Chinese Herbal Medicines 16 (2024) 313–326

Contents lists available at ScienceDirect

Chinese Herbal Medicines

journal homepage: www.elsevier.com/locate/chmed

Review

Chemical composition, pharmacological activity and development strategies of *Rubus chingii*: A review

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ARTICLE INFO

Article history:
Received 27 July 2023
Revised 10 October 2023
Accepted 11 January 2024
Available online 22 May 2024

Keywords:
applications
chemical compositions
processing
pharmacological effects
Rubus chingii Hu

ABSTRACT

Raspberries are used for both food and medicine, but it has not yet attracted widespread attention. In this paper, the chemical constituen of the original plant raspberry. *R. chingii* is one of the new "Zhe Bawei" medicinal materials selected in 2017. "Zhe Bawei" refers to eight kinds of genuine medicinal materials in Zhejiang Province. The chemical constituents, pharmacological effects, processing, and application of *Rubus chingii* Hu were reviewed to provide a reference for its further development. Relevant literature in recent years was collected in databases such as China Knowledge Network, Web of Science, Elsevier, PubMed, and X-Mol, using "raspberry", "*Rubus chingii*", "traditional use", "chemical composition", "pharmacology", etc. as keywords individually or in combination. The summary of pharmacological activities shows that the relationship between the pharmacological activities of raspberry is still not deep enough. More in-depth research should be carried out in this direction to explore the mechanism of action of its active ingredients and provide effective reference for the further development of the raspberry industry. In the future, with the participation of more researchers, it is expected to develop innovative drugs based on raspberry for the treatment of diseases.

Contents

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https://doi.org/10.1016/j.chmed.2024.01.007
1674-6384/

1. Introduction

Red raspberries are also known as "raspberry", "Marin", "*Rubus idaeus* L.", "*Rubus chingii* Hu", etc., and are valuable medicinal and food fruit (Fig. 1A) (Liu, Qin, & Wu, 2022). It has been an excellent medicinal and food plant for more than 1 500 years (Sheng et al., 2020). Raspberries include more than 400 species, the mainstream species used now is the East China raspberry (Wang et al., 2022). The original plants of raspberry mainly include *Rubus idaeus* L., *Rubus coreanus* Miq., *Rubus parvifolius* L., *Rubus niveus* Thunb., *Rubus corchorifolius* L.f., and *Rubus foliolosus* D.Don, etc. (Ke et al., 2021). Nowadays, all editions of *Chinese Pharmacopoeia*, including the latest edition of 2020, stipulate that *R. chingii* is the only original plant of raspberry, which reflects the unitynce, and the new "Zhe Bawei" refers to 16 kinds of Chinese medicinal materials initially identified in 2017 as new genuine medicinal materials in Zhejiang. The only variety included in the *Chinese Pharmacopoeia* is *R. chingii*, also named East China raspberry. East China raspberries are harvested as herbal medicine when the fruits dry and turn yellow. Its mature fruit is rich in nutrition and is recognized as the third generation of gold fruit in the world. Raspberry blossom and fruit in April, mature in late May, after green fruit, yellow fruit, and red fruit, in which mature red fruit is used as a fruit and not used as medicine (Sun et al., 2021). At present, raspberry is distributed in and outside China, such as in Zhejiang, Sichuan, Anhui, Fujian, Japan, Siberia, Central Asia, North America, Europe, and other places. As a medicinal food species, there are many studies on raspberry in and outside China, and the contents are updated rapidly, so it is necessary to compile a review of the literature in recent years to further understand raspberry and provide a reference for better clinical use of this herb.

Raspberry, which is slightly warm and sweet and sour, has the effect of benefiting the kidney, fixing the essence and reducing urination, nourishing the liver and brightening the eyes, and is a traditional kidney tonic herb and a major component of classical and famous formulas such as Wuzi Yanzong Pill. Wuzi Yanzong Pill is composed of *Rubus Chingii* (Fupenzi in Chinese), *Fructus Lycii* (Gouqizi in Chinese), *Cuscutae Semen* (Tusizi in Chinese), *Schisandrae Chinensis Fructus* (Wuweizi in Chinese), *Plantaginis Semen* (Cheqianzi in Chinese), which used for impotence and infertility due to kidney deficiency. In modern traditional Chinese medicine (TCM) clinics, it is commonly used to treat kidney yang deficiency symptoms such as enuresis, impotence and premature ejaculation, and dizziness (Zheng et al., 2022). The record of the efficacy of raspberry in *Chinese Pharmacopoeia* is basically the same as that in *Compendium of Materia Medica*. Raspberry has the effects of tonifying deficiency and kidney, nourishing liver and improving visual acuity. Raspberry contains a variety of biologically active ingredients, is rich in pharmacological effects, and has great potential for advancement.

2. Chemical compositions of raspberry

It has been documented that 105 compounds have been isolated from raspberry (Sheng et al., 2020), the main components

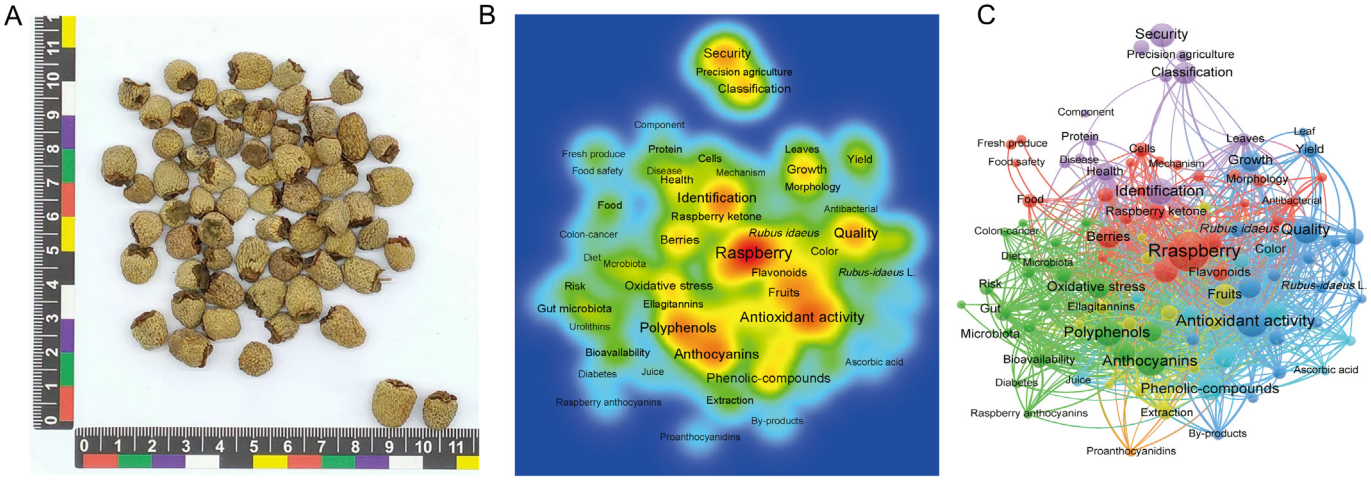

Fig. 1. (A) Medicinal herbs of *R. chingii*. (B) Density visualization by VOS viewer software. (C) Network visualization map was created by VOS viewer software.

include phenols, flavonoids, terpenes, organic acids, alkaloids, phenylpropanoids, coumarins, terpenes, etc. In addition, the newly discovered compounds in recent years are listed in Table 1, and the structures are drew in Fig. 2. Phytochemical studies have found that raspberry contains glycoproteins, flavonoid glycosides, polysaccharides (Ke, Bao, & Chen, 2021), and vitamins (A, B1, B2, B5, B6, C, and E). The contents of sugar and organic acid in the fruit were about 2.40%–10.67% and 0.62%–4.09%, respectively. The fruit mainly contains diterpenes, triterpenes, alkaloids, phenylpropanoids, organic acids, and other components (Wang et al., 2022). Raspberry leaves are used on a smaller scale than fruits and contain organic acids, flavonoids, tannins, and vitamin C. The main components of raspberry seeds are dietary fiber (64%) and essential fatty acids, and the main polyphenols are 1.2% ellagic acid and 0.45% flavan-3-ols (Majewski et al., 2020).

To gain a better understanding of raspberry research trends in recent years, we searched the Web of Science database from 2020 to 2022 by topic "raspberry", "*Rubus chingii* Hu", "*R. chingii*" and "*R. coreanus*" in the Web of Science core set to retrieve 3469 articles, generating density view and clustering view after removing irrelevant items ("product", "thing", "raspberry pi", "internet", "network", "strawberry", etc.). The network view can help us understand the intrinsic connections between different topics in literature, the role of high-frequency words, etc.

In the model (Fig. 1B), the colors indicate the study density of the keywords in the selected study. Red, yellow, green, and blue indicate the number of occurrences of the study object from most to least. The results show that the keywords around "raspberry", "polyphenols", "anthocyanins", "antioxidant activity", "quality", "security" and "identification" are the most frequent. "phenolic compounds", "polyphenols", "flavonoids", and "raspberry ketone", "ellagitannins", "quality", etc. reveal the active ingredients from raspberry fruits and the safety assessment of the study. The density view also reflects that polyphenols, among others, are hot compounds studied by researchers. On the Web of Science, "raspberry", "*Rubus chingii* Hu", "*R. chingii*" and "*R. coreanus*" are used as keywords to search the literature from 2020 to 2022, using the clustering view produced by VOS viewer. The model (Fig. 1C) found that "antioxidant activity", "fruits", "oxidative stress", "antibacterial", "food" etc. are the hot spots of research on raspberry.

2.1. Polyphenols

Polyphenols include phenolic acids, coumarins, flavonoids, stilbene, and lignans, and also include tannins (Hano & Tungmunnithum, 2020). Polyphenolic compounds, a class of herbal antioxidant factors, are split into two main groups: flavonoids and phenols. These components are significantly present in raspberry seed oil, some of them are listed in Table 1. Flavonoids are commonly found in edible and medicinal plants and are mainly composed of anthocyanins, condensed tannins, and hydrolyzed tannins (Li, Jiang, Chen, & Jackson, 2021). Total phenols are all

Table 1
Functional factors isolated from *R. chingii*.

Compound class	No.	Formula	Compounds	References
Phenolics	**1**	–	Butyl 2-(4-hydroxy-3-methoxyphenyl)-3-hydroxy propanoate (raspberry phenolic acid butyl ester)	Wang et al., 2022
Flavonoids	**2**	$C_9H_{10}O_5$	Syringic acid	Tomas, 2022
	3	$C_{16}H_{18}O_9$	Chlorogenic acid	
	4	$C_7H_6O_3$	Salicylic acid	
	5	$C_{15}H_{14}O_6$	Catechin	
	6	$C_{11}H_{12}O_5$	Sinapic acid	
	7	$C_9H_8O_3$	2-Hydroxycinnamic acid	
	8	$C_9H_8O_3$	*p*-Coumaric acid	
	9	$C_{27}H_{32}O_{14}$	Naringin	
	10	$C_{15}H_{10}O_8$	Myricetin	
	11	$C_{14}H_{12}O_3$	Resveratrol	
	12	$C_{10}H_{12}O_5$	Propyl gallate	
	13	$C_{15}H_{10}O_6$	Luteolin	
	14	$C_{16}H_{12}O_7$	Isorhamnetin	
	15	$C_{15}H_{10}O_7$	5,6,7,4′-Tetrahydroxy-flavonol	Wang et al., 2022
Diterpenoids	**16**	$C_{10}H_{14}$	*p*-Cymene (*p*-isopropyl toluene)	Balahbib et al., 2021
	17	$C_{26}H_{44}O_8$	19-*O*-*β*-Glucopyranosyl-13(*Z*)-ent-labda-8(17), 13(14)-diene-3*β*,15-diol	Liu et al., 2023
	18	$C_{26}H_{42}O_8$	15-*O*-*β*-Glucopyranosyl-13(*E*)-3-oxo-ent-labda-8(17), 13(14)-diene-15,19*β*-diol	Liu et al., 2023
	19	$C_{26}H_{44}O_8$	(13*S*)-19-*O*-*β*-*D*-Glucopyranosyl-labda-8(17),14-diene-3*β*,13-diol	
	20	$C_{26}H_{42}O_7$	(16*α*)-16,17-Dihydroxy-ent-Karan-2-one17-*O*-*β*-*D*-glucopyranoside	He et al., 2020
	21	$C_{20}H_{32}O_3$	(16*R*)-16,17-Dihydroxy-ent-kaurane-2-one	
Triterpenes	**22**	$C_{30}H_{48}O_4$	Alphitolic acid (2*α*,3*β*-dihydroxy-20(29)-lupen-28-oic acid)	Wang et al., 2022
	23	$C_{29}H_{40}O_5$	Negundonorin A	
Organic acid	**24**	$C_{30}H_{46}O_5$	3*β*,19*α*-Dihydroxy-1-oxo-olean-12-en-28-oic acid	
Polysaccharides	**25**	–	Pectin polysaccharide	Kong et al., 2022
	26	–	pRCP	Luo et al., 2023
Alkaloid	**27**	$C_{10}H_7NO_3$	2-oxo-1,2-Dihydroquinoline-4-carboxylic acid	Chen et al., 2022
Others	**28**	–	2,4,6-Trihydroxy acetophenone-6-*O*-*β*-*D*-glucopyranoside	Liu et al., 2021
	29	$C_{23}H_{20}O_{13}$	3,3′-di-*O*-Methyl ellagic acid 4-(5′′-acetyl)-*α*-*L*-arabinofuranoside	He et al., 2020
	30	–	1*β*,2*α*,19*α*-Trihydroxy-3-oxo-12-ursen-28-oic acid	Wang et al., 2022
	31	–	Methyl(*S*)-flavogallonate	Li, Sun, Chen, Jiang, & Jackson, 2021
	32	$C_{27}H_{38}O_{13}$	Rourinoside	
	33	$C_{20}H_{22}O_6$	3*β*-Hydroxy-manual-18-*O*-*β*-*D*-glucoside	Chen et al., 2022b
	34	$C_{11}H_{16}O_3$	3*β*,18-di-Hydroxy-ma	
	35	–	Pinoresinol	
	36	–	Loliolid	
	37	–	Dehydrovomifoliol	
	38	–	(−)-Syringaresino	

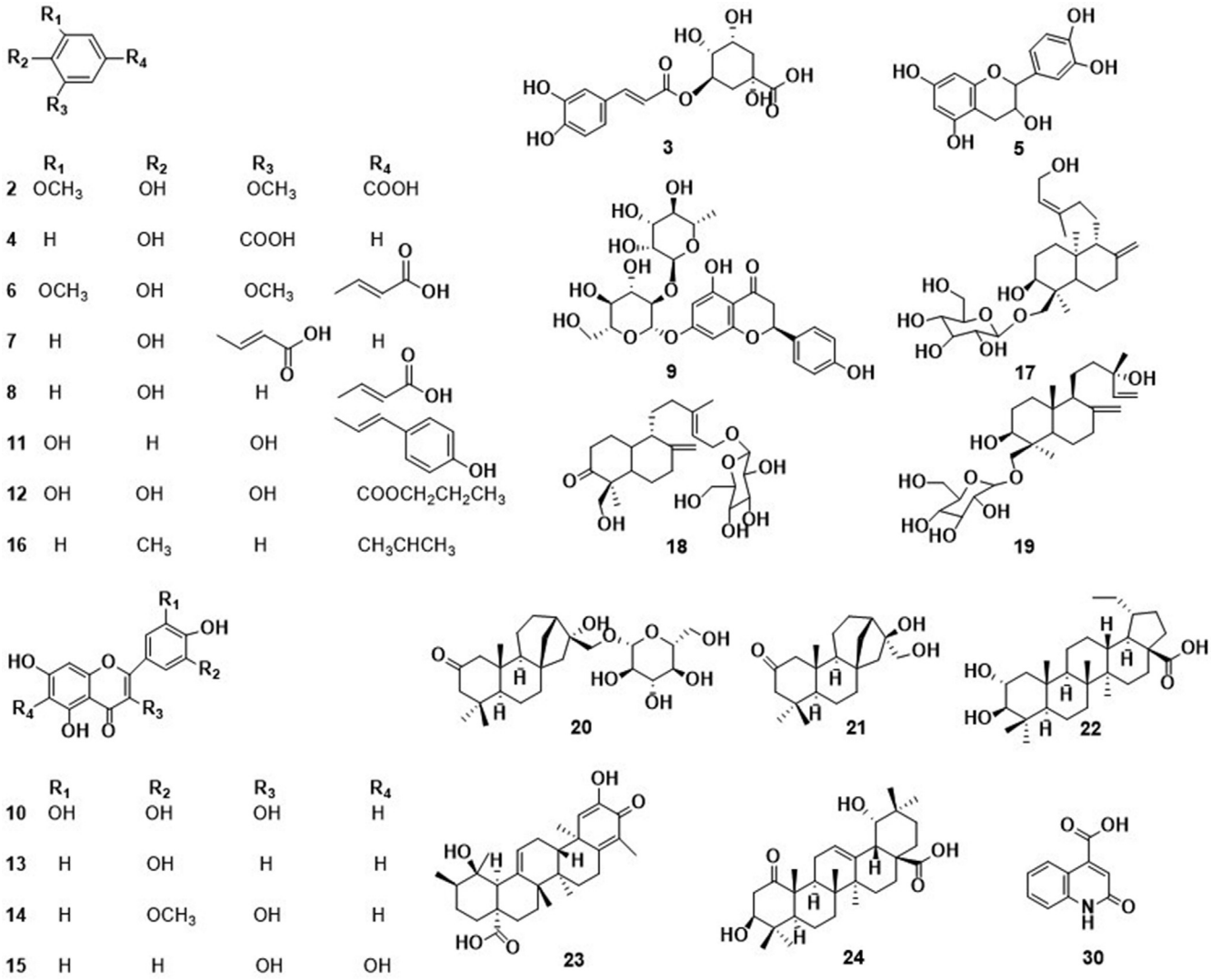

Fig. 2. Main chemical compounds structures in *R. chingii*.

phenolic substances, which include polyphenols and monophenols. Polyphenols are substances containing greater than or equal to two hydroxyl groups on a benzene ring and include flavonoids, tannins, phenolic acids, and anthocyanins phenols are found in plant foods. The total phenolic content of the raspberry leaf extract was higher than that of the stem or bark extract (Yao et al., 2021). Defatted raspberry seeds include a broad range of polyphenols, their extracts have antioxidant and antibacterial activity and are used in food, dietary supplements, cosmetics, the pharmaceutical industry, and as a high-value, inexpensive ingredient (Maric et al., 2022).

2.1.1. Phenolics

Phenolic family compounds are divided into flavonoids and non-flavonoids. There are six subclasses of flavonoids: anthocyanins, flavonols, flavanones, flavanols, flavonoids, and isoflavones. When sugars are linked in their chemical structure, anthocyanidins become anthocyanins. Non-flavonoids are divided into four subcategories: stilbenes, tannins, coumarins, and phenolic acids. Tannins are divided into concentrated tannins, hydrolyzed tannins, and compound tannins. Phenolic acids are divided into three categories: hydroxybenzoic acid, hydroxyphenyl acetic acid, and hydroxycinnamic acid (Lopez-Corona et al., 2022). Studies have shown that molecular imprinting technology can effectively separate the phenolic components of the ethyl acetate extract of raspberry (Wu et al., 2022). Butyl 2-(4-hydroxy-3-meth oxyphenyl)-3-hydroxy propanoate (**1**) (Table 1) is a new phenolic compound named raspberry phenolic acid butyl ester. 1β,2α,19α-trihydroxy-3-oxo-12-ursen-28-oic acid (**30**), 3β,19α-dihydroxy-1-oxo-olean-12-en-28-oic acid (**24**), alphitolic acid (**22**), negundonorin A (**23**) are isolated from this plant for the first time (Wang et al., 2022).

In most berries, the concentrations of total flavonoids and anthocyanins increased as the fruit approached maturity. However, in raspberries, the contents of flavonoids and anthocyanins in immature fruits were much higher than those in the late stage of fruit development. The decrease of flavonoids and anthocyanins in the late stage of fruit development was due to the down-regulation of phenylalanine and flavonoid biosynthesis. The mechanism of flavonoid biosynthesis seems to be unique to *R. chingii* and has not been reported in other fruit crops (Li et al., 2021).

Raspberry leaf extract has a higher content of active phenolic compounds than the fruit, with high antioxidant and biological activity, and can be used as an alternative to synthetic drugs for the treatment and prevention of diseases caused by poor lifestyles, as well as a food additive, thus improving the functional quality of food (Staszowska-Karkut & Materska, 2020). Raspberry stem extract has pro-oxidant activity and is dependent on solution pH

and temperature. It has been shown that free phenolics in raspberry pomace have the highest antioxidant activity in the DPPH assay (Yao et al., 2021). The total phenol content of raspberry leaf extract was two times higher than that of peel extract and three times higher than that of raspberry stem extract (Garjonyte, Budiene, Labanauskas, & Judzentiene, 2022). In summary, it can be seen that raspberry fruits, seeds, roots, stems and leaves have some biological activity, and the whole plant can be used medicinally, and it is conjectured that the flowers may also have some biological activity.

2.1.2. Flavonoids

There are mainly 14 flavonoid compounds in raspberry found in recent years (**2**–**15**) (Table 1). The flavonoids in raspberry mainly consist of quercetin and kaempferol-glycosides, which are mainly distributed in the epidermal hairs and placental parts of the fruit (Li et al., 2021). Raspberry is rich in anthocyanins, which are flavonoids. Anthocyanins can reduce inflammatory markers and have a beneficial effect on inflammation caused by obesity (Ngamsamer, Sirivarasai, & Sutjarit, 2022). Raspberries contain flavonoids and tannins that treat infectious diseases, and some of these compounds have been successfully used as major or additive ingredients in toothpaste or mouthwash to maintain oral health (Kovac et al., 2022), while others await further research or future uses.

2.2. Terpenoids

Terpenoids, including diterpenoids and triterpenoids. Six kinds of terpenoids have been isolated and identified from the fruits and leaves of *R. chingii* in recent years: 3 labdane-type diterpene glycosides (**17**–**19**) have been isolated from the fruits of *R. chingii*. (16α)-16,17-Dihydroxy-ent-kauran-2-one17-*O*-β-*D*-glucopyranoside (**20**) and (16R)-16,17-dihydroxy-ent-kaurane-2-one (**21**) were first isolated from raspberry as rare *p*-methane-type diterpenoids. Raspberry contains the monoterpene *p*-cymene (**16**), which has anti-inflammatory, anti-viral and anti-tumor activities. Its anti-tumor mechanism is related to the inhibition of apoptosis and the cell cycle (Balahbib et al., 2021).

2.3. Organic acids

Raspberries have been found to contain 56 organic acids, with phenolic acids being the most common, followed by fatty acids, with higher levels of organic acids such as gallic acid, salicylic acid, malic acid, citric acid, and ascorbic acid (Sheng et al., 2020; Yu et al., 2019). One new organic acid (**24**) found in recent years is listed in Table 1. Six phenolic acids were detected in raspberries: gallic acid, caffeic acid, chlorogenic acid, erucic acid, *p*-coumaric acid, and ferulic acid (Tomas, 2022). The main fatty acids in raspberry oil are linoleic acid (LA) and α-linolenic acid (ratio < 2: 1), and 10%–12% of the non-essential fatty acid, oleic acid, which can be synthesized by the body itself, is also present. The organic acid in red raspberry was mainly citric acid (22.87 g/L), which accounted for 90.9% of the total acid, resulting in excessive acidity of red raspberry wine and difficulty in microbial growth during fermentation (Chen, Tang, Feng, Sun, & Wang, 2020). *I. terricola* WJL-G4 fermentation could significantly degrade citric acid, improve the color and taste of red raspberry wine, increase the content of total flavonoids and total anthocyanins, and enhance the antioxidant activity of red raspberry wine (He et al., 2021).

2.4. Polysaccharides

The glycosyl group of raspberries is mainly composed of galacturonic acid and arabinose, the total ratio is 75.02% (Ke et al., 2021). Polysaccharides in raspberries have antioxidant, anti-inflammatory, and anti-tumor effects. Raspberries contain dietary fiber, which is a non-digestible polysaccharide that contributes to the activity of the gut microbiota and prevents obesity, diabetes, cardiovascular disease (Majewski et al., 2020), colon cancer, and other disease. The dietary fiber in raspberries can be used as a prebiotic component in the development of foods with enhanced nutritional properties. Pectin, an acidic heteropolysaccharide, is found in the cell walls of fruits and vegetables and is beneficial to health (Wu et al., 2020). Pectin polysaccharide RCHP-S is a new kind of polysaccharide in *R. chingii* Hu, which is composed of mannose, rhamnose, glucuronic acid, galacturonic acid, glucose, galactose, and arabinose with a molar ratio of 1.52: 19.08: 1.64: 41.98: 2.29: 20.61: 12.88 (Kong et al., 2022). Raspberry pectin (RP) is rich in phenolic compounds and can be used as a biomaterial for medical supplies or as a substitute for traditional plastic packaging for functional coatings and edible films. In addition, dietary supplements of RP may promote health. The addition of pectin to raspberry pulp reduces the amounts of bioavailable polyphenols, and the interaction between different components of the food matrix is important to guide the design of functional foods with improved nutritional quality and health benefits (Tomas, 2022).

Pectin polysaccharide (**25**) is a novel pectin polysaccharide found in *R. chingii* Hu. The homogeneous acid polysaccharide RPP-2a was composed of rhamnose-arabinose, galactose, glucose, xylose, galacturonic acid, and glucuronic acid, and the molar ratio of the above components was 15.4: 9.6: 7.6: 3.2: 9.1: 54.3: 0.8. As a potential natural immune enhancer, RPP-2a exhibits significant macrophage activation activity by increasing the production of nitric oxide, tumor necrosis factor-α, interleukin-6, and interleukin-1β (Yang et al., 2022). A novel acidic polysaccharide (RPP-3a) significantly promoted the viability of RAW264.7 macrophages by increasing the production of NO, tumor necrosis factor-α (TNF-α, interleukin-6 (IL-6), and interleukin-1β (IL-1β) at the expression and transcription levels. RPP-3a showed moderate reducing power and strong hydroxyl and superoxide anion radical scavenging ability. Immunostimulatory and antioxidant activities enable RPP-3a to be developed as a health-beneficial functional dietary supplement (Yang et al., 2022). A new immature raspberry polysaccharide, pRCP (**26**), is an acidic heteropolysaccharide that acts as a potential prebiotic to improve gut health by regulating gut flora, colonic inflammation, and oxidative stress induced by high-fat diet (HFD) in mice alleviated with pRCP (Luo et al., 2023).

2.5. Others

Raspberry contains 27 kinds of mineral elements, including Mg, Al, Ca, Mn, Ni, Pb, Ag, As, Cu, Fe, Cd, Se, and so on, among which Ca, Mn, Zn, Mg, K, and Fe are characteristic elements of raspberries, and Na, Ca, Mn, Zn, and Mg are the main constituent elements, among which Ca, Mn, Zn, and Mg have important roles in promoting reproductive health (Lu, 2020). Raspberries are rich in tannins, and other steroidal compounds, and also contain coumarins. There are seven alkaloids extracted from raspberry (Lu, 2020), and a new one was found in 2022, named 2-oxo-1,2-dihydroquinoline-4-carboxylic acid (**27**). Sixteen compounds were isolated from the 30% ethanol eluted part of the 70% ethanol extract of Raspberry, among which the compound 2,4,6-trihydroxyacetophenone-6-*O*-β-*D*-glucopyranoside (**28**) was first isolated. 3,3′-di-*O*-methylellagic acid 4-(5'-acetyl)-α-*L*-arabinofuranoside (**29**) were purified from the fruits of *R. chingii*. Methyl (*S*)-flavogallonate (**31**) and rourinoside (**32**) were first identified in *Rubus*. Other ingredients in raspberries include essential oils, amino acids, and polysaccharides. Raspberries contain vitamin C, sugars, and organic acids. Vitamin C has antioxidant properties that neutralize the negative effects of oxidative stress. In addition, raspberry also contains sev-

eral amino acids, such as threonine, valine, methionine, leucine, phenylalanine, lysine, and aspartic acid. 17 compounds were isolated from the stems of Raspberry, 3β-hydroxy-manool-18-*O*-β-*D*-glucoside (**33**) was a new compound, named raspberry glycoside B. 3β,18-di-hydroxy-manool (**34**) was a new natural product. Compounds pinoresinol (**35**), loliolid (**36**), dehydrovomifoliol (**37**), and (−)-syringaresino (**38**) were isolated from this plant for the first time (Chen et al., 2022a, 2022b).

3. Pharmacological effects and applications of raspberry

Pharmacological studies have shown that raspberry extract has anti-osteoporosis, regulates the central nervous system (Sheng et al., 2020), and reinforces kidney-yang, anti-aging, anti-mutagenic, anti-spotting, hepatoprotective (VandenAkker, Vendrame, Tsakiroglou, McGilvrey, & Klimis-Zacas, 2021), regulates immunity, hypoglycemic, antibacterial and anti-inflammatory effects.

Raspberry seed oil (RSO) is thought to be a source of polyphenols, fatty acids, unsaturated fat, tocopherols, tocopherols, carotenoids, flavonoids, phytosterols, antioxidants, monoterpenes, and many other compounds that have antibacterial, antioxidant, and anti-inflammatory properties, can be used in food, medicine, cosmetics, health products, and chemical industry (Ispiryan, Viškelis, & Viškelis, 2021). Studies have shown that raspberry leaf extract and raspberry leaf tea have significant antioxidant, antibacterial, anti-diabetic, and anti-inflammatory effects (Luo, Chen, Zhang, Jia, & Wang, 2020). Raspberry leaves have many therapeutic effects such as antidiarrheal, anti-bleeding, and regulating hormones (Chwil & Kostryco, 2020; Ke et al., 2021).

3.1. Kidney supplement

TCM uses raspberry to nourish the kidneys and boost yang energy. For more than 1 500 years, the unripe fruit of the raspberry has been utilized in TCM to treat different kidney-related illnesses such as dysuria, impotence, and seminal flow (Sheng et al., 2020). The raspberry alcoholic extract showed some improvement in kidney yang deficiency mice, and the active site of the protective effect of kidney yang deficiency was the n-butanol site. Raspberry contains rutin, ellagic acid, kaempferol-3-rutin glycoside, astragaloside, lily glycoside, and lycopodium F5, which can improve kidney function and prevent kidney injury (Zhou et al., 2021).

The formula Wuzi Yanzong Pill (WYP) contains salt raspberry, salt can enhance the effect of kidney essence fixation and urine reduction. Salt raspberry can regulate cAMP and cGMP of kidney-yang deficiency polyuria model rats and improve renal pathology (Zhang, Liao, Yang, Chen, & Hu, 2021). The optimal combination of five bioactive components in WYP was as follows: hyperoside 200 mg/kg, acteoside 100 mg/kg, schizandrol A 10 mg/kg, kaempferol 100 mg/kg, ellagic acid 1 mg/kg. This combination reduced the incidence of neural tube defects (NTDs) most significantly (Wang et al., 2023). The efficacy and potentiation mechanism of the formula after changing raspberry to salt-formed raspberry in the formula WYP are yet to be studied. In addition, the new edition of the *Chinese Pharmacopoeia* does not only include WYP, and it remains to be investigated whether processed raspberries will affect the efficacy of other prescriptions.

3.2. Antioxidation

Organic fertilizer increased the content of ellagic acid and gallic acid in raspberries, and high levels of caffeic acid, hydroxybenzoic acid, protocatechuic acid, and vitamin C were observed in organic raspberries during the overripening stage. The oxidative stress induced by organic fertilizer enhanced the antioxidant defense mechanism, the production of bioactive compounds, and the antioxidant capacity of raspberries (Frías-Moreno et al., 2021). The inhibitory effect of the red raspberry extract on activated hepatic stellate cells in cells and rats and the related molecular mechanisms showed that red raspberry is rich in bioactive components that can attenuate oxidative stress (Wu et al., 2021). Raspberry ketone (RK) showed antioxidant properties by increasing total antioxidant capacity (TAC). Up-regulated antioxidant enzymes, glutathione peroxidase (GSH-Px), nuclear factor erythroid-derived 2-related factor 2 (Nrf-2); down-regulation of malondialdehyde (MDA) and NADPH oxidases (NOXs); improve lipid peroxidation (Lim & Choi, 2021). Antioxidant substances can scavenge free radicals and attenuate inflammatory responses, while flavonoids and phenolic acids have good antioxidant activity. The total polyphenol content of the ethyl acetate extract of raspberry was the highest, and the 50% ethanol and water extract had good antioxidant activity, which could be developed as a natural antioxidant (Shi, Chen, Li, Wang, & Xie, 2023). The accumulation of fructose-dominated sugar mainly occurred in the later stage of raspberry fruit development, the contents of total phenol and total flavone were the highest in the green fruit stage, and the contents of anthocyanin were the highest in red fruit stage and purple fruit stage. The antioxidant capacity of raspberries was positively correlated with total phenol content. Flavonoids play a major role in antioxidant capacity, which is also related to substances such as vitamins (Huang et al., 2022).

3.2.1. Anti-aging

Wrinkles, uneven skin tone, and dryness are all signs of skin aging. Aging is caused by both intrinsic and extrinsic causes, including ultraviolet (UV)-induced oxidative free radicals. Vitamins C and E play a crucial protective role in the aging process and must be obtained from outside sources. Encapsulated extracts of vitamin C, vitamin E, and raspberry leaf cell culture extract have anti-aging and brightening effects, with significant improvements in skin tone, elasticity, and radiance, as well as significant improvements in smoothness, scaling, and wrinkles, with mild side effects such as tingling and tightness (Rattanawiwatpong, Wanitphakdeedecha, Bumrungpert, & Maiprasert, 2020).

Raspberry glycoproteins have high antioxidant activity and may be used to slow aging and prevent illness (Huo, Wang, Yang, Qu, & Zeng, 2020). Unripe raspberry (uRo) extract has a higher ellagic acid content and shows greater anti-aging and whitening effects than ripe raspberry extract (Oh et al., 2020). Raspberry contains the aromatic compound α-ionone, which inhibits UVB-mediated photoaging and barrier dysfunction of human epidermal keratinocyte forming cell line (HaCaT cells) and is a potential natural anti-photodamage agent. The levels of interleukin (IL)-1β, IL-6, IL-8, and tumor necrosis factor-α in HaCaT cells treated with α-ionone were significantly lower than those irradiated by UVB (Geng, Kang, Huang, & Tong, 2023).

3.2.2. Liver protection

Classical Chinese medicine records its role in the treatment of liver lesions, and in Hebei, Heilongjiang, and other places folk has long been used to treat hepatitis, cirrhosis, and other liver disease history of raspberry. Studies have shown that red raspberry extract (RBE) has an inhibitory effect on activated hepatic stellate cells (aHSC) in cells and rat models. RBE can reduce the accumulation of reactive oxygen species (ROS) in hepatic stellate cells. To induce apoptosis and regulate transdifferentiation of activated hepatic stellate cells, by inhibiting the activity of caspases/polymerase, the intracellular oxidative damage was eliminated, and the protein carbonylation was reduced. Up-regulation of nuclear factor erythroid 2-related factor 2 (Nrf2) / heme oxygenase-1 (HO-1) and proliferator-activated receptor gamma pathways effectively eliminate oxidative stress and alleviates HSC activation, thus providing

a basis for the development of new therapeutic strategies for chemical-induced liver fibrosis (Wu et al., 2021).

Some dietary polyphenols may alleviate alcoholic liver disease. The main chemical constituents of raspberry stems are polyphenols and flavonoids, which are the main active components acting as antioxidants and hepatoprotective agents. Raspberry polyphenols help induce metabolism to promote immune response and prevent liver damage caused by stress caused by obesity. Raspberry ketones act as a potent anti-inflammatory, antioxidant, and anti-apoptotic agent to protect the liver from acrylamide-induced injury in rats (Hamdy et al., 2022). The addition of raspberry polyphenol extracts and oligo-fructans or pectins to the diet may be considered as a dietary compound that may be effective in reducing diseases associated with nonalcoholic fatty liver disease caused by an obesogenic diet (Fotschki, Juśkiewicz, Jurgoński, & Sójka, 2021).

3.3. Anti-inflammatory and antibacterial

Ellagic acid is one of the raspberry phenolic acids that inhibit the nuclear factor-κB signaling pathway. It has a therapeutic effect on ulcerative colitis and can be used as a dietary supplement for patients with ulcerative colitis and related intestinal inflammatory diseases. Also, tannins and their derivatives in red raspberry are major anti-inflammatory polyphenolic substances and are expected to be compounds that reduce neuroinflammation (Garcia et al., 2020). RCHP-S has an anti-inflammatory effect on colitis mice and can be used as a food additive to develop anti-inflammatory agents for the treatment of intestinal inflammation (Kong et al., 2022). Ellagitannins and their derivatives are the main anti-inflammatory polyphenolic compounds with the potential to alleviate neuroinflammation (Garcia et al., 2020). Raspberry significantly down-regulated dextran sulfate sodium-induced circulating and local inflammatory factor IL-6, and significantly improved ulcerative colitis (Jiang, Shi, He, & Cai, 2022).

Raspberry contains antibacterial properties. Polyphenol compounds found in raspberry fruits have high antioxidant activity and antibacterial properties against pathogenic bacteria such as *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus* (Georgescu et al., 2022). Raspberry seed oil may be beneficial in destroying harmful bacteria in the mouth, and may also help to cure painful inflammation and irritating plaque deposition in the gums (Chang, Liu, Bao, Tao, & Liu, 2021). The phenolic acids such as ferulic acid, salicylic acid, and vanillic acid in raspberry fruit extract inhibited the activity of glucosyltransferase of *Streptococcus mutans*. The raspberry fruit extract containing phenolic acids may play a role in controlling and preventing dental caries without killing *Streptococcus mutans* by inhibiting the activity of *Streptococcus mutans* glucosyltransferase (Ham & Kim, 2020). Raspberry oil (RO) obtained from supercritical CO_2 may be beneficial in the chemoprevention or treatment of colon and breast cancers due to its rich composition. RO emulsion proved to have a good ability to spread free radicals and NO (Grajzer et al., 2021). Dietary (poly)phenols have been identified to have anti-inflammatory and neuroprotective effects. Raspberry with genotype 2 J19 enriched in ellagitannins and their degradation products and ellagic acid, attenuated pro-inflammatory markers and mediators CD40, NO, TNF-α, and intracellular superoxide via the NF-κB, MAPK, and NFAT pathways, and it also increased the release of the anti-inflammatory cytokine IL-10. Ellagitannin and its derivatives are major anti-inflammatory (poly)phenolic compounds that can be used to alleviate neuroinflammation (Garcia et al., 2020).

3.4. Anticancer and antitumor

The Raspberry seed oil contains a variety of micronutrients with high biological activity. It is an excellent source of polyunsaturated fatty acids (PUFA). It is reported that the content of PUFA in red raspberry seed oil is 85%, of which (expressed as a percentage of total fatty acids) contains 54% linoleic acid and 32% α-linolenic acid (Ispiryan et al., 2021). The antitumor activity of PUFA involves several mechanisms, including alterations in cell signaling (Pang, Chen, Xie, & Yao, 2021), chromatin remodeling, and DNA methylation. The active ingredients of raspberry rich in sterols, phenolic acids, and coumarins can act on key targets, and exert a multi-com ponent-multi-target-multi-pathway anti-tumor mechanism by inhibiting tumor cell proliferation and differentiation, inducing apoptosis, regulating glucose and lipid metabolism, hormone levels, and inflammatory responses (Pang et al., 2021). Raspberry oil contains large amounts of phytosterols and derivatives of 4,4-dimethyl phytosterols, 4,4-desmethyl phytosterols are a class of bioactive compounds commonly found in plant oils, naturally occurring 4,4-dimethyl phytosterols fight against various diseases such as inflammation, Parkinson's disease, Alzheimer's disease, cataracts, etc., and against skin, oral, liver, bladder and colon cancers (Zhang et al., 2020). The raspberry leaf extract extracted by steam distillation (SD) showed strong antioxidant capacity and moderate antibacterial activity against two bacteria, significant cytotoxic activity against tumor cell lines (Caco-2 and HL60), and a proliferation effect on healthy cells. Raspberry leaf extract has a good application prospect in food and cosmetics fields or dietary supplements (De Santis, Carbone, Garzoli, Laghezza Masci, & Turchetti, 2022).

Low-molecular catabolic products produced by raspberry polyphenols in the gastrointestinal tract may protect against colonic epithelial cell damage *in vivo* by reducing DNA damage. The (poly) phenolic compounds in raspberry are mediated by the gut microbiota to produce low molecular weight catabolic metabolites, which may protect against colorectal cancer *in vivo* by reducing DNA damage (Dobani et al., 2021). *R. coreanus* extract may exert anti-tumor immune effects by blocking the PD-1/PD-L1 axis, and its main component ellagic acid may be used as an effective anticancer immunotherapeutic agent (Kim, Kim, et al., 2020). The raspberry extract has anticancer activity against cervical cancer HeLa cells by upregulating the anti-proliferative molecule P53 and the pro-apoptotic molecule fatty acid synthetase (FAS) (Sham et al., 2021). Red raspberry extracts can inhibit the proliferation and apoptosis of hepatocellular carcinoma cells by inducing reactive oxygen species production, decreasing the apoptosis-related protein B-cell lymphoma-2 (Bcl-2)/Bax ratio, and significantly reducing the mitochondrial membrane potential of $HepG_2$ cells (Song, Li, Shi, & Yue, 2022). Ethyl carbamate (EC) is a human carcinogen mainly found in fermented foods and alcoholic beverages. Raspberry polysaccharides can protect against EC-induced toxicity by repairing redox imbalance, which indicates that mitochondrial membrane potential collapse is alleviated, excessive production of reactive oxygen species is reduced, and glutathione depletion is hindered (Ke, Bao, & Chen, 2021).

Raspberry can prevent, stop, delay, or reverse the initiation stage of carcinogenesis or the progression of tumor cells to malignancy, suggesting its great potential in prevention and cancer therapy.

3.5. Lowering blood lipids and anti-obesity

Raspberry leaf extract is rich in the antioxidant ellagitannin, which is not only non-toxic to erythrocytes and vascular endothelial cells, but also effectively protects them from free radicals, and its free radical inhibitory effect is more significant and effective than that of antioxidants for the prevention of diseases directly related to the cardiovascular system (Cyboran-Mikołajczyk et al., 2022). Raspberry ketone (RK) induces the expression of fibronectin type III domain protein 5 through the heme oxygenase-1 (HO-1)

signaling pathway. This study provides new evidence for the potential application of RK in the treatment of obesity. RK is highly bioavailable, rapidly metabolized, and exhibits significantly different pharmacokinetic behavior between obese and control mice, with white adipose tissue in obese mice being rich in lipids and serving as a direct target for RK (Zhao et al., 2020). RK has been used as an over-the-counter product for weight loss, the basic mechanisms of RK's protective effects include accelerated fatty acid oxidation, balanced serum glucose levels, and anti-inflammatory, and antioxidant processes. In human liver microsomes and cytosol, RK is reduced to rhodopsin, an active metabolite with anti-adipogenic effects, which may contribute to the anti-obesity effect of orally administered RK (Uramaru, Kawashima, Osabe, & Higuchi, 2023). Oral administration of 5% ethanol extract of immature plug field blisters and its bioactive compound ellagic acid resulted in a significant reduction in aortic and serum malonaldehyde levels. It was shown that both are useful alternative therapeutic agents for the regulation of blood cholesterol (Lee et al., 2020). Ellagic acid in immature plug field vesicles have hypocholesterolemic and anti-obesity activity, which effectively inhibits weight gain and enhances lipid profile (Kim, Jeong, et al., 2020). Red raspberry polyphenols from the pulp and whole fruit act as inhibitors of NOD-like receptor thermal protein domain associated protein 3 (NLRP3) inflammasome activation and epigenetic modifiers regulating adipogenesis, which confer resistance to diet-induced obesity and metabolic dysfunction (Fan et al., 2020).

A polyphenol extract from the whole fruit or pulp of red raspberry reduces high-fat diet-induced obesity in mice (Xian et al., 2021). Polyphenols in red raspberry pulp and whole fruit are inhibitors of NLRP3 inflammatory vesicle activation and epigenetic modifiers that regulate adipogenesis and resist diet-induced obesity and metabolic dysfunction (Fan et al., 2020). Anthocyanin is an antioxidant that eliminates reactive oxygen species by increasing antioxidant enzymes. Blocking the activation of nuclear factor-κB, thereby reducing the entire downstream cascade of pro-inflammatory mediators such as C-reactive protein (CRP), IL-6, and TNF-α, can also improve the imbalance of intestinal flora, restore the balance of intestinal flora, and anti-obesity effect (Ngamsamer et al., 2022). Raspberry as a dietary supplement can effectively improve obesity and exert beneficial effects, and its mechanism of action may be through the regulation of white fat browning, glycolipid metabolism, intestinal flora, and anti-inflammatory and antioxidant effects (Guan et al., 2023). Obesity, as a chronic metabolic disease, is deeply influenced by many factors such as genetics, lifestyle, and environment. There is a lack of clinical data on the improvement of obesity with raspberries and studies on the safety and efficacy of raspberries. Therefore, further clinical trials, epidemiology, and safety and efficacy evaluation of raspberries on improving obesity are needed to further elucidate the mechanism of action of raspberries on improving obesity. In addition, the pharmacodynamic substance basis for its weight loss effect is unclear, and further in-depth studies are needed.

3.6. Others

Raspberry leaves are used to treat certain eye diseases such as ocular pain, red eyes, and glaucoma (Sheng et al., 2020), as well as to treat fever, influenza, diabetes, diarrhea, and colic, and to promote childbirth (Bowman, Taylor, Muggleton, & Davis, 2021). Raspberry leaf extract contains potent antioxidants and other phytoactive components, has important lipid components of the epidermal hydro-lipid membrane, protects the skin from transepidermal water loss, and induces the expression of genes involved in molecular pathways that support skin hydration and moisturization, protects cells from oxidative stress, and has the potential to moisturize and nourish the skin (Rattanawiwatpong et al., 2020). In order to give birth more easily and harmoniously, many pregnant women ingest raspberry extract during pregnancy. However, studies have shown that raspberry leaf extract may lead to significant clinical down-regulation and inhibition of intestinal CYP3A4 (an element of the cytochrome P450 superfamily), thereby significantly changing the absorption and pharmacokinetics of the drugs taken, and even inhibiting the cervical ripening process. The ellagic acid contained in raspberry will shorten the clotting time and increase the activity of thrombin, which will lead to more pain in the delivery process (Socha et al., 2023). Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by abnormal glucose clearance and inadequate insulin response. If left uncontrolled, T2DM can lead to serious complications and death (Derrick, Kristo, Reaves, & Sikalidis, 2021). In patients with type 2 diabetes, red raspberry positively regulates inflammatory biomarker levels and shows a tendency to reduce insulin resistance (Moreno et al., 2022). Red raspberries are rich in anthocyanins and tannins. Regular addition of red raspberry and fructooligosaccharides to the diet can reduce diabetes and insulin resistance (Moreno et al., 2022).

Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most common neurodegenerative diseases. Resveratrol is a stilbene in Raspberry, which has a neuroprotective effect. Six phenolic compounds, ellagic acid, silver lindenoside, kaempferol-3-*O*-rutinoside, gallic acid, ferulic acid, and vanillic acid, may be effective in the treatment of Alzheimer's disease, and beneficial to the proliferation of murine microglial (BV2) cells at certain concentrations, and effectively inhibit the Lipopolysaccharide (LPS)-induced release of inflammatory factors such as NO, IL-6, TNF-α, and IL-1β and other inflammatory factors release. Among them, the first three compounds had relatively good inhibitory effects (Wu et al., 2022). Raspberry extract protects against chondrocyte catabolism and cartilage loss under inflammatory conditions (Bourmaud et al., 2021). In summary, the main chemical constituents and pharmacological effects of *R. chingii* were shown in Fig. 3.

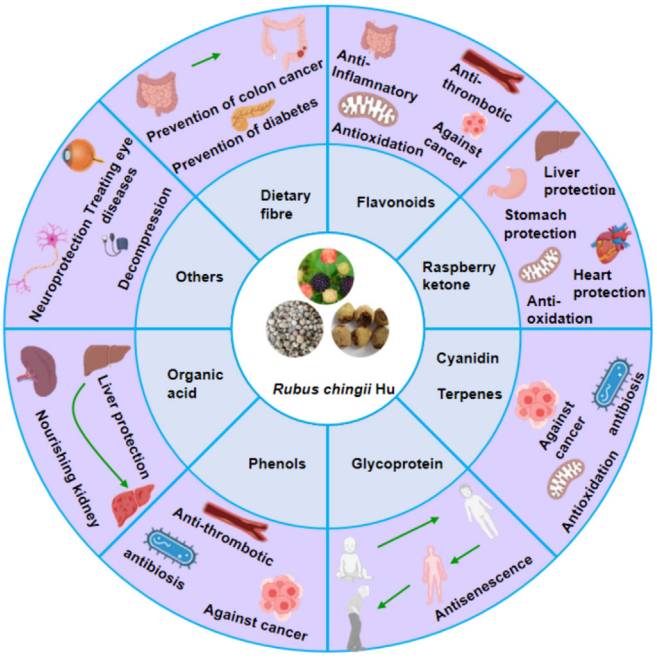

Fig. 3. Main chemical compounds and pharmacological effects of *R. chingii*.

4. Processing of raspberry

The processing methods of raspberry are mostly sun-dried or dried, and the processing methods include raw raspberry and salt raspberry in addition to wine raspberry. The processing methods include freezing, drying, juice extraction or powdering, and extraction of its bioactive components. To improve the quality of raspberry products and promote their further development, it is very important to determine the best processing conditions. It is more reasonable to steam kill and dry at 60 °C, which can preserve the active ingredients of raspberry at a higher level, but the effects of different preparation methods on the overall pharmacological activity of raspberry are still unclear and need to be further explored.

4.1. Identification

The identification of raspberry in the 2020 edition of the *Chinese Pharmacopoeia* includes powder microscopic identification and thin-layer chromatography identification. Most traditional means of identification of Chinese herbs are based on their external morphology, microstructure, or physicochemical identification, but as the plant has undergone crude processing and concoction of tablets, it is difficult to see its shape and color, and the microscopic features have been damaged to varying degrees, and the identification results are highly subjective. Physicochemical identification is only suitable for distinguishing pseudo products with obvious differences in chemical composition, and chemical composition is easily affected by a range of species, origin, growth cycle, storage conditions, concoction methods, transportation methods, etc., so the traditional method has certain limitations.

Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) is a specific molecular identification method, which can be used to specifically identify Raspberry in East China. This method does not require DNA sequencing and has high efficiency, low cost, stability, and specificity (Zheng et al., 2022). The protein fingerprints of raspberry fruit samples were analyzed by sodium dodecyl sulfate–polyacrylamide gel electrophoresis combined with advanced chemometrics, and the biomarkers obtained from the protein profiles of the berry seeds proved to be a powerful tool for the identification of their botanical origin and can be used to detect adulteration of berry-based products (Tan et al., 2022). Some scholars have shown that six components of raspberry: rutin, ellagic acid, kaempferol-3-rutinoside, zingiberin, silver linden glucoside, and saponin, can be used as quality markers of raspberry. Except for ellagic acid, the contents of the other five Q-markers were higher in Dexing raspberries from Jiangxi than in most other regions (Zhou et al., 2021).

4.2. Harvesting and processing

Global raspberry production averaged 846 515 tons from 2016 to 2020 (Tan et al., 2022). Among berry crops, the yield increase rate of raspberries are second only to that of blueberry. Russia is the largest producer of raspberries, and Poland, Serbia, and the United States have been among the top five (Lebedev et al., 2022). Modern East China raspberry's main production areas are Anhui, Jiangsu, Zhejiang, Jiangxi, Fujian, etc. The origin of *Rubi Fructus* is the dried fruit of *R. chingii*. *Rubi Fructus* harvested in wheat fields during May were the best. Besides, *R. chingii* with big, full, firm, yellow-green, sour-tasting, and free of impurities has the best quality (Liao et al., 2021). The main production area is Dexing County, Jiangxi Province, and Dexing raspberry is a national agricultural product with geographical indication, so it is also called Dexing raspberry. Fengqiu County, Henan, China, is a national demonstration area for the standardized cultivation of raspberries.

Modern records show that raspberries in Eastern China are mostly harvested in June and August when the fruits are still immature, whereas according to origin surveys and literature studies, raspberries are best harvested from late April to May before the fruits turn yellow (Sun et al., 2021). Raspberries soften when stored after harvesting, and fruit softening is an inevitable event in the ripening process of red raspberry fruit, even when stored under low-temperature refrigeration. It has been suggested that $CaCl_2$ treatment may retard the postharvest softening of red raspberry fruit stored at low temperatures by delaying cell wall degradation and starch hydrolysis (Lv et al., 2020). Preservation of raspberry fruits in trays sealed with compostable polylactic acid films and containing active film pads made from chitosan and mixed with green tea and rosemary ethanol extract prolonged their shelf life (Vieira, Alves, & Moldão Martins, 2022).

4.3. Thawing and drying

The common methods of thawing frozen raspberries are water bath thawing, microwave thawing, ultrasonic thawing, room temperature thawing, and refrigerated thawing. Microwave thawing is the most suitable method to maintain the flavor and sensory quality of raspberries (Liu, Lv, Meng, Xin, & Li, 2020).

Drying is one of the most widely used methods to increase the shelf life of raspberries. Seasonally fresh raspberries have a short shelf life due to their high moisture content and high respiration rate after maturation. Immediately after harvest, fresh raspberries should be processed using a suitable technology, such as cooling, freezing, canning, concentrating, drying, or making syrup, juice, and jam. Changes in bioactive components, color, and physical structure may occur during drying, so finding a suitable drying method is essential (Sadowska, Widerski, & Hallmann, 2020). The high content of bioactive compounds in the powder obtained by the fluidized bed airflow milling and drying method in a low-temperature simultaneous micronization process is more competitive. Methods for drying raspberries include hot air drying, vacuum drying, ultrasound-assisted vacuum drying, and freeze drying, among which ultrasound-assisted vacuum drying has lower drying time and shrinkage and higher bioactive content and color fixation and can be used as an alternative drying method (Tekin Cakmak, Kayacan Cakmakoglu, Avcı, Sagdic, & Karasu, 2021).

4.4. Extraction

Raspberry extraction methods include Soxhlet-sox, solid–liquid extraction (SLE), and two traditional extraction methods, supercritical fluid extraction (SFE) extraction and subcritical water extraction (SWE). The disadvantage of solid–liquid extraction is that the raw material must be pretreated first, and the reproducibility between batches is difficult to ensure. Compared with conventional methods, the use of the SFE method allows the recovery of high-quality edible raspberry seed oil, different varieties of raspberry seeds have a high content of high-quality oil for human nutrition and SFE can be used as an alternative green extraction technique for the recovery of raspberry seed oil (Mari, Pavli, Olovi, Abramovi, & Tesli, 2020). The bioactive compounds of raspberry by-products can be extracted by soxhlet extraction, hydrogenated distillation, maceration, cold press, and SFE. Raspberry pomace (RFP) could be a future source of recoverable bioactive compounds and fiber that could be investigated in the field of nutraceuticals, food preservation, and functional foods. Maceration maximized the extraction of quercetin and *p*-coumaric acid from RFP (Krivokapić, Vlaović, Damjanović, Perović, & Perović, 2021).

SFE is a green extraction method, the most commonly used solvent for SFE is carbon dioxide. It is an inert and environmentally safe method that allows the extraction of oil at relatively low temperatures and pressures. The use of this extraction technique allows us to overcome the problems that arise during the use of classical extraction methods, such as thermal degradation of the target compound, and residues of organic solvents in the extract. Moreover, it allows optimization of the extraction method and thus changes its parameters. The advantages of using SFE and cold pressing are reduced solvent use, lower energy consumption, shorter extraction time, and better quality. SFE can be a better technique for the green extraction of raspberry seed oil (Mari et al., 2020).

SWE, as a green extraction technique, is a non-toxic, non-flammable, environmentally friendly, efficient, safe, and low-cost conventional extraction technique that can selectively extract different types of bioactive compounds. The SWE method extracted anthocyanins from raspberries with significantly better antioxidant activity than conventional extraction methods. It is important to design a new functional beverage based on raspberry anthocyanins using the green extraction technique SWE (Wang, Ye, Wang, Yin, & Liang, 2021). The extraction of total raspberry flavonoid components using microwave-assisted low eutectic solvent was more effective, and the extracted and purified flavonoids were able to maintain good antioxidant and antibacterial activities and inhibit *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis* activities (Yu, Geng, & Zhang, 2023).

5. Development and application of raspberry

Raspberry leaf buds contain high levels of essential minerals such as Fe, Zn, K, Ca, Mg, Cu, and Mn, as well as high concentrations of bioactive substances with antioxidant and antibacterial properties (Krzepiłko, Prażak, & Święciło, 2021). Leaf buds can be an unconventional source of minerals, natural antioxidants, and antibacterial compounds, which can be used in the food, pharmaceutical, and cosmetic industries. It can also be used to produce dietary supplements, chemical therapeutic agents or substitutes for synthetic antioxidants and antibiotics, or preservatives for pharmaceuticals or cosmetics. Raspberry leaves have high phytochemical content and biological activity, including antioxidant, antidiabetic, antibacterial, and anti-inflammatory effects, indicating that eating these raspberries is beneficial to health. Raspberry seeds and pomace are rich in bioactive substances such as ω-3 fatty acids, vitamins, anthocyanins, and flavonoids. However, raspberry seeds and pomace are considered by-products or wastes during processing (Mari et al., 2020). The development and application of *R. chingii* products are drew in Fig. 4.

5.1. Raspberry daily products situation

Raspberry seed oil (RSO) extracted from raspberry seeds has anti-inflammatory activity and is used in anti-sunburn preparations, dental preparations, mouthwashes, after-shave preparations, antiperspirants, shampoos, lipsticks, etc. There are only a few domestic products about the application of raspberry in daily chemical products, such as the raspberry moisturizing invisible mask, and the raspberry skin-boosting facial mask.

Raspberry pomace can be used as a filler in the production of composites based on unplasticized polyvinyl chloride (Mirowski et al., 2021). Ellagitannin (ET) belongs to a group of raspberry phenolic compounds, and a functional edible film (LTEF) was formed using low-methoxyl pectin, and tara gum (TG). TG and ET have the potential to improve the properties of pectin films, and LTEF can be applied as a functional edible film in the food industry (Chen et al., 2020). The addition of TG and ET could improve the physical properties of low methoxylated pectin films, and the mixed edible films have good potential for application as food packaging films. Raspberry pomace extract contains anthocyanins, which are a promising colorant and antioxidant. Anthocyanins are the largest and most important water-soluble pigments in nature, they give berries their various colors and are widely distributed in red, purple, and blue plants (Gimeno, Gonzalez-Buesa, Oria, Venturini, & Arias, 2021). Cyanidins have pH-responsive properties and can change their color in response to changes in pH, however, are susceptible to external factors and reduce their stability (Yong & Liu, 2020). The colorimetric raspberry film PAXR15 prepared by incorporating raspberry pomace extract into pectin/sodium alginate/xanthan gum composite film (PAX) has the potential to become a pH-sensitive film for monitoring the freshness of protein-rich foods (Yang et al., 2021). Raspberry anthocyanin and curcumin were added to chitosan/starch/gelatin composite film (CSG), and the prepared binary color film could be used as a pH-sensitive indicator or packaging film (Duan et al., 2022).

The use of raspberry leaves for the removal of methylene blue from aqueous solutions provides a new method for the adsorption of dyes by natural material adsorbents and provides a theoretical basis for the use of raspberry leaf-based materials as adsorbents in wastewater treatment (Mosoarca, Popa, Vancea, Dan, & Boran, 2022). Cellulose was used as a carrier polymer for raspberry volatiles, and freeze-dried cellulose/raspberry complexes were prepared by complexation of raspberry juice and cellulose for use as a food flavoring ingredient (Vukoja, Pichler, Ivić, Šimunović, & Kopjar, 2020). Raspberry straw-derived biochar (BC)-Fe_3O_4/Fe_2O_3 composites and their urea-modified derivatives (BC-Fe-U) are effective tools for the simultaneous removal of As and Cr from water samples and may become water purification devices. This material can be simply separated from the solution and synthesized simply by using magnets, which makes agricultural waste management possible and low cost of preparation (Dobrzyńska, Wysokińska, & Olchowski, 2022). The non-glandular hairs in raspberry leaves can prevent the aggregation of the mixed components in the herb mixture and have high nutrient content, which can be used as a valuable raw material for preparing infusion solutions.

5.2. Raspberry-containing proprietary Chinese medicine preparations

At present, the efficacy of Chinese patent preparations containing raspberry in the market is mostly based on nourishing the liver and kidneys and aiding pregnancy. There are 15 kinds of Chinese patent medicines in the *Chinese Pharmacopoeia*, mainly for nourishing the kidneys. There are 259 prescriptions containing raspberries, but only a few formulations have been developed into preparations, and the functions are focused on reinforcing kidney essence, nourishing blood, and aiding pregnancy, while fewer raspberry formulations have been developed with the effects of lowering lipids, lowering sugar, protecting the liver, and regulating menstruation. Searching the Baiteng network, 944 patents were found with the keyword ‘‘raspberry and kidney tonic”, which indicates that there is a great prospect for developing raspberry kidney tonic drugs.

According to the records of *Compendium of Materia Medica*, the juice of raspberry leaves can brighten eyes and stop tears. However, at present, there are no eye care domestic products with raspberries as the main ingredient, and its market needs to be developed.

5.3. Raspberry food and health products situation

Raspberry fruit in the international fresh fruit market occupies the high-end market of fruit, known as ‘‘ruby”, ‘‘cancer’s nemesis”, and ‘‘the fruit of life”, often as a senior ingredient of Western cui-

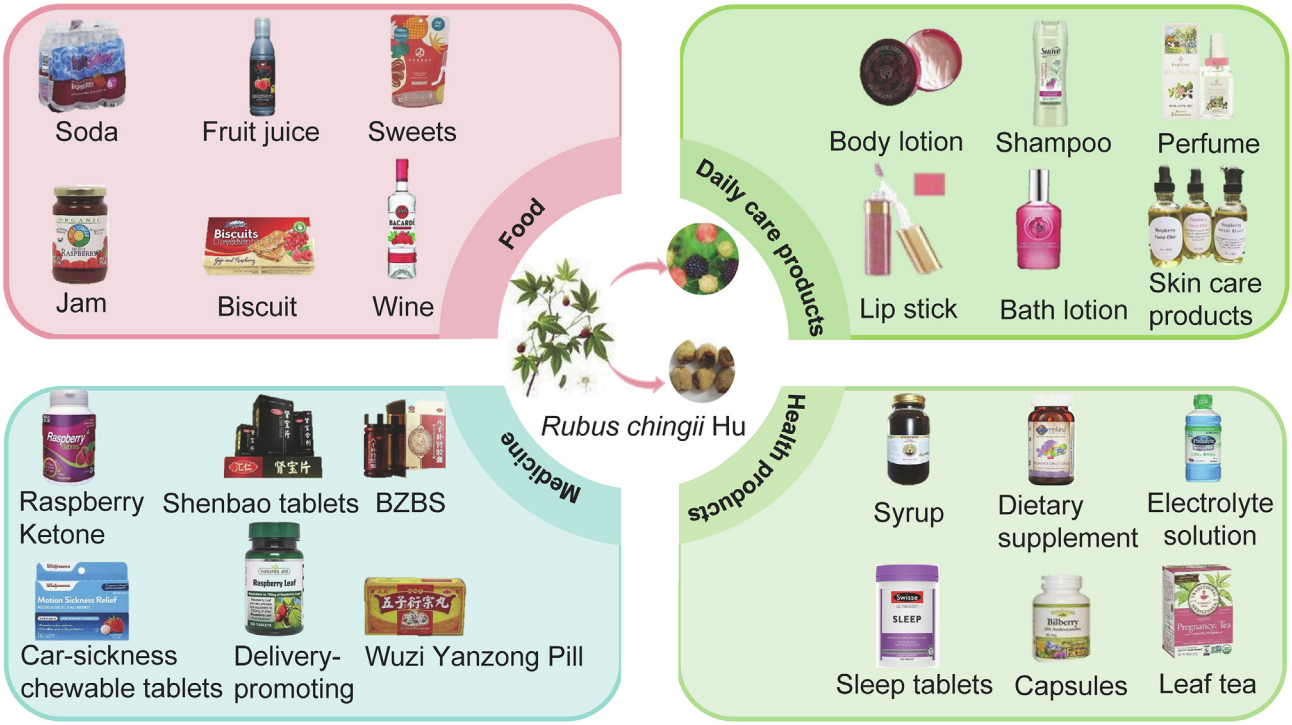

Fig. 4. Development and application of *R. chingii* products.

sine. In China's Western food industry development in the faster cities, raspberry fruit has quietly become a new favorite on the table. Raspberry fruit in addition to fresh food, can be processed into juice drinks, jam and fruit wine, and other products, but also as a food modifier, and fixing agent. In the UK and the US, raspberries have more than 100 categories of further processing, and thousands of varieties, including raspberry drinks, jams, yogurt, capsules, etc. In foreign countries, raspberry leaves have also been developed into a variety of therapeutic and health products, such as New Zealand red seal raspberry leaf tea, Australian raspberry water, German rose cranberry, etc. In China, there are only a few raspberry food and health care products, such as raspberry drinks, raspberry fruit tablets, Puzzle Ren brand yellow essence over benefit capsules, etc.

Raspberries have a shelf life of only 2–3 days and are also prone to deterioration during transportation (González-Orozco, Mercado-Silva, Castaño-Tostado, Vázquez-Barrios, & Rivera-Pastrana, 2020). Red raspberry wine brewing can extend its shelf life and increase the product value of red raspberries. In the fermentation process of red raspberry wine, the immobilized yeast of Penicillium flavum-producing has better fermentation power than free yeast, which can better retain the active ingredients such as anthocyanins and polyphenols in red raspberry wine, and also has an obvious antibacterial effect. Penicillium flavum-producing immobilized yeast improved the content of alcohols, lipids, and other aroma components in red raspberry fruit wine and maintained better fermentation performance after three consecutive fermentations (Liu et al., 2022).

The addition of raspberry juice gives wafers an attractive color and contributes to the phenolic content and antioxidant activity of the wafers. Raspberry juice can be used as a functional ingredient to enhance the nutritional value of wafers and to enhance health-promoting and organoleptic properties. Further studies are necessary, preferably starting with cellular models, which will make it possible to assess the degree of absorption of the compounds released from the food. Black raspberry phytochemicals have shown anticancer properties in experimental models, including prostate cancer (Szymanowska, Karaś, Złotek, & Jakubczyk, 2021). Studies using dried and ground raspberry pomace rich in polyphenols, dietary fiber, linoleic acid, and α-linolenic acid as a substitute for 30% gluten-free flour for cookies have shown that daily consumption of cookies containing raspberry pomace may have positive effects on certain cardiovascular risk factors and liver function indicators (Popović et al., 2022). The use of 4% or 5% raspberry aqueous extract as a new additive in the slurry may be considered a colorant and antioxidant for pasta processing to prevent color changes or lipid oxidation (Aksu, Erdemir, Turan, & Öz, 2022).

6. Conclusion and outlook

Raspberries and their ripe fruits have similar effects in terms of pharmacological action, raspberries have higher ellagic acid content and better anti-aging activity, making them more suitable for health product development. Raspberries have antioxidant, anti-aging, anti-cancer, lipid-lowering, and weight-loss effects, and have the potential to reduce the risk of chronic diseases and have great potential for the development of therapeutic food industry. Nowadays, raspberry fruit wine and jam products are mostly, fermented products are less, and the market prospect is broad, raspberries can be combined with suitable national body strains to develop fermented products, both through probiotic fermentation to improve the sensory quality of berry juice, but also to regulate the intestinal flora.

The *Chinese Pharmacopoeia* only stipulates the content of ellagic acid and kaempferol-3-*O*-rutinoside as the screening index of raspberry, and it is necessary to increase its quality markers. In the future, the correlation between the active components and pharmacological effects of raspberries should be deeply explored, and the quality identification system of raspberry should be estab-

lished to further improve the quality of raspberry products. In addition, the establishment of standards in other countries and regions also needs to be improved. At present, some of the chemical components of raspberry such as alkaloids, organic acids, oligosaccharides, dietary fiber and pectin polysaccharides, trace elements, etc. are less studied, and the relationship between pharmacological activity is still not deep enough, should be studied more deeply in this direction, to explore its active ingredients, mechanism of action, for the subsequent further development of the raspberry industry to provide an effective reference. At the same time, there are few raspberry products on the market, and most of them are mainly healthcare products, the development of other processing areas is still not deep enough, and there is a large gap in the market, the follow-up should increase the raspberry product development, in-depth processing research.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Xiangmei Xiong: Conceptualization, Software, Visualization, Writing – original draft, Writing – review & editing. **Zheng Liu:** Writing – review & editing. **Xiance Che:** Writing – review & editing, Visualization. **Xuemin Zhang:** Funding acquisition. **Xia Li:** Conceptualization, Funding acquisition, Resources, Supervision, Writing – review & editing. **Wenyuan Gao:** Conceptualization, Funding acquisition, Resources, Supervision.

Acknowledgments

This work was financially supported by the Innovation Team and Talents Cultivation Program of National Administration of Traditional Chinese Medicine (No. ZYYCXTD-D-202005), Tianjin Municipal Science and Technology Committee (No. 20YFZCSY00560), the Key Project at Central Government Level (No. 2060302) and National Natural Science Foundation of China (No. 82373982, 82173969).

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