunapoCoptidis Rhizoma57SY黃稲HuangboPolyporus Unbellatus (Pers)Fr.58SY黃稲Huangbo	33	SY	柴胡	Chaihu	Radix Bupleuri
35SY地骨皮DigupiLycii Cortex36SY獨活DuhuoRadix Angelicae Biseratae37SY防風ParaferagSophnikoviae Radix38SY茯苓FulingPoria Cocos (Schw.) Wolf.39SY覆盆子FupenziRubi Fructus40SY甘遂GansuiKansui Radix41SY枸杞子GouqiziLycii Fructus42SY南芥JingileSchizonepetae Herba43SY金銀花JinginhuaLonicerae Japonicae Flos44SY董蔘KushenSophorae Flavescentis Radix45SY使用MudapiCortex Moutan46SY牧乃皮MudapiCortex Moutan47SY南胡QianhuPuecedani Radix48SY前胡QianhuPuecedani Radix50SY熊子ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY敷褐SudihuangRehmanniae Radix Praeparata53SY東湾ZexieAlisma Orientale (Sam.) Juz.54SY如母ZhiniuAnemarrhenae Rhizoma55SY如母JulingPolyoprus Umbellatus (Pers)Fr.58SY黃稲JulingPolyoprus Umbellatus (Pers)Fr.59SY黃稲JulingOinhandie Rhizoma60SY黃稲JulingOinhandie Rhizoma54SY黃稲JulingOinhangie Rhizoma55SY如母<	34	SY	車前子	Cheqianzi	Plantaginis Semen
36SY獨活DuhoRadx Angelicae Biseratae37SY防風FangfengSaposhnikoviae Radix38SY茯苓FulningPoria Cocos (Schw.) Wolf.39SY覆盆子FuperaiRubi Fructus40SY間送GansuiKansui Radix41SY枸杞子GouqiziLycii Fructus42SY荊芥JingieSchizonepetae Herba43SY金銀花JinginhuaLonicerae Japonicae Flos44SY音夢KushenSophorae Flavescentis Radix45SY娘田MudanpiCortex Moutan46SY牧丹皮MudanpiCaulis Akebiae47SY村通QianhuPeucedani Radix48SY竹胡QianhuPeucedani Radix50SY城通ShazhuyuCortus Arctii51SY城通ShazhuyuCortus Officinalis Sleb, ET Zucc.52SY敷地黃ShudhuangRehmaniae Radix Praeparata53SY女参XuanshenFigwort Root54SY如母ZoiniAlemarchane Rhizoma55SY知母ZhinuAnemarchane Rhizoma56SYJuRZhuingPolporus Umbellatu (Pers)Fr.58SY黃石HuangboPolporus Umbellatu (Pers)Fr.58SY黃石HuangboGirdine Fructus59SYJuRZhuinuCoptidis Rhizoma60SY黃石Huangbo	35	SY	地骨皮	Digupi	Lycii Cortex
37SY防風FangfengSaposhnikoviae Radix38SY茯苓FulingPoria Cocos (Schw.) Wolf.39SY覆盆子FupenziRubi Fructus40SY甘遂GansuiKansui Radix41SY枸杞子GoujziLycii Fructus42SY荊芥JingileSchizonepetae Herba43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY苦香KushenSophorae Flavescentis Radix45SY邊懇MudanpiCortex Moutan46SY牧丹皮MudanpiCortex Moutan47SY牛蒡子NiubangziFurctus Arctii48SY牛蒡子QianhuPeucedani Radix50SY越差ShanzhuyuCortus Moutan51SY山塔更ShanzhuyuCortus Moutan52SY敷油黃ShudihuangRehmanniae Radix Praeparata53SY虹房ZuaneJingi54SY東富ZexieAlisma Orientale (Sam.) Juz.55SY如母ZhinuAnemarhenae Rhizoma56SYJafAHuangbianCoptidis Ribei, Fr.58SY黃香RhuangbianCoptidis Ribei, Sr.59SYJafAHuangboPhellodendri Chinrusis Cortex59SYJafAHuangbianCoptidis Rhizoma60SYJafARuisangGils Rizoma61SYJafARuisangGilbanu	36	SY	獨活	Duhuo	Radix Angelicae Biseratae
38SY茯苓FulngPoria Cocos (Schw.) Wolf.39SY覆盆子FupenziRubi Fructus40SY間遂GansuiKansui Radix41SY枸杞子GouqiziLycii Fructus42SY荊芥JingipeSohizonepetae Herba43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY萱蓼KushenSophorae Flavescentis Radix45SY連翹LianqiaoCortex Moutan46SY牧丹皮MudanpiCatlis Akebiae47SY木通MutongCatlis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY魚酸ShudhuangRehmanniae Radix Praeparta53SY素SudinuangRehmanniae Radix Praeparta54SY如母ZexieAlism Orientale (Sam.) Juz.55SY如母ZhimuGardeniae Fructus57SY操MaLullingPolyorus Umbellatus (Pers)Fr.58SY其相HuangboMyrha60SYJafeRuxiangOlisanun61SY乳香RuxiangOlisanu62TE白果BajzuiA. Dahurica (Fisch.) Benth. Et Hook64TEHāf-CBaizirenPiazirenPiaziredi Semen	37	SY	防風	Fangfeng	Saposhnikoviae Radix
39SY覆盆子FupenziRubi Fructus40SY甘遂GansuiKansui Radix41SY枸杞子GouqiziLycii Fructus42SY荊芥JingieSchizonepetae Herba43SY金銀花JinyinhuLonicerae Japonicae Flos44SY金銀花JinyinhuCortera Vaponicae Flos45SY塗銀MudanpiCortex Moutan46SY沙伊皮MudanpiCortex Moutan47SY大通MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianghuoNotoptergii Rhizoma Et Radix50SY黄海ShanzhuyuCornus Officinalis Sieb. Et Zucc.51SY其物ShudhunangRehmanniae Radix Praeparata53SY女参XuanshenFigwort Root54SY如母ZhinuAnemarhenae Rhizoma55SY如母ZhinuAnemarhenae Rhizoma56SY如母ZhinuAnemarhenae Rhizoma57SY類石HuangboPhellodendri Chinrusis Cortex58SY黃和HuangbianCoptidis Rhizoma60SY漢藥MagaMoyao61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaiguiAnbaircia (Fisch.) Benth. Et Hook64TEHaf-CBaizirenHaiguiae<	38	SY	茯笭	Fuling	Poria Cocos (Schw.) Wolf.
40SY甘遂GanuliKansui Radix41SY枸杞子GonqiziLycii Fructus42SY荊芥JingieSchzoneptae Herba43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY苦蔘KushanSophorae Flavescentis Radix45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCaulis Akebiae48SY牛蒡子NibangziFructus Arctii49SY前胡QianhuPucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY城東黄ShazhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黃ShazhuyuCornus Officinalis Sieb. Et Zucc.53SY太陽XuanshenFigwort Root54SY如母ZexieAlisma Orientale (Sam.) Juz.55SY如母JiniuAnemarthenae Rhizoma56SY如母ZhiziGardeniae Fructus57SY瀬香ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃稲HuangbinCortidis Rhizoma60SYJ藻MāRuxiang61SY梨香RuxiangOilbanun62TE白果BaiguoGinkgo Semen63TE白芷BaiziniA. Dahurica (Fisch.) Benth. Et Hook64TEHāBaizine <td>39</td> <td>SY</td> <td>覆盆子</td> <td>Fupenzi</td> <td>Rubi Fructus</td>	39	SY	覆盆子	Fupenzi	Rubi Fructus
41SY枸杞子GougiziLycii Fructus42SY荊芥JingipeSchizonepetae Herba43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY苦蔘KushenSophorae Flavescentis Radix45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MutongCatlis Akebiae47SY木通MutongCatlis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygi Rhizoma Et Radix51SY奥和黄ShanzhuyuCorrus Officinalis Sieb. Et Zucc.52SY東海XuanshenFigwort Root54SY基ShudihuangRehmanniae Radix Praeparata55SY知母ZhimuAnemarrhenae Rhizoma56SY如母JungAnemarrhenae Rhizoma57SY養布JuligPolyporus Umbellatus (Pers)Fr.58SY其佰HuangbianCoptidis Rhizoma59SYJuffaMugaiOtipianni60SY沒乘MoyaoMyrrha61SY乳香RuxiangOlibanun62TE白果BaizurenGinkgo Semen63TE白菜BaizurenPlatycladi Semen	40	SY	甘遂	Gansui	Kansui Radix
42SY荊芥JingieSchizonepetae Herba43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY苦蔘KushenSophorae Flavescentis Radix45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctti49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY火活ShanzhuyuCortus Officinalis Sieb. Et Zucc.52SY敷地黄ShudihuangRehmaniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY紫aJaniaZexieAlisma Orientale (Sam.) Juz.55SY如母JaniaJaniag56SYJafaJulingPolyporus Umbellatus (Pers)Fr.58SY黃相HuangbianCoptidis Rhizoma59SYJafaMoyaoMyrtha60SY沒藥MoyaoMyrtha61SYJafaRuxiangOlibanun62FE白果BaizuiA. Dahurica (Fisch.) Benth. Et Hook64FE柏子仁BaizirenPlatycladi Semen	41	SY	枸杞子	Gouqizi	Lycii Fructus
43SY金銀花JinyinhuaLonicerae Japonicae Flos44SY苦蔘KushenSophorae Flavescentis Radix45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY城華英ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黃ShudihuangRehmanniae Radix Praeparata53SYZs%XuanshenFigwort Root54SY如母ZhiiruAnemarthenae Rhizoma55SY如母ZhuingOalyporus Umbellatus (Pers)Fr.56SYJafaHuanglonPhellodendri Chinrusis Cortex57SY凝苓ZhulingOpyporus Umbellatus (Pers)Fr.58SYJafaHuanglanCoptidis Rhizoma60SYXamMoyaoMyrrha61SYNaRuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白星BaizirenPlatycidai Semen	42	SY	荊芥	Jingjie	Schizonepetae Herba
44SY苦夢KushenSophorae Flavescentis Radix45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCallis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygi Rhizoma Et Radix51SY山茱萸ShanzhuyuCorrus Officinalis Sieb. Et Zuce.52SY敷地黃ShudihuangRehmaniae Radix Praeparata53SY玄參XuanshenFigwort Root54SY如母ZhimuAnemarthenae Rhizoma55SY如母ZhinuGardeniae Fructus57SY養希ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃相HuangboPhellodendri Chinrusis Cortex59SYJ酒RuxiangMyrrha60SY溪藥MoyaoMyrrha61SY乳香RuxiangOilbanun62TE白尾BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TEHāfBaizirenPlatycladi Semen	43	SY	金銀花	Jinyinhua	Lonicerae Japonicae Flos
45SY連翹LianqiaoForsythiae Fructus46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY山茱萸ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熱地黃ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY如母ZexieAlisma Orientale (Sam.) Juz.55SY如母ZhiziGardeniae Fructus56SY山梔子ZhiziGardeniae Fructus57SY黄稻HuangboPolyporus Umbellatus (Pers)Fr.58SY其稻HuangboMellodendri Chinrusis Cortex59SY川黃連HuangboMyrtha61SY梨香RuxiangOlibanun62TE白尾BaizhiAnburica (Fisch.) Benth. Et Hook64TEHZBaizirenPalaycladi Semen	44	SY	苦蔘	Kushen	Sophorae Flavescentis Radix
46SY牧丹皮MudanpiCortex Moutan47SY木通MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygi Rhizoma Et Radix51SY山茱萸ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黃ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY如母ZhinuAnemarrhenae Rhizoma55SY如母ZhiziGardeniae Fructus56SY山梔子ZhiziGardeniae Fructus57SY黃福HuangboPhellodendri Chinrnsis Cortex58SY黃福MoyaoMyrtha60SY乳香RuxiangOlibanun61SY梨香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE柏千BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE柏千BaizhiA. Dahurica (Fisch.) Benth. Et Hook	45	SY	連翹	Lianqiao	Forsythiae Fructus
47SY木適MutongCaulis Akebiae48SY牛蒡子NiubangziFructus Arctii49SY前胡QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY山茱萸ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黃ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY烟母ZexieAlisma Orientale (Sam.) Juz.55SY如母ZhinuAnemarthenae Rhizoma56SY山梔子ZhinuGardeniae Fructus57SY橫橋HuangboPolyporus Umbellatus (Pers)Fr.58SY黃橋MutongCoptidis Rhizoma60SY淡藥MoyaoMyrtha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE柏花BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE柏子BaizirenPlatycladi Semen	46	SY	牧丹皮	Mudanpi	Cortex Moutan
48SY午旁子NiubangziFructus Arctii49SY前胡QianhuPeucedari Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY山茱萸ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黃ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY湖岡ZexieAlisma Orientale (Sam.) Juz.55SY如母ZhinuAnemarthenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SYガ名ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃梧HuangbianCoptidis Rhizoma60SY浅藥MoyaoMyrtha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TEHZBaizirenPlaycladi Semen64TE柏子BaizirenPlaycladi Semen	47	SY	木迪	Mutong	Caulis Akebiae
4951时的QianhuPeucedani Radix50SY羌活QianghuoNotopterygii Rhizoma Et Radix51SY山茱萸ShanzhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黄ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY澤瀉ZexieAlisma Orientale (Sam.) Juz.55SY知母ZhimuAnemarthenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SY猪苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃棺HuangboPhellodendri Chinrusis Cortex59SYJiāMoyaoMyrrha60SY溪RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TEHZBaizirenPlaycladi Semen64TE柏子仁BaizirenPlaycladi Semen	48	SY	午旁子 	Niubangzi	Fructus Arctii
5051元活QianghuoNotopterygii Rhizoma Et Radix51SY山茱萸ShazhuyuCornus Officinalis Sieb. Et Zucc.52SY熟地黄ShudihuangRehmanniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY澤瀉ZexieAlisma Orientale (Sam.) Juz.55SY知母ZhimuAnemarrhenae Rhizoma56SY如母ZhinuAnemarrhenae Rhizoma57SY猪苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃栢HuangboPhellodendri Chinrnsis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY乳香RuxiangOlibanun61SY乳香BaiguoGinkgo Semen62TE白尾BaigunoAnburica (Fisch.) Benth. Et Hook64TE柏子仁BaizirenPlatycladi Semen	49	SY	則的	Qiannu	Peucedani Radix
5151山来央SharzhuyuCorrus Officinalis Steb. Ef Zucc.52SY熟地黄ShudihuangRehmanniae Radix Praeparata53SY交参XuanshenFigwort Root54SY澤瀉ZexieAlisma Orientale (Sam.) Juz.55SY知母ZhinuAnemarrhenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SY矮AfterPolyporus Umbellatus (Pers)Fr.58SY黃相HuangboPhellodendri Chinrnsis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY淡藥MoyaoMyrrha61SY馬橋RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE柏千仁BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栖千仁BaizirenPlatycladi Semen	50	51	无 <u></u> 山茱萸	Qiangnuo	Notopterygii Knizoma Et Radix
52Sr熱地度ShudhuangRehmaniae Radix Praeparata53SY玄参XuanshenFigwort Root54SY澤瀉ZexieAlisma Orientale (Sam.) Juz.55SY知母ZhimuAnemarrhenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SY黃柏HuangboPolyporus Umbellatus (Pers)Fr.58SYJ插HuangboCoptidis Rhizoma59SYJiğiHuangbianCoptidis Rhizoma60SY沒藥MoyaoMyrrha61SY乳香RuxiangOilbanun62TE白果BaiguoGinkgo Semen63TE柏千仁BaizrenA. Dahurica (Fisch.) Benth. Et Hook	51	SY	山朱臾	Shanzhuyu	Cornus Officinalis Sieb. Et Zucc.
5.551法率》XuanshenFigwort Root54SY澤瀉ZexieAlisma Orientale (Sam.) Juz.55SY知母ZhinuAnemarrhenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SY猪苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃栢HuangboPhellodendri Chinrnsis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY溴藥MoyaoMyrtha61SY乳香RuxiangOilbanun62TE白果BaiguoGinkgo Semen63TE柏千仁BaizirenA. Dahurica (Fisch.) Benth. Et Hook	52	51	熱心東	Snuainuang	Kenmanniae Kadix Praeparata
5451澤湯ZexleAlisma Orientale (Sam.) Juz.55SY知母ZhimuAnemarrhenae Rhizoma56SY山梔子ZhiziGardeniae Fructus57SY豬苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃栢HuangboPhellodendri Chinrnsis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY没藥MoyaoMyrrha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栖子仁BaizirenPlaycladi Semen	53 F4	51	<u> </u>	Auansnen	rigwort Koot
5351741-4ZhunuAnemarthena e Ruizoma56SY山梔子ZhiziGardeniae Fructus57SY猪苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃棺HuangboPhellodendri Chinrnisis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY沒藥MoyaoMyrrha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栢子仁BaizirenPlaycladi Semen	54 EE	51 CV	/ 辛 / 乌 	Zexie	Anomorphonos Discorre
5051山根子ZhiZiGardeniae Fractus57SY豬苓ZhulingPolyporus Umbellatus (Pers)Fr.58SY黃稻HuangboPhellodendri Chinrusis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY沒藥MoyaoMyrrha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栢子仁BaizirenPlaycladi Semen	55	SI	カウ	Zhiniu	Anemarmenae Rinzoma
57513134%ZhungFolyous Unbenatus (Fers)FL58SY黃栢HuangboPhellodendri Chinrasis Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY沒藥MoyaoMyrrha61SY児香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栢子仁BaizirenPlatycladi Semen	50	SI	山他丁 球茶	Zhuling	Baluparus Imballatus (Bars)Er
5051與由HuanglooPhenotential Channels Cortex59SY川黃連HuanglianCoptidis Rhizoma60SY沒藥MoyaoMyrrha61SY乳香RuxiangOlibanun62TE白果BaiguoGinkgo Semen63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栖子仁BaizirenPlatycladi Semen	58	SV	加下	Huangho	Dhellodendri Chinrasis Cortey
60 SY 没藥 Moyao Myrrha 61 SY 乳香 Ruxiang Olibanun 62 TE 白果 Baiguo Ginkgo Semen 63 TE 白芷 Baizhi A. Dahurica (Fisch.) Benth. Et Hook 64 TE 栢子仁 Baiziren Platycladi Semen	50	SV	奥10 川苦浦	Huandian	Contidis Rhizoma
61 SY 凡香 Ruxiang Olibanun 62 TE 白果 Baiguo Ginkgo Semen 63 TE 白芷 Baizhi A. Dahurica (Fisch.) Benth. Et Hook 64 TE 栢子仁 Baiziren Platycladi Semen	60	SV	治藥	Movao	Myrrha
62 TE 白果 Baiguo Ginkgo Semen 63 TE 白芷 Baizhi A. Dahurica (Fisch.) Benth. Et Hook 64 TE 栢子仁 Baiziren Platycladi Semen	61	SV	· / / / / / / / / / / / / / / / / / / /	Ruviang	Olibanun
63TE白芷BaizhiA. Dahurica (Fisch.) Benth. Et Hook64TE栢子仁BaizirenPlatycladi Semen	62	TE	九日 白里	Raiguo	Ginkao Semen
64 TE 相子仁 Baiziren Platycladi Semen	63	TE	白花	Baizhi	A Dahurica (Fisch) Benth Et Hook
	64	TE	山 <u>山</u> 石子仁	Baiziren	Platycladi Semen
65 TE 五昧子 Beiwuweizi Schisandrae Chinensis Eructus	65	TE	五味子	Beiwijweizi	Schisandrae Chinensis Fructus
66 TE – Tš – Dahuane – Badiu Rhoi Fr Rhizoma	66	TE	大黃	Dahuang	Radix Rhei Et Rhizome
67 TE YA Fining Shiradelae Herba	67	TE	浮萍	Funing	Spirodelae Herba
68 TE ŠĀA Gaoben Lieustici Rhizoma Et Radix	68	TE	藁本	Gaoben	Ligustici Rhizoma Et Radix

(continued on next page)

Table 1 (continued)

	Sasang type	Chinese name	Pronunciation	English name
69	TE	葛根	Gegen	Radix Puerariae
70	TE	芯蒂	Guadi	Calyx Cucumis
71	TE	黃芩	Huangqin	Scutellariae Radix
72	TE	桔梗	Jiegeng	Platycodon Grandiforus
73	TE	款冬花	Kuandonghua	Farfarae Flos
74	TE	蘿葍子	Laifuzi	Raphani Semen
75	TE	麻黃	Mahuang	Ephedra Herba
76	TE	牛黃	Niuhuang	Bovis Calculus
77	TE	蒲黄	Puhuang	Pollen Typhae
78	TE	桑白皮	Sangbaipi	Mori Cortex
79	TE	山藥	Shanyao	Rhizoma Dioscoreae
80	TE	升麻	Shengma	Cimicifugae Rhizoma
81	TE	石菖蒲	Shichangpu	Acoritataninowii Rhizoma
82	TE	使君子	Shijunzi	Quisqualis Indica
83	TE	酸枣仁	Suanzaoren	Ziziphi Spinosae Semen
84	TE	天門冬	Tiandong	Asparagi Radix
85	TE	烏梅	Wumei	Mume Fructus
86	TE	甘菊花	Yejuhua	Chrysanthemi Indici Flos
87	TE	薏苡仁	Yiyiren	Coicis Semen
88	TE	皂角	Zaojiaoci	Gleditsiae Spina
89	TY	蘆根	Lugen	Phragmitis Rhizoma
90	TY	太太	Mugau	Chaenomeles Sinensis (Thouin) Koehne
91	TY	松花	Songhuafen	Pine Pollen
92	TY	松節	Songjie	Lignum Pini Nodi

SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

1. Introduction

Sasang Constitutional Medicine (SCM) is a type of traditional Korean medicine, in which patients are classified into one of four Sasang constitution types (Sasang type): So-Eum (SE), So-Yang (SY), Tae-Eum (TE), and Tae-Yang (TY) [1]. The herbs are classified into four groups corresponding to the four Sasang types. For example, *Panax Ginseng* is used only for SE patients and *Ephedra herba* is used for TE patients. In addition, SCM is well-known for its personalized medicine characteristics, which means that despite the similar symptoms, the medications consisting of various medicinal herbs are prescribed differently depending on the patient's Sasang type.

Despite the importance of personalized medicine, however, it is only possible to assume the classification principle of SCM because the classification criteria for the herbs into four Sasang type groups or the meaning of each herb belonging to each Sasang type are largely unknown. Thus far, although various studies have been conducted to find the criteria and the meaning of herbal classification [2–4], most studies were conducted by applying the theoretical concepts of herbs used in conventional traditional medicine or by narratively reviewing the results for each Sasang type [3, 5]. Recently, chemical property-based various machine learning approaches have been applied to investigate natural products including herbal medicines [6, 7].

To gain a better understanding of the personalized medicine characteristics of SCM and its operation, we conducted a detailed investigation of the compound information that composes the Sasang type-specific personalized herbal medicines on both multivariate and univariate levels in this study. Using machine learning (ML) techniques and statistical analyses, compound patterns and specific compounds that enable Sasang type classification were found, and the chemical characteristics of the important compounds contributing to the classification were analyzed. The Sasang types of medicinal herbs, whose Sasang types were unidentified, were predicted based on compound information, and the prediction results were confirmed by a simple functional assay.

2. Methods

2.1. Identification of herbs

The list of herbs for each Sasang constitution type was obtained from 『Donguisusebowon Sinchukbon』(『東醫壽世保元 辛丑 本』; Longevity and Life Preservation of the Eastern Medicine), a book in which Jema Lee, the founder of SCM, presented the final result of his categorization of herbs by Sasang type. Previous studies [8, 9] that identified the medicinal herbs belonging to each Sasang type were also referenced. As a result, 144 herbs (47 for SE type, 37 for SY type, 44 for TE type, and 16 for TY type) were included in this study.

2.2. Construction of an herb-compound matrix dataset

Traditional Chinese Medicine Systems Pharmacology and Analysis Platform (TCMSP) (https://old.tcmsp-e.com/tcmsp.php), a database containing information on 499 herbs and 29,384 compounds, was used to extract compound information for each herb [10]. TCMSP was selected because the number of compounds included in the database has a greater advantage than other databases. When 144 herbs were analyzed using the database, 92 medicinal herbs (31 for the SE type, 30 for the SY type, 27 for the TE type, and 4 for the

TY type) were included, allowing further analysis (Table 1).

The compound information for each herb was extracted from the database and transformed into a simplified molecular-input lineentry system (SMILES) string [11]. A vector containing all compounds of 92 herbs was constructed using one-hot encoding (size of $1 \times$ 4745). As a result, a herb-compound matrix (size of 92×4745) was constructed and used in analyses in this study. All data preprocessing and analysis were performed using Pandas, a Python library for data manipulation and analysis, and Scikit-learn, a Python module that integrates a broad range of machine learning algorithms [12].

2.3. Machine learning (ML) experimental details

2.3.1. ML model selection

Five well-known supervised machine-learning algorithms for classification were applied in this study. The models compared are as follows: extremely randomized trees (ERT), extreme gradient boosting (XGBoost), linear and nonlinear support vector machine (SVM), and multinomial logistic regression (Mlogit).

The ERT classifier is a decision tree-based ensemble method that is similar to random forests but uses randomly selected cut-off values rather than the optimal one. The strength of the ERT classifier is that it is robust to noise and can thus lead to a further decrease in overall variance while performing largely equal to or better than other tree-based classifiers [13]. Furthermore, the ensemble method can rank the importance of features used in a classification problem [14]. The XGBoost is a kind of Machine Learning algorithm belonging to a decision-tree-based ensemble and enrolls an advanced framework of gradient boosting [15]. The SVM classifier searches for the optimal hyperplane that maximizes the margin between classes in high-dimensional space [16]. The SVM classifier can be used as linear or nonlinear classifiers according to the applied kernel. The radial basis function (Gaussian kernel) was applied for the nonlinear SVM classifier. The one-vs.-rest scheme was used to apply the SVM, a binary classifier, into a multi-class problem. The Mlogit classifier is used to predict a nominal dependent variable with more than two categories [17]. The strength of the Mlogit model is that it measures how relevant a predictor (coefficient size) is and the direction of association (positive or negative) of the predictor.

2.3.2. Feature selection

The optimal number of features was selected by calculating the performance (accuracy) of the model while increasing the number of features from 10 to 4700 in increments of 10. The features were included from the feature (compound) with the highest feature importance score. It was calculated by a double nested cross-validation. This procedure was repeated ten times to avoid inconsistent results caused by randomness. Sixty features showed the best performance. The sixty features (compounds) showing the highest feature importance scores were selected by a nested cross-validation performance. All the feature selection procedures were conducted in the nested training set of each fold to avoid data leakage.

2.3.3. Hyperparameter optimization

For hyperparameter optimization, a randomized search on hyperparameters with nested cross-validation to avoid data leakage was conducted. The hyperparameter configuration can be varied across the folds because the hyperparameters were tuned for each fold. Supplementary Table S1summarizes the searched hyperparameters and their range for each ML model.

2.4. Model performance assessment

2.4.1. K-fold cross-validation

Each model was trained with stratified k-fold cross-validation (k = 4), in which the dataset was divided randomly into k disjoint subsets of approximately equal size according to the Sasang type.

2.4.2. AUROC, precision, recall, f1 score, and accuracy

The AUC was used to evaluate how well the ML model distinguishes the Sasang types with the compounds configuration of each herb. The area under the receiving operating characteristic (AUROC) curve was calculated using the implementation in the Scikit-learn Python package. The precision, recall, f1 score, and accuracy (equations (1)-(4)) were used to evaluate the performance of the machine-learning model.

$$precision = \frac{tp}{tp + fp}$$
(1)
$$recall = \frac{tp}{tp + fn}$$
(2)
$$f1 \ score = \frac{2 * precision * recall}{precision + recall}$$
(3)
$$accuracy = \frac{tp + tn}{tp + tn + fp + fn}$$
(4)

4



Fig. 1. Basic characteristics of Sasang herb data (A) Box plot of the compounds data used in the analysis. The number of compounds for each Sasang type was analyzed using a box plot, and the average number of compounds for each type was calculated. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type; TY, Tae-Yang type. (B) Result of one-way ANOVA. The data were plotted as a function of the means and 95% confidence intervals. Tukey was conducted as a post-hoc analysis. (C) Venn diagram of the compounds belonging to each Sasang type.

S.-Y. Park et al.

In this equation, tp denotes the true positive; fp, false positive; tn, true negative; fn, false negative. Macro-average methods that treat all classes equally were used to calculate the average values in multi-class classification settings.

2.5. Cell-based analysis

2.5.1. Cell culture and reagents

AGS (derived from the stomach), HepG2 (derived from the liver) and NRK-52E (derived from the kidney) cells were obtained from American Type Culture Collection (ATCC, Rockville, MD). The cells were maintained in Dulbecco's modified Eagle's medium liquid (DMEM) with high glucose levels, 10% fetal bovine serum (FBS), 50 units/ml penicillin, and 50 µg/ml streptomycin at 37 °C in a humidified atmosphere containing 5% CO2. For all experiments, the cells were starved for 12 h in FBS-free media [18]. *Curcuma longa* Radix, *Houttuynia cordata* and *Leonurus japonicus* Houtt were extracted using the medicinal standard herbs, which are guaranteed by Korea FDA and produced by the pharmaceutical company (Daewon pharmacy, Korea) approved as the good manufacturing practice (GMP) system as previously described [19, 20].

2.5.2. MTT assay

The cells were plated at a density of 1×10^5 cells per well in 48-well culture plates and incubated in an FBS-free medium for 12 h. AGS and NRK-52E cell were incubated with drugs for 24 h [18]. HepG2 cells were incubated with drugs for 1 h, followed by a treatment with AA (10 μ M) for 12 h and then iron (5 μ M) for 6 h. The cell viability was defined as relative to the untreated control [i.e., viability (% of control) = 100 × (absorbance of the treated sample)/(absorbance of control)] as previously described [19,20].

2.6. Statistical analysis

Analysis of variance (ANOVA) test was used to assess the differences in the number of compounds belonging to the four Sasang types. Fisher's exact test was used to determine if there are non-random associations between each compound and each Sasang type, at a univariate level. Multiple comparison correction was not conducted because the purpose of Fisher's exact test was to suggest relevant compound candidates.

3. Results

3.1. Basic characteristics of the compounds comprising the SCM medicinal herbs

Ninety-two medicinal herbs were analyzed (31 for the SE type, 30 for the SY type, 27 for the TE type, and four for the TY type) in the current study (Table 1). Before examining whether it was possible to discriminate the Sasang type using the compound information composing each herb, we first described the basic characteristics of the compound information. The average numbers of compounds were 99.3, 95.2, 65.0, and 34.5 for SE, SY, TE, and TY types, respectively (Fig. 1A). We examined the difference between the number of compounds among the different Sasang type groups. Although the difference of compound number among the Sasang types was marginally significant (F-stat = 2.68, p-val = 0.052), it seems that the TY type is the primary factor, as the compound number of the other types appears comparable. (Fig. 1B). The overlap of compound lists belonging to each Sasang type was also examined using a Venn diagram (Fig. 1C).

3.2. Classification of each herb to a specific sasang type being explained by the multivariate level compound information

ML classifiers were trained for Sasang type and their performance of the classifiers was assessed to find out whether the Sasang type information can be explained by compound combination at the multivariate level, i.e., whether it is possible to discriminate the corresponding Sasang type using the compound information composing each herb. Four TY-type herbs were excluded because of their small sample size [21,22]. Four samples were too small for the model to learn the generalizable pattern. As a result, 88 herbs were used for subsequent analyses.

Table 2			
Overall classification	performance for	or each	model.

	Precision	Recall	F1 score	Accuracy
Model				
ERT	0.505 ± 0.125	0.522 ± 0.139	0.498 ± 0.129	0.511 ± 0.121
XGBoost	0.394 ± 0.064	0.436 ± 0.078	0.374 ± 0.077	0.397 ± 0.067
SVM (RBF)	0.475 ± 0.066	0.482 ± 0.062	0.467 ± 0.070	0.489 ± 0.067
SVM(Linear)	0.441 ± 0.087	0.514 ± 0.109	0.420 ± 0.092	0.455 ± 0.085
Mlogit	0.464 ± 0.061	0.446 ± 0.061	0.422 ± 0.049	0.466 ± 0.067

Mean \pm SD. ERT, extremely randomized trees; XGBoost, extreme gradient boosting; SVM, support vector machine; Mlogit, multinomial logistic regression.

Five well-known classification ML models were applied for this study. The ML models compared in this study were as follows: ERT, XGBoost, linear and nonlinear (RBF) SVM, and Mlogit (see Materials and Methods for more details). Since the ERT model outperformed the other models (Table 2), the ERT classifier was selected. The macro-averaged accuracy and f1 score of the ERT classifier were 0.511 \pm 0.121 and 0.498 \pm 0.129, respectively (mean \pm SD).

The ERT classifier was investigated more thoroughly for a detailed analysis of the classifier performance. The macro-average AUROC of the classifier was 0.73 (Fig. 2). The classification performance of the ERT model for the individual Sasang type was as follows: the average precision, recall, and f1 score for the SE type were 0.612, 0.671, and 0.621, respectively; 0.464, 0.451, and 0.434, respectively, for the SY type; 0.440, 0.443, and 0.439, respectively, for TE type (Table 3, Supplementary Figure S1). The result showed statistically significant classification performance for the SE and SY type, suggesting that the configuration of the compound composing each herb has information to discriminate the Sasang type of each herb. In other words, the classification of each herb to a specific type can be explained by the compound configuration of the herbs.

3.3. Most compounds showing selectivity for particular sasang type

To avoid curse of dimensionality, feature selection was conducted. The optimal number of features was chosen by the double nested cross-validation performance (see the Methods 2.3.2). Sixty turned out to be the optimal number and the sixty features (compounds) that have the highest feature importance scores were selected by the nested cross-validation performance. The sixty features (compounds) were analyzed to understand which compounds are processed in a distributed manner and which are processed in a labeled-line manner for the purpose of classifying the Sasang type information. The sixty compounds were clustered based on the cosine similarity between each vector of the sixty compounds (size of 88×1) and representative Sasang type vector for each type (size of 88×1), representing the distribution of each compound and each Sasang type within 88 herbs, respectively. To define the clusters, the dendrogram was cut at the second level, resulting in three clusters and one compound (Fig. 3). We found that the three clusters corresponded to TE-prominent (n = 8), SY-prominent (n = 9), and SE-prominent compound groups (n = 42), which suggests that the majority of compounds have selectivity for particular Sasang type.

3.4. Chemical characteristics of the sasasng type-prominent compounds

To identify the chemical characteristics of the Sasang type-prominent compounds, firstly, the chemical taxonomy of each cluster, i. e., the structural classification of chemical entities using ClassyFire [23], was identified (Supplementary Tables S2, S3, and S4). Many of the TE-prominent compounds showed a class of fatty acyls (7/8). Unlike TE-prominent compounds, SY-prominent compounds showed heterogeneous composition with various classes: prenol lipids (2/9), fatty acyls (2/9), coumarins and derivatives (2/9), carboxyl acids and derivatives (1/9), cinnamic acids and derivatives (1/9), and organooxygen compounds (1/9). The SE-prominent compounds were identified as prenol lipids (21/42), flavonoids (9/42), and benzene and substituted derivatives (4/42).

Furthermore, a review of the biosynthetic characteristics of the major secondary metabolites in sixty compounds that are crucial in the Sasang type classification could suggest an interesting point of view [24]. As shown in Supplementary Table S2, the majority of the components in the medicinal herbs classified as TE type were fatty acid-based substances synthesized via a polyketide biosynthetic pathway that requires various polyketide synthases. In the case of compounds from the medicinal herbs for the SY type, the shikimate, mevalonate, and polyketide pathways were involved in biosynthesizing these metabolites. As in the case of SY type, the compound list for the SE type showed that various biosynthetic pathways were involved for these compounds, but terpenoids appeared most commonly, basically biosynthesized through the mevalonic (isoprenoid) pathway [25].



Fig. 2. Classification performance of the Sasang type decoder. Receiver operating characteristic (ROC) curve of 88 herbs with 60 compound features. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

Table 3

Classification performance of the extremely randomized trees classifier for individual Sasang type.

	Precision	Recall	F1 score	Accuracy
SE	0.612 ± 0.155	0.671 ± 0.132	0.621 ± 0.076	0.511 ± 0.121
SY	0.464 ± 0.271	0.451 ± 0.127	0.434 ± 0.189	
TE	0.440 ± 0.132	0.443 ± 0.185	0.439 ± 0.159	
Average	0.505	0.522	0.498	0.511

Mean \pm SD. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.



Fig. 3. Clustered heatmap of the 60 compounds showing SC-prominent compounds. Each row represents each compound, and the column represents each SC type. The color represents the similarity (cosine similarity) between the distribution of each compound and that of each SC type. The data was clustered with respect to rows. The compounds were clustered into three groups at the second level dendrogram, resulting in TE-prominent, SY-prominent, and SE-prominent compounds, respectively. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

3.5. Identification of sasasng type-specific compounds from a univariate level analysis

A univariate level statistical test (Fisher's exact test) was conducted on the sixty compounds showing a high feature importance score to find the compounds that are more relevant to the Sasang type, i.e., the Sasang type-specific compounds. Fourteen Sasang type-specific compounds were found accordingly, and the relative ratio of each compound for each Sasang type was analyzed (Fig. 4). Among them, ten, three, and one compound are relevant to the SE, SY, and TE types, respectively. Guaiene, -cis-.beta.-Elemene diastereomer, naringin, 3691-11-0, *o*-cymol, cadalin, cadinene, alpha-terpineol, germacrene, l-limonen are found to be SE-specific



Fig. 4. SC type-specific compounds. Fourteen compounds showed significant relevance with the SC type (according to Fisher's exact test). The bar graph represents the relative frequency of each compound, indicating which SC type compound shows relevance. The relative frequency is # herbs including the compound for each SC type (A) SE-specific compounds. (B) SY-specific compounds. (C) TE-specific compound. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

compounds (Fig. 4A); FER, marmesin, decyl acetate to be SY-specific compounds (Fig. 4B); and arachidonic acid to be TE-specific compounds (Fig. 4C).

3.6. Sasang type prediction of unidentified medicinal herbs based on compound level information, and their investigations by functional assay

The trained ML classifier was applied to predict the Sasang type of medicinal herbs whose Sasang types are unidentified as a further application. Thirty medicinal herbs were selected according to the amount of the usage [26].

The trained ML classifier successfully predicted the Sasang type of the thirty herbs with the probability of which Sasang type each herb belongs. The prediction procedure was repeated 10 times for each herb, and the mean probability was presented to provide stability (Fig. 5 and Table 4). As a result, seven kinds of herbs (from number 1 to number 7), including *Curcuma longa* Radix and *Eriobotrya japonica* Lindley corresponded to SE type (Fig. 5A), and thirteen herbs (from number 8 to number 20), such as *Houttuynia cordata, Cistanche deserticola,* and *Lindera strychnifolia* Vill. are related to the SY type (Fig. 5B). Ten herbs (from number 21 to number 30) containing *Leonurus japonicus* Houtt. and *Benincasa hispida* Cogniaux were categorized as the TE type (Fig. 5C).

Additionally, we wanted to know whether the predicted herbs with the highest rank in each type have a biological function in each organ corresponding to the Sasang type. According to SCM theory, each Sasang type is highly related to specific organs (i.e. SE, kidney; SY, stomach; TE, liver) [1, 2, 3]; Thus, we tested the anti-cancer effects of *Curcuma longa* Radix (SE) in the NRK-52E kidney cancer cell line and *Houttuynia cordata* (SY) in the AGS stomach cancer cell line as well as anti-oxidant effects of *Leonurus japonicus* Houtt (TE) in the HepG2 hepatocyte (Fig. 6A–C). The water extract of *Curcuma longa* Radix (the first ranking herb in SE) and *Houttuynia cordata* (the first ranking herb in SY) significantly inhibited the proliferation of cancer derived from kidney and stomach, respectively. *Leonurus japonicus* Houtt (the first ranking herb in TE) markedly inhibited the oxidative damage induced by AA + iron.

Heliyon 9 (2023) e13692



Fig. 5. Predicted result of top 30 unidentified medicinal herbs using trained ERT model. The Sasang type of the 30 medicinal herbs was predicted using the trained ERT model. The bar represents the mean probability (ten trials repeated) of which constitution each medicinal herb belongs. The predicted Sasang type of each herb is visualized using background colors, and the herbs are clustered based on their predicted Sasang type. In each herbal group, the herbs were sorted according to their probability. The numbers indicate the name of herbs in Table 4 (A) Compounds 1–7 predicted as SE type. (B) Compounds 8–15 predicted as SY type. (C) Compounds 16–30 predicted as TE type. SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

Table	Δ	
IaDIC	4	

Prediction probability for the top 30 unidentified medicinal herbs to belong to which constitution.

	Chinese name	English name	SE	SY	TE
1	鬱金	Curcuma longa Radix	0.766	0.125	0.110
2	枇杷葉	Eriobotrya japonica Lindley	0.519	0.231	0.250
3	防己	Sinomenium acutum Rehder et Wilson	0.459	0.298	0.243
4	丹蔘	Salvia miltiorrhiza Bunge	0.427	0.202	0.371
5	艾葉	Artemisia princeps Pampanini	0.426	0.239	0.335
6	丁香	Syzygium aromaticum Merrill et Perry	0.414	0.296	0.290
7	龍膽草	Gentiana scabra Bunge	0.354	0.304	0.342
8	魚腥草	Houttuynia cordata	0.129	0.665	0.206
9	肉蓯蓉	Cistanche deserticola	0.137	0.610	0.253
10	烏藥	Lindera strychnifolia Vill.	0.243	0.580	0.177
11	淫羊藿	Epimedium koreanum Nakai	0.282	0.569	0.149
12	肉荳蔲	Myristica fragrans	0.170	0.563	0.266
13	北沙參	Glehnia littoralis Fr. Schmidt ex Miquel	0.258	0.540	0.202
14	細辛	Asarum sieboldii Miq.	0.268	0.532	0.199
15	辛夷	Magnolia denudata Desrousseaux	0.268	0.532	0.199
16	檳榔子	Areca catechu Linné	0.205	0.530	0.265
17	百合	Lilium lancifolium Thunberg	0.201	0.475	0.324
18	小茴香	Foeniculum vulgare	0.275	0.451	0.274
19	蛇床子	Torilis japonica	0.330	0.388	0.282
20	紫蘇葉	Perillae Folium	0.336	0.379	0.285
21	益母草	Leonurus japonicus Houtt	0.101	0.220	0.679
22	冬瓜子	Benincasa hispida Cogniaux	0.153	0.210	0.637
23	決明子	Cassia tora Linné	0.301	0.143	0.556
24	杜仲	Eucommia ulmoides Oliver	0.294	0.162	0.543
25	白蒺藜	Tribulus terrestris	0.183	0.386	0.430
26	釣鉤藤	Uncariae Ramulus cum Uncus	0.352	0.239	0.409
27	麥芽	Hordeum vulgare Linné	0.257	0.337	0.405
28	川貝母	Fritillariae Cirrhosae Bulbus	0.293	0.310	0.397
29	牛膝	Twotoothed Achyranthes	0.366	0.266	0.368
30	威靈仙	Chinese Clematis	0.343	0.291	0.366

SE, So-Eum type; SY, So-Yang type; TE, Tae-Eum type.

4. Discussion

SCM is a unique form of personalized medicine in traditional Korean medicine, in which the patients are classified into one of four Sasang constitution types: SE, SY, TE, or TY. In SCM, herbal medicines (composed of various medicinal herbs) are prescribed based on the patients' Sasang type, in addition to their symptoms, and the applied medicinal herbs were divided into four groups corresponding to the four Sasang types; the herbs themselves are inextricably linked to the concept of Sasang type. Furthermore, a study of the herbs could provide more objective insight than investigating the Sasang type-diagnosed patients by SCM experts to understand the intrinsic principle of SCM, in that the agreement rate for diagnosed Sasang type among three qualified SCM experts is between 52.5% and 68.4% [2,27]. Using a novel drug-centric approach, this study examined the compound patterns that enable Sasang type classification and the chemical characteristics of each herbal group that contributes to the medicinal effect of SCM via ML techniques.

A previous study examined the major botanical compounds, such as phenol, alkaloid, and terpenoid, contained in each herb from a biomedical point of view. Lim et al. reported that phenolics were dominant in the TY-type herbs, iridoids and triterpenes were in the SY-type herbs, saponins were in the TE-type herbs, and monoterpene and sesquiterpenes were in SE type herbs [3]. On the other hand, because this research was still limited as a review on the characteristics of each herb, more systematic and data-driven group-level characteristics of each constitutional herbal group consisting of corresponding medicinal herbs have not been identified.

This study aimed to identify the principle/criteria for classifying medicinal herbs into the Sasang types using a data-driven approach. The current study examined whether the principle of distribution is explainable at the multi-compound-level by multi-variate analyses, such as ML [28]. The Sasang type classification could be explained by multi-compound configuration, being confirmed by statistical significance in the classification performance of the ML classifier on the SE and SY type herbs. Various patterns made by multiple compounds would help classify different type groups at the multivariate level. Although the classification performance for the TE type was statistically insignificant (p value = 0.25), the herbs were only investigated at the compound level in this study. Other factors, in addition to the compound factor, would help account for the Sasang type classification principles. It is important how much the Sasang type classification can be explained by other characteristics, such as traditional theory-based taste and action information, in addition to the compound information in further analyses.

This study investigated which compounds play important roles in type discrimination to interpret the multi-compound patterns derived from ML analysis. The 60 compounds deducted by the ML pattern analysis were examined using hierarchical clustering, and 14 Sasang type-specific compounds were found by statistical analysis. On the other hand, because this result reflects only univariate-level investigation, much more remains to be investigated for multivariate-level interpretation.

The characteristics of these compounds were analyzed using chemical information. The secondary metabolites in the plants were biosynthesized by the action of various enzymes and generally constituted the active ingredients of medicinal plants [29,30]. It was



Fig. 6. Cell viability in three types of cells. The cells were plated at a density of 1×10^5 cells per well in 48-well culture plates and incubated in an FBS-free medium for 12 h. (A and B) AGS and NRK-52E cells were incubated with drugs for 24 h. (C) HepG2 cells were incubated with drugs for 1 h, followed by a treatment with AA (10 μ M) for 12 h and then iron (5 μ M) for 6 h. All data represent means \pm SD of 4 independent experiments (* $\rho < 0.05$ and ** $\rho < 0.01$ vs. control group; ## $\rho < 0.01$ vs. AA + iron-treated group). AA, arachidonic acid; con, vehicle-treated control.

also reported that the building blocks that make up the drug target of the bodies and a line of enzymes normally involved in the biosynthesis of secondary metabolites [31,32]. Although it is difficult to assume that the compounds listed in Fig. 4 have the representative activity of each herbal medicine and there is little scientific evidence to directly connect the biosynthetic pathway of some of the representative compounds to SCM, the potential and novelty of these attempts themselves cannot be ignored. In the TE type, fatty acid-based materials are normally synthesized through the polyketide biosynthetic pathway. On the other hand, the shikimate, mevalonate, and polyketide pathways were involved in the SY constitution. In the case of SE, one of the most abundant components, terpenoids, was related to the mevalonic (isoprenoid) pathway. Although this analysis alone is not enough to explain the characteristics of herbal medicines in the SCM, at least there are some differences for each Sasang type in terms of the biosynthetic pathway.

This study has some limitations. Owing to the small sample size, medicinal herbs of the TY type were excluded from the analyses. The TY type frequently has a small sample size in other studies regarding Sasang type diagnosis because of the rarity of the TY type in the population distribution in SCM. The majority of studies excluded the TY type from their analyses. The same situation occurred in this study although we adopted a drug-centric approach. In addition, in this study, the herb-compound matrix was constructed using one-hot encoding, not considering the chemical similarity between compounds. It would be better to consider vector embedding in future research. In addition, in this study, we provided information about the predictive type of the medicinal herbs using a trained ML classifier. However, readers should note that this prediction is only a result of nonlinear pattern computation based on compound information, not based on the whole information comprising the Sasang type, implying that this predictive information was not recommended for direct clinical application. If there exists a discrepancy between the prediction result and the clinical application, this indicates that additional information is needed to the dataset. Refining the model remains to conduct additional research in the future.

5. Conclusions

Here, we comprehensively investigated the compounds composing the Sasang type-specific personalized herbal medicines. We confirmed that most of the 60 compounds showing high feature importance determined by the ERT classifier have selectivity for particular Sasang type. We found that most compounds showed selectivity for particular Sasang type. We also investigated taxonomic

and biosynthetic characteristics of the 59 Sasang-prominent compounds (8, 9, and 42 compounds for TE, SY, and SE, respectively). Furthermore, we identified 14 Sasang type-specific compounds showing statistically significance with the Sasang type at a univariate level. Lastly, using a trained ERT classifier, we predicted the Sasang type of commonly used but unidentified medicinal herbs, and indirectly confirmed the prediction result with a simple *in vitro* experiment examining the biological function of herbs.

Declarations

Author contribution statement

Ji-Hwan Kim: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data. Chang-Eop Kim: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper; Analyzed and interpreted the data.Sa-Yoon Park, Young Woo Kim: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Yu Rim Song, Young Pyo Jang, Young Pyo Jang: Performed the experiments.

Funding statement

Prof. Ji-Hwan Kim was supported by National Research Foundation of Korea [NRF-2017R1C1B5017048 and NRF-2022R111A2066653]. Prof. Chang-Eop Kim was supported by National Research Foundation of Korea [2020M3A9E4103843]; Ministry of Health and Welfare [HF20C0087].

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

Supplementary content related to this article has been published online at [URL].

Acknowledgement

Kim YW would like to thank to the Ph.D.'s program of Kyungpook National University for completing the thesis through this work.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.heliyon.2023.e13692.

References

- [1] J.Y. Kim, D.D. Pham, Sasang constitutional medicine as a holistic tailored medicine, Evid. base Compl. Alternative Med. 6 (S1) (2009) 11–19.
- [2] S.Y. Park, M. Park, W.Y. Lee, C.Y. Lee, J.H. Kim, S. Lee, C.E. Kim, Machine learning-based prediction of Sasang constitution types using comprehensive clinical information and identification of key features for diagnosis, Integr. Med. Res. 10 (3) (2021), 100668.
- [3] S.H. Lim, E.S. Jeon, J. Lee, S.Y. Han, H. Chae, Pharmacognostic outlooks on medical herbs of Sasang typology, Integr. Med. Res. 6 (3) (2017 Sep) 231–239, https://doi.org/10.1016/j.imr.2017.06.005.
- [4] E.J. Kim, Y.S. Hong, S.H. Seo, S.E. Park, C.S. Na, H.S. Son, Metabolite markers for characterizing Sasang constitution type through GC-MS and 1H NMR-based metabolomics study, Evid. base Compl. Alternative Med. 2019 (2019).
- [5] W.Y. Lee, C.Y. Lee, C.E. Kim, J.H. Kim, Investigating the biomarkers of the sasang constitution via network pharmacology approach, J. Evidence-Based Complementary Altern. Med. 2021 (2021), 6665130.
- [6] H.W. Kim, M. Wang, C.A. Leber, L.F. Nothias, R. Reher, K.B. Kang, G.W. Cottrell, NPClassifier: a deep neural network-based structural classification tool for natural products, J. Nat. Prod. 84 (11) (2021) 2795–2807.
- [7] R. Zhang, X. Li, X. Zhang, H. Qin, W. Xiao, Machine learning approaches for elucidating the biological effects of natural products, Nat. Prod. Rep. 38 (2) (2021) 346–361.
- [8] J.H. Kim, The study on the selection of sasang constitution-specific herbs in ^Fdongyisusebowon sinchuk-bon_a from TCMID and TCMSP, Journal of Sasang Constitutional Medicine 31 (3) (2019) 19–33.
- [9] K.Y. Kim, J.Y. Kim, A research on the classification of herbal medicines based on the Sasang constitution (Taeumin and Taeyangin Part), Journal of Sasang Constitutional Medicine 14 (1) (2002) 1–9.
- [10] J. Zhao, F. Lin, G. Liang, Y. Han, N. Xu, J. Pan, M. Luo, W. Yang, L. Zeng, Exploration of the molecular mechanism of polygonati rhizoma in the treatment of osteoporosis based on network Pharmacology and molecular docking, Front. Endocrinol. 12 (2022 Jan 5), 815891.

- [11] H. El-Behery, A.F. Attia, N. El-Feshawy, H. Torkey, Efficient machine learning model for predicting drug-target interactions with case study for Covid-19, Comput. Biol. Chem. 93 (2021), 107536.
- [12] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, et al., Scikit-learn: machine learning in Python, J. Mach. Learn. Res. 12 (2011) 2825–2830.
- [13] P. Geurts, D. Ernst, LJMl Wehenkel, Extremely randomized trees 63 (1) (2006) 3-42.
- [14] Robust feature selection using ensemble feature selection techniques, in: Y. Saeys, T. Abeel, Y. Van de Peer (Eds.), Joint European Conference on Machine Learning and Knowledge Discovery in Databases, Springer, 2008.
- [15] X. Wang, X. You, L. Zhang, D. Huang, B. Aramini, L. Shabaturov, G. Jiang, J. Fan, A radiomics model combined with XGBoost may improve the accuracy of distinguishing between mediastinal cysts and tumors: a multicenter validation analysis, Ann. Transl. Med. 9 (23) (2021) 1737.
- [16] I. Steinwart, A. Christmann, Support Vector Machines, Springer Science & Business Media, 2008.
- [17] D.J. Bohning, S.M. Aotio, Multinomial logistic regression algorithm, Ann. inst. Stat. Math. 44 (1) (1992) 197–200.
- [18] U.J. Yun, S.J. Bae, Y.R. Song, Y.W. Kim, A critical YAP in malignancy of HCC is regulated by evodiamine, Int. J. Mol. Sci. 23 (3) (2022) 1855.
- [19] Y.R. Song, B. Jang, S.M. Lee, S.J. Bae, S.B. Bak, Y.W. Kim, *Angelica gigas* NAKAI and its active compound, decursin, inhibit cellular injury as an antioxidant by the regulation of AMP-activated protein kinase and YAP signaling, Molecules 27 (6) (2022) 1858.
- [20] E.H. Lee, S.Y. Baek, J.Y. Park, Y.W. Kim, Emodin in Rheum undulatum inhibits oxidative stress in the liver via AMPK with Hippo/Yap signalling pathway, Pharm. Biol. 58 (1) (2020 Dec) 333–341.
- [21] S.H. Park, M.G. Kim, S.J. Lee, J.Y. Kim, H. Chae, Temperament and character profiles of sasang typology in an adult clinical sample, J. Evidence-Based Complementary Altern. Med. 2011 (2011), 794795.
- [22] S.H. Lee, M. Hwang, S.H. Choi, H.J. Kim, E.J. Lee, C.Y. Kwon, S.Y. Chung, J.W. Kim, G.T. Chang, Analysis of the bio-psychological characteristics of Sasang typology in Korean preschool children using the ponderal index and the temperament and character inventory, J. Compl. Integr. Med. 18 (1) (2020) 175–183.
 [23] Y. Djoumbou Feunang, R. Eisner, C. Knox, L. Chepelev, J. Hastings, G. Owen, E. Fahy, C. Steinbeck, S. Subramanian, E. Bolton, R. Greiner, D.S. Wishart,
- ClassyFire: automated chemical classification with a comprehensive, computable taxonomy, J. Cheminf. 8 (2016) 61.
- [24] R. Jan, S. Asaf, M. Numan, Lubna, K.M. Kim, Plant secondary metabolite biosynthesis and transcriptional regulation in response to biotic and abiotic stress conditions, Agronomy 11 (2021) 968.
- [25] Y. Zhou, X. Lu, L. Chen, P. Zhang, J. Zhou, Q. Xiong, Y. Shen, W. Tian, Polysaccharides from Chrysanthemun indicum L. enhance the accumulation of polysaccharide and atractylenolide in Atractylodes macrocephala Koidz, Int. J. Biol. Macromol. 190 (2021 Nov 1) 649–659.
- [26] M. Park, C.Y. Lee, T.H. Lee, Y.S. Kim, C.E. Kim, Identifying theoretical characteristics of traditional medicines in Korea, China, and Japan through the herb usage data, Journal of Physiology & Pathology in Korean Medicine 32 (3) (2018) 149–156.
- [27] Y.H. Baek, H.S. Kim, S.W. Lee, E.S. Jang, The concordance and validity assessment of diagnosis for the expert in sasang constitution, Journal of Sasang constitutional medicine 26 (3) (2014) 295–303.
- [28] Y. Shi, L. Zhang, Z. Wang, X. Lu, T. Wang, D. Zhou, Z. Zhang, Multivariate machine learning analyses in identification of major depressive disorder using restingstate functional connectivity: a multicentral study, ACS Chem. Neurosci. 12 (15) (2021 Aug 4) 2878–2886.
- [29] T. Wu, S.M. Kerbler, A.R. Fernie, Y. Zhang, Plant cell cultures as heterologous bio-factories for secondary metabolite production, Plant Commun 2 (5) (2021), 100235.
- [30] R. Bisht, A. Bhattacharyya, A. Shrivastava, P. Saxena, An overview of the medicinally important plant type III PKS derived polyketides, Front. Plant Sci. 12 (2021), 746908.
- [31] U. Gani, R.A. Vishwakarma, P. Misra, Membrane transporters: the key drivers of transport of secondary metabolites in plants, Plant Cell Rep. 40 (1) (2021) 1–18.
- [32] E. Ancheeva, G. Daletos, P. Proksch, Bioactive secondary metabolites from endophytic fungi, Curr. Med. Chem. 27 (11) (2020) 1836–1854.