

An updated review of composition, health benefits, and applications of phenolic compounds in *Ficus Carica L.*

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Abstract

Ficus carica L. (FC) is rich in phenolic compounds such as phenolic acids, flavonoids, and anthocyanins. Phenolic compounds in FC show remarkable health benefits and applications. The composition of phenolic compounds in FC can vary with some factors, such as variety, ripeness, geographical location, extraction methods and processing methods. New techniques such as supercritical fluid extraction, subcritical water extraction and ionic liquid extraction should be further developed and combined with traditional techniques to obtain higher quality sources of phenolic compounds. Numerous in vivo and in vitro studies reported healthy benefits of phenolic compounds in FC, such as anti-oxidant, anti-inflammatory, anti-diabetic, anti-obesity, anti-cancer and anti-Alzheimer's. Further works are required to reveal mechanisms and structure-activity relationships, such as targeted metabolomics and pharmacological studies. In terms of applications, phenolic compounds in FC as prebiotics on the intestinal flora need to be further studied to expand their applicability in food fermentation. In a word, this review highlights the remarkable health benefits and application value of phenolic compounds in FC.

KEYWORDS

application, composition, *Ficus carica L.*, health benefits, phenolic compounds

1 | INTRODUCTION

Ficus carica Linn. (FC) belongs to the genus *Ficus* within the family Moraceae, it is one of the most ancient fruits cultivated in the Mediterranean region. Meanwhile, it has high production rates in Mediterranean countries, including Turkey, Egypt, Greece, Algeria, Italy, and Spain (Hussain et al., 2021). FC is widely utilized in the food industry, for instance, fresh figs are common foods and dried figs could be used as jam. Additionally, figs could also be applied as juice and fermented fruit wine (Ayuso et al., 2022). Besides, fig juice can cure mild constipation (Rtibi et al., 2018), leaves can be used as animal feed (Hassanien, 2023), fig latex can be utilized to help rennet dairy products (Castelli &

López, 2021), edible oils and fats can be extracted from seeds (Badgujar et al., 2014). Hence, FC plays a vital role in the extensive processing of fruits.

All parts of FC are abundant in bioactive compounds, such as fresh fruit, leaves, and latex. Fresh fruit extract contains a variety of nutrients and bioactive ingredients such as free sugars, organic acids, phenolic compounds and fatty acids (Kiralán et al., 2023). Flavonoids, flavonols and proanthocyanidins are found in leaves (Bashir et al., 2023). Fig latex also contains numerous bioactive compounds, triterpenoids, phytosterols, fatty acids, proteases, organic acids and amino acids (Castelli & López, 2021). All of the bioactive compounds in FC have health benefits such as antibacterial, anti-oxidant, anti-diabetic, acetylcholinesterase

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inhibition, immune regulation, anti-cancer, etc. (Surendran et al., 2020). In traditional medicine, FC is applied to various reproductive, digestive, endocrine and respiratory diseases, and is effective in the treatment of diabetes, anemia, cancer, leprosy, liver diseases, skin diseases and ulcers (Ayuso et al., 2022; Morovati et al., 2022; Salah et al., 2022; Yahiaoui et al., 2022). And it is also listed in the Western Pharmacopoeia and herbal treatment guidelines (Barolo et al., 2014).

The powerful health benefits of FC are associated with their high levels and diversity of phenolic compounds; and mainly phenolic compounds in FC are phenolic acids, flavonoids and anthocyanins (Aicha & Menadi, 2023; Rezagholizadeh et al., 2022). The content and composition of phenolic compounds in FC vary based on factors such as fruit quality, processing method and extraction techniques in particulars (Oluwaseun Ruth Alara et al., 2021; Shahinuzzaman et al., 2020). Traditional solvent extraction, ultrasonic-assisted extraction, ionic liquid extraction, microwave-assisted extraction, and supercritical fluid extraction are effective methods for extracting phenolic compounds from FC. Among them, the traditional solvent extraction methods are very time-consuming and require more solvents than other methods, which are more suitable for SMEs in developing countries (Alara et al., 2018; Shahinuzzaman et al., 2020). Ultrasonic-assisted extraction, ionic liquid extraction, microwave-assisted extraction and supercritical fluid extraction require relatively less solvent, and they can separate phenolic compounds efficiently with good reproducibility. The characteristics of low extraction temperature and time-saving are also more suitable for industrial production (Alara et al., 2018; Morgan, 2013; Shirzad et al., 2017).

Numerous studies have demonstrated the health benefits of phenolic compounds in FC, such as anti-oxidant, anti-inflammatory, anti-obesity, anti-diabetic, anti-inflammatory, anti-cancer and anti-Alzheimer's (Aicha & Menadi, 2023; Kiralan et al., 2023; Moyo & Tavengwa, 2023). For example, quercetin in FC is a powerful natural anti-oxidant and anti-inflammatory (Lesjak et al., 2018). Cyanidin is a natural flavonoid with therapeutic effects on cardiovascular disease and atherosclerosis, and it can reduce cellular lipid accumulation in macrophages and hepatocytes (Shen et al., 2022). Caffeic acid and Chlorogenic acid are phenolic acid compounds with various physiological activities such as anti-oxidant, anti-inflammatory and antibacterial (Birková, 2020). Catechin is derivative of flavanols in FC, it shows anti-oxidant, anti-inflammatory, and cardiovascular benefits (Zeng et al., 2020). FC is also very high in rutin, a flavonoid compound with a variety of health benefits. Rutin is found to be effective in the treatment of several diseases like varicosities, haemorrhoids and internal haemorrhage (Patel & Patel, 2019; Veberic et al., 2008).

With the rise of nutritional supplements and functional foods in the world, scientists are increasingly

interested in phenolic compounds, and the phenolic compounds in FC are also attracting attention from several industries (González-Romero et al., 2022). In the food industry, phenolic compounds can act as coloring agents, functional ingredients, nutritional enhancers, preservatives and antioxidants (Alara et al., 2021; Ayuso et al., 2022). Phenolic compounds can also be used in the development of novel drug formulations as well as in a variety of clinical disease studies (Alamgeer et al., 2017; Morovati et al., 2022). Because of their anti-oxidant and antimicrobial properties, phenolic compounds can also be combined with a variety of polymers to create food packaging materials that preserve the freshness of various foods (Wang et al., 2019; Zeng et al., 2019). Furthermore, phenolic compounds extracted from FC have great potential in clinical medicine, green food packaging materials and the food industry (Albuquerque et al., 2021).

2 | COMPOSITION OF PHENOLIC COMPOUNDS IN FC

The main forms of phenolic compounds in FC are glycosides, monomers, polymers, and substrates or free-binding molecules (Nakilcioğlu-Taş & Ötleş, 2021). According to the biosynthetic pathway or structural features, phenolic compounds are divided into simple phenolic acids, flavonoids, tannins, coumarins, lignans and astragals (Abegaz & Kinfe, 2019; Rehab & Amira, 2018). The major phenolic compounds in FC are flavonoids and phenolic acids (Figure 1) (Francini et al., 2021). FC contains phenolic acids such as chlorogenic acid, flavanols such as (+) catechin and (−) epicatechin, flavonols such as quercetin, 3-O-glucoside, kaempferol-3-O-glucoside and rutin, flavonoids such as lignan-8-C-glucoside, anthocyanins such as cyanidin-3-O-rutinoside, and many other phenolic compounds (Hssaini et al., 2022; Prgomet et al., 2021; Slatnar et al., 2011).

2.1 | Total phenols, total flavonoids, and total anthocyanins in FC

The content of total phenols, total flavonoids and total anthocyanins in FC varies based on a variety of factors, including fruit part, variety, ripeness, growth location and processing method. There were also significant differences in the composition of phenolic compounds among different parts of FC. Tables 1 and 2 summarize the total phenolic, total flavonoid and total anthocyanin contents of each part of FC. It is reported that the total phenolic content of FC leaves was higher than other parts of the fruit such as peel, pulp and root (Oliveira et al., 2009). And more flavonoid compounds in FC leaves may be linked to the photosynthesis (Treutter, 2006). The total phenolic content of the skin

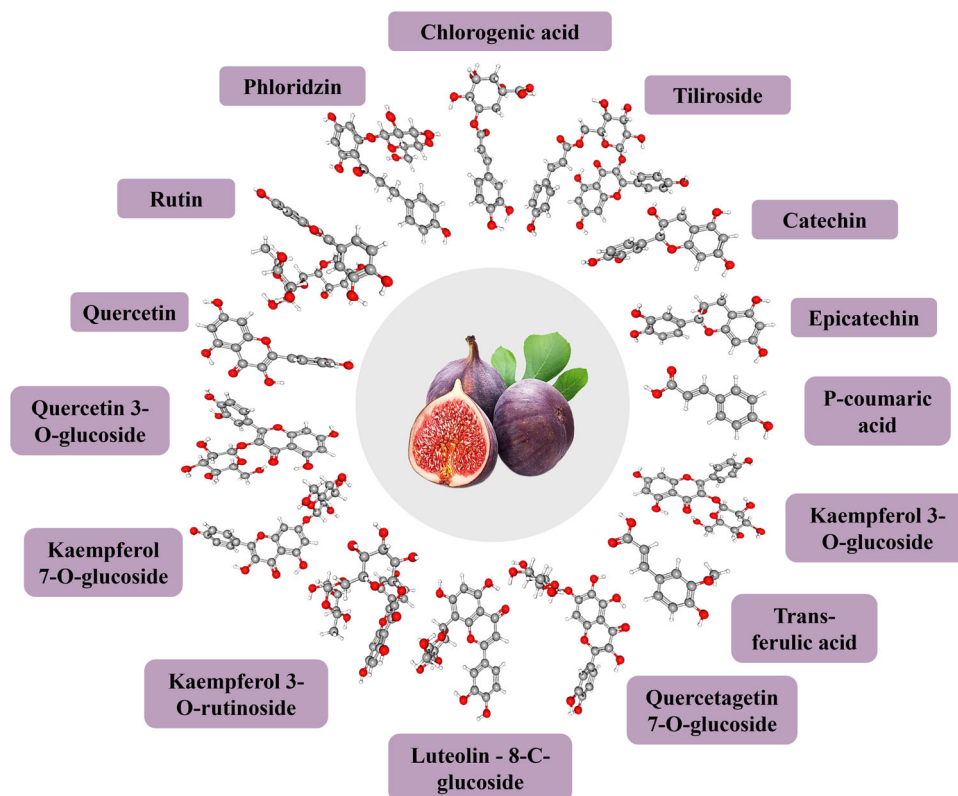


FIGURE 1 Main phenolic compounds in FC. FC, *Ficus carica L.*

part of FC is also higher than the pulp part (Solomon et al., 2006). Anthocyanins are the most abundant phenolic compounds in the peel part of FC, and latex in FC tree is an important source of phenolic compounds, which contains various phenolic compounds such as psoralen and bergamot lactone (Salah et al., 2022). The content of phenolic compounds in FC varied with varieties, for instance, phenolic compounds in the latex of 18 varieties of FC were extracted by maceration and ultrasound-assisted extraction with 75% ethanol, and the types and contents of phenolic compounds in the latex of 18 varieties of FC are found to be different (Shahinuzzaman et al., 2020). Significant differences were also found in the total phenolic content of 10 different varieties of dried figs (Wojdyło et al., 2016). In addition, dark-skinned fig varieties have higher phenolic acids and flavonoids than light-skinned varieties (Arvaniti et al., 2019; Kebal et al., 2022). For example, extracts of darker varieties showed higher contents of polyphenols, flavonoids, and anthocyanins compared to lighter colored varieties, the total phenolic content of Mission variety is 281 mg gallic acid equivalents (GAE)/100 g, while the light colored variety Kadota had a total phenolic content of only 49 mg GAE/100 g (Solomon et al., 2006). Ripeness is also a factor affecting the content of phenolic compounds in FC, this is because phenolic compounds accumulate during ripening (Hssaini et al., 2021). In highly ripe

figs, especially dark-colored varieties, more anthocyanin could be accumulated in the pericarp (Pereira et al., 2017). Moreover, location is another factor affecting the total phenolic content, and figs grown in Turkey usually have higher total phenolic than in other countries (Kamiloglu & Capanoglu, 2015).

The total phenolic, total flavonoid and total anthocyanin content in FC decreased during drying process. Anthocyanins in FC are unstable phenolic compounds, and naturally drying figs have the greatest loss of anthocyanins. The total phenolic content of yellow and purple FC decreased by 8% and 15% after the solar drying process, and the total anthocyanin content of purple and yellow FC decreased by 83% and 98%, respectively (Kamiloglu & Capanoglu, 2015). Meanwhile, the total phenolic content of greenhouse-dried figs was higher than that of open-air drying (Radojcin et al., 2021). And the total phenols and total flavonoids of freeze-dried figs were also substantially reduced (Bachir Bey et al., 2017). Besides, during the freezing process, the contents of total phenols, total flavonoids and total anthocyanins also decreased significantly. With the concentrations of these phenolic compounds in fresh figs are 31.0 mg GAE/100 g, 11.4 mg quercetin equivalent (QE)/100 g and 0.8 mg cyanidin-3-glucoside (C3G)/100 g, compared to only 14.0 mg GAE/100 g, 3.6 mg C3G/100 g and no detectable QE/100 g in frozen figs (Petkova et al., 2019).

TABLE 1 Total phenols in FC.

Sample (part/tissue)	Variety, origin	Assay method	Concentration	References
Dried figs (whole)	White figs (<i>Ficus carica</i>) from Beni Maouche	Solid Liquid Extraction	2190.10 ± 17.55 CE/100 g FW	Amessis-Ouchemoukh et al. (2017)
Peel Pulp Leaves	<i>F. carica</i> (var. Pingo de Mel and var. Branca Tradicional), Northeast Portugal	HPLC-DAD	600.6–723 mg/kg lyophilized extract (Peel) 36.6–130.3 mg/kg lyophilized extract (pulp) 32412.0–34473.6 mg/kg lyophilized extract (leaves)	Oliveira et al. (2009)
Leaves	Two Iranian fig cultivars namely Sabz and Torsh	Spectrometric-Folin-Ciocalteu	18.52–23.604 mg GAE/g DW	Abdolinejad et al. (2021)
Stem barks	Prikro (city of Brobo, Côte d'Ivoire)	Solid Liquid Extraction	115.51 ± 1.60 mg GAE/g DW	Sieniawska et al. (2022)
Fresh fruit	Ten different fig cultivars, Spanish	UPLC-PDA-FL	715–186 mg/100 g FW	Wojdyło et al. (2016)
Fresh fruit	Twenty-seven Tunisian ecotypes	Spectrometric-Folin-Ciocalteu	51.50–100.23 mg GAE/100 g FW	Fateh et al. (2020)
Fresh fruit	Ten different fig cultivars, Morocco	Spectrometric-Folin-Ciocalteu	90.75–524.74 mg GAE/100 g FW	Hssaini et al. (2020)
Latex	Eighteen different fig cultivars, Malaysia	Spectrometric-Folin-Ciocalteu	The maceration extraction method 233.14–311.83 µg GAE/mL Ultrasound-assisted Extraction 224.37–291.98 µg GAE/mL	Shahinuzzaman et al. (2020)
Fresh fruit	Durban, South Africa	Ethanol extraction	104.67 ± 5.51 µg/mL	Mopuri et al. (2018)
Fig seed	–	Spectrometric-Folin-Ciocalteu	665.12 ± 0.52 mg GAE/100 g DW	Bölek (2021)
Fig seed	Sarilop variety, Turkey	50% (vol/vol) methanol in water	714 mg GAE/kg DW	Nakilcioğlu-Taş & Ötleş (2021)
Leaves	Pakistan	Spectrometric-Folin-Ciocalteu	71.208 ± 2.89 mg/g GAE DW	Asghar et al. (2023)

Abbreviations: DAD, diode-array detection; FL, fluorescence detectors; GAE, gallic acid equivalents; HPLC, high-performance liquid chromatography; PAD, photodiode array.

2.2 | Individual phenolic compounds in FC

The variety of individual phenolic compounds in FC is diverse, and their content varies based on the variety, color, ripening and drying method. Variety affects the composition of individual phenolic compounds in FC, with the highest content of quercetin-3-O-rutinoside in the Verdal Brevas variety at 328 mg/100 g dry weight (DW) (Wojdyło et al., 2016). Chlorogenic acid is a phenolic acid with different content in different parts, 1.9–8 mg/100 g DW in the whole fruit, 12–21 mg/100 g DW in the peel, and 0.5–6 mg/100 g DW in the pulp of fresh figs (Kamiloglu & Capanoglu, 2015). The flavonoid compounds in FC mainly included lignan 6C-hexose-8C-pentose and apigenin-rutinoside, which were mainly concentrated in the peel,

0.1–1.9 mg/100 g FW and 0.8–2.4 mg/100 g fresh weight (FW), respectively (Vallejo et al., 2012). Anthocyanin in FC is mainly anthocyanin-3-O-rutinoside, with the highest content of 116 mg/100 g DW in alfalfa varieties (Wojdyło et al., 2016). Darker figs had higher levels of anthocyanin-3-O-rutinoside and quercetin-3-O-rutinoside, and brown, green, and yellow-green varieties contained the highest levels of chlorogenic acid (Pereira et al., 2017). The pericarp contains higher levels of anthocyanin-3-O-rutinoside, anthocyanin-3-O-glucoside, and geranin-3-O-rutinoside than the flesh at various stages of fig ripening. Chlorogenic acid, ellagic acid, quercetin-3-O-rutinoside, quercetin-3-acetylglucoside, anthocyanin-3-O-rutinoside, and anthocyanin-3-O-rutinoside were significantly lower in unripe figs than in ripe figs (Pereira et al., 2017).

TABLE 2 Total flavonoids and total anthocyanins in FC.

Sample (part/tissue)	Variety, origin	Total flavonoids	Total anthocyanins	References
Fresh fruit	Four Tunisian fig varieties	410–830 mg/kg	–	Soltana et al. (2018)
Leaves	Ten Algerian cultivars	11.667–16.211 mg QE/g	–	E. Maghsoudlou et al. (2016)
Leaves	Turkey	252.5 ± 1.1 mg QE/g	–	Orhan et al. (2011)
Leaves	–	43.92 mg QE/g dry leave extract	–	Yassien et al. (2022)
Whole, skin, pulp	Two Turkish cultivars Sarilop-yellow Bursa siyahi- purple	Sarilop-yellow 7–63 mg CE/100 g DW Bursa siyahi-purple 66–234 mg CE/100 g DW	Sarilop-yellow 0.8–5.9 mg of C3G/100 g DW Bursa siyahi-purple 14.5–196 mg C3G/100 g DW	Kamiloglu & Capanoglu (2015)
Fresh fruit	Twenty-seven Tunisian ecotypes	0.33–17.59 mg QE/100 g FW	1.61–11.67 mg C3G/100 g FW	Fateh et al. (2020)
Fresh fruit	Ten different fig cultivars, Morocco	14.59–83.71 mg CE/100 g DW	3.1–24.8 mg C3R/100 g DW	Hssaini et al. (2020)
Fresh fruit	Three dark fig varieties	84.63–151.47 mg/100 g DW	–	Bachir Bey et al. (2017)
Fresh fruit	Two native Algerian fig varieties, azendjar (Az) and taamriouth (Ta)	Az 428.34 ± 15.42 QE mg/100 g DW Ta 307.63 ± 7.94 QE mg/100 g DW	–	Kebal et al. (2022)
Fresh fruit	Ten different Spanish fig cultivars	–	0.4–122 mg/100 g DW	Wojdyło et al. (2016)

Abbreviations: CE, catechin equivalent; C3G, cyanidin-3-glucoside; C3R, cyaniding-3-O-rutinoside; DW, dry weight; FW, fresh weight; QE, quercetin equivalent.

Drying is an important factor affecting the content of individual phenolic compounds in FC. The predominant phenolic acid in dried figs is gallic acid, up to 5.04 mg/100 g DW, while in whole fresh figs the concentration of gallic acid is up to 6.98 mg/100 g DW (Arvaniti et al., 2019). Drying methods also affect the content of individual phenolic compounds in FC, kaempferol-3-O-glucoside in FC is 0.31–0.59 mg/100 g FW after sun drying and 0.56–1.43 mg/100 g FW after oven drying (Slatnar et al., 2011).

3 | EXTRACTION OF PHENOLIC COMPOUNDS FROM FC

3.1 | Conventional solvent extraction

Methanol, ethanol, acetone, petroleum ether and dimethylformamide are conventional used solvents for the extraction of phenolic compounds from FC (Nakilcioğlu-Taş & Ötleş, 2021). Both water and 50% ethanol are used as solvents to extract total phenols from fig leaves, and total phenolic contents of 21.2 mg GAE/g DW and 17.1 mg GAE/g DW were reported, respectively (Alcántara et al., 2020). Both Bucic-Kojic et al. (Çalışkan & Aytekin Polat, 2011) and Debib et al. (2014) reported

that 80% ethanol is the best for extraction of polyphenol from FC. A green alternative to toxic organic solvents is low eutectic solvents (DES). DES consisting of glycerol, xylitol, and D-(–)-fructose in a 3:3:3 molar ratio showed higher extraction rates for the five polyphenolic compounds simultaneously compared to conventional ethanol, and the extraction rates of caffeoyl malic acid, glucoside psoralen, rutin, psoralen and bergamot lactone were 6.48, 16.34, 5.21, 15.22, and 2.46 mg/g, respectively (T. Wang et al., 2017). Obviously, compared with conventional solvent extraction, DES has no significant advantages for the extraction of phenolic compounds, and it is also a challenge to completely remove DES from phenolic extracts.

It is very important to select suitable extraction solvent for polyphenol extraction. But, identifying suitable solvents to develop standard methods for all forms of phenolic compounds in FC can be a difficult task. In addition, the ability of the solvents to establish hydrogen bonds is decisive, specifically for the achievement of solvation and release of the matrix-bound species, the greater the diffusivity of the solvent within the matrix, the easier the destabilization of the hydrogen bond network within its structure and higher the solvation of the target phenolic compounds (Alara et al., 2021; Gil-Martín et al., 2022). Thus, a variety of

extraction solvent factors must be considered, such as solvent capacity, solvent polarity, solvent boiling point, solvent reactivity, solvent viscosity, solvent stability and safety issues.

3.2 | Ultrasonic-assisted extraction

Ultrasonic technology is a green extraction technology that uses the cavitation effect to accelerate chemical reactions, and it is widely used in the extraction of functional ingredients (Cui et al., 2021; Nie et al., 2021). Ultrasound-assisted extraction initiates cell rupture and creates a path for the release of intracellular polyphenols at optimized conditions, and numerous studies have reported that ultrasonic extraction can improve the extraction efficiency of polyphenols (Hadidi et al., 2020; Selvakumar et al., 2021). Ultrasonic extraction of spruce bark yields phenolic compounds 1.1–7.1 times higher than conventional solvent extraction. Using an appropriate solvent system is a key step in achieving high yields of phenolic compounds in ultrasonic assisted extraction (Bouafia et al., 2021), ethanol is the best solvent for extracting phenolic compounds from rice bran extract, bay laurel and mango pericarp under ultrasonic condition (Peanparkdee et al., 2019; Rincón et al., 2019; Rodsamran & Sothornvit, 2019). Ultrasound-assisted surfactant, dimethyl sulfoxide extraction of polyphenols from pomegranate peel yielded a total phenolic content of 43.58 ± 1.0 mg GAE/g DW (Selvakumar et al., 2021). Compared with the results of Alcantara et al. (2020), it is 2.76 times that of water extraction and 3.72 times that of 50% ethanol extraction. Further research is critical to solve the scaling-up of the ultrasonic assisted extraction for industrial purposes. Main aspects to be analyzed are related to the configuration of the ultrasonic emitter and the extraction vessel, the increase of the ratio dried material-solvent and the design of the cooling system to keep mild temperatures during the ultrasonic assisted extraction.

3.3 | Ionic liquid extraction

As a class of novel and promising media, ionic liquids (ILs) have shown infusive potential applications in energy production (Singh, et al., 2022). Meanwhile, ILs are undergoing development as extractants for phenolic compounds from wastewater due to their outstanding properties (Skoronski et al., 2020). By utilizing 1-butyl-3-methylimidazole hexafluorophosphate solution as an extractant, the phenolic compounds present in fig leaves, pulp and pericarp, comprising of gallic acid, chlorogenic acid, rutin, psoralen and bergamot lactone, can be quickly and effectively extracted under ultrasonic-assisted conditions. This process leads to a remarkable enhancement in the extraction yield and a reduction in the extraction time

(Qin et al., 2015). The advantages of ILs extraction for phenolic compounds are high efficiency, good selectivity, non-toxicity and environmentally-friendly. However, ionic liquids are costly, and more research is required for their selection and design. Hence, future research should focus on selecting and designing ionic liquids to achieve higher extraction efficiencies and lower costs.

3.4 | Microwave-assisted extraction

Microwave-assisted extraction rapidly heats samples using high-frequency oscillation and molecular friction to extract plant compounds (Sarfarazi et al., 2020). It offers multiple advantages over conventional solvent extraction, including high extraction rates, short extraction times, and low solvent consumption (Mustapa et al., 2015). In recent years, microwave assisted extraction has also been used to extract phenolic compounds from FC (Singh, Kim, et al., 2022). Microwave-assisted surfactants are used to extract five phenolic compounds from fig leaves. The extraction rates of caffeoyl malic acid, psoralen glucoside, rutin, psoralen, and bergamot lactone reached 9.72, 5.95, 4.77, 15.65, and 3.49 mg/g, respectively, and the final extraction rates were much higher than water extraction and 50% ethanol extraction (Yu et al., 2020). Additionally, employing microwave-assisted extraction with low eutectic solvents in the extraction of fig leaves has resulted in higher contents of polyphenols and furanocoumarins (Wang et al., 2017). In general, microwave-assisted extraction is a promising extraction method of phenolic compounds in FC, but the application is still very limited (Moyo & Tavengwa, 2023). It should also be noted that microwave-assisted extraction is also technically challenging and requires good control of microwave power, extraction time and other parameters in the extraction process of phenolic compounds.

3.5 | Subcritical water extraction

Subcritical water refers to the temperature between 100°C and 374°C, the pressure is large enough and maintained in the liquid state of water (the critical state of water parameters for 374°C, 22 Mpa) (Di Domenico Ziero et al., 2020). Water exhibits a robust hydrogen bonding force at room temperature, binding tightly to the phenolic hydroxyl group. However, as the temperature increases, the dielectric constant of water ϵ decreases, drastically weakening the hydrogen bonding force. This weakening leads to a decrease in both density and polarity, ultimately making the phenolics more soluble (Yan et al., 2020). Using subcritical water extraction, total phenolics and total flavonoids are efficiently extracted from the pulp and skin (Maghsoudlou et al., 2017). As a cost-effective, abundant, and environmentally sustainable polar solvent,

subcritical water extraction offers several benefits, including high extractant quality, short extraction time, low solvent volume, and minimal expenses (Ko et al., 2020). Subcritical water extraction is a productive and eco-friendly process for obtaining phenolic compounds from FC. Therefore, it is vital to acquire phenolic compounds that possess the utmost anti-oxidant activity to support their potential application as natural antioxidants in the industry. The utilization of the subcritical water extraction method to extract phenolic compounds from figs remains limited, and additional potential applications warrant further exploration in the future.

3.6 | Supercritical fluid extraction

Supercritical carbon dioxide represents a popular technique for extracting phenolic compounds from plants (Sridhar et al., 2021). Four phenolic compounds found in agave can be extracted using supercritical carbon dioxide. These include artemisinin C, 3-prenyl-4-hydroxycinnamic acid, p-coumaric acid, and kaempferol. And when the extraction conditions of supercritical carbon dioxide are 60°C and 40 MPa, the extraction rates of kaempferol, artemisinin C and 3-prenyl-4-hydroxycinnamic acid were 156%, 98%, and 64% higher than those of ethanol extract, respectively (Piantino et al., 2008). However, the non-polar character of carbon dioxide does not allow extraction of most polyphenols, and requires the use of co-solvents to change the polarity of carbon dioxide to extract non-volatile polyphenols (Chañi-Paucar et al., 2022). Supercritical carbon dioxide extraction with ethanol (80% vol/vol) as co-solvent is effective in the extraction of polyphenols from oats (Escobedo-Flores et al., 2018). By optimizing extraction conditions such as temperature, pressure, extraction time and other parameters, higher yields and higher quality phenolic compounds can be obtained. In supercritical carbon dioxide extraction of phenolic compounds from black rose hips, total phenolic and total anthocyanin contents of 76.58 ± 4.25 mg GAE/g DW and 10.89 ± 1.56 mg cyanidin-3-O-glucoside equivalent per g of the dry fruits, the extraction rate can reach several times that of conventional solvent extraction (Kasapoğlu et al., 2023). Using aqueous methanol as a co-solvent, the caffeic acid content of dried potato peel is extracted to 0.75 mg/g, when extraction conditions are 80°C, 350 bar, 20% methanol concentration and a CO₂ flow rate of 18.0 g/min, total phenol and caffeic acid recoveries of 37% and 82%, respectively (de Andrade Lima et al., 2021). However, no specific application of supercritical fluids in phenolic compounds of FC extraction has been found yet, and further exploration is required. In addition, some studies have explored the application of other supercritical fluids in functional substances, such as supercritical alcohol and supercritical ethyl acetate, but also requires further research and validation.

4 | HEALTH BENEFITS OF PHENOLIC COMPOUNDS IN FC

4.1 | Anti-oxidant activity

Compared to vitamin C and vitamin E, FC contains superior anti-oxidant properties, and it can enrich plasma lipoproteins. Within 4 h of fig consumption, the anti-oxidant capacity of human plasma increases significantly, lasts 6 h (Vinson et al., 2005). Phenolic compounds in FC play a key role in anti-oxidant composition (Gong et al., 2022), the anti-oxidant principle is to capture free radicals to protect cells from damage caused by oxidative stress, thus maintaining cell health and normal life activities (Khutami et al., 2022). The ethanolic extract of fig leaf at 1 mg/mL shows strong anti-oxidant activity with 75.7% DPPH scavenging capacity (Abdel-Rahman et al., 2021), but the total anti-oxidant activity in this study was lower than that determined by Nadia et al. by using Ascorbic as standard (Amessis-Ouchemoukh et al., 2017). Total phenolics and total flavonoids in the pericarp of Peggy's red figs are higher than those of green figs, which can effectively improve the activity of anti-oxidant enzymes (S. Liu, Xiao, & Wang, 2022). Thus, darker fig varieties containing more polyphenols, flavonoids, flavonols, anthocyanins and proanthocyanidins (Bey & Louaileche, 2015). A total of 27 fig species originating from Tunisian ecotypes show good anti-oxidant capacity, with total polyphenol contents ranging from 51.50 to 100.23 mg GAE/g DW and ABTS inhibition ranging from 263.7 to 676.13 mg vitamin C equivalent/100 g FW (Fateh et al., 2020). Moreover, the pericarp extract can also be used as an anti-oxidant to improve the oxidative stability of rapeseed oil and has higher anti-oxidant activity than tert-butylhydroquinone (Elahe Maghsoudlou et al., 2017). Regardless of the part of the FC, it contains high levels of phenolic compounds, all of which are great sources of natural antioxidants.

4.2 | Anti-inflammatory

Phenolic compounds of Fig fruit, leaves and latex exert anti-inflammatory effect (Rezagholidzadeh et al., 2022). For instance, quercetin and naringenin are essential in pharmacology for their anti-inflammatory properties (Cheng et al., 2019). Fig leaf extract is rich in phenolic compounds and inhibits the production of the pro-inflammatory cytokines tumor necrosis factor- α (TNF- α) and prostaglandin E2 (PGE2) (Bouyahya et al., 2016). Results indicated that TNF- α and interleukin 1 α (IL-1 α) could be downregulated by phenolic compounds of FC (Turkoglu et al., 2017). In addition, caffeoyl malic acid and rutin in fig leaves can reduce allergy and atopic dermatitis symptoms in animals (Abe et al., 2022). Morin hydrate, hesperidin, and rutin are extracted from FC, they are effective in reducing the inflammatory

cytokines interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and TNF- α in diabetic animals (Ginwala et al., 2019). And naringenin, lignan, and quercetin can also modify proliferator-activated receptor γ (PPAR- γ), which activates insulin sensitivity to regulate inflammation (Saini, 2010). Morin hydrate also significantly reduces the expression of TNF- α , IL-6, cyclooxygenase 2 (COX-2) and PGE2 in 1,2-dimethylhydrazin-induced colon cancer by downregulating the nuclear factor kappa B (NF- κ B) pathway, thus exerting an effective anti-inflammatory effect (Sharma et al., 2018). Latex and leaves of FC are natural sources of psoralen, which can attenuate the inflammatory response and inhibited LPS-induced IL-1 β and IL-8 mRNA expression in studies of periodontitis (Abdel-Aty et al., 2019; Li et al., 2018). Flavonoid compounds in FC may cooperate with glutathione, tocopherol or protective enzymes to counteract the destructive effects of oxidative stress, which can enhance resistance to CCl4-induced oxidative stress and hepatotoxicity in rats, and may be used clinically to treat acute hepatitis, chronic hepatitis, cirrhosis and toxic liver injury (Debib et al., 2016). However, many of these phenolic compounds were not phenolic compounds from figs, and specific mechanism on the anti-inflammatory effects of figs phenolic compounds are not clear.

4.3 | Anti-cancer

Fig fruits, bark, leaves, latex and roots have strong anti-cancer properties (Idolo et al., 2010; Khodarahmi et al., 2011; Patil & Patil, 2011). The anti-cancer properties of FC are mainly due to phenolic compounds (Yahiaoui et al., 2022). These phenolic compounds can suppress a wide range of cancers, including adenocarcinoma, breast, brain, cervical, colon, and stomach cancers (Morovati et al., 2022). Fig latex contains various phenolic compounds, fig latex has toxic effects on U251 cells (Human glioma cell line), and stops the cancer cell cycle and inhibits DNA synthesis, leading to cancer cell apoptosis (Wang et al., 2008). In U-87 MG, T98 G and U-138 MG glioblastoma cells, fig latex also specifically inhibits cell viability and induces apoptosis (Amessis-Ouchemoukh et al., 2017; Tezcan et al., 2015). In MCF-7 cell line, fig tree latex extract promotes ROS production and inhibits cell activity (Abdel-Aty et al., 2019). In addition, fig latex extract inhibits the viability of MDA-MB-231 cells derived from triple-negative breast cancer by downregulating signal-regulated kinase 2, cyclic AMP response-binding protein and AKT Serine/Threonine Kinase 2 (AKT2) (AlGhalban et al., 2021). Treatment of Hela and Caski cervical cancer cells with fig latex extracts, it can reduce cell viability and proliferation by decreasing Ki67 protein. Furthermore, latex extracts have the potential to induce cycle block and inhibit clonogenic capacity, invasion and migration by upregulating pRb and P53 tumor-boosting proteins (Ghanbari et al., 2019).

The ethanolic extract of fig leaf also has anti-cancer activity against breast, hepatocellular, colon and laryngeal cancers, and the total phenolic content of the ethanolic extract is positively correlated with anti-cancer activity (Abdel-Rahman et al., 2021). Treatment of MCF-7 and CaCo-2 cells with the ethanolic extract of fig leaf also shows significant cytotoxicity, and both Hep2 and HepG2 cells are also strongly inhibited, with inhibition rates ranging from 80.7% to 66.9% (Abdel-Rahman et al., 2021). Fig extract also induces apoptosis in human colorectal cancer cells HCT-116 and HT-29, shows the strong antiproliferative activities and achieves anti-cancer effects (Soltana et al., 2019). Prenylated isoflavone derivatives from FC exhibits pronounced antiproliferative activities against diverse human cancer cell lines in vitro, which can significantly reduce nitric oxide production (Liu et al., 2019). In conclusion, the anti-cancer mechanism of phenolic compounds in FC is not clear, FC may prevent cancer development and progression by modulating multi-targeted pathways, such as numerous dysregulated signaling cascades involved in cell proliferation, cell cycle regulation, apoptosis, autophagic inflammatory processes, metastasis, invasion and angiogenesis.

4.4 | Anti-diabetic and anti-obesity

A large number of previous studies have proved that various dietary polyphenols may influence blood glucose at different levels and may also help control and prevent diabetes complication (Aryaeian et al., 2017). Phenolics may provide a protective effect against hyperglycemia-induced chronic diseases through dual protection of antioxidant and inhibition of starch digestion (Ali Asgar, 2013). Various extracts of fig fruits and leaves significantly inhibited alpha-amylase and alpha-glucosidase activities, with phenolic compounds playing the most prominent anti-diabetic role (Mopuri et al., 2018; Wojdyło et al., 2016). Flavonoid-rich fig pericarp extracts also have significant inhibitory effects on α -glucosidase (Meziant et al., 2021; Ramadan et al., 2021). Fig leaves contain a significant quantity of phenolic compounds (71.208 ± 2.89 mg/g GAE DW) upregulated the expression of GCK, GLUT4, and IGF, and downregulated G6P, and significantly ameliorated streptozotocin-induced diabetes mellitus in rats (Asghar et al., 2023). A total of 40, 60, and 80 mg of ethanolic extract of fig leaf are fed to rats, respectively, after giving treatment to each group for 14 days, all significantly reduce blood glucose levels in rats (Kurniawan & Yusuf, 2021). Strong α -glucosidase inhibitory activity is also observed in the high caffeic acid content of fig latex (Yahiaoui et al., 2022). Fig extract glucose drinks significantly reduce postprandial glycaemic index and insulin response in humans compared to regular glucose drinks (Atkinson et al., 2019). More clinical trials are needed to determine

the effects of polyphenols-rich foods, their effective dose, and mechanisms of their effects in managing diabetes.

FC also has anti-obesity properties, it can reduce animal body weights and serum low-density lipoprotein levels (Arafa et al., 2020). Preparation of three different concentrations of figs, 100, 150, and 200 mg/kg (rat body weight) fed to rats, which can significantly reduce body weight, cholesterol, triglyceride, low-density lipoprotein, very low density lipoprotein levels and increased high-density lipoprotein levels in rats (Surendran et al., 2020). Furthermore, the ethanol extract from figs' fruit comprises a significant quantity of polyphenols and flavonoids ($104.67 \pm 5.51 \mu\text{g/mL}$ and $81.67 \pm 4.00 \mu\text{g/mL}$). The IC_{50} value of fig ethanol extract on pancreatic lipase was $230.475 \pm 9.65 \mu\text{g/mL}$, which can reduce the body's digestion and absorption of fat, and has a good anti-obesity effect (Mopuri & Islam, 2016). Fig leaves are rich in psoralen and bergamot lactone, which significantly reduce gene expression of $\text{PPAR}\gamma$, $\text{C/EBP}\alpha$, leptin, adiponectin and GLUT4, and decreases lipid content (Pucci et al., 2022). Phenols in FC have significant anti-diabetic and anti-obesity effects, but existing studies have failed to correlate for monomeric phenols, and specific mechanisms have not been validated.

4.5 | Anti-Alzheimer's disease (AD)

AD, as a neurodegenerative disease, seriously threatens about over 6% of the elderly aged 65 (Liu et al., 2021). The pathogenesis is related to acetylcholine disorder, in clinical medicine, acetylcholinesterase inhibitors are mostly used to improve symptoms of AD (Ossenkoppele et al., 2015). Phenolic compounds such as rutin, lignans, quercetin and chlorogenic acid, which are abundant in fig latex, also show potent inhibitory activity against acetylcholinesterase (Yahiaoui et al., 2022). The pericarp of Peggy's Red Fig is rich in phenolic compounds, which can effectively reduce the aggregation of β -amyloid in the AD transgenic nematode CL4176, alleviate the paralysis of the organism, improve the activity of anti-oxidant enzymes, and reduce the toxicity of $\text{A}\beta$ 1-42. Thus playing a good role in the fight against AD (Liu et al., 2022). And the potential mechanism of quercetin in FC against AD is shown in Figure 2.

Adding fig fruits to the diet of APPsw/Tg2576 mice, it can significantly inhibit inflammatory cytokines in the plasma of the mouse brain, reduce $\text{A}\beta$ 1-40 and $\text{A}\beta$ 1-42 levels in the brain, and delay the formation of age spots (Essa et al., 2015). Moreover, adding 4% Oman fig fruit to the diet of mice, it shows significant improvement in memory deficits, reduction in anxiety-related behaviors, enhancement of spatial and positional discrimination learning and motor coordination in mice (Subash et al., 2016). Taking together, dietary supplement of figs may help improve cognitive and behavioral deficits in patients with AD, and the disease-modifying mechanism

is closely linked to the phenolic compounds in FC. Furthermore, the anti-alzheimer's mechanism of phenols may be closely related to gut microbes as well, and based on the reciprocal mechanism of the gut-brain axis, polyphenols may be able to ameliorate neuroinflammation in the brain and improve cognitive functioning and social deficits in patients with AD by increasing SCFAs.

5 | POTENTIAL APPLICATION OF PHENOLIC COMPOUNDS OF FC

5.1 | Applications in the food industry

5.1.1 | Food additives

The application of fig by-products as functional ingredients in the development of novel food formulations has shown promise as colorants, texture enhancers and preservatives (Ayuso et al., 2022). Food additives and colorants are key ingredients used in the food industry to improve food quality and safety (Sun et al., 2021). There is a growing consumer demand for natural colors to enhance the nutritional and functional properties of food, such as anti-oxidant, anti-cancer and antibacterial. Due to their excellent anti-oxidant and antimicrobial activities, phenolic compounds in FC can be used as alternatives to chemical additives in the food industry, and they can be applied to oils, seafood, meat and beverages as antioxidants, antimicrobials and preservatives (Wu & Zhou, 2021). Anthocyanins are also widely used in the beverage industry as both coloring agents and functional ingredients (Morata et al., 2019). FC contains anthocyanins and carotenoids that can be utilized as colorants, stabilizers and functional ingredients in a variety of beverage products (Zhang et al., 2020). And anthocyanins in pericarp of FC are novel anthocyanin-based food colorants, which also have great research potential in confectionery and bakery products (Backes et al., 2020) Figure 3.

Phenolic compounds in fig fruit, leaves and roots have good inhibitory activity against a variety of bacteria (Mahmoudi et al., 2016). In the food industry, phenolic compounds are promising alternatives to synthetic antimicrobials. For example, epicatechin is added to ultrahigh-temperature processed milk, it inhibits the occurrence of the milk-maillard reaction under high-temperature conditions, and reduces the formation of off-flavors in milk (Colahan-Sederstrom & Peterson, 2005). addition of phenolic compounds to baked goods can reduce advanced glycation end-products in baked goods, and adding epicatechin to cookies can reduce glyoxal and methylglyoxal in cookies (Ou et al., 2018). Sardine oil oxidation can be effectively inhibited by quercetin, rutin, and caffeic acid (Chandrasekar et al., 2016). Caffeic acid can effectively inhibit the oxidation of hickory oil, the anti-oxidant effect is significantly better

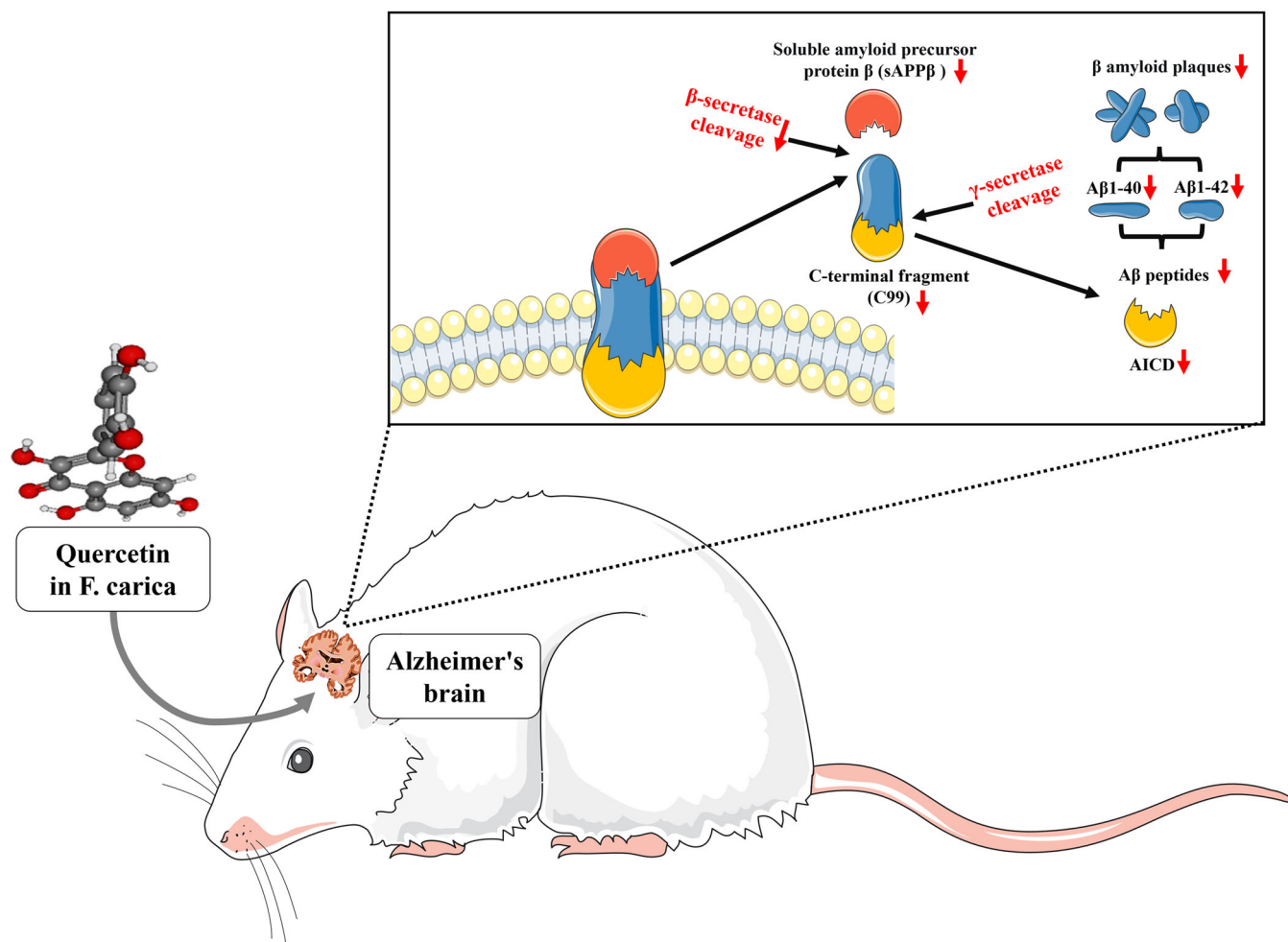


FIGURE 2 Potential mechanism of quercetin in FC against Alzheimer's disease (AICD: β -amyloid precursor protein intracellular domain). FC, *Ficus carica* L.

than butylated hydroxytoluene and butylatedhydroxyanisole (Zhang et al., 2018). Quercetin and rutin applied to soybean oil also shows excellent anti-oxidant activity (Lee et al., 2017). Meanwhile, chlorogenic acid, caffeic acid, rutin, catechin and quercetin in FC, which can also be used as antioxidants in the storage process of various types of oils and fats (Olszowy, 2019). Therefore, in the food industry, phenolic compounds extracted from FC have a great potential application value.

5.1.2 | Green food packaging materials

Phenolic compounds can also be added to food packaging materials, especially green food packaging materials made from polymers (such as polysaccharides, lipids and proteins), applied in the form of films and coatings for the preservation of various types of food (Singh et al., 2022). The preparation of green packaging materials containing

phenolic compounds usually involves several steps, incorporation of phenolic compounds into polymers, structural characterization using various modern instruments, testing of barrier and mechanical properties and biological activity of the material, application to food packaging, and finally evaluation of the food by sensory, physical, chemical and biological indicators (Wu & Zhou, 2021). For example, composite coating prepared with chitosan and chlorogenic acid for peach preservation significantly reduces ROS levels in peach fruits and maintains postharvest quality of peach fruits (Jiao et al., 2019). Gallic acid loaded nanofibers is found to be an efficient active packaging material, it can reduce oxidation reaction of walnuts during storage (Aydogdu et al., 2019). Curcumin, gallic acid, quercetin and other phenolic compounds mixed with gelatine to make a composite gelatine coating film for chicken meat preservation, which can significantly inhibit the growth of *Salmonella typhimurium* and *Escherichia coli* in the chicken meat, thus prolonging the freshness period

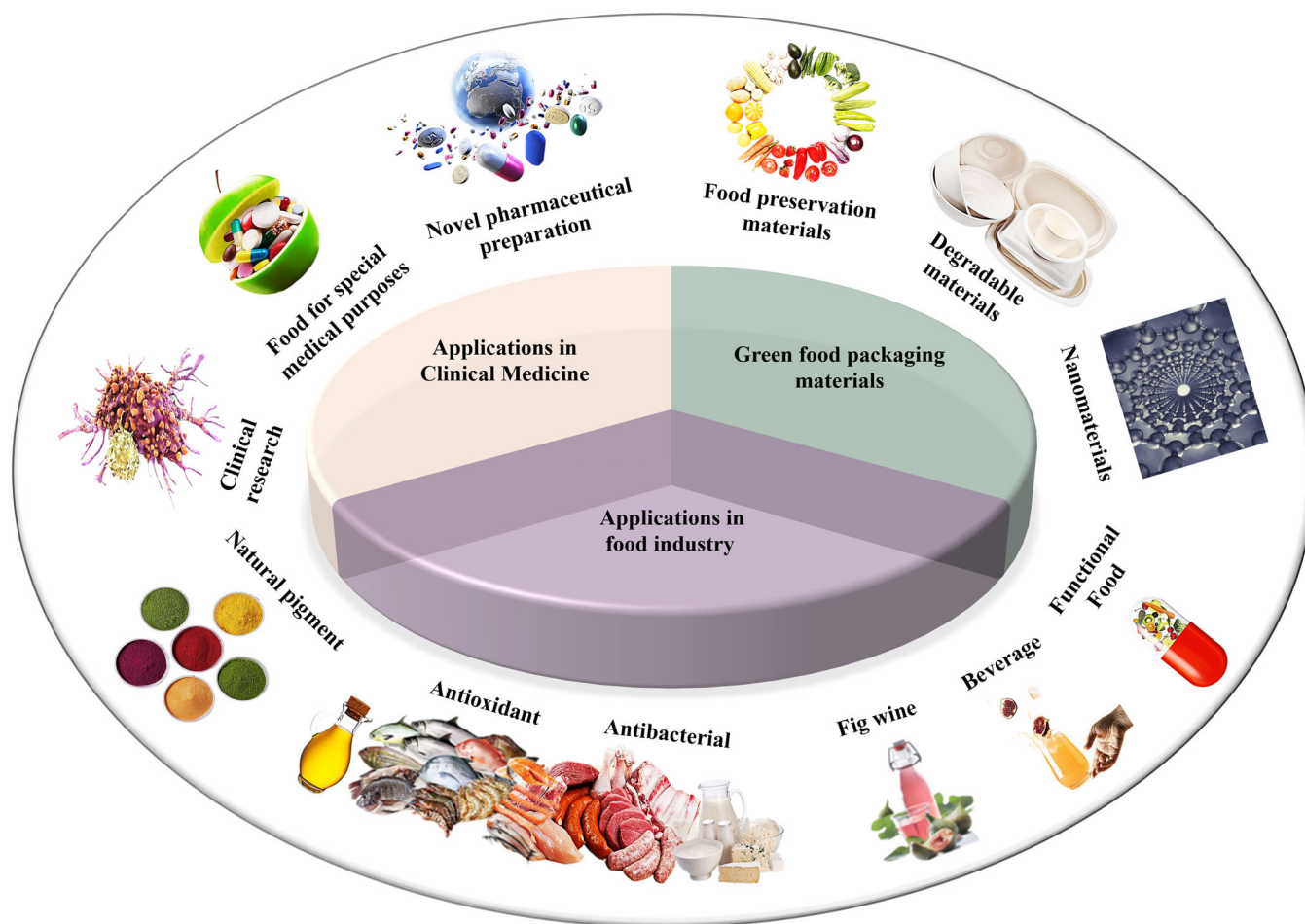


FIGURE 3 Potential application of phenolic compounds of FC. FC, *Ficus carica* L.

of the chicken meat (Khan et al., 2020). Therefore, phenolic compounds extracted from FC can also be blended with various natural polymers to produce green food packaging materials, which can be used in preserving and storing a wide variety of fruits and vegetables, nuts, eggs and meats.

5.2 | Applications in clinical medicine

FC has many beneficial effects on human health, it can be utilized in pharmacobiology for new drug formulations and clinical applications. Health benefits of FC are mainly attributed to its rich phenolic compounds (Salehi et al., 2021; Yao et al., 2021). Numerous epidemiologic data, animal studies and cell culture evidence support the medicinal value of FC in anti-oxidant, anti-cancer, anti-diabetic, anti-inflammatory, cardiovascular protection and anti-AD (Alamgeer et al., 2017). And FC is also traditionally used as antispasmodic and anti-inflammatory medicine, leaves and roots are used for various diseases such as gastrointestinal (colic, indigestion, loss of appetite and diarrhea), respiratory diseases (sore throat, cough and

bronchial problems), and cardiovascular diseases (Hesam Shahrajabian et al., 2021; Misbah et al., 2013). Phenolic compounds in FC are clinically effective as laxatives, fig juice mixed with honey is used for bleeding disorders. Indian medicine also uses figs as a mild laxative, expectorant, and diuretic.

The aqueous extract of FC is rich in phenolic acids (such as gallic acid, chlorogenic acid, prunic acid and ellagic acid) and flavonoids, which have a natural laxative effect without causing diarrhea and improve functional gastrointestinal disorders (Rtibi et al., 2018). FC is also excellent source of proanthocyanidins, lignan-6-C-pentose and apigenin. And proanthocyanidins are a powerful anti-oxidant, especially in the dark figs, which can effectively reduce α -glucosidase and α -amylase activities, flavonoids and polyphenols in FC have anti-diabetic effects, and they are natural anti-diabetic ingredients that can be used in the development of natural hypoglycemic drugs (Irudayaraj et al., 2016; Khadhraoui et al., 2019; Mopuri et al., 2018). Several studies have reported that the flavonoids in FC have potent free radical scavenging and metal chelating activities, and it can inhibit the activities of key enzymes

associated with many chronic diseases, such as tyrosinase, α -glucosidase, urease, and cholinesterase (Meziant et al., 2021; Zhang et al., 2022).

Phenolic compounds in FC are also a promising antitumor drug for the clinical adjuvant treatment of a variety of cancers, including adenocarcinoma, breast cancer, brain cancer, cervical cancer, colon cancer, mature glioblastoma, hepatocellular carcinoma, leukemia, lung cancer, melanoma, oral cancer, osteosarcoma, prostate cancer, and gastric cancer, which facilitates the research of new natural anti-cancer agents (Abdel-Rahman et al., 2021; Morovati et al., 2022). Four new structurally diverse allylisoflavone derivatives are isolated from FC, which also exhibit significant in vitro anti-proliferative activity against various human HL-60 cancer cell (Liu et al., 2019). Quercetin and naringenin attenuate the expression of tumor necrosis factor (Cheng et al., 2019). Fig extract has a good inhibitory effect on *Candida albicans* and *Klebsiella pneumoniae*, and it can protect human from infection (Debib et al., 2014). FC also has hepatoprotective effects in clinical practice, inhibits free radical production and counteracts the damaging effects of oxidative stress on the liver (Debib et al., 2016). Dietary supplementation with figs can improve cognitive and behavioral deficits in alzheimer's mouse (Subash et al., 2016). Furthermore, fig extracts have shown great results in protecting bone microarchitecture, and have great potential in replacing estrogen as an anti-osteoporosis treatment for postmenopausal women (Adlina Mohammad et al., 2018). However, in the application of food additives and clinical medicine, the dosage and safety problems of phenolic compounds in FC should be considered. For instance, high-dose (7 mg/kg body weight) chlorogenic acid can induce inflammation reactions and oxidative stress injury in rats (Du et al., 2013). Therefore, phenolic compounds as food additives and clinical medicine should undergo rigorous exposure assessment as well as multi-stage toxicological studies.

6 | CONCLUSION AND PROSPECT

FC is a fruit with important nutritional and economic values, and phenolic compounds in FC are valuable natural resources. Phenolic compounds in FC mainly include phenolic acids, flavonoids and anthocyanin glycoside. Exploitation of the full potential of phenolic compounds in FC lies in the development of prudent and efficient methods for their detection, isolation, and analysis. Traditional solvent extraction method is still the widely used technique for the extraction of phenolic compounds. Future research should consider modern extraction techniques and green solvents, such as supercritical fluid extraction, subcritical water extraction, ionic liquid extraction method, microwave-assisted extraction, and ultrasonic-assisted extraction. These

methods have the advantages of being more efficient and environmentally friendly in the extraction of phenolic compounds. A combination of different extraction methods is also used to extract phenolic compounds from FC when a single extraction technique is not sufficient to completely extract the target phenolic compounds from FC. Efficient extraction of gallic acid, chlorogenic acid, rutin, psoralen, and bergamot from fig leaves, pulp, and pericarp using ionic liquid-based ultrasound-assisted extraction of five phenolic acids. Ionic liquid-based ultrasound-assisted extraction is a fast, simple, and environmentally friendly combination technique. On this basis, microwave technology can also be applied in combination with ionic liquids, which promises a more efficient extraction of phenolic compounds from FC.

Numerous in vitro and in vivo studies on the mechanism of biological activity of phenolic compounds in FC will also provide strong support for clinical applications and natural functional products. Targeted metabolomics and pharmacological studies can further explain the bioactivity and medicinal value of the phenolic compounds in FC.

At present, phenolic compounds in FC are mainly utilized in food industry, clinical medicine and green food packaging materials. Colorants, functional ingredients, food fortifiers, preservatives and antioxidants are the most common forms of application of phenolic compounds from FC in food industry. In addition, phenolic compounds have functions as prebiotic components, which are closely related to the regulation of intestinal flora. To obtain packaging materials with better performance and freshness preservation, in the production of green food packaging materials by adding phenolic compounds from FC, optimal process parameters are necessary to determine phenolic compound concentrations within the safe range. Despite phenolic compounds have many health benefits, some studies have reported that ingestion of high concentrations of phenolic compounds may act as pro-oxidants and cause toxicological effects. Therefore, while phenolic compounds from FC in clinical medicine and the preparation of novel pharmaceutical formulations, they must be preceded by clinical studies to determine the safe concentration range for the ingestion of these phenolic compounds.

AUTHOR CONTRIBUTIONS

Qinqiu Zhang: conceptualization; investigation; methodology; writing—original draft. **Yue Peng:** investigation. **Fan Li:** investigation. **Yi Xu:** investigation. **Qing Zhang:** writing—review & editing. **Dingtao Wu:** writing—review & editing. **Mingrui Chen:** writing—review & editing. **Shang Lin:** writing—review & editing. **Wen Qin:** funding acquisition; project administration; supervision; writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ETHICS STATEMENT

This article do not make use of human or animal subjects and/or tissue, there are no ethical problems.

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