Polish Journal of Agronomy
2021, 44, 22–29

doi: 10.26114/pja.iung.452.2021.452.04

A review of chemical constituents, traditional and modern pharmacology of fig (*Ficus carica* L.), a super fruit with medical astonishing characteristics

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Abstract. Fig (*Ficus carica* L.) belongs to Moraceae family, is clearly of greatest importance as a source of human food and nutrition. The fig's fruits are a good natural source of nutrients, phytochemicals, and minerals which may improve human health and nutrition. All relevant papers in English language were collected. The keywords of pharmacology, traditional medicine, phytochemistry, fig and health promoting were searched in Google Scholar, Scopus, Research Gate and PubMed. The most important pharmacological characteristics of *Ficus carica* are anticancer, antioxidant, antiparasitic, antiviral, antibacterial, antimutagene, anti-inflammatory, anti-angiogenic, antidiabetic, antipyretic, reproductive, antiplatelet, endocrine, immunological, dermatological, antispasmodic, hypolipidemic, nootropic, antidiarrheal, nephro- and hepato-protective and anti-warts effects. Fruits have anti-oxidative, anti-spasmodic and nephroactivity protective, branches have both anti-oxidant and anti-inflammatory characteristics. Leaves have anti-inflammatory, anti-pyretic, anti-diabetic, helpato-protective, anti-angiogenic, immunomodulatory, anti-nematicidal effect, inhibit of osteoclastogenesis, and are used in the case of ischemia and reperfusion injuries. Latex has anti-cancer, anti-bacterial, anti-angiogenic, antiviral and anthelmintic properties. Moreover, fig's stem bark has anti-diabetic characteristics. The aim of this review was to go through some important studies on chemical constituents and pharmacological effects of fig. The obtained findings show potential of different parts of the fig plant as an additive in the food and pharmaceutical industries.

Keywords: pharmacology, traditional medicine, phytochemistry, fig, health promoting

FIG OCCURRENCE AND CULTIVATION

Traditional medicine has been used for thousands of years by many generations in Asian countries and other parts of the world (Shahrajabian et al., 2019a,b,c; Sun et al., 2019a,b). Traditional medicine is an important component of complementary and alternative medicine (Shahrajabian et al., 2020a,b). Cultivation and use of medicinal herbs and fruits significantly helps to promote sustainable agricultural development via growing demand for organic agricultural production in different countries (Shahrajabian et al., 2020c,d,e,f; Sun et al., 2020a,b). Fig (*Ficus carica* L.) is a deciduous tree belonging to the Moraceae family, is one of the oldest cultivated trees with both fresh and dry consumption in all over the world (Mehraj et al., 2013; Allegra et al., 2017). It is reported to be under cultivation from 2000–3000 BC in the eastern Mediterranean region (Marpudi et al., 2013). The most of the world's fig production is provided by Mediterranean countries (Gozlekci, 2010). Some countries like Turkey, Egypt, Algeria and Morocco account for more than 65% of the world production, and Turkey is the leading country in both fresh and dry figs, accounting for 51% of fig fruit world exports (Allegra et al., 2018). The bark is a smooth and silvery gray. The leaves are bright green and single. The tiny flowers of the fig are out of sight, clustered inside the green multiple fruit called syconium. The matured fruit has a tough peel (pure green, green suffused with brown or purple), often cracking upon ripeness and exposing the pulp beneath. Seeds are large, medium, small and their number can changes from 30 to 1600 per fruits. Among the commonly consumed fruits and beverages, dried fig is one of food with highest content of polyphenols (Bachir Bey et al., 2014). The skin color of fig fruit varies from yellow to black; so, figs can be divided depending on their skin color into two groups: the light skin fig varieties with a yellow, yellow-green or green color and dark ones with a red, purple, black or brown skin color (Bachir Bey and Louaileche, 2015).

FIG NUTRITIONAL COMPOSITION AND CHEMICAL CONSTITUENTS

The genotype is the main factor that determines difference in the composition of bioactive compounds in figs and provide information on putative health benefits of different genotypes (Ercisli et al., 2012; Bachir Bey and Louaileche,

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2015). *Ficus carica* species are rich source of naturally occurring antioxidant and antimicrobial activity, and its compounds play an important role in preventing innumerable health disorders related to oxidative stress including cardiovascular diseases, neurodegenerative and cancer (Ahmad et al., 2013). Li et al. (2011) reported that the major components detected in volatile oil of the leaves were psoralen (10.12%), β-damascenone (10.17%), benzyl alcohol (4.56%), behenic acid (4.79%), and bergapten (1.99%), but the major components detected in volatile oil of the fruits were furfural (10.55%), 5-methyl-2-furaldehyde (10.1%), and benzeneacetaldehyde (6.59%). They have identified a total of 121 volatile constituents in the leaves and 108 in the fruits, and 18 volatile constituents are identified in both leaves and fruits. Ikegami et al. (2013) also mentioned that fig leaves, fruit, and latex all contain anticancer components, among which bergapten and psoralen are two important ones. Bergapten has inhibitory effects on the liver cancer cell lines, stomach cancer cell line, and NPC cells, the mechanism of which may include direct killing, arresting the cell cycle and inducing apoptosis (Santoro et al., 2016). Chemical examination of *Ficus* spp. have shown the presence of psoralen, bergapten, umbelliferone, β-sitosterol, campesterol, stigmasterol, fucosterol, fatty acids, 6-(2-methoxy-Z-vinyl)-7-methyl-pyranocoumarin and 9,19-cycloarlane triterpenoid, 6-O-acyl-a-D-glycosyl- and 6-O-acyl-β-glucosyl-β-sitosterol and lupeol acetate (Khodarahmi et al., 2011). Mujic et al. (2012) described that the major volatile compound in dried figs was benzaldehyde, and after benzaldehyde, the most abundant aldehyde in dried figs was hexanal. Sagili et al. (2018) reported that fig is important source of vitamins, amino acids and antioxidants, and it is nutritious fruit rich in fiber, potassium, calcium, and iron with higher level than other fruit such as apples, grapes and strawberries. The dried fig contains phenolic substances which contribute to its quality, and the phenolic compounds of dried figs can produce a significant increase of the antioxidant capacity of human plasma and can protest plasma lipoproteins from oxidation (Vinson, 1999). The peels and pulps have variable levels of polyphenols, flavonoids, anthocyanins, tannins and antioxidant activity; fig fruit peels, especially those with a dark color, contained the highest concentrations of phytochemicals and exhibited the highest antioxidant activity compared to fig fruit pulps (Mahmoudi et al., 2018). Pourghayoumi et al. (2016) suggested that the chlorogenic acid played a trifling role in determination of antioxidant capacity of the fruits. Soni et al. (2014) showed the presence of vitamin E, β-amyrin, stigmasterol, campesterol, oleic acid, isoamyl laurate and ϒ tocopherols majorly. They have also stated that the extract shows antibacterial activity and showed zone of inhibition against *Proteus mirabilis* and *Bacillus subtilis*. Figure 1 shows chemical structures of compounds identified in the ethanol extract of *Ficus carica* L. fruit by

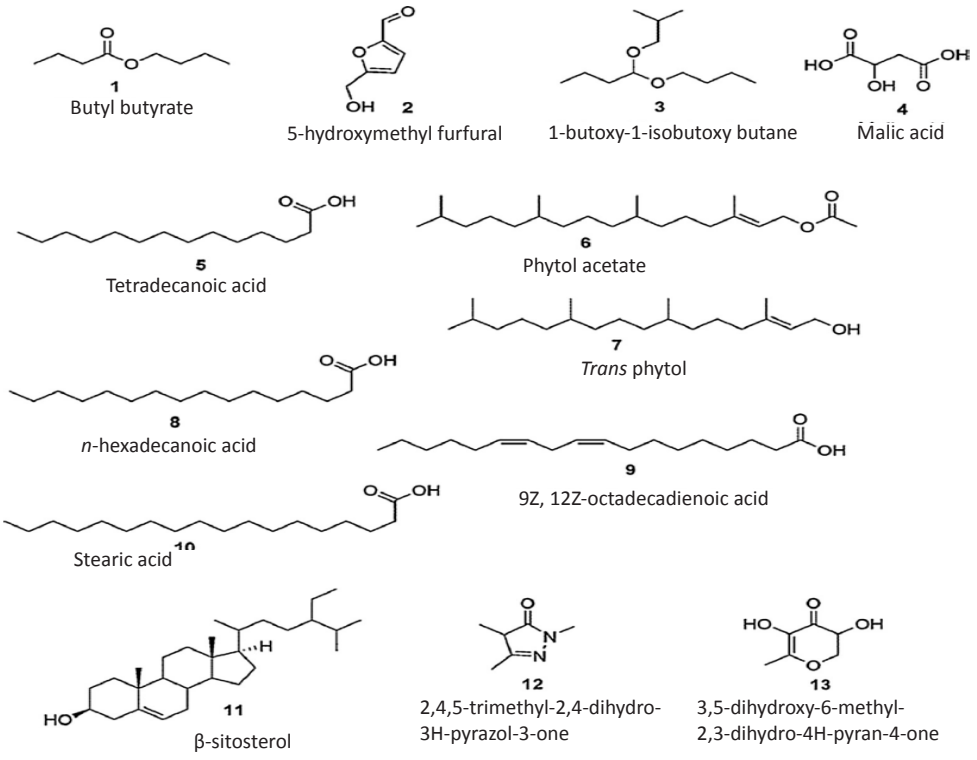

Figure 1. Chemical structures of compounds identified in the ethanolic extract of *Ficus carica* L. fruit by GC-MS. (GC-MS= gas chromatography-mass spectroscopy) (Mopuri et al., 2018).

GC-MS. Mopuri et al. (2018) showed the presence of a number of bioactive compounds such as butyl butyrate, 5-hydroxymethyl furfural, 1-butoxy-1-isobutoxy butane, malic acid, tetradecanoic acid, stearic acid, sitosterol, 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, and 2,4,5-trimethyl-2,4-dihydro-3H-pyrazol-3-one. Chemical and nutritional composition of fig's leaves are water (65.90%), ash (5.30%), proteins (5.90%), lipids (0.81%), fiber (4.50%), and carbohydrates (17.50%) (El-Shobaki et al., 2010).

Phytochemical constituents of unpolar fractions obtaining from fig leaves are n-Dodecane, Glycerol, n-Tridecane, n-Tetradecane, 3-Octadecene (E), n-Tetradecanoic acid (Myristicacid), n-Hexadecanoic acid (Palmitic acid), n-Heptadecanoic acid (Margaric acid), 1-Octadecanol, Phytol, Linoleic acid, α-Linolenic acid, Stearic acid, n-Eicosanoic acid (Arachidic acid), 1-Docosanol (Behenyl alcohol), 1-Hexadecanoylglycerol (1-Palmitoylglycerol), n-Docosanoic acid (Behenic acid), Tetracosan-1-ol (Lignocerylalcohol), Squalene, Tetracosan-1-ol (Lignocerylalcohol), Squalene, Tetracosanoicacid (Lignoceric acid), Pentacosan-1-ol, n-Octacosane, 1-Hexacosanol (Ceryl alcohol), Hexacosanoicacid (Cerotic acid), Heptacosan-1-ol, Octacosan-1-ol (Montanylalcohol), α-Tocopherol, Stigmasterol, Triacontan-1-ol (Melissyl alcohol), β-Sitosterol, α-Amyrin, Germanicol, Lanosterol, β-Amyrin, Lupeol acetate and β-Amyrin acetate (Li et al., 2011; Ivanov et al., 2018). The main ingredients of fruits of figs are cyaniding-3-O-glucoside, cyaniding-3-Orhamnoglucoside, saturated fat, cholesterol, sodium, insoluble sugars, protein, vitamin A, vitamin C, calcium and iron, and the most important ingredients of ripe dried fruit are alkaloids, flavonoids, coumarins, saponins and terpenes (Soni et al., 2014; Rahmani and Aldebasi, 2017).

MEDICINAL USES AND POTENTIAL HEALTH BENEFITS IN MODERN PHARMACEUTICAL SCIENCE AND TRADITIONAL MEDICINE

Turan et al. (2018) stated that figs are rich in antioxidant and phenol substances, therefore, consumption of figs can help the antioxidant defense system to cope with parameters that increase oxidative stress such as ethanol which may accelerate the adaptation of organisms. Bachir Bey and Louaileche (2015) indicated that dried fig is a good source of various non-enzymatic antioxidants which

Table 1. Pharmacological properties of *Ficus carica* (Bouyahya et al., 2016).

Activity	Part of plant	Type of extract/compound
Antibacterial activity	Leaves	Ethanolic extract
	Leaves	Methanolic extract
	Fruit	Ethanolic and methanolic extract
	Leaves	Methanolic extract
	Leaves	Hexane, chloroform, ethyl acetate and aqueous alcoholic extract
	Leaves	Methanolic extract
Antioxidant activity	Leaves	Methanolic extract
	Fruit pulp, Peel and pulp	Methanolic extract
	Leaves, pulps and peels	Aqueous extract
	Leaves	Phenols and flavonoids
	Latex	Phenol and flavonoids
	Leaves	Methanolic extract
	Fruit	Ethanolic extract
	Leaves	Methanolic extract
Anticancer activity	Fruit, Leaves and latex	Ethanolic, ethyl acetate and dichloromethane extract
	Fruit	Ethanolic
	Latex	Latex
	-	polysaccharides
	Latex	6-O-acyl-beta-D-glucosyl-beta-sitosterols, acyl moiety and linoleyl with minor amounts of stearyl and oleyl
Anti-inflammatory activity	Leaves	Methanolic extract
	Leaves	Petroleum ether
	Latex	Pure extract
	Leaves	Methanolic extract
	Fruit	Hydroalcoholic extract
	Leaves	Petroleum ether, chloroform and ethanolic extract
Antipyretic activity	Leaves	Ethanolic extract
Anti-acne activity	Fruit and leaves	Petroleum ether, chloroform, methanol and distilled water extract

Table 2. Pharmacological activities of some phytoconstituents reported in different parts of Ficus carica (Badgujar et al., 2014).

Part used	Type	Examples	Pharmacological activities
Leaf	Coumarin	4′, 5′-Dihydropsoralen, umbelliferone, marmesin, bergapten	Sunscreen agent, cytotoxic, photosensitizer
Fruit	Coumarin	Umbelliferone, scopoletin	Anticancer, anemia, antioxidant
Leaf	Flavonoid	Rutin	Anticancer, coloring agent
Fruit	Alkaloid	Quinines	Antimalarial
Leaf	Sterol	Bauerenol, 24-methylenecycloartanol, *ψ*-taraxasterol ester, lupeol	Anticancer, antiprotozoal, chemopreventive, anti-inflammatory
Leaf	Triterpenoid	Ficusogenin	Anticancer, anti-inflammatory
Leaf, root	Coumarin	Psoralen	Sunscreen, tanning activator
Leaf, root	Sterol	β-Sitosterol	Hypolipidemic
Fruit	Anthocyanin	Cyanidin-3-*O*-glucoside, cyaniding-3-*O*-rhamnoglucoside	Antioxidant and radical scavenging actions
Latex	Triterpenoid	6-*O*-Linoleyl-β-$_D$-glucosyl-β-sitosterol, 6-*O*-Oleyl-β-$_D$-glucosyl-β-sitosterol, 6-*O*-palmitoyl-β-D-glucosyl-β-sitosterol	Hypolipidemic
Fruit	Hydrocarbon	Stilbenes	Antioxidant, hemoptysis, antiseptic

Table 3. Pharmaceutical benefits of fig.

Benefits	Mechanism and impacts	Reference
Antioxidant activity	a. The leaves extracts of *F. carica* may ameliorate hyperglycemia, hyperlipidaemia and antioxidant status in diabetic rats.	Allahyari et al. (2014) Bachir Bey et al. (2014) Turan and Celik (2016) Belguith-Hadriche et al. (2017) Sedaghat and Rahemi (2018)
Anti-inflammatory activity	a. The fruit paste is applied to swellings and inflammation for relieving pain.	Guarrera (2005) Mawa et al. (2013)
Anticancer activity	a. A mixture of 6-*O*-acyl-*β*-d-glucosyl-*β*-sitosterols has been isolated as an effective cytotoxic agent from fig latex which showed *in vitro* inhibitory effects of on proliferation of various cancer cell lines. b. *F. carica* leaf extract had a higher anticancer activity compared with its fruit extracts.	Rubnov et al. (2001) Yancheva et al. (2005) Zhang et al. (2018) Purnamasari et al. (2019)
Anti-diabetic activity	a. The leaves of *Ficus carica* L. used to cure diabetes, and can be used as additive source in nutraceutical and biopharmaceutical industries.	Khan et al. (2011) Mopuri et al. (2018)
Alzheimer's disease	a. The dietary supplementation of figs may be useful for the improvement of cognitive and behavioral deficits in Alzheimer's disease.	Subash et al. (2016)
Hypoglycaemic activity	a. *Ficus carica* extract showed a clear hypoglycaemic effect in diabetic rats.	Perez et al. (2000)
Hepatoprotective activity		Gond and Khadabadi (2008)
Antibacterial and antifungal activity	a. The combination impacts of methanol extract with ampicillin or gentamicin were synergistic against oral bacteria which showed that figs could act as a natural antibacterial agent. b. Hexane, chloroform, ethyl acetate, and methanol extracts of *F. carica* latex showed antimicrobial activities.	Jeong et al. (2009) Aref et al. (2010)
Antituberculosis activity		Khadabadi et al. (2007)
Antimutagenic	a. Its plant extract verified the ability to decrease the genotoxicity of environmental mutagens.	Agabeili and Kasimova (2005)
Nematicidal activity	a. The leaf extract of *F. carica* showed the strongest nematicidal activity.	Liu et al. (2011)

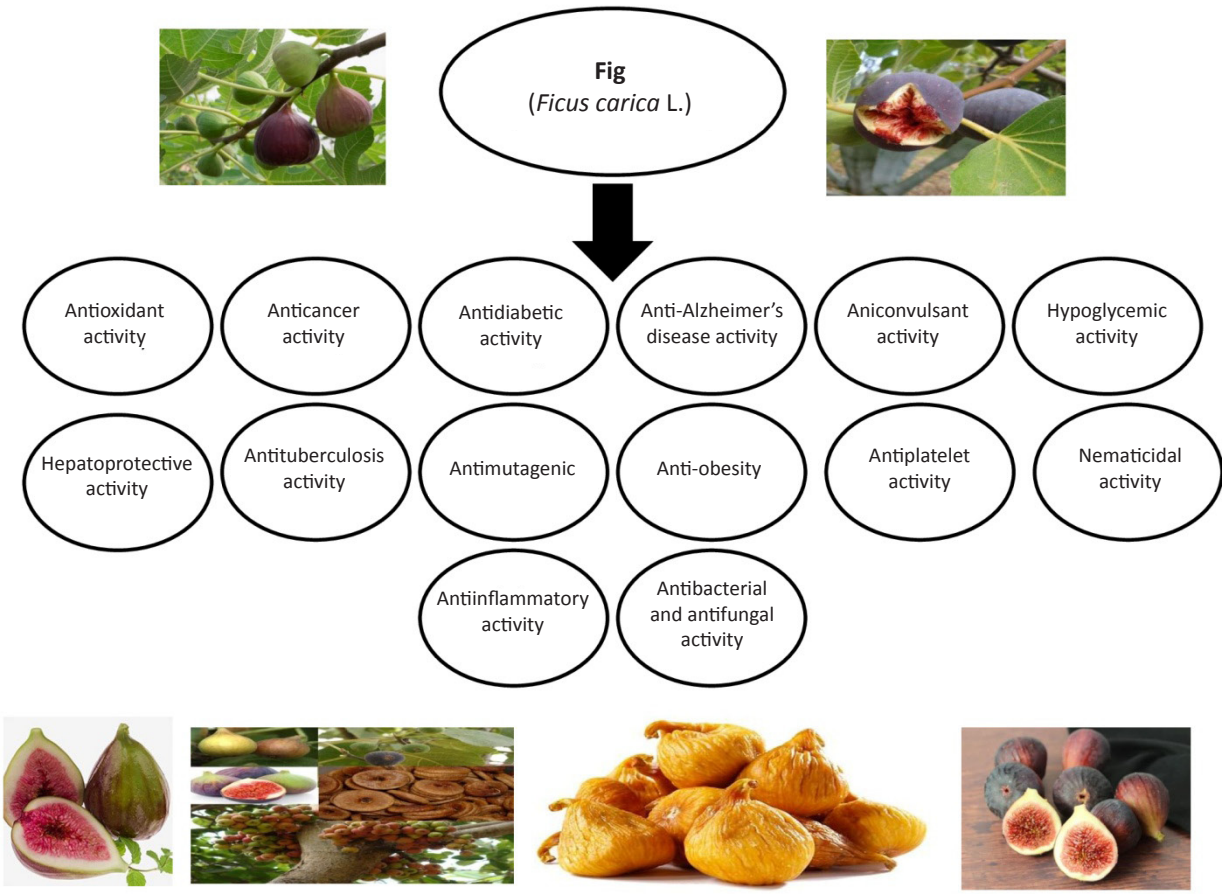

Figure 2. The most important health benefits of fig.

may improve human health, because the fig varieties with a dark skin contain higher levels of polyphenols, flavonoids, flavonols, anthocyanins and proanthocyanidins, and exhibit better antioxidant activity than light ones. Palaniyappan et al. (2013) noted that the ethanolic extract of fruits of *Ficus carica* showed the aphrodisiac activity and it is dose dependent. Ghandehari and Fatemi (2018) suggested that fig latex could decrease tumor growth without having any adverse effect on hematological and histological factors. Fathy et al. (2017) reported that the olive oil with fig and date-palm fruit extracts together could be used synergistically to decrease the bad side effects of chemotherapy and radiotherapy. Patil et al. (2010) showed that the test extract possessed promising immuno-stimulant properties of figs. Sharma et al. (2017) observed that the *Ficus carica* can improve CCl_4-induced hepatotoxicity. Jeong et al. (2009) suggested that figs could be employed as a natural antibacterial agent in oral care products. Mopuri et al. (2018) concluded that the ethanolic extract of the fruit of *F. carica* may have potential antidiabetic and antiobesogenic agents. Idrus et al. (2018) showed that *Ficus carica* has beneficial effects on bone health due to its high minerals content and inhibition of osteoclastogenesis via RANKL pathway, and therefore, it has a potential to be used as a pharmaceutical product for bone health. Its fruit, root and leaves are used in the native system of medicine in different disorders, such as colic, indigestion, diarrhea, sore throats, coughs, bronchial problems, inflammatory, cardiovascular disorders, ulcerative diseases, and cancers (Gilani et al., 2008). Information on medicinal uses of figs against potential cancer and diseases with cancer-related etiologies are included in ancient, medieval and early modern herbals from the Middle East and Europe (Chawla et al., 2012). The fruit's juice of *F. carica* mixed with honey is used for haemorrhage (Mawa et al., 2013). In Indian medicine, fruits are used as a mild laxative, expectorant, and diuretic (Solomon et al., 2006). Mawa et al., (2013) reported that fruit paste is applied to swellings, tumours, and inflammation for relieving pain. It has been reported that figs have been conventionally used for their therapeutic benefits as laxative, cardiovascular, respiratory, antispasmodic, and anti-inflammatory remedies (Guarrera, 2005). Pharmacological properties of *Ficus carica* are shown in Table 1. Pharmacological activities of some phytoconstituents reported in different parts

of *Ficus carica* are presented in Table 2. Pharmaceutical benefits of fig are presented in Table 3 and in Figure 2.

CONCLUSION

The fig (*Fiscus carica* L.) is famous for its nutritive values, and is consumed both fresh and dried fruit in all over the world. It belongs to the Moraceae family. Fig has been broadly used as traditional medicine in many countries. The leaves and fruits of fig are rich in phenolic compounds, organic acids, and volatiles. The leaves of fig contain polyphenols with antioxidant and radical scavenging properties which are potentially beneficial for human health. In traditional medicine, fig leaves have been used to treat diabetes and liver disorders. The most important characteristics of figs are antioxidant activity, anti-inflammatory activity, gastric activity, antimicrobial and antiparasitic activity, hypoglycemic activity etc. Further researches should be done to isolate and characterize the active component of fig and make a connection between traditional medicinal science and modern science.

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received – 20 December 2020
revised – 8 March 2021
accepted – 26 March 2021