Advances in understanding of health-promoting benefits of medicine and food homology using analysis of gut microbiota and metabolomics

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REVIEW ARTICLE

Advances in understanding of health-promoting benefits of medicine and food homology using analysis of gut microbiota and metabolomics

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Abstract

The health-promoting benefits of medicine and food homology (MFH) are known for thousands of years in China. However, active compounds and biological mechanisms are unclear, greatly limiting clinical practice of MFH. The advent of gut microbiota analysis and metabolomics emerge as key tools to discover functional compounds, therapeutic targets, and mechanisms of benefits of MFH. Such studies hold great promise to promote and optimize functional efficacy and development of MFH-based products, for example, foods for daily dietary supplements or for special medical purposes. In this review, we summarized pharmacological effects of 109 species of MFH approved by the Health and Fitness Commission in 2015. Recent studies applying genome sequencing of gut microbiota and metabolomics to explain the activity of MFH in prevention and management of health consequences were extensively reviewed. We discussed the potentiality in future to decipher functional activities of MFH by applying metabolomics-based polypharmacokinetic strategy and multiomics technologies. The needs for personalized MFH recommendations and comprehensive databases have also been highlighted. This review emphasizes current achievements and challenges of the analysis of gut microbiota and metabolomics as a new avenue to understand MFH.

KEYWORDS
gut microbiota, medicine and food homology, metabolomics, multiomics technology

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Abbreviations: IBD, inflammatory bowel disease; LPS, lipopolysaccharide; MFH, medicine and food homology; SCFA, short-chain fatty acid; TCMIO, a comprehensive database of traditional Chinese medicine on immuno-oncology; WEGL, water extract of *Ganoderma lucidum mycelium*

1 | INTRODUCTION

Medicine and food homology (MFH) has been practiced for thousands of years in China. Historically, the concept of “medicine and food homology” was proposed in Huang Di Nei Jing Su Wen (475 BC–221 BC): “eating as food and administering to the patient as medication,” meaning that MFH can be scientifically and practically used as both food and medicine (Gong, Ji, Xu, Zhang, & Li, 2020; Hou & Jiang, 2013). Over the past decades, an increasing number of studies have demonstrated health-promoting effects of MFH for prevention and treatment of diseases, such as obesity, cardiovascular disease, diabetes, and several types of cancer (e.g., Cheng et al., 2019; Deng et al., 2012; Ge et al., 2018; Ren et al., 2019; Wang, Gao, et al., 2015). As of 2015, the Health and Fitness Commission has approved 109 MFH species, and Table 1 summarizes their pharmacological effects. Randomized controlled trails, animal experiments, and in vitro analysis have shown that MFH species exhibited antioxidant (Gupta, Bansal, Babu, & Maithil, 2013; Karimi et al., 2019; Yang, Yue, Runwei, & Guolin, 2010), antihyperglycemic (Camacho et al., 2015; Su, Bao, Xie, Xu, & Chen, 2020), antiaging (Wang, Huo, Liu, Yang, & Zeng, 2020), and anti-inflammatory activities (Choi, Woo, Ham, & Lee, 2017; Li, Zhang, Chen, et al., 2020; Li, Zhang, Liu, et al., 2020).

There is a vast number and wide concentration range of compounds present in MFH (Gao et al., 2019; Ji et al., 2020; Lan & Jia, 2010; Xie, Wang, et al., 2018). Advances in analytical technology have made possible characterization of hundreds of bioactive components in MFH and their nutritional value, health properties, and pharmacological effects. Among them, saponins, flavonoids, alkaloids, terpenoids, and polysaccharides are the most well-studied (see Cui, Wang, et al., 2018; Gong et al., 2019, 2020; Ji et al., 2020). Despite marked achievements in understanding MFHs, mechanisms responsible for their beneficial health effects are largely unknown. Most importantly, the traditional approach to understanding the pharmacology of a multicomponent MFH is to study the biochemical or genetic effects of a single component and gradually assemble the findings to reflect an entire picture of such a complex biosystem (Lan, Xie, & Jia, 2013). Due to the highly complex interactions associated with the targets of a diseased state, such an approach cannot accurately capture the complexity of MFH.

Recent advancements in genome sequencing technologies, for example, 16S rRNA sequencing and metagenomics, have contributed to the groundbreaking characterization of the gut microbiome and its function in host health and disease. Studies pertaining to traditional Chinese medicines, including most MFH species, have investigated the potential of gut microbiota in therapeutic effects, yielding rich information for understanding of MFH (Feng, Ao, Peng, & Yan, 2019; Yue et al., 2019). In addition, metabolomics is an emerging “omics” science that provides a comprehensive characterization of metabolites and metabolism in biological systems, which is a new frontier to uncover mechanisms of the beneficial effects of MFH (Abula et al., 2020; Kim & Kim, 2020). Of note, a metabolomics-based polypharmacokinetic strategy has been successfully applied to elucidate complex interactions between multicomponent agents, such as Chinese traditional medicines, Chinese material medical therapy and foods, and metabolic system in relation with health outcomes (Lan & Jia, 2010; Wang, Bao, Han, Han, & Yang, 2016).

In this review, we summarized and discussed recent studies regarding genome sequencing of gut microbiota and metabolomics that have facilitated understanding of the activity of MFH in prevention and management of health, based on randomized clinical trials or animal experiments. A total of 90 studies (from 2015 to 2020) were collected from resources such as PubMed, SciFinder Scholar, and Web of Science using the following search terms: each of MFH species (Latin name and/or English name), together with metabolomics and/or intestinal microbiota (gut microbiota) (Figure 1). Only clinical trials and original articles of animal experiments published from 2015 to 2020 were included. The articles were retrieved and extensively reviewed by three independent researchers. Most studies focus on the effects of MFH on noncommunicable diseases, including cardiovascular diseases, diabetes, obesity, and certain types of cancers (Table S1). We also discussed the potential for assessing the nutritional value and personalized medication of MFH based on gut microbiota and circulating metabolome. This review aimed to provide a comprehensive overview of current achievements and challenges that need to be emphasized and addressed when using metabolome and analysis of gut microbiota as a new avenue to understand MFH.

2 | GUT MICROBIOTA AND MECHANISMS OF MFH

Accumulating evidence has proved that gut microbiota have significant activities in maintenance and improvement of health (Brial, Le Lay, Dumas, & Gauguier, 2018; Feng et al., 2019; Gurung et al., 2020). MFHs contain various compounds that belong to different chemical classes, which could interact with gut microbiota after ingestion. Several studies have shown effects of MFH on the promotion, inhibition, elimination, and/or colonization of new species of gut microbiota (Feng et al., 2019; Yue et al., 2019). Recently, studies have consistently shown that MFH may achieve their therapeutic effects by modulation of gut microbiota composition and functions, and regulation of microbiota-related metabolism (Feng et al., 2019). The effects of changes in gut microbiota have been examined mostly for diabetes and its complications, inflammatory bowel disease (IBD), depression, and several cancers (Table S1).

Specifically, *Hericium erinaceus*, a traditional edible mushroom, has been shown to alleviate IBD by regulating and improving intestinal bacteria and the immune system (Chen et al., 2017). Similarly, 2-O-β-D-glucopyranosyl-L-ascorbic acid from *Lycium barbarum* L. improved serum physiological and biochemical indicators, blocked proinflammatory cytokines, promoted the production of short-chain fatty acids (SCFAs), and modulated the composition of the gut microbiota in a rat model of IBD (Huang, Dong, et al., 2019). Zhang, Zhao, et al. (2018) demonstrated antitumor effects of polysaccharides extracted

TABLE 1 The pharmacological effects of 109 medicine and food homology species approved by the Health and Fitness Commission in 2015

Latin name	English Name	Ingredients	Health-promoting effects
Eugenia caryophyllata Thunb	Clove	Eugenol	Antimicrobial (Cui, Zhang, Li, & Lin, 2018)
Illicium verum Hook. f.	Star Anise	Phenolic compounds and flavonoid Phenolic compounds	Antimycotoxigenic (Aly, Sabry, Shaheen, & Hathout, 2016) Antioxidant activity (Aly et al., 2016; Padmashree et al., 2007) Antibacterial (Ibrahim, Mattar, Abdel-Khalek, & Azzam, 2017)
Canavalia gladiate (Jacq.) DC.	Sword Bean		
Foeniculum vulgare Mill.	Little Fennel	Essential oil	Antioxidant activity (Ahmed, Shi, Liu, & Kang, 2019) Antibacterial (Diao, Hu, Zhang, & Xu, 2014) Antidiabetic (Mostafa et al., 2015)
Cirsium setosum (Willd.) MB.	Common Cephalanoplos Herb		
Dioscorea opposita Thunb.	Chinese Yam	Polysaccharide	Antiobesity (Cheng et al., 2019) Antiaging (Wang, Huo, et al., 2020)
Crataegus pinnatifida Bunge	Hawthorn	Polysaccharide Organic acid and flavonoids	Hypotension (Cloud, Vilcins, & McEwen, 2019) Antiglycation (Zhu et al., 2019) Aid digestion (Wang, Lv, et al., 2019)
Portulaca oleracea L.	Purslane	Phenolics Flavonoids and lipopolysaccharide Polysaccharide	Antioxidant activity (Alu'datt et al., 2019) Anti-inflammation (Miao et al., 2019) Enhancing immunity (YouGuo, ZongJi, & XiaoPing, 2009) Hepatorenal protective (Seif, Madboli, Marrez, & Aboulthana, 2019)
Zaocys dhumnades (Cantor)	Zaocys Dhumnade		
Prunus mume (Sieb.) Sieb.etZuce.	Dark Plum Fruit		
Chaenomeles speciosa (Sweet) Nakai	Pawpaw	Heteropolysaccharide Polysaccharide Essential oil	Antitumor (Cheng et al., 2020) Antioxidant activity (Xie, Zou, & Li, 2016) Antimicrobial (Xianfei, Xiaoqiang, Shunying, & Guolin, 2007)
Cannabis sativa L.	Fructus Cannabis	Total flavonoid Essential oil	Antimicrobial (Frassinetti, Gabriele, Moccia, Longo, & Di Gioia, 2020) Cancer suppression (Bala, Mukherjee, Braga, & Matsabisa, 2018) Antioxidant activity (Nafis et al., 2019)
Citrus aurantium L. var. *amara* Engl.	Seville Orange Flower		
Polygonatum odoratum (Mill.) Druce	Polygonatum Odoratum	Saponin and flavonoid	Antidiabetic (Deng et al., 2012)
Glycyrrhiza uralensis Fisch.	Liquorice	Phenolic compounds Total flavones and licochalcone A	Antioxidant activity (Quintana et al., 2019) Antimicrobial (Quintana et al., 2019) Antihyperglycemic (Luo et al., 2019)
Angelicae Dahuricae Radix	Angelica Dahurica	Imperatorin Coumarins	Antiobesity (Lu et al., 2016) Fight fatty liver (Lu et al., 2016) Antioxidant activity (Bai et al., 2016) Antiproliferative (Bai et al., 2016)
Ginkgo biloba L.	Ginkgo	Polysaccharide, acids, ginkgol, and flavonoids Lipids or polar metabolites	Neuroprotective effects (Wang & Zhang, 2019) Cardioprotective effect (Wang, Zhang, Ren, & Dong, 2016)
Dolichos lablab L.	White Hyacinth Bean		
Dolichos lablab L.	Flos Lablab Album		

(Continues)

TABLE 1 (Continued)

Latin name	English Name	Ingredients	Health-promoting effects
Dimocarpus longan Lour.	Arillus Longan	Polyphenol Total phenolic compounds	Antifungal (Rangkadilok et al., 2012) Antihyperglycemic (Li et al., 2015) Antioxidant activity (Pan et al., 2008)
Catsia tora Linn	Semen Cassiae	Anthraquinones naphtopyrones Polysaccharide	Antidiabetic (Wang, Zhou, et al., 2019) Renoprotective effects (Wang, Zhou, et al., 2019) Antioxidant activity (Liu, Liu, Sun, Jiang, & Yan, 2014)
Lilium brownie F. E. Brown var. *viridulum* Baker	Lily		Antidepressant (Chi et al., 2019)
Myristica fragrans Houtt.	Nutmeg	Total phenolic	Antioxidant activity (Gupta et al., 2013; Su et al., 2007) Antimicrobial (Gupta et al., 2013)
Cinnamomum cassia Presl	Cinnamon	Essential oil Cinnamaldehyde	Anti-inflammatory (Sun et al., 2016) Antibacterial (Wang, Yang, et al., 2018) Antidiabetes (Habtemariam, 2019) Antiobesity and antiHyperglycemic (Camacho et al., 2015)
Phyllanthus emblica L.	Emblic Leafflower Fruit	Polyphenols Quercetin	Antioxidant activity (Li, Zhang, Chen, et al., 2020) Anti-inflammatory (Li, Zhang, Chen, et al., 2020) Antidiabetic (Srinivasan, Vijayakumar, Kothandaraman, & Palani, 2018)
Citrus medica L. var. *sarcodactylis* Swingle	Fingered Citron	Essential oil Polysaccharides	Antibacterial (Wang, You, et al., 2020) Antioxidant activity (Wu, Li, Tu, Yang, & Zhan, 2013)
Prunus armeniaca L.	Almond	Total polyphenols	Antioxidant activity (Wani et al., 2017)
Hippophae rhamnoides L.	Sea-Buckthorn	Polyphenols Homogalacturonan Phenolics and flavonoids Polyunsaturated fatty acids	Antioxidant activity (Radenkovs, Püssa, Juhnevica-Radenkova, Anton, & Seglina, 2018) Anticancer (Wang, Gao, et al., 2015) Antiproliferation (Guo, Guo, Li, Fu, & Liu, 2017) Immunomodulatory (Suryakumar & Gupta, 2011)
Euryale ferox Salisb.	Semen Euryales	Glucan Polysaccharides	Antihyperglycemic (Zhang, Su, Gong, et al., 2019) Antioxidant activity (Wu et al., 2014)
Zanthoxylum bungeanum Maxim.	Pepper	Indole-3-lactic acid Indole-3-propionic acid Indole-3-acetic acid Indole-3-aldehyde	Antioxidant activity (Sakurai, Odamaki, & Xiao, 2019) Antibacterial (Sakurai et al., 2019) Anticancer (Sakurai et al., 2019)
Vigna umbellata Ohwi et Ohashi	Small Red Bean		
Equus asinus L.	Donkey-Hide Gelatin	Low-molecular-weight peptides	Antiphotoaging (Kim, Kim, Kim, & Jang, 2018)
Gallus gallus domesticus Brisson	Endothelium Corneum Gigeriae Galli	Polysaccharides	Antioxidant activity (Xiong et al., 2014)
Hordeum vulgare L.	Hordei Fructus Germinatus	Total phenolic Total flavonoid	Antiobesity (Thatiparthi, Dodoala, Koganti, & Kvsrg, 2019)
Ecklonia kurome Okam.	Hordei Fructus Germinatus		
Ziziphus jujuba Mill.	Jujube	Polysaccharides Cyclic adenosine monophosphate	Antioxidant activity (Ji, Hou, Yan, Shi, & Liu, 2020) Immunomodulatory (Lin, Liu, Lai, et al., 2018) Antiallergy (Jiang et al., 2019)
Siraitia grosvenorii (Swingle.) C. Jeffrey ex A. M. Lu & Z. Y. Zhang	Momordica Grosvenori	Cucurbitane glycosides	Anti-inflammatory (Pan, Yang, Tsai, Sang, & Ho, 2009) Anticancer (Takasaki et al., 2003)
Prunus japonica Thunb.	Semen Pruni		
Lonicera japonica Thunb.	Honeysuckle	Polysaccharide HP-02 Polyphenols	Immunomodulatory (Feng et al., 2019) Treatments of fatty liver (Liu et al., 2018)

(Continues)

TABLE 1 (Continued)

Latin name	English Name	Ingredients	Health-promoting effects
Canarium album Raeusch.	Fructus Canarii		
Houttuynia cordata Thunb.	Cordate Houttuynia	Houttuynia polyphenols and volatile oils Houttuynia polyphenols and volatile oils	Anti-inflammatory (Shingnaisui, Dey, Manna, & Kalita, 2018) Antioxidant activity (Shingnaisui et al., 2018)
Zingiber officinale Rosc.	Ginger	Phenolics and total carotenoids Phenolic compounds	Antioxidant activity (Ghafoor et al., 2020) Prevent obesity (Wang, Li, Wang, Hu, & Chen, 2019)
Hovenia dulcis Thunb.	Hovenia Dulcis Thunb		Anti-inflammatory (Choi et al., 2017) Antisteatotic (Choi et al., 2017)
Lycium barbarum L.	Fructus Lycii	Chlorogenic acid, quercetin, kaempferol, and isorhamnetin Glycitein, quercetin, atropine, sitosterol alpha1, cycloartenol, and fucosterol Betaine	Antioxidant activity (Zhang, Chen, Yang, & Shi, 2018) Treatment of Retinitis Pigmentosa (Hou-Pan et al., 2019) Prevention of Alzheimer's disease (Ye et al., 2015)
Gardenia jasminoides Ellis	Gardenia		
Amomum villosum Lour.	Amomun Villosum	Polysaccharides	Antioxidant activity (Zhang, Li, Xiong, Jiang, & Lai, 2013)
Sterculia lychnophora Hance	Scaphium Scaphigerum	Polysaccharides Kaempferol-3-O-β-D-glucoside, kaempferol-3-O-D-rutinoside, and isorhamnetin-3-O-D-rutinoside Not available	Anti-inflammatory (Oppong, Li, Banahene, Fang, & Qiu, 2018) Antiobesity (Oppong et al., 2018) Antiulcer (Oppong et al., 2018)
Poria cocos (Schw.) Wolf	Poria Cocos	Polysaccharides Triterpenoids	Antidepressant and Immunosuppressive (Zhang, Chen, Li, Zhao, & Duan, 2018) Diuretic (Hu, Huang, Zhang, Xiao, & Jia, 2017)
Citrus medica L.	Citrus Medica Limonum	Essential oil Heteropolysaccharide Phenols and flavonoids	Antimicrobial (Gao, Zhong, Chen, Tang, & Guo, 2020) Immunomodulatory (Peng et al., 2019) Antioxidant activity (Menichini et al., 2011) Hypoglycemic potential (Menichini et al., 2011) Anti-inflammatory (Menichini et al., 2011)
Elsholtzia ciliata (Thunb.) Hyland.	Chinese Mosla Herb		
Prunus persica (L.) Batsch	Peach Seed		
Morus alba L.	Mulberry Leaf	Rutin, chlorogenic acid, Moracin NTricetin, gallic acid, and chlorogenic acid	Antiobesity (He et al., 2019) Antioxidant activity (Tu et al., 2019) Antidiabetes (Ge et al., 2018)
Morus alba L.	Mulberry	1-Deoxynijirimycin Phenols	Hypoglycemic (Thaipitakwong, Supasyndh, Rasmi, & Aramwit, 2020) Antineuroinflammatory (Xu, Huang, Xu, He, & Wang, 2020) Antioxidant activity (Xu et al., 2020)
Citrus reticulata Blanco	Vermilion	Phenolic and flavonoid	Antioxidant activity (Zhang, Yang, & Zhou, 2018)
Platycodon grandiflorum (Jacq.) A. DC.	Platycodon Grandiflorum	Saponin Platycodin D	Prevention of eccentric exercise-induced muscle damage (Kim, Oh, et al., 2018) Ameliorating nephrotoxicity (Kim et al., 2012)
Alpinia oxyphylla Miq.	Bitter Cardamon	5-Hydroxymethylfurfural Diphenylheptanes Sesquiterpenes Flavones	Antioxidant (Liu et al., 2014) Antidiarrheal effect (Wang, Zhao, et al., 2015)
Nelumbo nucifera Gaertn.	Folium Nelumbinis	Polysaccharides	Immunomodulatory activity (Hu et al., 2019)
Raphanus sativus L.	Semen Raphani	Isothiocyanates	Anticancer (Pocasap, Weerapreeyakul, Tanthanuch, & Thumanu, 2017)

(Continues)

TABLE 1 (Continued)

Latin name	English Name	Ingredients	Health-promoting effects
Nelumbo nucifera Gaertn.	Lotus Seed	Oligosaccharides Protein	Regulating gut microbiota (Su et al., 2019) Anti-inflammatory activity (Moon, Ahn, Oh, & Je, 2019) Antioxidant activity (Moon et al., 2019)
Alpinia officinarum Hance	Galangal	Polyphenols	Antimicrobial (Tang, Xu, Yagiz, Simonne, & Marshall, 2018) Antioxidant activity (Tang et al., 2018)
Lophatherum gracile Brongn.	Lophatherum Gracile	Flavonoids	Antiviral activity (Chen, Zhong, et al., 2019)
Glycine max (L.) Merr.	Fermented Soybean	Isoflavones	Antioxidant activity (Li, Zhang, Liu, et al., 2020) Anti-inflammatory activity (Li, Zhang, Liu, et al., 2020)
Chrysanthemum morifolium Ramat.	Chrysanthemum	Polysaccharides Phenolics	Anti-inflammatory activity (Li, Yang, et al., 2019) Antioxidant activity (Li, Yang, et al., 2019)
Cichorium intybus L.	Chicory	Chicoric acid Chlorogenic acid Flavonoids Phenolic acids	Antidiabetic effect (Ferrare et al., 2018) Antioxidant activity (Abbas et al., 2015)
Brassica juncea (L.) Czern & Coss	Brassica Juncea Czerm. Et Coss		
Polygonatum kingianum	Rhizoma Polygonatum	Polysaccharides Flavonoids Phenolics	Antioxidant activity (Allen et al., 2018) Antimicrobial (Allen et al., 2018) Antidiabetes (Blacher, Levy, Tatirovsky, & Elinav, 2017)
Perilla frutescens (L.) Britt.	Perilla Frutescens	Lipopolysaccharides Essential oils	Anti-inflammatory (Wang, Li, et al., 2018) Antioxidant activity (Chen et al., 2020)
Perilla frutescens (L.) Britt.	Perilla Seed	Phenolic phytochemicals	Antioxidant (Kim & Lee, 2019) Inhibition of α-glucosidase and aldose reductase (Ha et al., 2012)
Pueraria lobata (Willd.) Ohwi	The Root Of Kudzu Vine	Polysaccharides	Immunomodulatory activity (Dong et al., 2019) Antioxidant activity (Cui et al., 2008)
Sesamum indicum L.	Semen Sesami Nigrum	Fatty acids Phytosterols	Antibacterial (Zafar et al., 2020) Neuroprotective effect (Botelho et al., 2014)
Piper nigrum L.	Black Pepper	Piperine Capsaicinoids	Improvements of cardiometabolic risk markers associated to Western-style diet (Sina, Nasrollahzadeh, Shokraei, Rismanchi, & Foroughi, 2018) Normalized the glucose and liver enzyme activities (Sarfraz, Khaliq, Khan, & Aslam, 2017)
Sophora japonica L.	Sophora Flower Bud	Polysaccharides Phenolics	Prevention of UVB radiation (Li, Huang, et al., 2019) Antioxidant activity (Guo et al., 2020)
Sophora japonica L.	Flos Sophorae	Rutin	Antioxidant activity (Tang et al., 2019)
Taraxacum mongolicum Hand.-Mazz.	Dandelion	Chicoric acid	Antioxidant activity (Lis, Jedrejek, Moldoch, Stochmal, & Olas, 2019) Hemostasis (Lis et al., 2019) Anticancer (Ren et al., 2019)
Apis cerana Fabricius	Honey	Polyphenolics Minerals Ascorbic acid	Treatments of diabetic wounds (Chaudhary, Bag, Banerjee, Chatterjee, & Medicine, 2019) Antialcoholic effect (Guo, Deng, & Lu, 2019) Stimulating glucose uptake (Lori et al., 2019)
Torreya grandis Fort.	Chinese Torreya	Alkaloids Flavonoids Tannins Terpenoids Saponins	Anti-inflammatory activity (Saeed et al., 2010) Antioxidant activity (Shi et al., 2018)

(Continues)

TABLE 1 (Continued)

Latin name	English Name	Ingredients	Health-promoting effects
Ziziphus jujuba Mill. var. *spinose* (Bunge) Hu ex H. F. Chou	Semen Ziziphi Spinosae	Flavonoids	Hypnotic effects (Yan et al., 2019) Antioxidant activity (Yan et al., 2020)
Imperata cylindrical Beauv. var. *major* (Nees) C. E. Hubb.	Fresh Rhizoma Imperatae		
Phragmites communis Trin.	Fresh Rehmannia Root		
Agkistrodon acutus (Güenther)	Pallas Pit Viper		
Citrus reticulata Blanco	Orange Peel	Polymethoxyflavones	Anticancer (Lu, Lee, Chu, Ho, & Sheen, 2019) Antibacterial (Amanulla & Sundaram, 2019)
Mentha haplocalyx Briq.	Mentha Haplocalyx	Polysaccharides	Antiaging activities (Jiang et al., 2020) Antioxidant activity (Chen, Fang, et al., 2019)
Coix lacryma-jobi L. var. *mayuen.* (Roman.) Stapf	Coix Seed	Polysaccharides	Anticancer (Qu et al., 2016)
Allium macrostemon Bunge.	Allium Macrostemon	Macrostemonoside A	Antidepressant-like activity (Lee et al., 2010) Treatments of hyperglycemia and hyperlipidemia and visceral obesity (Xie et al., 2008)
Rubus chingii Hu	Raspberry	Pelargonidin-3-O-glucoside	Antidiabetes (Su, Bao, et al., 2020) Improving lipid metabolism (Kowalska, Olejnik, Zielińska-Wasielica, & Olkowicz, 2019)
Pogostemon cablin (Blanco) Benth.	Wrinkled Gianthyssop Herb	Flavonoids Phenolics	Xanthine oxidase inhibitory activities (Liu, Deng, et al., 2017) Anti-inflammatory activity (Wu et al., 2018)
Panax ginseng C. A. Mey	Ginseng	Sapogenins Polysaccharides	Antiobesity (Lin, Lee, et al., 2019) Hypoglycemic, anti-inflammatory, and lipid-lowering effect (Xu et al., 2019)
Flos Lonicerae Confusae	Wild Honeysuckle Flower Bud	Polyphenols	Antioxidant activity (Xie et al., 2019)
Coriandrum sativum L.	Cilantro	Phenolics	Antioxidant activity (Wong & Kitts, 2006) Antibacterial (Wong & Kitts, 2006)
Rosa rugosa Thunb or *Rose rugosa* cv. Plena	Rugosa Rose	Polyphenols	Antidiabetes (Liu, Tang, Zhao, Xin, & Aisa, 2017) Antihypertensive activity (Xie & Zhang, 2012)
Pinus massoniana Lamb.	Pini Pollen	Polysaccharides	Preventing *P. mirabilis* infection (Zhou et al., 2017)
Pueraria thomsonii Benth.	Puerariae Thomsonii Radix.	Isoflavonoids Daidzein Genistein	Antidiabetes (Wong, Razmovski-Naumovski, Li, Li, & Chan, 2015) Treatment of Parkinson's disease (Lin et al., 2010)
Microcos paniculata L.	Microctis Folium	Flavonoids	Anti-inflammatory activity (Li, He, et al., 2018)
Prunella vulgaris L.	Prunellae Spica	Polysaccharides Phenolics Flavonoids	Antiviral effect (Ma et al., 2016) Hepatoprotective activity (Ahmad et al., 2020)
Angelica sinensis (Oliv.) Diels	Angelicae Sinensis Radix	Volatile oils Polysaccharides	Anti-inflammatory activity (Zhong et al., 2016) Blood-replenishing (Tao, Hong-Guo, Yong-Li, Peng-Ling, & Yan-Ming, 2016)
Kaempferia galanga L.	Galanga Resurrectionlily Rhizome	Diarylheptanoids Phenolics Total flavonoid content	Anti-inflammatory (Yao, Huang, Wang, & He, 2018) Antioxidant activity (Ali, Yesmin, Satter, Habib, & Yeasmin, 2018) Antineoplastic activities (Ali et al., 2018)
Crocus sativus L.	Crocus Sativus	Phenolics	Antidiabetes (Karimi-Nazari et al., 2019) Antioxidant activity and enzyme inhibitory activities (Menghini et al., 2018)
Amomum tsao-ko Crevost et Lemaire	Fructus Tsaoko	Essential oil	Antibacterial (Min, Cheng, & Fenghui, 2016) Antioxidant activity (Yang et al., 2010)

(Continues)

TABLE 1 (Continued)

Latin name	English Name	Ingredients	Health-promoting effects
Curcuma longa L.	Turmeric	Curcuminoids	Antioxidant activity (Karimi et al., 2019) Antimicrobial (Karimi et al., 2019) Anticancer (Zhou et al., 2019)
Piper longum L.	Fructus Piperis Longi	Piperine	Neuroprotective effects (Peng et al., 2019) Anti-inflammatory activity (Wang et al., 2017)
Codonopsis pilosula (Franch.) Nannf.	Codonopsis Radix	Tryptophan Syringin, Tangshenoside I Codonopyrrolidium A Lobetyolin	Hematopoietic and improving immunologic functions (Gao et al., 2019)
Cistanches Herba	Desertliving Cistanche Herb	Phenylethanoid glycosides Cistanche polysaccharides	Improving immune function (Tian, Li, Bai, Wu, & Wei, 2019), improvements of the gut microbiota diversity (Fu et al., 2020)
Dendrobium officinale Kimura et Migo	Herba Dendrodii Officinalis	Polysaccharides	Immunomodulatory (Tao et al., 2019) Antidiabetes (Liu, Yang, et al., 2020)
Panacis Quinquefolii Radix	American Genseng	Panax quinquefolium saponin	Anti-inflammatory (Xie, Chen, et al., 2018) Treating acute central nervous system injury (Dou, Chen, Ran, & Jiang, 2018)
Astragali Radix	Milkvetch Root	Sucrose fatty acid esters Polysaccharide	Anti-inflammatory activity (Li et al., 2013) Antidiabetes (Liu et al., 2019)
Ganoderma	Ganoderma Lucidum	Lanostane triterpenoids	Anti-inflammatory activity (Su, Peng, et al., 2020) Antibacterial activities (Ghafoor et al., 2020) Antiobesity (Diling et al., 2020)
Gastrodia elata Bl.	Gastrodiae Rhizoma	Compounds of high polarity	Anti-inflammatory activity (Xu et al., 2020) Antioxidant activities (Xu et al., 2020)
Cornus officinale Sieb. et Zucc	Dogwood	Polyphenols	Anti-inflammatory activity (David et al., 2020)
Folium eucommiae	Eucommia Ulmoides Leaf	Chlorogenic acid Geniposidic acid Aucubin	Treatments of photoimmunosuppression (Hiramoto, Yamate, Hirata, & Fujikawa, 2018), prevention of vascular disease (Lee et al., 2018)

from *Glycyrrhiza uralensis*, which could be explained by modulation of the gut microbiota composition, that is, a remarkable increase in the genus *Lachnospiraceae*_UCG_001, *Enterorhabdus*, *Odoribacter*, *Enterococcus*, and *Ruminiclostridium*_5. Moreover, Ginseng (Knight et al., 2018), *Polygonatum kingianum* (Yan et al., 2017), Mulberry (Chen et al., 2018), and *Alpinia oxyphylla* Miq. (Xie, Xiao, et al., 2018) have alleviated diabetes in animal models by modulating gut microbiota (Table S1). Although distinct molecular pathways involved in the health benefits of MFH have not been identified, associations between MFH-induced alterations of relative abundances of gut microbiota and improvements in clinical parameters (i.e., anthropological measurements and blood biochemical indicators) have been consistently observed. These findings further indicate that MFH may prevent or mitigate diseases by interacting with gut microbiota, particularly by influencing the composition of gut microbiota and/or regulating their metabolism (Feng et al., 2019).

Interactions between gut microbiota and MFH undoubtedly contribute to variations in both microbiota composition and the levels of metabolites produced by gut microbiota. Many gut microbiota-derived metabolites have been identified, such as lipopolysaccharide (LPS), SCFAs, bile acids, choline metabolites, organic acids, indole derivatives, and several species of lipids. Of note, these metabolites often exert extensive effects on the host, thereby producing the therapeutic effects of MFH. For instance, Yan et al. (2017) reported that total saponins and total polysaccharides extracted from *Polygonatum kingianum* improved fasting blood glucose, fasting insulin, body weight, and LPS. Improvements of these parameters correlated with alterations in the relative abundance of gut microbiota and SCFAs in a rat model of type 2 diabetes. Zeng et al. (2017) found that, in mice, Lotus seed resistant starch type 3 enhanced production of SCFAs and intestinal absorption of calcium, magnesium, and iron by regulating gut microbiota.

It should be noted that most bioactive compounds in MFH often exhibit poor bioavailability (Feng et al., 2019; Lin, Luo, et al., 2019). The gut microbiota could be one of the main ways in which herbal medicines act on human health through reshaping the microbial structure and/or processing the herbal ingredients to form bioactive metabolites (Chen et al., 2016). For instance, ginsenosides are a series of active constituents in Panax ginseng. However, orally, the bioavailability of ginsenosides is usually around 0.1% to 0.5% of amount administered. Interestingly, certain gut microbiota such as *Bacteroides*, *Bifidobacterium*, *Eubacterium*, *Prevotella oris*, and *Fusobacterium* can metabolize ginsenosides and generate new compounds with health-promoting effects and dramatically improved bioavailability, for example,

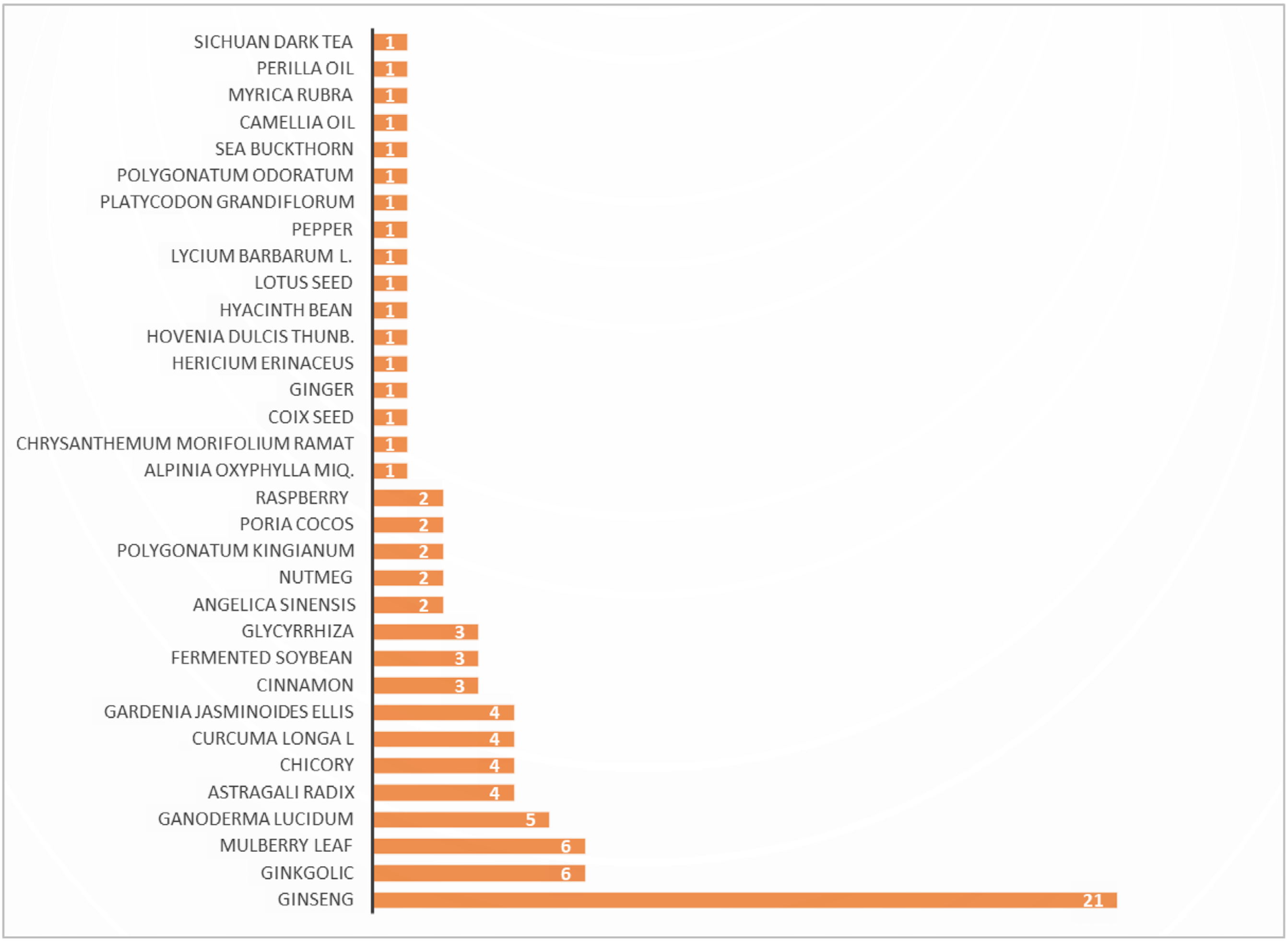

FIGURE 1 A summary of 90 studies that investigated effects of medicine and food homology using metabolomics and/or analysis of gut microbiota from 2015 to 2020

20-O-(b-D-glucopyranosyl)-20(S)-protopanaxadiol. Moreover, polyphenols are active compounds that are abundant in MFH, but polyphenol bioavailability is less than 10%. The gut microbiota influences polyphenol bioavailability by modifying the structures of aglycones, glycosides, and conjugates. As a consequence, polyphenols are converted to catabolites, which may be nonnegligible contributors to the health effects of parental polyphenols (Clavel & Mapesa, 2013; Kawabata, Yoshioka, & Terao, 2019; Pino et al., 2000; Teng & Chen, 2019; Yen-Ling et al., 2006). Besides, intestinal bacteria has been highlighted to possess distinct polysaccharide preferences and polysaccharides may favor the growth of specific bacterial species (Koropatkin, Cameron, & Martens, 2012). It has been shown that the water extract of *Ganoderma lucidum mycelium* (WEGL) and its high-molecular-weight polysaccharides may be used as prebiotics to reduce body weight gain, chronic inflammation, and insulin resistance in obese individuals (Chang et al., 2015). The beneficial effects induced by WEGL may be attributed to specific alterations in the gut microbiota, leading to an improved bioavailability by interacting with gut microbiota. Characteristics of typical MFH compounds, such as saponins, flavonoids, sennoside, and rhapontin and their corresponding microbial metabolites have been summarized and discussed elsewhere (Lin, Luo, et al., 2019).

In sum, the health-promoting effects of MFH could be attributed to their direct effects on gut microbiota composition and on the levels and bioavailability of beneficial metabolites or catabolic products produced by gut microbiota. However, most of the active components in MFH are not well-defined and their functional activities have not been confirmed. Moreover, knowledge regarding microbial metabolites of bioactive MFH compounds is extremely limited. More studies are warranted to investigate molecular interactions between MFH and gut microbiota to understand benefits of MFH.

3 | METABOLOMICS AND MECHANISMS OF MFH

Beneficial effects of MFH have been studied for many years and interest in MFH is growing worldwide. Large effects have been paid to isolate and characterize for single bioactive compounds and to test their nutritional and clinical value individually (Wang et al., 2005; Wu et al., 2012). Although such approach has been done over decades with great success, the synergetic effects of complex components of MFH on holistic perturbations in relation to health and disease status were largely unexplored (Commisso, Strazzer, Toffali, Stocchero, & Guzzo, 2013; Wang et al., 2011). Metabolomics represents a global understanding of the metabolite complement of living systems and dynamic responses to changes in endogenous and exogenous factors, which opens up the possibility to explore impacts of the multicomponent mixtures and their complex interactions on biological systems in a holistic manner (Hu & Xu, 2014; Lan & Jia, 2010; Shi et al., 2016). By effectively characterizing biochemical phenotype of MFH, in particularly, low-molecular-weight metabolic intermediates and end products of metabolism, including primary metabolites, for example, sugars, amino acids, fatty acids, and organic acids and secondary metabolites, for example, phenylpropanoids and alkaloids, metabolomics not only aids in identifying the chemical constituents of MFH and screening the active components, but also evaluates their efficacy, and determine mechanisms of MFH's health-promoting effects (Hu & Xu, 2014; Li, Liu, et al., 2018; Song, Zhang, Yan, Liu, & Wang, 2017; Wang et al., 2011; Wang, Zhu, et al., 2019; Xie, Wang, et al., 2018). In the preceding 5 years, there have been 65 investigations that used high-throughput metabolite profiling technology to characterize the effects of MFH on disease prevention and treatment (Table S1).

Specifically, the mulberry leaf is widely recognized for its therapeutic effect on diabetes and its complications; however, the mechanism is unknown. Using metabolomics, investigators have shown that protective effects of mulberry leaf might be related to the regulation of insulin receptor and TGF-/Smads signaling pathway (Zhang, Su, Zhu, et al., 2019), influences on lipid metabolism, amino acid metabolism, and glucose metabolism that are involved in the pathogenesis of diabetes (Hu, Thakur, et al., 2017), and modulation of glycometabolism (Wen, Lin, Dong, & Deng, 2016). Moreover, in the toxicity study of *Tripterygium wilfordii*, Chen et al. (2008) used mass spectrometry-based metabolomics to study the changes of rat urine metabolome caused by *Tripterygium* glycosides and for the first time showed the time-dependent toxicity of high-dose *Tripterygium wilfordii* glycosides, leading to negative impacts-involved energy metabolism and choline metabolism. Furthermore, several studies investigated wide range of therapeutic and pharmacological effects of ginseng that were produced by the ginseng rather than from an isolated compound, and also studied certain metabolic pathways related with health status (Feng, Yue, et al., 2016; Lin, Liu, Pi, et al., 2018; Lin, Lee, et al., 2019; Wang, Zhu, et al., 2019; Wu et al., 2012; Yang et al., 2016). Such investigations help to elucidate chemical bases to assure the efficacy and quality of ginsengs. For instance, most of animal metabolomic studies have investigated effects of ginseng, Panax ginseng, and American ginseng (Table S1). Ginseng beneficially affects circulating metabolites in different metabolic pathways, such as bile acids, amino acids, lipids, and phytosphingosine (Feng, Liu, et al., 2016; Feng, Yue, et al., 2016; Li, Liu, et al., 2018; Lin, Liu, Pi, et al., 2018; Lin et al., 2016; Tao et al., 2019; Wang, Zhu, et al., 2019; Zhu et al., 2015), which may partly explain the mechanism of therapeutic effects of ginsengs on Alzheimer's disease, stress, TNBS-induced colitis, cognitive impairment, and cisplatin nephrotoxicity. Of note, the dried leaf of *Platycodon grandiflorum* is known for its anti-inflammatory and antioxidative activities. Wang, Lin, et al. (2019) for the first time investigated the antidepressant-like effects of *Platycodins Folium* and its potential mechanism in attenuating depression in a mouse model of LPS-induced depression. *Platycodins Folium* improved metabolisms of lipids, amino acids, energy, arachidonic acid, glutathione, and inositol phosphate, which were associated with a therapeutic effect on depression.

Most interestingly, there are only a few studies that have combined metabolomics with analysis of gut microbiota to examine the metabolic characteristics of MFH and reveal their probably activities in disease prevention and treatment (Table S1). The integration of metabolomics and gut microbiota (mainly taxonomic information) is an excellent tool to explain the complex interaction between host and gut microbiota at a system level and to screen microorganisms and bioactive compounds responsible for therapeutic effects of MFH. For instance, by combining intestinal community modulation and metabolite analysis, Li, Liu, Liu, Liao, and Zou (2019) found that different components of mulberry leaves (i.e., crude powder, mulberry leaf fiber, and mulberry leaf polyphenols) promoted weight loss by reducing the relative abundance of lachnespiraceae, bacillus, lactobacillales, lactobacillus, and lactobacillus_gasseri species, which improved lipid profiles. Wang, Yu, et al. (2016) found that American Ginseng alleviated colitis and colorectal cancer induced by azoxymethane/dextran sulfate sodium by the joint study of metabolomics and intestinal microflora. By integrating gut microbiota and bile acids in serum and feces, Huang, Zheng, et al. (2019) shed light on the mechanisms behind the cholesterol- and lipid-lowering effects of Pu-erh tea, a famous traditional Chinese tea prepared by microbial fermentation of fresh *Camellia sinensis* leaves. This study for the first time demonstrated the mechanistic link between theabrownin, the characteristic component of Pu-erh tea, and changes in the gut microbiota, FXR signaling, and bile acids synthesis in the modulation of cholesterol levels in serum and liver. Zhou et al. (2016) studied beneficial effects of ginseng polysaccharides and ginsenosides in Du-Shen-Tang, the decoction of ginseng, on over-fatigue and acute cold stress by analyzing gut microbiota and metabolome. Results showed that ginseng polysaccharides improved intestinal metabolism and reinstated the perturbed holistic gut microbiota. Li, Shi, et al. (2019) evaluated the effects of Yi Nian Kang Bao tea, a medicine–food formulation based on Sichuan dark tea, on dyslipidemia and investigated the mechanism underlying its correlation with gut microbiota and serum metabolite regulation. Their findings highlight the health-promoting effects of Yi Nian Kang Bao tea on prevention of dyslipidemia. Moreover, integrating gut microbiota analysis and metabolomics revealed molecular mechanisms of the benefits of polysaccharides from *Aralia elata* root barks for the treatment of some hepatic disorders through decreasing the inflammatory markers in liver (Xia, Wang, Yu, Liang, & Kuang, 2019).

In conclusion, metabolomics has shown irreplaceable potentials to improve understanding diseases and to explore the function and essence of MFH constitutes, thereby providing a unique perspective for elucidating the action mechanism of MFH. Although thousands of years of observing the health benefits of MFH and modern clinical research have proven the efficacy of MFH, obscurity of the functions and potential therapeutic targets are the main limitations for clinical practice. Further research and development are still required to elucidate the underlying mechanism of action.

4 | PERSPECTIVES FOR THE FUTURE

4.1 | Application of polypharmacokinetic strategy to MFH

Because MFH contains hundreds of chemical components that coexist and, likely, interactions, it may be necessary to establish an MFH research model that uses a metabolomics-based polypharmacokinetic strategy (Xie, Wang, et al., 2018). A polypharmacokinetic study for complex exposures, that is, MFH, integrates phytochemical and metabolomics to simultaneously identify and characterize “what are absorbed (the bioavailable phytochemical compounds)” and “what are produced (the new compounds produced through biotransformation)” and a time-dependent response of biochemical substances should be captured. By using advanced multivariate statistics and bioinformatics to compare a disease-model profile with the intervention-response profile, investigators can reveal the influence of MFH substances on the metabolic network of organisms from a holistic perspective, providing comprehensive insights in molecular mechanism of nutritional and therapeutic efficacy of MFH. Such an approach could greatly accelerate the pharmacological evaluation of core functional compounds and advance therapeutic development (Jia, Fan, Wang, & Xie, 2015; Lan et al., 2013; Xie, Wang, et al., 2018; Zhang, Xiao, et al., 2018).

The polypharmacokinetic strategy has been successfully used in studies of traditional Chinese medicine and formulas, and it has led to several promising achievements. Specifically, Xie, Wang, et al. (2018) characterized the time-dependent concentration profiles of bioavailable compounds of Huangqi decoction consisting of *Radix Astragali* and *Radix Glycyrrhizae*, secondary metabolite profiles in plasma, and the dynamic changes of metabolic endpoints in healthy Chinese volunteers. Findings revealed the relationships between multiple compounds of Huangqi decoction, their corresponding metabolites, and their effects on metabolism, providing unprecedented understanding of the mechanisms of action of Huangqi decoction. Very recently, Wang, Li, Tao, et al. (2019) performed pharmacokinetic evaluation of rats after oral administration of eight constituents in Yuanhu Zhitong tablets (Ping et al., 2019) or Yuanhu Zhitong prescription (i.e., a commonly used clinical herb preparation recorded in the China Pharmacopoeia for the treatment of stomach pain, hypochondriac pain, headache, and dysmenorrhea), Corydalis yanhusuo, and Angelica dahurica (Hoffm.).

To the best of our knowledge, there is a lack of research on the absorption, distribution, and metabolism of multicomponents of MFH. Metabolomics-based pharmacokinetic profiling of MFH and their products enables clarification of metabolic processes and better understanding of associated nutritional value and therapeutic mechanisms. It integrates phytochemical and metabolomic profiling to simultaneously monitor the pharmacokinetic behaviors of multiple constituents. However, challenges lie predominately in the fact that MFH comprises a large number of complex constituents with diverse chemical structures that are present in a wide concentration range. Chemical characteristics and the ADME system (i.e., absorption, distribution, metabolism, and excretion) of constituents should be both considered. The limited use of this state-of-the-art profiling technique may be due to the major investment in analytical equipment, methods, and availability of analytical standards required for its implementation that could simultaneously and precisely generate information on exposure and corresponding absorbed constituents. Comprehensive databases for metabolite identification are also urgently needed to be developed. Moreover, the lack of user-friendly and robust statistical methods that could deal with multivariate time-series and high-dimension datasets limits the application of pharmacokinetic profiling, which need to be overcome.

4.2 | Application of multiomics-based randomized controlled trials

Despite great achievements in investigating benefits of MFH, most evidence is from animal studies. Randomized controlled trails are the gold standard for assessing efficacy of drugs in humans. However, evidence from randomized controlled trails of health-promoting effects of MFH is extremely limited and prior studies, unfortunately, had limited sample sizes, short intervention periods, and a lack of dose information. For instance, Mohammadi et al. (2019) conducted a systematic search of all available randomized controlled trials up to June 2018 to evaluate the efficacy of ginseng on serum inflammatory biomarkers. Only seven studies existed, and the findings were not robust, which highlighted a need for long-term dose-escalating trials. Phimarn, Wichaiyo, Silpsavikul, Sungthong, and Saramunee (2017) performed a meta-analysis of 13 studies to assess efficacy of Mulberry on improvements in blood glucose and lipid profiles. However, several studies in this group were composed of a small number of participants, thus, they lacked statistical power.

The advent of -omics technologies (i.e., genomics, transcriptomics, proteomics, and metabolomics) in the preceding two decades has improved understanding of the interplay between MFH and health, an outcome that has attracted attention worldwide. Rational integration and scientific analysis of multiple omics technologies, together with network pharmacology and bioinformatics, reveal the material basis and mechanism of MFH efficacy from a systems-wide perspective (Lin et al., 2012). Especially, integration of metagenomic and metabolomic data shows great potential to uncover the intricate relationship between key functional gut microbiota and MFH and endogenous co-metabolites of biological importance (Feng, Gao, Meng, Xue, & Qin, 2020; Li, Liu, et al., 2019; Wang, Yu, et al., 2016). Pan et al. (2019) integrated gene targets and metabolomics data, and pathway analysis revealed significantly associations between metabolism of pyruvate, purine, and glucose with the effects of Guan-Jie-Kang, a prescription modified from a traditional Chinese medicine

"Wu Tou Decoction," in arthritis treatment, elucidating multi-pathway mechanisms.

In summary, multiomics-based randomized controlled trials can provide fundamental information to seek leads for discovery of nutritional and therapeutic targets (Yang & Lao, 2019), direct future studies to manipulate specific gut microbiota and target defined microbial pathways, and to promote and optimize functional efficacy and development of MFH-based products, for example, foods for special medical purposes and daily dietary supplements. Thus, future efforts will require an integrated/holistic multiomics approach to decipher the biology and activities of MFH.

However, it is worth mentioning that suggested mechanisms from -omics studies should be confirmed with other experiments. It is also important to be aware that the key immediate challenge is how to develop the standardized methodological and analytical workflows for these multiomics platforms. Importantly, although animal studies can definitely provide comprehensive information that is not able to be provided by in vitro studies or computer modeling, such as biological mechanisms underlying functional effects, the translatability of observed findings from animal studies to humans is always a substantial challenge. The differences in the pharmacokinetic and pharmacodynamic phases between human and animal models could inevitably lead to some degree of error in extrapolation of findings regardless of the dose conversion method used (Wojcikowski & Gobe, 2014). However, MFH species have been practiced for thousands of years. The traditional use and documented prescriptions of pharmacopoeia of the People's Republic prescription deserve to be tested.

4.3 | Personalized MFH recommendations

It is of great interest to have a holistic picture of the plasticity and individual variability in response to the administration of MFH. This information would facilitate personalized, precise recommendations as a complement to the general "one-fits-all" population-based advice. Given the large individual variation in physical and psychological response to environmental factors, a detailed metabolic profile could help to identify people who can benefit more from a specific MFH intervention adapted to their genotype and phenotype. This phenomenon has also been seen in randomized controlled trails that investigated effect of diet, another important modifiable lifestyle factor in health outcomes (Palmnas et al., 2020). Variations in gut microbiota composition and function have been suggested as a key determinant of differential responses to Chinese herbs, traditional Chinese medicine formula (Yue et al., 2019), and daily meals (Palmnas et al., 2020; Shukla, Murali, & Brilliant, 2015; Zmora, Zeevi, Korem, Segal, & Elinav, 2016). Individual variations in gut microbiota at baseline significantly influence the anti-obesogenic effects and the metabolism of ginsenosides (Dong et al., 2017; Song, Kim, & Kim, 2014). Similarly, Peterson et al. (2018) found that the gut microbiota response to curcumin, a phenolic compound mainly isolated from the pleiotropic herb *Curcuma longa* L., was highly personalized, leading to responders and nonresponders who exhibited response concordance in a double-blind, randomized, placebo-controlled trial. However, these findings need to be validated in large-scale studies.

During the preceding 3 years, grouping individuals based on similarities in metabolic phenotype, that is, metabotypes, has been a novel concept that has attracted worldwide attention for improved prevention and management of noncommunicable chronic diseases (Palmnas et al., 2020). Randomized controlled trials that evaluate metabotype-specific responses are a fundamental step required to bridge the current gap of knowledge with regard to the efficacy of MFH strategies. Advances in high-throughput metabolomics technology and rapid development of bioinformatics enable us to extract differences and similarities in complex and high-dimension metabolomics data, which we are extensively working on (Ghafoor et al., 2020; Palmnas et al., 2020; Riedl, Gieger, Hauner, Daniel, & Linseisen, 2017; Shi et al., 2019; Shi, Brunius, Johansson, et al., 2018; Shi, Brunius, Lehtonen, et al., 2018).

Although promising, it is noteworthy that achieving accurate quantitation of food and nutrient consumption is still challenging (Maruvada et al., 2020), which hinders our investigation on nutrient status across diverse populations. Moreover, important points need to be stressed in order to achieve comparable results between studies. For instance, because postprandial time, habitual dietary pattern, and frequency of participating training session affect an individual's metabolic characteristics, the standardized documentations for those information are certainly required prior to collection of biological samples at rest and pre-exercise. Investigators must take replicate samples and/or intra-experiments to evaluate the reproducibility of metabolite measurements and to determine the true magnitude of intervention effects in relation to measurement errors.

4.4 | Comprehensive databases

Implementation of network and web-based databases could facilitate assessing the effects of MFH on health and point to likely mechanisms to accelerate development of MFH-inspired products with nutritional and therapeutic value. Although there are no databases specifically for MFH, several databases include information on traditional Chinese medicine that could be used as substitutes. The Traditional Chinese Medicine Database has over 400 species of Chinese herbs, including some MFH, and chemical structures for 37,170 compounds (Chen, 2011). The TCMGeneDIT database and Traditional Chinese Medicines Integrated Database include information of Chinese medicine, targeted genes, associated diseases, and pharmacological effects. BATMAN-TCM is a bioinformatics analysis tool specially designed for research of molecular mechanisms (Liu et al., 2016). It could be used for ingredient target prediction, functional analyses of targets including biological pathway, Gene Ontology and disease enrichment analyses, the visualization of ingredient-target-pathway/disease association network, and KEGG biological pathway with highlighted targets. FooDB (http://www.foodb.ca/) is the world's largest and most comprehensive information resource that provides information on food constituents and their potential biological functions (Wishart, 2018). It provides information on both macronutrients and micronutrients,

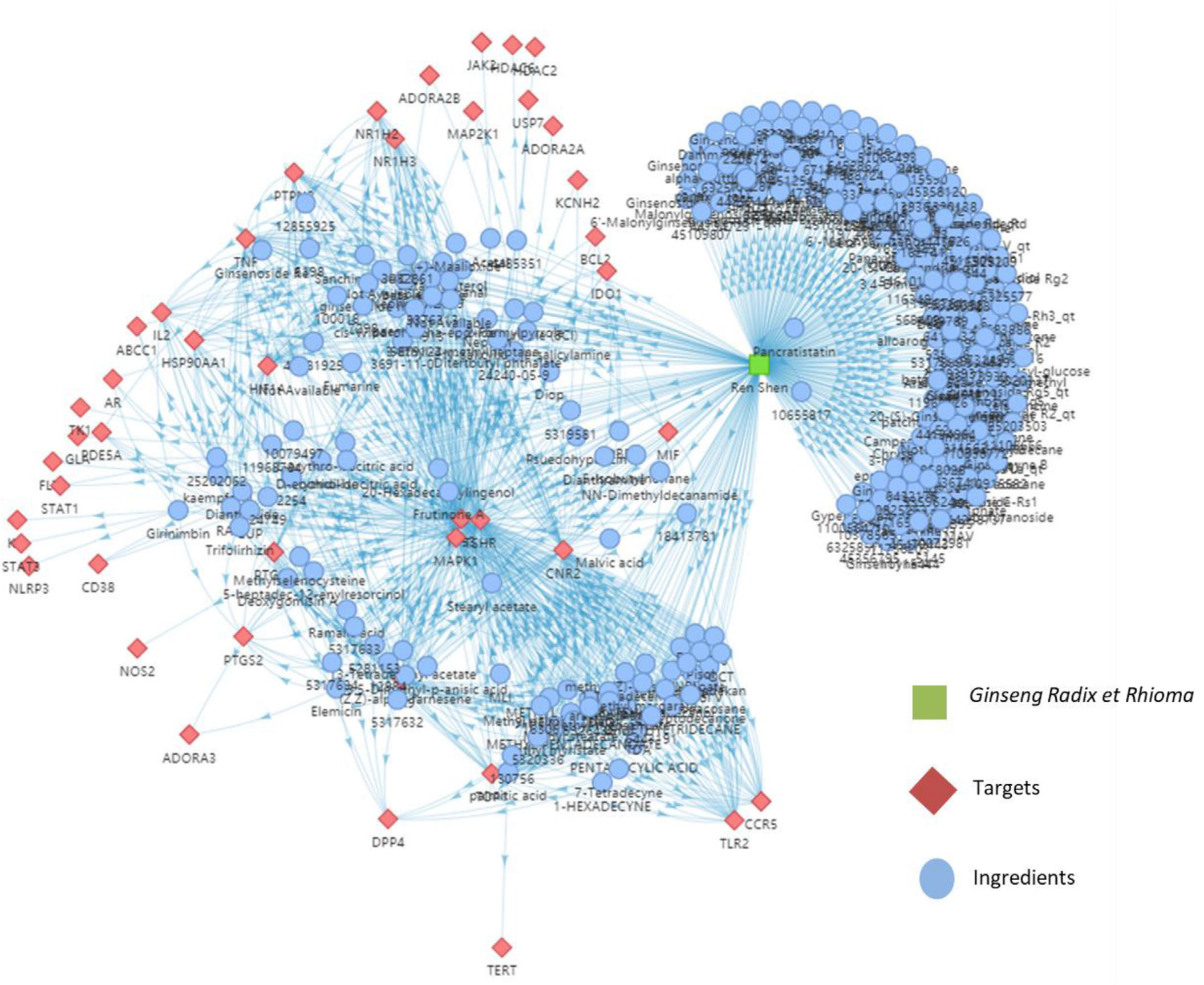

FIGURE 2 The *Ginseng Radix et Rhioma*–ingredient–target network for the mechanism of action exploration. The network consists of 367 interactions connecting 324 ingredients and 43 protein targets involved in multiple metabolisms

as well as data on the compound's physiological and presumptive health effects that are summarized from published studies. FlavorDB (http://cosylab.iiitd.edu.in/flavordb) is a database of flavor molecules (Garg et al., 2018), which comprises of 25,595 flavor molecules representing an array of tastes and odors. It provides dynamic, user-friendly interface of the resource and facilitates exploration of flavor molecules and improved understanding of flavor mechanisms in relation to their nutritional values.

A promising achievement is the development of TCMIO, a comprehensive database of traditional Chinese medicine on immuno-oncology (Liu, Cai, et al., 2020). This database includes 400 immuno-oncology targets, 1,493 prescriptions extracted from the Chinese Pharmacopoeia, 618 species of Chinese herbs, 13,403 prescription–traditional Chinese medicine relations extracted from the Chinese Pharmacopoeia, 126,972 small-molecule ligands against immuno-oncology targets, 16,437 ingredients of traditional Chinese medicine, 32,847 medicine species–ingredient relations, 41,527 ingredient–immuno-oncology targets relations based on network prediction, and 157,195 ligand–targets relations. Along with chemical and bioinformatics mining tools, this database is a comprehensive resource for research on mechanisms of Chinese medicine, particularly for cancer immunity and development of cancer immunotherapy drugs. For instance, the ingredient–target network of *Ginseng Radix et Rhioma* constructed by TCMIO consists of 367 interactions connecting 324 ingredients (e.g., pisol, 9-hexadecenoic acid, methyl myristate, pentadecylic acid, methyl linoleate, and panaxynol) and 43 protein targets (Figure 2). The high correlativity between *Ginseng Radix et Rhioma*. and pathways in cancer, central carbon metabolism in cancer, sphingolipid signaling pathway, and IBD (Benjamini adjusted $p < .05$) has been revealed by KEGG enrichment analysis (Table S2). Results indicate the multiple metabolism pathways that may be mediated by *Ginseng Radix et Rhioma*. We urgently need network and web-based databases that include species of MFH and their biological activities, such as TCMIO and other user-friendly web-based databases.

In addition, oral administration of MFH leads to perturbations of hundreds, even thousands, of endogenous molecules that vary widely in stability and concentration. The current databases commonly store hundreds of metabolites, but they are limited when it comes to determining MFH-induced alterations in the metabolome of a complex biological system. Therefore, it is essential to expand databases for metabolites and overcome the obstacle to identification of metabolites in complex biological mixtures.

5 | CONCLUSIONS

MFH has been used for thousands of years; however, mechanisms of their health-promoting effects are largely unknown. Obscure functions and unclear therapeutic targets are the main limitations for clinical practice of MFH. Advances in genome sequencing technologies, for example, 16S rRNA sequencing and metagenomics, and metabolomics have yielded rich information for better understanding of the activities of MFH in host health. Up to now, among 109 MFH species approved by the Health and Fitness Commission, a large number of MFH has, however, not been investigated by state-of-the-art high-throughput omics technologies. Moreover, existing evidence is based on animal models, and randomized controlled trials with different populations are required to determine the true effects of MFH in humans. Most importantly, future researches are urgently required to investigate multi-components of MFH using polypharmacokinetic strategy, decipher the biology and functional activities of MFH using multiomics technology, identify personalized responses to MFH and key determinants, and to develop comprehensive databases. Focusing on these aspects will help identify the pharmacodynamic constituents of MFH and their therapeutic mechanisms of action, and efficacious MFH-based products, for example, foods for special medical purposes or dietary supplementation.

AUTHOR CONTRIBUTIONS

MMY, TY, MY, and LS conceived the review, collected literatures, and drafted and revised the manuscript. RXG, JK, PW, YHZ, and HFZ summarized and reviewed literatures. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENTS

This research did not include any human subjects and animal experiments.

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REFERENCES

Abbas, Z. K., Saggu, S., Sakeran, M. I., Zidan, N., Rehman, H., & Ansari, A. A. (2015). Phytochemical, antioxidant and mineral composition of hydroalcoholic extract of chicory (*Cichorium intybus* L.) leaves. *Saudi Journal of Biological Sciences 22*(3), 322–326.

Abula, K., Beckmann, J., He, Z., Cheong, C., Lu, F., & Gropel, P. (2020). Autonomy support in physical education promotes autonomous motivation towards leisure-time physical activity: Evidence from a sample of Chinese college students. *Health Promotion International*, *35*(1), e1–e10. https://doi.org/10.1093/heapro/day102

Ahmad, G., Masoodi, M. H., Tabassum, N., Mir, S. A., & Iqbal, M. J. (2020). In vivo hepatoprotective potential of extracts obtained from floral spikes of *Prunella vulgaris* L. *Journal of Ayurveda and Integrative Medicine*. https://doi.org/10.1016/j.jaim.2019.08.003

Ahmed, A. F., Shi, M., Liu, C., & Kang, W. (2019). Comparative analysis of antioxidant activities of essential oils and extracts of fennel (*Foeniculum vulgare* Mill.) seeds from Egypt and China. *Food Science and Human Wellness*, *8*(1), 67–72. https://doi.org/10.1016/j.fshw.2019.03.004

Ali, H., Yesmin, R., Satter, M. A., Habib, R., & Yeasmin, T. (2018). Antioxidant and antineoplastic activities of methanolic extract of *Kaempferia galanga* Linn. Rhizome against Ehrlich ascites carcinoma cells. *Journal of King Saud University - Science*, *30*(3), 386–392.

Allen, J. M., Mailing, L. J., Cohrs, J., Salmonson, C., Fryer, J. D., Nehra, V., … Woods, J. A. (2018). Exercise training-induced modification of the gut microbiota persists after microbiota colonization and attenuates the response to chemically-induced colitis in gnotobiotic mice. *Gut Microbes*, *9*(2), 115–130. https://doi.org/10.1080/19490976.2017.1372077

Alu'datt, M. H., Rababah, T., Alhamad, M. N., Al-Tawaha, A., Al-Tawaha, A. R., Gammoh, S., … Kubow, S. (2019). Herbal yield, nutritive composition, phenolic contents and antioxidant activity of purslane (*Portulaca oleracea* L.) grown in different soilless media in a closed system. *Industrial Crops and Products*, *141*, 111746. https://doi.org/10.1016/j.indcrop.2019.111746

Aly, S. E., Sabry, B. A., Shaheen, M. S., & Hathout, A. S. (2016). Assessment of antimycotoxigenic and antioxidant activity of star anise (*Illicium verum*) in vitro. *Journal of the Saudi Society of Agricultural Sciences*, *15*(1), 20–27. https://doi.org/10.1016/j.jssas.2014.05.003

Amanulla, A. M., & Sundaram, R. J. M. T. P. (2019). Green synthesis of TiO_2 nanoparticles using orange peel extract for antibacterial, cytotoxicity and humidity sensor applications. *Materials Today: Proceedings*, *8*, 323–331.

Bai, Y., Li, D., Zhou, T., Qin, N., Li, Z., Yu, Z., & Hua, H. (2016). Coumarins from the roots of *Angelica dahurica* with antioxidant and antiproliferative activities. *Journal of Functional Foods*, *20*, 453–462. https://doi.org/10.1016/j.jff.2015.11.018

Bala, A., Mukherjee, P. K., Braga, F. C., & Matsabisa, M. G. (2018). Comparative inhibition of MCF-7 breast cancer cell growth, invasion and angiogenesis by *Cannabis sativa* L. sourced from sixteen different geographic locations. *South African Journal of Botany*, *119*, 154–162. https://doi.org/10.1016/j.sajb.2018.07.022

Blacher, E., Levy, M., Tatirovsky, E., & Elinav, E. (2017). Microbiome-modulated metabolites at the interface of host immunity. *The Journal of Immunology*, *198*(2), 572–580. https://doi.org/10.4049/jimmunol.1601247

Botelho, J. R. S., Medeiros, N. G., Rodrigues, A. M., Araujo, M. E., Machado, N. T., Santos, A. G., … Junior, R. N. C. (2014). Black sesame (*Sesamum indicum* L.) seeds extracts by CO_2 supercritical fluid extraction: Isotherms of global yield, kinetics data, total fatty acids, phytosterols and neuroprotective effects. *The Journal of Supercritical Fluids*, *93*, 49–55.

Brial, F., Le Lay, A., Dumas, M. E., & Gauguier, D. (2018). Implication of gut microbiota metabolites in cardiovascular and metabolic diseases. *Cellular and Molecular Life Sciences*, *75*(21), 3977–3990. https://doi.org/10.1007/s00018-018-2901-1

Camacho, S., Michlig, S., De Senarclensbezencon, C., Meylan, J., Meystre, J., Pezzoli, M., … Coutre, J. L. (2015). Anti-obesity and anti-hyperglycemic effects of cinnamaldehyde via altered ghrelin secretion and functional impact on food intake and gastric emptying. *Scientific Reports*, *5*(1), 7919–7919.

Chang, C., Lin, C., Lu, C., Martel, J., Ko, Y., Ojcius, D. M., … Young, J. D. (2015). Ganoderma lucidum reduces obesity in mice by modulating the composition of the gut microbiota. *Nature Communications*, *6*(1), 7489–7489.

Chaudhary, A., Bag, S., Banerjee, P., & Chatterjee, J. (2019). Wound healing efficacy of Jamun honey in diabetic mice model through reepithelialization, collagen deposition and angiogenesis. *Journal of Traditional and Complementary Medicine*. https://doi.org/10.1016/j.jtcme.2019.10.002

Chen, C., You, L. J., Huang, Q., Fu, X., Zhang, B., Liu, R. H., & Li, C. (2018). Modulation of gut microbiota by mulberry fruit polysaccharide treatment of obese diabetic db/db mice. *Food & Function*, *9*(7), 3732–3742. https://doi.org/10.1039/c7fo01346a

Chen, C. Y. (2011). TCM Database@Taiwan: The world's largest traditional Chinese medicine database for drug screening in silico. *PLoS One*, *6*(1), e15939. https://doi.org/10.1371/journal.pone.0015939

Chen, D. L., Yang, X., Zheng, C. Q., Yang, J., Tang, X. C., Chen, J., … Xie, Y. Z. (2017). Extracts from Hericium erinaceus relieve inflammatory bowel disease by regulating immunity and gut microbiota. *Oncotarget*, *8*(49), 85838–85857. https://doi.org/10.18632/oncotarget.20689

Chen, F., Liu, S., Zhao, Z., Gao, W., Ma, Y., & Wang, X. (2020). Ultrasound pretreatment combined with microwave-assisted hydrodistillation of essential oils from *Perilla frutescens* (L.) Britt. leaves and its chemical composition and biological activity. *Industrial Crops and Products*, *143*, 111908.

Chen, F., Wen, Q., Jiang, J., Li, H. L., Tan, Y. F., Li, Y. H., & Zeng, N. J. J. O. E. (2016). Could the gut microbiota reconcile the oral bioavailability conundrum of traditional herbs. *Journal of Ethnopharmacology*, *179*, 253–264.

Chen, G., Fang, C., Chen, X., Wang, Z., Liu, M., & Kan, J. (2019). High-pressure ultrasonic-assisted extraction of polysaccharides from *Mentha haplocalyx*: Structure, functional and biological activities. *Industrial Crops and Products*, *130*, 273–284.

Chen, L.-F., Zhong, Y.-L., Luo, D., Liu, Z., Tang, W., Cheng, W., … Li, M.-M. (2019). Antiviral activity of ethanol extract of *Lophatherum gracile* against respiratory syncytial virus infection. *Journal of Ethnopharmacology*, *242*, 111575.

Chen, M., Ni, Y., Duan, H., Qiu, Y., Guo, C., Jiao, Y., … Jia, W. (2008) Mass spectrometry-based metabolic profiling of rat urine associated with general toxicity induced by the multiglycoside of *Tripterygium wilfordii* Hook. f. *Chemical Research in Toxicology*, *21*, 288–294.

Cheng, X., Shi, S., Su, J., Xu, Y., Ordaz-Ortiz, J. J., Li, N., … Wang, S. (2020). Structural characterization of a heteropolysaccharide from fruit of *Chaenomeles speciosa* (Sweet) Nakai and its antitumor activity. *Carbohydrate Polymers*, *236*, 116065. https://doi.org/10.1016/j.carbpol.2020.116065

Cheng, Z., Hu, M., Tao, J., Yang, H., Yan, P., An, G., & Wang, H. (2019). The protective effects of Chinese yam polysaccharide against obesity-induced insulin resistance. *Journal of Functional Foods*, *55*, 238–247. https://doi.org/10.1016/j.jff.2019.02.023

Chi, X., Wang, S., Baloch, Z., Zhang, H., Li, X., Zhang, Z., … Ma, K. (2019). Research progress on classical traditional Chinese medicine formula Lily Bulb and Rehmannia Decoction in the treatment of depression. *Biomedicine & Pharmacotherapy*, *112*, 108616. https://doi.org/10.1016/j.biopha.2019.108616

Choi, R.-Y., Woo, M.-J., Ham, J. R., & Lee, M.-K. (2017). Anti-steatotic and anti-inflammatory effects of *Hovenia dulcis* Thunb. extracts in chronic alcohol-fed rats. *Biomedicine & Pharmacotherapy*, *90*, 393–401. https://doi.org/10.1016/j.biopha.2017.03.077

Clavel, T., & Mapesa, J. O. (2013). Phenolics in human nutrition: Importance of the intestinal microbiome for isoflavone and lignan bioavailability. In K. G. Ramawat & J. M. Merillon (Eds.), *Natural* products (pp. 2433–2463). Amsterdam, the Netherlands: Elsevier.

Cloud, A. M. E., Vilcins, D., & McEwen, B. J. (2019). The effect of hawthorn (*Crataegus* spp.) on blood pressure: A systematic review. *Advances in Integrative Medicine*. https://doi.org/10.1016/j.aimed.2019.09.002

Commisso, M., Strazzer, P., Toffali, K., Stocchero, M., & Guzzo, F. (2013). Untargeted metabolomics: An emerging approach to determine the composition of herbal products. *Computational and Structural Biotechnology Journal*, *4*(5), e201301007. Retrieved from http://www.sciencedirect.com/science/article/pii/S2001037014600507. doi:https://doi.org/10.5936/csbj.201301007

Cui, H., Liu, Q., Tao, Y., Zhang, H., Zhang, L., & Ding, K. J. C. P. (2008). Structure and chain conformation of a (1→ 6)-α-D-glucan from the root of *Pueraria lobata* (Willd.) Ohwi and the antioxidant activity of its sulfated derivative. *Carbohydrate Polymers*,*74*(4), 771–778.

Cui, H., Zhang, C., Li, C., & Lin, L. (2018). Antimicrobial mechanism of clove oil on *Listeria monocytogenes*. *Food Control*, *94*, 140–146. doi:https://doi.org/10.1016/j.foodcont.2018.07.007

Cui, X., Wang, S., Cao, H., Guo, H., Li, Y., Xu, F., … Han, C. (2018). A review: The bioactivities and pharmacological applications of *Polygonatum sibiricum* polysaccharides. *Molecules*, *23*(5), 1170. https://doi.org/10.3390/molecules23051170

David, L., Moldovan, B., Baldea, I., Olteanu, D., Bolfa, P., Clichici, S., … Filip, G. A. (2020). Modulatory effects of *Cornus sanguinea* L. mediated green synthesized silver nanoparticles on oxidative stress, COX-2/NOS2 and NFkB/pNFkB expressions in experimental inflammation in Wistar rats. *Materials Science and Engineering: C*, *110*, 110709.

Deng, Y., He, K., Ye, X., Chen, X., Huang, J., Li, X., … Li, P. (2012). Saponin rich fractions from *Polygonatum odoratum* (Mill.) Druce with more potential hypoglycemic effects. *Journal of Ethnopharmacology*, *141*(1), 228–233. https://doi.org/10.1016/j.jep.2012.02.023

Diao, W.-R., Hu, Q.-P., Zhang, H., & Xu, J.-G. (2014). Chemical composition, antibacterial activity and mechanism of action of essential oil from seeds of fennel (*Foeniculum vulgare* Mill.). *Food Control*, *35*(1), 109–116. https://doi.org/10.1016/j.foodcont.2013.06.056

Diling, C., Yinrui, G., Longkai, Q., Xiaocui, T., Yadi, L., Jiaxin, F., … Dongdong, W. (2020). Metabolic regulation of *Ganoderma lucidum* extracts in high sugar and fat diet-induced obese mice by regulating the gut-brain axis. *Journal of Functional Foods*, *65* 103639.

Dong, W.-W., Xuan, F.-L., Zhong, F.-L., Jiang, J., Wu, S., Li, D., & Quan, L.-H. (2017). Comparative analysis of the rats' gut microbiota composition in animals with different ginsenosides metabolizing activity. *Journal of Agricultural and Food Chemistry*, *65*(2), 327–337. https://doi.org/10.1021/acs.jafc.6b04848

Dong, Z., Zhang, M., Li, H., Zhan, Q., Lai, F., & Wu, H. (2019). Structural characterization and immunomodulatory activity of a novel polysaccharide from *Pueraria lobata* (Willd.) Ohwi root. *International Journal of Biological Macromolecules*, *154*, 1556–1564.

Dou, H.-C., Chen, J.-Y., Ran, T.-F., & Jiang, W.-M. (2018). *Panax quinquefolius saponin* inhibits endoplasmic reticulum stress-mediated apoptosis and neurite injury and improves functional recovery in a rat spinal cord injury model. *Biomedicine & Pharmacotherapy*, *102*, 212–220.

Feng, J., Chang, X., Zhang, Y., Lu, R., Meng, X., Song, D., … Nie, G. (2019). Characterization of a polysaccharide HP-02 from Honeysuckle flowers and its immunoregulatory and anti-*Aeromonas hydrophila* effects in Cyprinus carpio L. *International Journal of Biological Macromolecules*, *140*, 477–483. https://doi.org/10.1016/j.ijbiomac.2019.08.041

Feng, L., Liu, X. M., Cao, F. R., Wang, L. S., Chen, Y. X., Pan, R. L., … Chang, Q. (2016). Anti-stress effects of ginseng total saponins on hindlimb-unloaded rats assessed by a metabolomics study. *Journal of Ethnopharmacology*, *188*, 39–47. https://doi.org/10.1016/j.jep.2016.04.028

Feng, L., Yue, X. F., Chen, Y. X., Liu, X. M., Wang, L. S., Cao, F. R., … Chang, Q. (2016). LC/MS-based metabolomics strategy to assess the amelioration effects of ginseng total saponins on memory deficiency induced by simulated microgravity. *Journal of Pharmaceutical and Biomedical Analysis*, *125*, 329–338. https://doi.org/10.1016/j.jpba.2016.04.002

Feng, W., Ao, H., Peng, C., & Yan, D. (2019). Gut microbiota, a new frontier to understand traditional Chinese medicines. *Pharmacological Research*, *142*, 176–191. https://doi.org/10.1016/j.phrs.2019.02.024

Feng, Y., Gao, X. X., Meng, M. D., Xue, H. H., & Qin, X. M. (2020). Multi-omics reveals the mechanisms of antidepressant-like effects of the low polarity fraction of Bupleuri Radix. *Journal of Ethnopharmacology*, *256*, 112806. https://doi.org/10.1016/j.jep.2020.112806

Ferrare, K., Bidel, L. P., Awwad, A., Poucheret, P., Cazals, G., Lazennec, F., … Tousch, D. (2018). Increase in insulin sensitivity by the association of chicoric acid and chlorogenic acid contained in a natural chicoric acid extract (NCRAE) of chicory (*Cichorium intybus* L.) for an antidiabetic effect. *Journal of Ethnopharmacology*, *215*, 241–248.

Frassinetti, S., Gabriele, M., Moccia, E., Longo, V., & Di Gioia, D. (2020). Antimicrobial and antibiofilm activity of *Cannabis sativa* L. seeds extract against *Staphylococcus aureus* and growth effects on probiotic *Lactobacillus* spp. *LWT*, *124*, 109149. https://doi.org/10.1016/j.lwt.2020.109149

Fu, Z., Han, L., Zhang, P., Mao, H., Zhang, H., Wang, Y., … Liu, E. (2020). Cistanche polysaccharides enhance echinacoside absorption in vivo and affect the gut microbiota. *International Journal of Biological Macromolecules*, *149*, 732–740.

Gao, S., Liu, J., Wang, M., Liu, Y., Meng, X., Zhang, T., … Sun, X. (2019). Exploring on the bioactive markers of Codonopsis Radix by correlation analysis between chemical constituents and pharmacological effects. *Journal of Ethnopharmacology*, *236*, 31–41.

Gao, Z., Zhong, W., Chen, K., Tang, P., & Guo, J. (2020). Chemical composition and anti-biofilm activity of essential oil from *Citrus medica* L. var. sarcodactylis Swingle against *Listeria monocytogenes*. *Industrial Crops and Products*, *144*, 112036. https://doi.org/10.1016/j.indcrop.2019.112036

Garg, N., Sethupathy, A., Tuwani, R., Nk, R., Dokania, S., Iyer, A., … Shukla, S. J. (2018). FlavorDB: A database of flavor molecules. *Nucleic Acids Research*, *46*(D1), D1210–D1216.

Ge, Q., Chen, L., Tang, M., Zhang, S., Liu, L., Gao, L., … Chen, K. (2018). Analysis of mulberry leaf components in the treatment of diabetes using network pharmacology. *European Journal of Pharmacology*, *833*, 50–62. https://doi.org/10.1016/j.ejphar.2018.05.021

Ghafoor, K., Al Juhaimi, F., Özcan, M. M., Uslu, N., Babiker, E. E., & Mohamed Ahmed, I. A. (2020). Total phenolics, total carotenoids, individual phenolics and antioxidant activity of ginger (*Zingiber officinale*) rhizome as affected by drying methods. *LWT*, *126*, 109354. https://doi.org/10.1016/j.lwt.2020.109354

Gong, X., Chen, N., Ren, K., Jia, J., Wei, K., Zhang, L., … Li, M. (2019). The fruits of *Siraitia grosvenorii*: A review of a Chinese food-medicine. *Frontiers in Pharmacology*, *10*, 1400. https://doi.org/10.3389/fphar.2019.01400

Gong, X., Ji, M., Xu, J., Zhang, C., & Li, M. (2020). Hypoglycemic effects of bioactive ingredients from medicine food homology and medicinal health food species used in China. *Critical Reviews in Food Science and Nutrition*, *60*, 1–24. https://doi.org/10.1080/10408398.2019.1634517

Guo, P., Deng, Q., & Lu, Q. J. (2019). Anti-alcoholic effects of honeys from different floral origins and their correlation with honey chemical compositions. *Food Chemistry*, *286*, 608–615.

Guo, R., Guo, X., Li, T., Fu, X., & Liu, R. H. (2017). Comparative assessment of phytochemical profiles, antioxidant and antiproliferative activities of Sea buckthorn (*Hippophaë rhamnoides* L.) berries. *Food Chemistry*, *221*, 997–1003. https://doi.org/10.1016/j.foodchem.2016.11.063

Guo, Z., Wu, X., Zhao, X., Fan, J., Lu, X., Wang, L., & Life, S. (2020). An edible antioxidant film of *Artemisia sphaerocephala* Krasch. gum with sophora japonica extract for oil packaging. *Food Packaging and Shelf Life*, *24*, 100460.

Gupta, A. D., Bansal, V. K., Babu, V., & Maithil, N. (2013). Chemistry, antioxidant and antimicrobial potential of nutmeg (*Myristica fragrans* Houtt). *Journal of Genetic Engineering and Biotechnology*, *11*(1), 25–31. https://doi.org/10.1016/j.jgeb.2012.12.001

Gurung, M., Li, Z., You, H., Rodrigues, R., Jump, D. B., Morgun, A., & Shulzhenko, N. (2020). Role of gut microbiota in type 2 diabetes pathophysiology. *EBioMedicine*, *51*, 102590. https://doi.org/10.1016/j.ebiom.2019.11.051

Ha, T. J., Lee, J. H., Lee, M.-H., Lee, B. W., Kwon, H. S., Park, C.-H., … Jang, D. S. (2012). Isolation and identification of phenolic compounds from the seeds of *Perilla frutescens* (L.) and their inhibitory activities against α-glucosidase and aldose reductase. *Food Chemistry*, *135*(3), 1397–1403.

Habtemariam, S. (2019). The chemical and pharmacological basis of cinnamon (*Cinnamomum* species) as potential therapy for type-2 diabetes and associated diseases. In S. Habtemariam (Ed.), *Medicinal foods as potential therapies for type-2 diabetes and associated diseases* (pp. 505–550). Cambridge, MA: Academic Press.

He, X., Li, H., Gao, R., Zhang, C., Liang, F., Sheng, Y., … Huang, K. (2019). Mulberry leaf aqueous extract ameliorates blood glucose and enhances energy expenditure in obese C57BL/6J mice. *Journal of Functional Foods*, *63*, 103505. https://doi.org/10.1016/j.jff.2019.103505

Hiramoto, K., Yamate, Y., Hirata, T., & Fujikawa, T. J. (2018). Preventive effects of *Eucommia ulmoides* leaf extract and its components on UVB-induced immunosuppression in mice. *Journal of Functional Foods*, *48*, 351–356.

Hou-Pan, S., Mei-Yan, Z., Xiao-Juan, C., Xin-Yi, C., Yi-Jing, Y., Ya-Sha, Z., … Jun, P. (2019). A network pharmacology approach to uncover the molecular targets and associated potential pathways of *Lycii Fructus* for the treatment of retinitis pigmentosa. *Digital Chinese Medicine*, *2*(3), 136–146. https://doi.org/10.1016/j.dcmed.2019.12.002

Hou, Y., & Jiang, J. G. (2013). Origin and concept of medicine food homology and its application in modern functional foods. *Food & Function*, *4*(12), 1727–1741. https://doi.org/10.1039/c3fo60295h

Hu, C., & Xu, G. (2014). Metabolomics and traditional Chinese medicine. *TrAC Trends in Analytical Chemistry*, *61*, 207–214. https://doi.org/10.1016/j.trac.2014.06.007

Hu, G.-S., Huang, C.-G., Zhang, Y., Xiao, W., & Jia, J.-M. (2017). Accumulation of biomass and four triterpenoids in two-stage cultured *Poria cocos* mycelia and diuretic activity in rats. *Chinese Journal of Natural Medicines*, *15*(4), 265–270. https://doi.org/10.1016/S1875-5364(17)30043-2

Hu, W., Jiang, Y., Xue, Q., Sun, F., Zhang, J., Zhou, J., … Shen, T. (2019). Structural characterisation and immunomodulatory activity of a polysaccharide isolated from lotus (*Nelumbo nucifera* Gaertn.) root residues. *Journal of Functional Foods*, *60*, 103457.

Hu, X. Q., Thakur, K., Chen, G. H., Hu, F., Zhang, J. G., Zhang, H. B., & Wei, Z. J. (2017). Metabolic effect of 1-deoxynojirimycin from mulberry leaves on db/db diabetic mice using liquid chromatography-mass spectrometry based metabolomics. *Journal of Agricultural and Food Chemistry*, *65*(23), 4658–4667. https://doi.org/10.1021/acs.jafc.7b01766

Huang, F., Zheng, X., Ma, X., Jiang, R., Zhou, W., Zhou, S., … Jia, W. (2019). Theabrownin from Pu-erh tea attenuates hypercholesterolemia via modulation of gut microbiota and bile acid metabolism. *Nature Communications*, *10*, 4971. https://doi.org/10.1038/s41467-019-12896-x

Huang, K., Dong, W., Liu, W., Yan, Y., Wan, P., Peng, Y., … Cao, Y. (2019). 2-O-beta-d-glucopyranosyl-l-ascorbic acid, an ascorbic acid derivative isolated from the fruits of *Lycium barbarum* L., modulates gut microbiota and palliates colitis in dextran sodium sulfate-induced colitis in mice. *Journal of Agricultural and Food Chemistry*, *67*(41), 11408–11419. https://doi.org/10.1021/acs.jafc.9b04411

Ibrahim, M. K., Mattar, Z. A., Abdel-Khalek, H. H., & Azzam, Y. M. (2017). Evaluation of antibacterial efficacy of anise wastes against some multidrug resistant bacterial isolates. *Journal of Radiation Research and Applied Sciences*, *10*(1), 34–43. https://doi.org/10.1016/j.jrras.2016.11.002

Ji, M. Y., Bo, A., Yang, M., Xu, J. F., Jiang, L. L., Zhou, B. C., & Li, M. H. (2020). The pharmacological effects and health benefits of *Platycodon grandifloras*—A medicine food homology species. *Foods*, *9*(2), 142. https://doi.org/10.3390/foods9020142

Ji, X., Hou, C., Yan, Y., Shi, M., & Liu, Y. (2020). Comparison of structural characterization and antioxidant activity of polysaccharides from jujube

(*Ziziphus jujuba* Mill.) fruit. *International Journal of Biological Macromolecules*, *149*, 1008–1018. https://doi.org/10.1016/j.ijbiomac.2020.02.018

Jia, W., Fan, T. P., Wang, X. N., & Xie, G. X. (2015). The polypharmacokinetics of herbal medicines. *Science*, *350*(6262), S76–S79.

Jiang, P., Meng, W., Shi, F., Chen, C., Sun, Y., & Jiao, L. (2020). Structural characteristics, antioxidant properties and antiaging activities of galactan produced by *Mentha haplocalyx* Briq. *Carbohydrate Polymers*, *234*, 115936.

Jiang, T., He, F., Han, S., Chen, C., Zhang, Y., & Che, H. (2019). Characterization of cAMP as an anti-allergic functional factor in Chinese jujube (*Ziziphus jujuba* Mill.). *Journal of Functional Foods*, *60*, 103414. https://doi.org/10.1016/j.jff.2019.06.016

Karimi-Nazari, E., Nadjarzadeh, A., Masoumi, R., Marzban, A., Mohajeri, S. A., Ramezani-Jolfaie, N., & Salehi-Abargouei, A. (2019). Effect of saffron (*Crocus sativus* L.) on lipid profile, glycemic indices and antioxidant status among overweight/obese prediabetic individuals: A double-blinded, randomized controlled trial. *Clinical Nutrition ESPEN*, *34*, 130–136.

Karimi, N., Ghanbarzadeh, B., Hajibonabi, F., Hojabri, Z., Ganbarov, K., Kafil, H. S., … Kamounah, F. S. (2019). Turmeric extract loaded nanoliposome as a potential antioxidant and antimicrobial nanocarrier for food applications. *Food Bioscience*, *29*, 110–117.

Kawabata, K., Yoshioka, Y., & Terao, J. (2019). Role of intestinal microbiota in the bioavailability and physiological functions of dietary polyphenols. *Molecules*, *24*(2), 370. https://doi.org/10.3390/molecules24020370

Kim, D., & Lee, J. (2019). Comparative evaluation of phenolic phytochemicals from perilla seeds of diverse species and screening for their tyrosinase inhibitory and antioxidant properties. *South African Journal of Botany*, *123*, 341–350.

Kim, G., & Kim, J. H. (2020). Impact of skeletal muscle mass on metabolic health. *Endocrinology and Metabolism*, *35*(1), 1–6. https://doi.org/10.3803/EnM.2020.35.1.1

Kim, J.-S., Kim, D., Kim, H.-J., & Jang, A. (2018). Protection effect of donkey hide gelatin hydrolysates on UVB-induced photoaging of human skin fibroblasts. *Process Biochemistry*, *67*, 118–126. https://doi.org/10.1016/j.procbio.2018.02.004

Kim, T.-W., Song, I.-B., Lee, H.-K., Lim, J.-H., Cho, E.-S., Son, H.-Y., … Yun, H.-I. (2012). Platycodin D, a triterpenoid sapoinin from *Platycodon grandiflorum*, ameliorates cisplatin-induced nephrotoxicity in mice. *Food and Chemical Toxicology*, *50*(12), 4254–4259.

Kim, Y.-A., Oh, S.-H., Lee, G.-H., Hoa, P. T., Jin, S. W., Chung, Y. C., … Jeong, H.-G. (2018). Platycodon grandiflorum-derived saponin attenuates the eccentric exercise-induced muscle damage. *Food and Chemical Toxicology*, *112*, 150–156.

Knight, R., Vrbanac, A., Taylor, B. C., Aksenov, A., Callewaert, C., Debelius, J., … Dorrestein, P. C. (2018). Best practices for analysing microbiomes. *Nature Reviews Microbiology*, *16*(7), 410–422. https://doi.org/10.1038/s41579-018-0029-9

Koropatkin, N. M., Cameron, E. A., & Martens, E. C. (2012). How glycan metabolism shapes the human gut microbiota. *Nature Reviews Microbiology*, *10*(5), 323–335.

Kowalska, K., Olejnik, A., Zielińska-Wasielica, J., & Olkowicz, M. (2019). Raspberry (*Rubus idaeus* L.) fruit extract decreases oxidation markers, improves lipid metabolism and reduces adipose tissue inflammation in hypertrophied 3T3-L1 adipocytes. *Journal of Functional Foods*, *62*, 103568.

Lan, K., & Jia, W. (2010). An integrated metabolomics and pharmacokinetics strategy for multi-component drugs evaluation. *Current Drug Metabolism*, *11*(1), 105–114. https://doi.org/10.2174/138920010791110926

Lan, K., Xie, G., & Jia, W. (2013). Towards polypharmacokinetics: Pharmacokinetics of multicomponent drugs and herbal medicines using a metabolomics approach. *Evidence-Based Complementary and Alternative Medicine*, *2013*, 819147. https://doi.org/10.1155/2013/819147

Lee, G.-H., Lee, H.-Y., Choi, M.-K., Choi, A.-H., Shin, T.-S., & Chae, H.-J. (2018). *Eucommia ulmoides* leaf (EUL) extract enhances NO production in ox-LDL-treated human endothelial cells. *Biomedicine & Pharmacotherapy*, *97*, 1164–1172.

Lee, S., Kim, D. H., Lee, C. H., Jung, J. W., Seo, Y. T., Jang, Y. P., & Ryu, J. H. (2010). Antidepressant-like activity of the aqueous extract of *Allium macrostemon* in mice. *Journal of Ethnopharmacology*, *131*(2), 386–395.

Li, C., Zhang, B., Liu, C., Zhou, H., Wang, X., Mai, K., … He, G. (2020). Effects of dietary raw or Enterococcus faecium fermented soybean meal on growth, antioxidant status, intestinal microbiota, morphology, and inflammatory responses in turbot (*Scophthalmus maximus* L.). *Fish & Shellfish Immunology*, *100*, 261–271.

Li, J., Liu, Y., Li, W., Wang, Z., Guo, P., Li, L., & Li, N. (2018). Metabolic profiling of the effects of ginsenoside Re in an Alzheimer's disease mouse model. *Behavioural Brain Research*, *337*, 160–172.

Li, K., He, Z., Wang, X., Pineda, M., Chen, R., Liu, H., … Guo, J. (2018). Apigenin C-glycosides of *Microcos paniculata* protects lipopolysaccharide induced apoptosis and inflammation in acute lung injury through TLR4 signaling pathway. *Free Radical Biology and Medicine*, *124*, 163–175.

Li, L., Huang, T., Lan, C., Ding, H., Yan, C., & Dou, Y. (2019). Protective effect of polysaccharide from *Sophora japonica* L. flower buds against UVB radiation in a human keratinocyte cell line (HaCaT cells). *Journal of Photochemistry and Photobiology B: Biology*, *191*, 135–142.

Li, L., Shi, M., Salerno, S., Tang, M., Guo, F., Liu, J., … Ma, L. (2019). Microbial and metabolomic remodeling by a formula of Sichuan dark tea improves hyperlipidemia in apoE-deficient mice. *PLoS One*, *14*(7), e0219010.

Li, L., Xu, J., Mu, Y., Han, L., Liu, R., Cai, Y., & Huang, X. (2015). Chemical characterization and anti-hyperglycaemic effects of polyphenol enriched longan (*Dimocarpus longan* Lour.) pericarp extracts. *Journal of Functional Foods*, *13*, 314–322. https://doi.org/10.1016/j.jff.2015.01.006

Li, Q., Liu, F., Liu, J., Liao, S., & Zou, Y. (2019). Mulberry leaf polyphenols and fiber induce synergistic antiobesity and display a modulation effect on gut microbiota and metabolites. *Nutrients*, *11*(5), 1017. https://doi.org/10.3390/nu11051017

Li, W., Sun, Y. N., Yan, X. T., Yang, S. Y., Song, S. B., Lee, Y. M., … Kim, Y. H. (2013). NF-κB inhibitory activity of sucrose fatty acid esters and related constituents from *Astragalus membranaceus*. *Journal of Agricultural and Food Chemistry*, *61*(29), 7081–7088.

Li, W., Zhang, X., Chen, R., Li, Y., Miao, J., Liu, G., … Cao, Y. (2020). HPLC fingerprint analysis of *Phyllanthus emblica* ethanol extract and their antioxidant and anti-inflammatory properties. *Journal of Ethnopharmacology*, *254*, 112740. https://doi.org/10.1016/j.jep.2020.112740

Li, Y., Yang, P., Luo, Y., Gao, B., Sun, J., Lu, W., … Yu, L. L. (2019). Chemical compositions of chrysanthemum teas and their anti-inflammatory and antioxidant properties. *Food Chemistry*, *286*, 8–16.

Lin, C.-M., Lin, R.-D., Chen, S.-T., Lin, Y.-P., Chiu, W.-T., Lin, J.-W., … Lee, M.-H. J. P. (2010). Neurocytoprotective effects of the bioactive constituents of *Pueraria thomsonii* in 6-hydroxydopamine (6-OHDA)-treated nerve growth factor (NGF)-differentiated PC12 cells. *Phytochemistry*, *71*(17-18), 2147–2156.

Lin, H., Liu, Z., Pi, Z., Men, L., Chen, W., & Liu, Z. (2018). Urinary metabolomic study of the antagonistic effect of P. ginseng in rats with estrogen decline using ultra performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. *Food & Function*, *9*(3), 1444–1453. https://doi.org/10.1039/c7fo01680h

Lin, H., Pi, Z., Men, L., Chen, W., Liu, Z., & Liu, Z. (2016). Urinary metabonomic study of *Panax ginseng* in deficiency of vital energy rat using ultra performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. *Journal of Ethnopharmacology*, *184*, 10–17. https://doi.org/10.1016/j.jep.2016.02.031

Lin, J.-N., Lee, P.-S., Mei, N.-W., Cheng, A.-C., Yu, R.-C., & Pan, M.-H. (2019). Effects of ginseng dietary supplementation on a high-fat diet-induced obesity in C57BL/6 Mice. *Food Science and Human Wellness*, *8*, 344–350.

Lin, L., Luo, L., Zhong, M., Xie, T., Liu, Y., Li, H., & Ni, J. (2019). Gut microbiota: A new angle for traditional herbal medicine research. *RSC Advances*, *9*(30), 17457–17472. https://doi.org/10.1039/c9ra01838g

Lin, L. L., Wang, Y. H., Lai, C. Y., Chau, C. L., Su, G. C., Yang, C. Y., … Juan, H. F. (2012). Systems biology of meridians, acupoints, and Chinese herbs in disease. *Evidence-Based Complementary and Alternative Medicine*, *2012*, 372670. https://doi.org/10.1155/2012/372670

Lin, T., Liu, Y., Lai, C., Yang, T., Xie, J., & Zhang, Y. (2018). The effect of ultrasound assisted extraction on structural composition, antioxidant activity and immunoregulation of polysaccharides from *Ziziphus jujuba* Mill var. spinosa seeds. *Industrial Crops and Products*, *125*, 150–159. https://doi.org/10.1016/j.indcrop.2018.08.078

Lis, B., Jedrejek, D., Moldoch, J., Stochmal, A., & Olas, B. (2019). The anti-oxidative and hemostasis-related multifunctionality of L-chicoric acid, the main component of dandelion: An in vitro study of its cellular safety, antioxidant and anti-platelet properties, and effect on coagulation. *Journal of Functional Foods*, *62*, 103524.

Liu, A., Zhao, X., Li, H., Liu, Z., Liu, B., Mao, X., … Jia, Y. (2014). 5-Hydroxymethylfurfural, an antioxidant agent from *Alpinia oxyphylla* Miq. improves cognitive impairment in Aβ1-42 mouse model of Alzheimer's disease. *International Immunopharmacology*, *23*(2), 719–725.

Liu, C., Liu, Q., Sun, J., Jiang, B., & Yan, J. (2014). Extraction of water-soluble polysaccharide and the antioxidant activity from Semen cassiae. *Journal of Food and Drug Analysis*, *22*(4), 492–499. https://doi.org/10.1016/j.jfda.2014.01.027

Liu, F., Deng, C., Cao, W., Zeng, G., Deng, X., & Zhou, Y. J. B. (2017). Phytochemicals of *Pogostemon cablin* (Blanco) Benth. aqueous extract: Their xanthine oxidase inhibitory activities. *Biomedicine & Pharmacotherapy*, *89*, 544–548.

Liu, L., Tang, D., Zhao, H., Xin, X., & Aisa, H. A. (2017). Hypoglycemic effect of the polyphenols rich extract from *Rose rugosa* Thunb on high fat diet and STZ induced diabetic rats. *Journal of Ethnopharmacology*, *200*, 174–181.

Liu, M., Tan, J., He, Z., He, X., Hou, D.-X., He, J., & Wu, S. (2018). Inhibitory effect of blue honeysuckle extract on high-fat-diet-induced fatty liver in mice. *Animal Nutrition*, *4*(3), 288–293. https://doi.org/10.1016/j.aninu.2018.06.001

Liu, Y., Liu, W., Li, J., Tang, S., Wang, M., Huang, W., … Gao, X. (2019). A polysaccharide extracted from *Astragalus membranaceus* residue improves cognitive dysfunction by altering gut microbiota in diabetic mice. *Carbohydrate Polymers*, *205*, 500–512.

Liu, Y., Yang, L., Zhang, Y., Liu, X., Wu, Z., Gilbert, R. G., … Wang, K. (2020). Dendrobium officinale polysaccharide ameliorates diabetic hepatic glucose metabolism via glucagon-mediated signaling pathways and modifying liver-glycogen structure. *Journal of Ethnopharmacology*, *248*, 112308.

Liu, Z., Cai, C., Du, J., Liu, B., Cui, L., Fan, X., … Xie, L. (2020). TCMIO: A comprehensive database of traditional Chinese medicine on immuno-oncology. *Frontiers in Pharmacology*, *11*, 439. https://doi.org/10.3389/fphar.2020.00439

Liu, Z., Guo, F., Wang, Y., Li, C., Zhang, X., Li, H., … He, F. (2016). BATMAN-TCM: A bioinformatics analysis tool for molecular mechANism of traditional Chinese medicine. *Scientific Reports*, *6*, 21146. https://doi.org/10.1038/srep21146

Lori, G., Cecchi, L., Mulinacci, N., Melani, F., Caselli, A., Cirri, P., … Paoli, P. (2019). Honey extracts inhibit PTP1B, upregulate insulin receptor expression, and enhance glucose uptake in human HepG2 cells. *Biomedicine & Pharmacotherapy*, *113*, 108752.

Lu, K.-H., Lee, H.-Y., Chu, Y.-L., Ho, C.-T., & Sheen, L.-Y. (2019). Bitter orange peel extract induces endoplasmic reticulum-mediated autophagy in human hepatoma cells. *Journal of Functional Foods*, *60*, 103404.

Lu, X., Yuan, Z.-Y., Yan, X.-J., Lei, F., Jiang, J.-F., Yu, X., … Du, L.-J. (2016). Effects of *Angelica dahurica* on obesity and fatty liver in mice. *Chinese Journal of Natural Medicines*, *14*(9), 641–652. https://doi.org/10.1016/S1875-5364(16)30076-0

Luo, Z., Guo, Z., Xiao, T., Liu, H., Su, G., & Zhao, Y. (2019). Enrichment of total flavones and licochalcone A from licorice residues and its hypoglycemic activity. *Journal of Chromatography B*, *1114–1115*, 134–145. https://doi.org/10.1016/j.jchromb.2019.01.026

Ma, F.-W., Kong, S.-Y., Tan, H.-S., Wu, R., Xia, B., Zhou, Y., & Xu, H.-X. (2016). Structural characterization and antiviral effect of a novel polysaccharide PSP-2B from *Prunellae Spica*. *Carbohydrate Polymers*, *152*, 699–709.

Maruvada, P., Lampe, J. W., Wishart, D. S., Barupal, D., Chester, D. N., Dodd, D., … Zeisel, S. H. (2020). Perspective: Dietary biomarkers of intake and exposure—Exploration with omics approaches. *Advances in Nutrition*, *11*(2), 200–215. https://doi.org/10.1093/advances/nmz075

Menghini, L., Leporini, L., Vecchiotti, G., Locatelli, M., Carradori, S., Ferrante, C., … Leone, S. (2018). *Crocus sativus* L. stigmas and byproducts: Qualitative fingerprint, antioxidant potentials and enzyme inhibitory activities. *Food Research International*, *109*, 91–98.

Menichini, F., Loizzo, M. R., Bonesi, M., Conforti, F., De Luca, D., Statti, G. A., … Tundis, R. (2011). Phytochemical profile, antioxidant, anti-inflammatory and hypoglycemic potential of hydroalcoholic extracts from *Citrus medica* L. cv Diamante flowers, leaves and fruits at two maturity stages. *Food and Chemical Toxicology*, *49*(7), 1549–1555. https://doi.org/10.1016/j.fct.2011.03.048

Miao, L., Tao, H., Peng, Y., Wang, S., Zhong, Z., El-Seedi, H., … Xiao, J. (2019). The anti-inflammatory potential of *Portulaca oleracea* L. (purslane) extract by partial suppression on NF-κB and MAPK activation. *Food Chemistry*, *290*, 239–245. https://doi.org/10.1016/j.foodchem.2019.04.005

Min, D., Cheng, P., & Fenghui, S. (2016). Anti-infectious efficacy of essential oil from Caoguo (*Fructus Tsaoko*). *Journal of Traditional Chinese Medicine*, *36*(6), 799–804.

Mohammadi, H., Hadi, A., Kord-Varkaneh, H., Arab, A., Afshari, M., Ferguson, A. J. R., & Ghaedi, E. (2019). Effects of ginseng supplementation on selected markers of inflammation: A systematic review and meta-analysis. *Phytotherapy Research*, *33*(8), 1991–2001. https://doi.org/10.1002/ptr.6399

Moon, S. W., Ahn, C.-B., Oh, Y., & Je, J.-Y. (2019). Lotus (*Nelumbo nucifera*) seed protein isolate exerts anti-inflammatory and antioxidant effects in LPS-stimulated RAW264.7 macrophages via inhibiting NF-κB and MAPK pathways, and upregulating catalase activity. *International Journal of Biological Macromolecules*, *134*, 791–797.

Mostafa, D. M., Abd El-Alim, S. H., Asfour, M. H., Al-Okbi, S. Y., Mohamed, D. A., & Awad, G. (2015). Transdermal nanoemulsions of *Foeniculum vulgare* Mill. essential oil: Preparation, characterization and evaluation of antidiabetic potential. *Journal of Drug Delivery Science and Technology*, *29*, 99–106. https://doi.org/10.1016/j.jddst.2015.06.021

Nafis, A., Kasrati, A., Jamali, C. A., Mezrioui, N., Setzer, W., Abbad, A., & Hassani, L. (2019). Antioxidant activity and evidence for synergism of *Cannabis sativa* (L.) essential oil with antimicrobial standards. *Industrial Crops and Products*, *137*, 396–400. https://doi.org/10.1016/j.indcrop.2019.05.032

Oppong, M. B., Li, Y., Banahene, P. O., Fang, S.-M., & Qiu, F. (2018). Ethnopharmacology, phytochemistry, and pharmacology of *Sterculia lychnophora* Hance (Pangdahai). *Chinese Journal of Natural Medicines*, *16*(10), 721–731. https://doi.org/10.1016/S1875-5364(18)30112-2

Padmashree, A., Roopa, N., Semwal, A. D., Sharma, G. K., Agathian, G., & Bawa, A. S. (2007). Star-anise (*Illicium verum*) and black caraway (*Carum nigrum*) as natural antioxidants. *Food Chemistry*, *104*(1), 59–66. https://doi.org/10.1016/j.foodchem.2006.10.074

Palmnas, M., Brunius, C., Shi, L., Rostgaard-Hansen, A., Torres, N. E., Gonzalez-Dominguez, R., … Landberg, R. (2020). Perspective: Metabotyping-A potential personalized nutrition strategy for precision prevention of cardiometabolic disease. *Advances in Nutrition*, *11*, 524–532. https://doi.org/10.1093/advances/nmz121

Pan, H. D., Zheng, Y. F., Liu, Z. Q., Yuan, Z. W., Ren, R. T., Zhou, H., … Liu, L. (2019). Deciphering the pharmacological mechanism of Guan-Jie-Kang in treating rat adjuvant-induced arthritis using omics analysis. *Frontiers of Medicine*, *13*(5), 564–574. https://doi.org/10.1007/s11684-018-0676-2

Pan, M.-H., Yang, J.-R., Tsai, M.-L., Sang, S., & Ho, C.-T. (2009). Anti-inflammatory effect of *Momordica grosvenori* Swingle extract through suppressed LPS-induced upregulation of iNOS and COX-2 in murine macrophages. *Journal of Functional Foods*, *1*(2), 145–152. doi:https://doi.org/10.1016/j.jff.2009.01.003

Pan, Y., Wang, K., Huang, S., Wang, H., Mu, X., He, C., … Huang, F. (2008). Antioxidant activity of microwave-assisted extract of longan (*Dimocarpus Longan* Lour.) peel. *Food Chemistry*, *106*(3), 1264–1270. https://doi.org/10.1016/j.foodchem.2007.07.033

Peng, B., Yang, J., Huang, W., Peng, D., Bi, S., Song, L., … Yu, R. (2019). Structural characterization and immunoregulatory activity of a novel heteropolysaccharide from bergamot (*Citrus medica* L. var. *sarcodactylis*) by alkali extraction. *Industrial Crops and Products*, *140*, 111617. https://doi.org/10.1016/j.indcrop.2019.111617

Peterson, C. T., Vaughn, A. R., Sharma, V., Chopra, D., Mills, P. J., Peterson, S. N., & Sivamani, R. K. (2018). Effects of turmeric and curcumin dietary supplementation on human gut microbiota: A double-blind, randomized, placebo-controlled pilot study. *Journal of Evidence-Based Integrative Medicine*, *23*. https://doi.org/10.1177/2515690x18790725

Phimarn, W., Wichaiyo, K., Silpsavikul, K., Sungthong, B., & Saramunee, K. (2017). A meta-analysis of efficacy of *Morus alba* Linn. to improve blood glucose and lipid profile. *European Journal of Nutrition*, *56*(4), 1509–1521. https://doi.org/10.1007/s00394-016-1197-x

Ping, W., Tinglan, Z., Guohua, Y., Mengjie, L., Jin, S., Jiaqi, Z., … Hongjun, Y. (2019). Poly-pharmacokinetic strategy-delineated metabolic fate of bioactive compounds in a traditional Chinese medicine formula, Yuanhu Zhitong tablets, using parallel reaction monitoring mode. *Phytomedicine*, *53*, 53–61. Retrieved from http://www.sciencedirect.com/science/article/pii/S0944711318303076.

Pino, A. M., Valladares, L. E., Palma, M. A., Mancilla, A. M., & Albala, C. (2000). Dietary isoflavones affect sex hormone-binding globulin levels in postmenopausal women. *Journal of Clinical Endocrinology & Metabolism*, *85*(8), 2797–2800.

Pocasap, P., Weerapreeyakul, N., Tanthanuch, W., & Thumanu, K. (2017). Sulforaphene in *Raphanus sativus* L. var. *caudatus* Alef increased in late-bolting stage as well as anticancer activity. *Asian Pacific Journal of Tropical Biomedicine*, *7*(11), 998–1004.

Qu, D., Sun, W., Liu, M., Liu, Y., Zhou, J., & Chen, Y. (2016). Bitargeted microemulsions based on coix seed ingredients for enhanced hepatic tumor delivery and synergistic therapy. *International Journal of Pharmaceutics*, *503*(1-2), 90–101.

Quintana, S. E., Cueva, C., Villanueva-Bermejo, D., Moreno-Arribas, M. V., Fornari, T., & García-Risco, M. R. (2019). Antioxidant and antimicrobial assessment of licorice supercritical extracts. *Industrial Crops and Products*, *139*, 111496. https://doi.org/10.1016/j.indcrop.2019.111496

Radenkovs, V., Püssa, T., Juhnevica-Radenkova, K., Anton, D., & Seglina, D. (2018). Phytochemical characterization and antimicrobial evaluation of young leaf/shoot and press cake extracts from *Hippophae rhamnoides* L. *Food Bioscience*, *24*, 56–66. https://doi.org/10.1016/j.fbio.2018.05.010

Rangkadilok, N., Tongchusak, S., Boonhok, R., Chaiyaroj, S. C., Junyaprasert, V. B., Buajeeb, W., … Satayavivad, J. (2012). In vitro antifungal activities of longan (*Dimocarpus longan* Lour.) seed extract. *Fitoterapia*, *83*(3), 545–553. https://doi.org/10.1016/j.fitote.2011.12.023

Ren, F., Li, J., Yuan, X., Wang, Y., Wu, K., Kang, L., … Yuan, Z. (2019). Dandelion polysaccharides exert anticancer effect on Hepatocellular carcinoma by inhibiting PI3K/AKT/mTOR pathway and enhancing immune response. *Journal of Functional Foods*, *55*, 263–274.

Riedl, A., Gieger, C., Hauner, H., Daniel, H., & Linseisen, J. (2017). Metabotyping and its application in targeted nutrition: An overview. *British Journal of Nutrition*, *117*(12), 1631–1644.

Saeed, M. K., Deng, Y., Dai, R., Li, W., Yu, Y., & Iqbal, Z. (2010). Appraisal of antinociceptive and anti-inflammatory potential of extract and fractions from the leaves of *Torreya grandis* Fort Ex. Lindl. *Journal of Ethnopharmacology*, *127*(2), 414–418.

Sakurai, T., Odamaki, T., & Xiao, J. Z. (2019). Production of indole-3-lactic acid by *Bifidobacterium* strains isolated fromhuman infants. *Microorganisms*, *7*(9), 340. https://doi.org/10.3390/microorganisms7090340

Sarfraz, M., Khaliq, T., Khan, J. A., & Aslam, B. (2017). Effect of aqueous extract of black pepper and ajwa seed on liver enzymes in alloxan-induced diabetic Wister albino rats. *Saudi Pharmaceutical Journal*, *25*(4), 449–452.

Seif, M. M., Madboli, A.-N., Marrez, D. A., & Aboulthana, W. M. K. (2019). Hepato-renal protective effects of Egyptian purslane extract against experimental cadmium toxicity in rats with special emphasis on the functional and histopathological changes. *Toxicology Reports*, *6*, 625–631. https://doi.org/10.1016/j.toxrep.2019.06.013

Shi, J., Cao, B., Wang, X.-W., Aa, J.-Y., Duan, J.-A., Zhu, X.-X., … Liu, C.-X. (2016). Metabolomics and its application to the evaluation of the efficacy and toxicity of traditional Chinese herb medicines. *Journal of Chromatography B*, *1026*, 204–216. https://doi.org/10.1016/j.jchromb.2015.10.014

Shi, L.-K., Mao, J.-H., Zheng, L., Zhao, C.-W., Jin, Q.-Z., & Wang, X.-G. (2018). Chemical characterization and free radical scavenging capacity of oils obtained from *Torreya grandis* Fort. ex. Lindl. and *Torreya grandis* Fort. var. Merrillii: A comparative study using chemometrics. *Industrial Crops and Products*, *115*, 250–260.

Shi, L., Brunius, C., Bergdahl, I. A., Johansson, I., Rolandsson, O., Donat Vargas, C., … Landberg, R. (2019). Joint analysis of metabolite markers of fish intake and persistent organic pollutants in relation to type 2 diabetes risk in Swedish adults. *Journal of Nutrition*, *149*(8), 1413–1423. https://doi.org/10.1093/jn/nxz068

Shi, L., Brunius, C., Johansson, I., Bergdahl, I. A., Lindahl, B., Hanhineva, K., & Landberg, R. (2018). Plasma metabolites associated with healthy Nordic dietary indexes and risk of type 2 diabetes-a nested case-control study in a Swedish population. *American Journal of Clinical Nutrition*, *108*(3), 564–575. https://doi.org/10.1093/ajcn/nqy145

Shi, L., Brunius, C., Lehtonen, M., Auriola, S., Bergdahl, I. A., Rolandsson, O., … Landberg, R. (2018). Plasma metabolites associated with type 2 diabetes in a Swedish population: A case-control study nested in a prospective cohort. *Diabetologia*, *61*(4), 849–861. https://doi.org/10.1007/s00125-017-4521-y

Shingnaisui, K., Dey, T., Manna, P., & Kalita, J. (2018). Therapeutic potentials of *Houttuynia cordata* Thunb. against inflammation and oxidative stress: A review. *Journal of Ethnopharmacology*, *220*, 35–43. https://doi.org/10.1016/j.jep.2018.03.038

Shukla, S. K., Murali, N. S., & Brilliant, M. H. (2015). Personalized medicine going precise: From genomics to microbiomics. *Trends in Molecular Medicine*, *21*(8), 461–462. https://doi.org/10.1016/j.molmed.2015.06.002

Sina, Z., Nasrollahzadeh, J., Shokraei, S., Rismanchi, M., & Foroughi, F. (2018). Black and red peppers attenuates plasma and lipopolysaccharide-induced splenocytes production of tumor necrosis factor-α in mice fed a high-fat, high-sucrose diet. *Journal of Functional Foods*, *50*, 158–163.

Song, M.-Y., Kim, B.-S., & Kim, H. (2014). Influence of Panax ginseng on obesity and gut microbiota in obese middle-aged Korean women. *Journal of Ginseng Research*, *38*(2), 106–115. https://doi.org/10.1016/j.jgr.2013.12.004

Song, Q., Zhang, A.-H., Yan, G.-L., Liu, L., & Wang, X.-J. (2017). Technological advances in current metabolomics and its application in tradition Chinese medicine. *RSC Advances*, *7*(84), 53516–53524. https://doi.org/10.1039/c7ra02056b

Srinivasan, P., Vijayakumar, S., Kothandaraman, S., & Palani, M. (2018). Anti-diabetic activity of quercetin extracted from *Phyllanthus emblica* L. fruit: In silico and in vivo approaches. *Journal of Pharmaceutical Analysis*, *8*(2), 109–118. https://doi.org/10.1016/j.jpha.2017.10.005

Su, H.-G., Peng, X.-R., Shi, Q.-Q., Huang, Y.-J., Zhou, L., & Qiu, M.-H. (2020). Lanostane triterpenoids with anti-inflammatory activities from *Ganoderma lucidum*. *Phytochemistry*, *173*, 112256.

Su, H., Bao, T., Xie, L., Xu, Y., & Chen, W. (2020). Transcriptome profiling reveals the antihyperglycemic mechanism of pelargonidin-3-O-glucoside extracted from wild raspberry. *Journal of Functional Foods*, *64*, 103657.

Su, H., Chen, J., Miao, S., Deng, K., Liu, J., Zeng, S., … Toxicology, C. (2019). Lotus seed oligosaccharides at various dosages with prebiotic activity regulate gut microbiota and relieve constipation in mice. *Food and Chemical Toxicology*, *134*, 110838.

Su, L., Yin, J.-J., Charles, D., Zhou, K., Moore, J., & Yu, L. (2007). Total phenolic contents, chelating capacities, and radical-scavenging properties of black peppercorn, nutmeg, rosehip, cinnamon and oregano leaf. *Food Chemistry*, *100*(3), 990–997. https://doi.org/10.1016/j.foodchem.2005.10.058

Sun, L., Zong, S.-B., Li, J.-C., Lv, Y.-Z., Liu, L.-N., Wang, Z.-Z., … Xiao, W. (2016). The essential oil from the twigs of *Cinnamomum cassia* Presl alleviates pain and inflammation in mice. *Journal of Ethnopharmacology*, *194*, 904–912. https://doi.org/10.1016/j.jep.2016.10.064

Suryakumar, G., & Gupta, A. (2011). Medicinal and therapeutic potential of Sea buckthorn (*Hippophae rhamnoides* L.). *Journal of Ethnopharmacology*, *138*(2), 268–278. https://doi.org/10.1016/j.jep.2011.09.024

Takasaki, M., Konoshima, T., Murata, Y., Sugiura, M., Nishino, H., Tokuda, H., … Yamasaki, K. (2003). Anticarcinogenic activity of natural sweeteners, cucurbitane glycosides, from *Momordica grosvenori*. *Cancer Letters*, *198*(1), 37–42. https://doi.org/10.1016/S0304-3835(03)00285-4

Tang, R., Luo, J., Wang, W., Liu, D., Wang, G., & Guo, X. (2019). Rutin's natural source Flos Sophorae as potential antioxidant and improver of fungal community in Chinese sausages. *LWT*, *101*, 435–443.

Tang, X., Xu, C., Yagiz, Y., Simonne, A., & Marshall, M. R. (2018). Phytochemical profiles, and antimicrobial and antioxidant activities of greater galangal [*Alpinia galanga* (Linn.) Swartz.] flowers. *Food Chemistry*, *255*, 300–308.

Tao, S., Lei, Z., Huang, K., Li, Y., Ren, Z., Zhang, X., … Chen, H. (2019). Structural characterization and immunomodulatory activity of two novel polysaccharides derived from the stem of Dendrobium officinale Kimura et Migo. *Journal of Functional Foods*, *57*, 121–134.

Tao, W., Hong-Guo, S., Yong-Li, H., Peng-Ling, L., & Yan-Ming, W. (2016). Urine metabonomic study for blood-replenishing mechanism of *Angelica sinensis* in a blood-deficient mouse model. *Chinese Journal of Natural Medicines*, *14*(3), 210–219.

Teng, H., & Chen, L. (2019). Polyphenols and bioavailability: An update. *Critical Reviews in Food Science and Nutrition*, *59*(13), 2040–2051. https://doi.org/10.1080/10408398.2018.1437023

Thaipitakwong, T., Supasyndh, O., Rasmi, Y., & Aramwit, P. (2020). A randomized controlled study of dose-finding, efficacy, and safety of mulberry leaves on glycemic profiles in obese persons with borderline diabetes. *Complementary Therapies in Medicine*, *49*, 102292. https://doi.org/10.1016/j.ctim.2019.102292

Thatiparthi, J., Dodoala, S., Koganti, B., & Kvsrg, P. (2019). Barley grass juice (*Hordeum vulgare* L.) inhibits obesity and improves lipid profile in high fat diet-induced rat model. *Journal of Ethnopharmacology*, *238*, 111843. https://doi.org/10.1016/j.jep.2019.111843

Tian, S., Li, X.-M., Bai, M., Wu, Y.-Y., & Wei, Z.-Z. (2019). Study on neuroendocrine-immune function of Phenylethanoid Glycosides of Desertliving Cistanche herb in perimenopausal rat model. *Journal of Ethnopharmacology*, *238*, 111884.

Tu, J., Shi, D., Wen, L., Jiang, Y., Zhao, Y., Yang, J., … Yang, B. (2019). Identification of moracin N in mulberry leaf and evaluation of antioxidant activity. *Food and Chemical Toxicology*, *132*, 110730. https://doi.org/10.1016/j.fct.2019.110730

Wang, B., Zhang, Y., Huang, J., Dong, L., Li, T., & Fu, X. (2017). Anti-inflammatory activity and chemical composition of dichloromethane extract from *Piper nigrum* and *P. longum* on permanent focal cerebral ischemia injury in rats. *Revista Brasileira de Farmacognosia*, *27*(3), 369–374.

Wang, C., Lin, H., Yang, N., Wang, H., Zhao, Y., Li, P., … Wang, F. (2019). Effects of *Platycodins folium* on depression in mice based on a UPLC-Q/TOF-MS serum assay and hippocampus metabolomics. *Molecules*, *24*(9), 1712. https://doi.org/10.3390/molecules24091712

Wang, C. Z., Yu, C., Wen, X. D., Chen, L., Zhang, C. F., Calway, T., … Yuan, C. S. (2016). American ginseng attenuates colitis-associated colon carcinogenesis in mice: Impact on gut microbiota and metabolomics. *Cancer Prevention Research*, *9*(10), 803–811. https://doi.org/10.1158/1940-6207.Capr-15-0372

Wang, F., You, H., Guo, Y., Wei, Y., Xia, P., Yang, Z., … Yang, D. (2020). Essential oils from three kinds of fingered citrons and their antibacterial activities. *Industrial Crops and Products*, *147*, 112172. https://doi.org/10.1016/j.indcrop.2020.112172

Wang, G. W., Bao, B., Han, Z. Q., Han, Q. Y., & Yang, X. L. (2016). Metabolic profile of Fructus Gardeniae in human plasma and urine using ultra high-performance liquid chromatography coupled with high-resolution LTQ-orbitrap mass spectrometry. *Xenobiotica*, *46*(10), 901–912. https://doi.org/10.3109/00498254.2015.1132793

Wang, H.-Y., & Zhang, Y.-Q. (2019). The main active constituents and detoxification process of *Ginkgo biloba* seeds and their potential use in functional health foods. *Journal of Food Composition and Analysis*, *83*, 103247. https://doi.org/10.1016/j.jfca.2019.103247

Wang, H., Gao, T., Du, Y., Yang, H., Wei, L., Bi, H., & Ni, W. (2015). Anticancer and immunostimulating activities of a novel homogalacturonan from *Hippophae rhamnoides* L. berry. *Carbohydrate Polymers*, *131*, 288–296. https://doi.org/10.1016/j.carbpol.2015.06.021

Wang, H., Yang, Z., Ying, G., Yang, M., Nian, Y., Wei, F., & Kong, W. (2018). Antifungal evaluation of plant essential oils and their major components against toxigenic fungi. *Industrial Crops and Products*, *120*, 180–186. https://doi.org/10.1016/j.indcrop.2018.04.053

Wang, J., Li, D., Wang, P., Hu, X., & Chen, F. (2019). Ginger prevents obesity through regulation of energy metabolism and activation of browning in high-fat diet-induced obese mice. *The Journal of Nutritional Biochemistry*, *70*, 105–115. https://doi.org/10.1016/j.jnutbio.2019.05.001

Wang, M., Lamers, R. J. A., Korthout, H. A., van Nesselrooij, J. H., Witkamp, R. F., van der Heijden, R., … van der Greef, J. (2005). Metabolomics in the context of systems biology: Bridging traditional Chinese medicine and molecular pharmacology. *Phytotherapy Research*, *19*(3), 173–182.

Wang, P., Li, K., Tao, Y., Li, D. F., Zhang, Y., Xu, H. Y., & Yang, H. J. (2019). TCM-ADMEpred: A novel strategy for poly-pharmacokinetics prediction of traditional Chinese medicine based on single constituent pharmacokinetics, structural similarity, and mathematical modeling. *Journal of Ethnopharmacology*, *236*, 277–287. https://doi.org/10.1016/j.jep.2018.07.008

Wang, Q., Zhou, J., Xiang, Z., Tong, Q., Pan, J., Wan, L., & Chen, J. (2019). Anti-diabetic and renoprotective effects of *Cassiae semen* extract in the streptozotocin-induced diabetic rats. *Journal of Ethnopharmacology*, *239*, 111904. https://doi.org/10.1016/j.jep.2019.111904

Wang, S., Zhao, Y., Zhang, J., Huang, X., Wang, Y., Xu, X., … Liu, L. (2015). Antidiarrheal effect of *Alpinia oxyphylla* Miq. (Zingiberaceae) in experimental mice and its possible mechanism of action. *Journal of Ethnopharmacology*, *168*, 182–190.

Wang, X.-F., Li, H., Jiang, K., Wang, Q.-Q., Zheng, Y.-H., Tang, W., & Tan, C.-H. (2018). Anti-inflammatory constituents from Perilla frutescens on lipopolysaccharide-stimulated RAW264.7 cells. *Fitoterapia*, *130*, 61–65.

Wang, X., Huo, X.-Z., Liu, Z., Yang, R., & Zeng, H.-J. (2020). Investigations on the anti-aging activity of polysaccharides from Chinese yam and their regulation on klotho gene expression in mice. *Journal of Molecular Structure*, *1208*, 127895. https://doi.org/10.1016/j.molstruc.2020.127895

Wang, X., Sun, H., Zhang, A., Sun, W., Wang, P., & Wang, Z. (2011). Potential role of metabolomics approaches in the area of traditional Chinese medicine: As pillars of the bridge between Chinese and Western medicine. *Journal of Pharmaceutical and Biomedical Analysis*, *55*(5), 859–868. https://doi.org/10.1016/j.jpba.2011.01.042

Wang, Y., Lv, M., Wang, T., Sun, J., Wang, Y., Xia, M., … Wan, J. (2019). Research on mechanism of charred hawthorn on digestive through modulating "brain-gut" axis and gut flora. *Journal of Ethnopharmacology*, *245*, 112166. https://doi.org/10.1016/j.jep.2019.112166

Wang, Y., Zhu, D., Chen, Y., Jiang, R., Xu, H., Qiu, Z., … Luo, H. (2019). Metabonomics study of ginseng glycoproteins on improving sleep quality in mice. *BioMed Research International*, *2019*, 2561828. https://doi.org/10.1155/2019/2561828

Wang, Z., Zhang, J., Ren, T., & Dong, Z. (2016). Targeted metabolomic profiling of cardioprotective effect of *Ginkgo biloba* L. extract on myocardial ischemia in rats. *Phytomedicine*, *23*(6), 621–631. https://doi.org/10.1016/j.phymed.2016.03.005

Wani, S. M., Jan, N., Wani, T. A., Ahmad, M., Masoodi, F. A., & Gani, A. (2017). Optimization of antioxidant activity and total polyphenols of dried apricot fruit extracts (*Prunus armeniaca* L.) using response surface methodology. *Journal of the Saudi Society of Agricultural Sciences*, *16*(2), 119–126. https://doi.org/10.1016/j.jssas.2015.03.006

Wen, C. W., Lin, X. D., Dong, M. J., & Deng, M. J. (2016). An evaluation of 1-deoxynojirimycin oral administration in Eri silkworm through fat body metabolomics based on (1) H nuclear magnetic resonance. *BioMed Research International*, *2016*, 4676505. https://doi.org/10.1155/2016/4676505

Wishart, D. (2018). *FooDB: The food database*. Retrieved from http://www.foodb.ca/

Wojcikowski, K., & Gobe, G. (2014). Animal studies on medicinal herbs: Predictability, dose conversion and potential value. *Phytotherapy Research*, *28*(1), 22–27. https://doi.org/10.1002/ptr.4966

Wong, K. H., Razmovski-Naumovski, V., Li, K. M., Li, G. Q., & Chan, K. (2015). Comparing morphological, chemical and anti-diabetic characteristics of Puerariae Lobatae Radix and Puerariae Thomsonii Radix. *Journal of Ethnopharmacology*, *164*, 53–63.

Wong, P. Y., & Kitts, D. D. (2006). Studies on the dual antioxidant and antibacterial properties of parsley (*Petroselinum crispum*) and cilantro (*Coriandrum sativum*) extracts. *Food Chemistry*, *97*(3), 505–515.

Wu, C., Wang, X., Wang, H., Shen, B., He, X., Gu, W., & Wu, Q. (2014). Extraction optimization, isolation, preliminary structural characterization and antioxidant activities of the cell wall polysaccharides in the petioles and pedicels of Chinese herbal medicine Qian (*Euryale ferox* Salisb.). *International Journal of Biological Macromolecules*, *64*, 458–467. https://doi.org/10.1016/j.ijbiomac.2013.12.025

Wu, J.-Z., Liu, Y.-H., Liang, J.-L., Huang, Q.-H., Dou, Y.-X., Nie, J., … Su, Z.-R. (2018). Protective role of β-patchoulene from *Pogostemon cablin* against indomethacin-induced gastric ulcer in rats: Involvement of anti-inflammation and angiogenesis. *Phytomedicine*, *39*, 111–118.

Wu, W., Song, F., Guo, D., Mi, J., Qin, Q., Yu, Q., & Liu, S. (2012). Mass spectrometry-based approach in ginseng research: A promising way to metabolomics. *Current Analytical Chemistry*, *8*(1), 43–66.

Wu, Z., Li, H., Tu, D., Yang, Y., & Zhan, Y. (2013). Extraction optimization, preliminary characterization, and in vitro antioxidant activities of crude polysaccharides from finger citron. *Industrial Crops and Products*, *44*, 145–151. https://doi.org/10.1016/j.indcrop.2012.11.008

Xia, Y.-G., Wang, T.-L., Yu, S.-M., Liang, J., & Kuang, H.-X. (2019). Structural characteristics and hepatoprotective potential of *Aralia elata* root bark polysaccharides and their effects on SCFAs produced by intestinal flora metabolism. *Carbohydrate Polymers*, *207*, 256–265.

Xianfei, X., Xiaoqiang, C., Shunying, Z., & Guolin, Z. (2007). Chemical composition and antimicrobial activity of essential oils of *Chaenomeles speciosa* from China. *Food Chemistry*, *100*(4), 1312–1315. https://doi.org/10.1016/j.foodchem.2005.12.011

Xie, G. X., Wang, S. L., Zhang, H., Zhao, A. H., Liu, J. J., Ma, Y. M., … Jia, W. (2018). Poly-pharmacokinetic study of a multicomponent herbal medicine in healthy Chinese volunteers. *Clinical Pharmacology & Therapeutics*, *103*(4), 692–702. https://doi.org/10.1002/cpt.784

Xie, J.-J., Chen, J., Guo, S.-K., Gu, Y.-T., Yan, Y.-Z., Guo, W.-J., … Chen, L. (2018). *Panax quinquefolium saponin* inhibits endoplasmic reticulum stress-induced apoptosis and the associated inflammatory response in chondrocytes and attenuates the progression of osteoarthritis in rat. *Biomedicine & Pharmacotherapy*, *97*, 886–894.

Xie, T., Bai, S., Zhang, K., Ding, X., Wang, J., Zeng, Q., … Xuan, Y. (2019). Effects of *Lonicera confusa* and *Astragali Radix* extracts supplementation on egg production performance, egg quality, sensory evaluation, and antioxidative parameters of laying hens during the late laying period. *Poultry Science*, *98*(10), 4838–4847.

Xie, W., Zhang, Y., Wang, N., Zhou, H., Du, L., Ma, X., … Cai, G. (2008). Novel effects of macrostemonoside A, a compound from Allium macrostemon Bung, on hyperglycemia, hyperlipidemia, and visceral obesity in high-fat diet-fed C57BL/6 mice. *European Journal of Pharmacology*, *599*(1-3), 159–165.

Xie, X., Zou, G., & Li, C. (2016). Purification, characterization and in vitro antioxidant activities of polysaccharide from Chaenomeles speciosa. *International Journal of Biological Macromolecules*, *92*, 702–707. https://doi.org/10.1016/j.ijbiomac.2016.07.086

Xie, Y., Xiao, M., Ni, Y., Jiang, S., Feng, G., Sang, S., & Du, G. (2018). *Alpinia oxyphylla* Miq. extract prevents diabetes in mice by modulating gut microbiota. *Journal of Diabetes Research*, *2018*, 4230590. https://doi.org/10.1155/2018/4230590

Xie, Y., & Zhang, W. (2012). Antihypertensive activity of *Rosa rugosa* Thunb. flowers: Angiotensin I converting enzyme inhibitor. *Journal of Ethnopharmacology*, *144*(3), 562–566.

Xiong, Q., Li, X., Zhou, R., Hao, H., Li, S., Jing, Y., … Shi, Y. (2014). Extraction, characterization and antioxidant activities of polysaccharides from *E. corneum gigeriae galli*. *Carbohydrate Polymers*, *108*, 247–256. https://doi.org/10.1016/j.carbpol.2014.02.068

Xu, H., Ruan, L.-Y., Chen, C., Fan, J.-T., Chen, J.-F., Zhao, W.-L., … Zheng, Q. (2020). Therapeutic assessment of fractions of Gastrodiae Rhizoma on chronic atrophic gastritis by 1H NMR-based metabolomics. *Journal of Ethnopharmacology*, *254*, 112403.

Xu, J., Liu, H., Su, G., Ding, M., Wang, W., Lu, J., …… Zhao, Y. (2019). Purification of ginseng rare sapogenins 25-OH-PPT and its hypoglycemic, antiinflammatory and lipid-lowering mechanisms. *Journal of Ginseng Research*. https://doi.org/10.1016/j.jgr.2019.11.002

Xu, X., Huang, Y., Xu, J., He, X., & Wang, Y. (2020). Anti-neuroinflammatory and antioxidant phenols from mulberry fruit (*Morus alba* L.). *Journal of Functional Foods*, *68*, 103914. https://doi.org/10.1016/j.jff.2020.103914

Yan, H., Lu, J., Wang, Y., Gu, W., Yang, X., & Yu, J. (2017). Intake of total saponins and polysaccharides from *Polygonatum kingianum* affects the gut microbiota in diabetic rats. *Phytomedicine*, *26*, 45–54.

Yan, Y., Fu, C., Cui, X., Pei, X., Li, A., Qin, X., … Du, H. (2020). Metabolic profile and underlying antioxidant improvement of Ziziphi Spinosae Folium by human intestinal bacteria. *Food Chemistry*, *320*, 126651.

Yan, Y., Qiang, L., Hui-Zhi, D., Chen-Xi, S., Ai-Ping, L., Xiang-Ping, P., … Xue-Mei, Q. (2019). Determination of five neurotransmitters in the rat brain for the study of the hypnotic effects of Ziziphi Spinosae Semen aqueous extract on insomnia rat model by UPLC-MS/MS. *Chinese Journal of Natural Medicines*, *17*(7), 551–560.

Yang, L., Yu, Q. T., Ge, Y. Z., Zhang, W. S., Fan, Y., Ma, C. W., … Qi, L. W. (2016). Distinct urine metabolome after Asian ginseng and American ginseng intervention based on GC-MS metabolomics approach. *Scientific Reports*, *6*, 39045. https://doi.org/10.1038/srep39045

Yang, M. X., & Lao, L. X. (2019). Emerging applications of metabolomics in traditional Chinese medicine treating hypertension: Biomarkers, pathways and more. *Frontiers in Pharmacology*, *10*, 16. https://doi.org/10.3389/fphar.2019.00158

Yang, Y., Yue, Y., Runwei, Y., & Guolin, Z. (2010). Cytotoxic, apoptotic and antioxidant activity of the essential oil of *Amomum tsao-ko*. *Bioresource Technology*, *101*(11), 4205–4211.

Yao, F., Huang, Y., Wang, Y., & He, X. (2018). Anti-inflammatory diarylheptanoids and phenolics from the rhizomes of kencur (*Kaempferia galanga* L.). *Industrial Crops and Products*, *125*, 454–461.

Ye, M., Moon, J., Yang, J., Hwa Lim, H., Bin Hong, S., Shim, I., & Bae, H. (2015). The standardized Lycium chinense fruit extract protects against Alzheimer's disease in 3xTg-AD mice. *Journal of Ethnopharmacology*, *172*, 85–90. https://doi.org/10.1016/j.jep.2015.06.026

Yen-Ling, Low, Alison, M., Dunning, Mitch, … Research, L. J. C. (2006). Implications of gene-environment interaction in studies of gene variants in breast cancer: An example of dietary isoflavones and the D356N polymorphism in the sex hormone-binding globulin gene. *Cancer Research*, *66*, 8980–8983.

YouGuo, C., ZongJi, S., & XiaoPing, C. (2009). Evaluation of free radicals scavenging and immunity-modulatory activities of *Purslane polysaccharides*. *International Journal of Biological Macromolecules*, *45*(5), 448–452. https://doi.org/10.1016/j.ijbiomac.2009.07.009

Yue, S. J., Wang, W. X., Yu, J. G., Chen, Y. Y., Shi, X. Q., Yan, D., … Tang, Y. P. (2019). Gut microbiota modulation with traditional Chinese medicine: A system biology-driven approach. *Pharmacological Research*, *148*, 104453. https://doi.org/10.1016/j.phrs.2019.104453

Zafar, S., Ashraf, A., Ijaz, M. U., Muzammil, S., Siddique, M. H., Afzal, S., … Ahmed, Z. (2020). Eco-friendly synthesis of antibacterial zinc nanoparticles using *Sesamum indicum* L. extract. *Journal of King Saud University - Science*, *32*(1), 1116–1122.

Zeng, H., Huang, C., Lin, S., Zheng, M., Chen, C., Zheng, B., & Zhang, Y. (2017). Lotus seed resistant starch regulates gut microbiota and increases short-chain fatty acids production and mineral absorption in mice. *Journal of Agricultural and Food Chemistry*, *65*(42), 9217–9225. https://doi.org/10.1021/acs.jafc.7b02860

Zhang, D., Li, S., Xiong, Q., Jiang, C., & Lai, X. (2013). Extraction, characterization and biological activities of polysaccharides from *Amomum villosum*. *Carbohydrate Polymers*, *95*(1), 114–122. https://doi.org/10.1016/j.carbpol.2013.03.015

Zhang, H., Yang, Y.-F., & Zhou, Z.-Q. (2018). Phenolic and flavonoid contents of mandarin (*Citrus reticulata* Blanco) fruit tissues and their antioxidant capacity as evaluated by DPPH and ABTS methods. *Journal of Integrative Agriculture*, *17*(1), 256–263.

Zhang, L., Su, S., Zhu, Y., Guo, J., Guo, S., Qian, D., … Duan, J. A. (2019). Mulberry leaf active components alleviate type 2 diabetes and its liver and kidney injury in db/db mice through insulin receptor and TGF-beta/Smads signaling pathway. *Biomedicine & Pharmacotherapy*, *112*, 108675. https://doi.org/10.1016/j.biopha.2019.108675

Zhang, W.-N., Su, R.-N., Gong, L.-L., Yang, W.-W., Chen, J., Yang, R., … Chen, Y. (2019). Structural characterization and in vitro hypoglycemic activity of a glucan from *Euryale ferox* Salisb. seeds. *Carbohydrate Polymers*, *209*, 363–371. https://doi.org/10.1016/j.carbpol.2019.01.044

Zhang, W., Chen, L., Li, P., Zhao, J., & Duan, J. (2018). Antidepressant and immunosuppressive activities of two polysaccharides from *Poria cocos* (Schw.) Wolf. *International Journal of Biological Macromolecules*, *120*, 1696–1704.

Zhang, X.-F., Chen, J., Yang, J.-L., & Shi, Y.-P. (2018). UPLC-MS/MS analysis for antioxidant components of Lycii Fructus based on spectrum-effect relationship. *Talanta*, *180*, 389–395. https://doi.org/10.1016/j.talanta.2017.12.078

Zhang, X., Zhao, S., Song, X., Jia, J., Zhang, Z., Zhou, H., … Bian, Y. (2018). Inhibition effect of glycyrrhiza polysaccharide (GCP) on tumor growth through regulation of the gut microbiota composition. *Journal of Pharmacological Science*, *137*(4), 324–332. https://doi.org/10.1016/j.jphs.2018.03.006

Zhang, Y. T., Xiao, M. F., Liao, Q., Liu, W. L., Deng, K. W., Zhou, Y. Q., … Yang, Y. T. (2018). Application of TQSM polypharmacokinetics and its similarity approach to ascertain Q-marker by analyses of transitivity in vivo of five candidates in Buyanghuanwu injection. *Phytomedicine*, *45*, 18–25. https://doi.org/10.1016/j.phymed.2018.03.012

Zhong, L.-J., Hua, Y.-L., Ji, P., Yao, W.-L., Zhang, W.-Q., Li, J., & Wei, Y.-M. (2016). Evaluation of the anti-inflammatory effects of volatile oils from processed products of *Angelica sinensis* radix by GC–MS-based metabolomics. *Journal of Ethnopharmacology*, *191*, 195–205.

Zhou, J.-L., Zheng, J.-Y., Cheng, X.-Q., Xin, G.-Z., Wang, S.-L., & Xie, T. (2019). Chemical markers' knockout coupled with UHPLC-HRMS-based metabolomics reveals anti-cancer integration effects of the curcuminoids of turmeric (*Curcuma longa* L.) on lung cancer cell line. *Journal of Pharmaceutical and Biomedical Analysis*, *175*, 112738.

Zhou, J., Wei, K., Wang, C., Dong, W., Ma, N., Zhu, L., … Zhu, R. (2017). Oral immunisation with Taishan *Pinus massoniana* pollen polysaccharide adjuvant with recombinant *Lactococcus lactis*-expressing *Proteus mirabilis* ompA confers optimal protection in mice. *Allergologia et Immunopathologia*, *45*(5), 496–505.

Zhou, S.-S., Xu, J., Zhu, H., Wu, J., Xu, J.-D., Yan, R., … Wang, Z. (2016). Gut microbiota-involved mechanisms in enhancing systemic exposure of ginsenosides by coexisting polysaccharides in ginseng decoction. *Scientific Reports*, *6*(1), 1–13.

Zhu, H., Long, M. H., Wu, J., Wang, M. M., Li, X. Y., Shen, H., … Li, S. L. (2015). Ginseng alleviates cyclophosphamide-induced hepatotoxicity via reversing disordered homeostasis of glutathione and bile acid. *Scientific Reports*, *5*, 17536. https://doi.org/10.1038/srep17536

Zhu, R., Zhang, X., Wang, Y., Zhang, L., Wang, C., Hu, F., … Chen, G. (2019). Pectin oligosaccharides from hawthorn (*Crataegus pinnatifida* Bunge. Var. major): Molecular characterization and potential antiglycation activities. *Food Chemistry*, *286*, 129–135. https://doi.org/10.1016/j.foodchem.2019.01.215

Zmora, N., Zeevi, D., Korem, T., Segal, E., & Elinav, E. (2016). Taking it personally: Personalized utilization of the human microbiome in health and disease. *Cell Host & Microbe*, *19*(1), 12–20. https://doi.org/10.1016/j.chom.2015.12.016

SUPPORTING INFORMATION

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