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REVIEW ARTICLE

Taxonomy, traditional uses and biological activity of *Ficus carica* L. (Moraceae): A review

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Abstract

Ficus carica L. (Moraceae), a tree native to the tropics and subtropics that has been used traditionally in folk medicine. The crude extracts have been the focus of many studies due to its wide range of biological effects. Even though the species has been the subject of numerous pharmacologically based studies, very few studies have published on their findings. Attempts to bridge this knowledge gap are being made to enhance the species' utility in modern research. The following review looks at all research articles on anti-diabetic, antioxidant, antibacterial, antimicrobial, drugs, antiviral, traditional medicine, ethnopharmacology, toxicity, and cytotoxic activity. Therapeutically, some of the more fascinating impacts are on cancer prevention, liver diseases, blood sugar and antimicrobial activity. While the leaves, fruits and latex of the *F. carica* plant have been the primary focus of biological research, the stem and roots have got almost minimal attention. The results of this investigation indicate that extracts from all parts of *F. carica* are non-toxic. However, further well-planned clinical trials are required to confirm preclinical findings because the safety and effectiveness of *F. carica* have not been fully evaluated in humans. It is important to investigate the extract's mechanism of action. Establishing the standard dose and safety is necessary.

Keywords

Ficus carica; antioxidant; antibacterial; plants; medicinal plants

Introduction

Plants have been used as a source of medicine, both for their traditional medicinal uses and for the extraction of novel active chemicals including numerous blockbuster medications (1). *Ficus carica* (Moraceae), most popularly known as fig or "*kerma*" in the local Arabic language, is one of the most commercially valuable medicinal plants native to the Mediterranean (2). The edible fruit of *F. carica*, also called "fig" for short, has propelled this species to widespread renown among many *Ficus* species. Due to its medicinal and pharmacological effects as an antioxidant, anti-mutagenic or anti-carcinogenic, anti-inflammatory and antibacterial, this plant is among the most essential components of the Mediterranean diet (3). The chemical composition of *F. carica* and its purported health benefits have garnered a lot of interest. Traditional medicine has long made use of this species as a remedy for numerous ailments (4, 5). Few researchers have published a report on their findings (6–9), even though several studies based on pharmacological studies have been undertaken on the species. Subsequent investigations seek to close this knowledge gap to improve the species' use

in contemporary research. The following reviews sought to update the previous reviews (7, 10, 11) and provide current details about *F. carica*.

Taxonomy, distribution and abundance

The genus *Ficus* L. is the most diverse in the family Moraceae; it contains over 750 different species and is found mostly in tropical and subtropical areas (12). *Ficus carica* is a member of the order Urticales (6). The mulberry tree, of which the fig is a species, is one of the world's oldest fruiting plants. The great variety in the species' habits makes the genus interesting (13). It is classified as a dicot (14). Some of them are female in function and produce only fruit with seeds, while others are male in function and generate only pollen and wasp offspring. The *F. carica* tree is small. Woody plants include trees and shrubs (15). Its bark is grey and slightly roughened and it does not have any adventitious roots. A palmately lobed, cordately based, undulate or irregularly dentate edge, acute to obtuse apex and scabrous pubescent leaf blade characterize the stipulated and petiolate leaves (6). It is one of the earliest plants cultivated by humans (16). Its primary distribution is in the tropics and subtropics (15). It is generally accepted that domestication started in the Early Neolithic in several locations around the Mediterranean basin (17). The fig tree grows in temperate climates such as southwest Asia and the eastern Mediterranean (18). From this region, cultivated figs have spread to every continent where they may flourish (17). The bulk of them are located in the tropics and subtropics (12). *F. carica*, a characteristic Mediterranean fruit species, is grown commercially across most of the Middle East, Africa and South Europe (17). The common fig has likely been cultivated for at least 11000 years, according to fossil records (17).

Traditional uses

Ficus carica fruits have been discovered to work well as laxatives, cough suppressants, emollients, relievers, emmenagogues and in the control of hypercholesterolemia (14). It has been employed to assist digestion and treat ulcerative inflammation and eruption (13). A decoction made from dried *F. carica* is beneficial in treating respiratory tract inflammation, kidney inflammation, pneumonia, pleurisy, measles, scarlet fever, smallpox and skin illnesses (4, 5). It also boosts the immune system and helps avoid hypertension (4). The leaves are used as an antidiabetic, vermifuge and in the treatment of contact dermatitis (6). Warts, epilepsy, toothache, haemorrhoids, snake bites and cough were all reportedly alleviated by applying fresh fig latex (19). Metabolic, cardiovascular and respiratory disorders as well as haemorrhoids and skin infections, have all been treated with it in traditional medicine (16). Figs have been used to treat malignant ulcers, sores, swellings and as a beneficial therapy for chronic illnesses, according to both ancient and modern herbal books (20). *F. carica* leaves, bark, buds, fruits, seeds and latex have traditionally been used to treat jaundice, diabetes, diarrhea, nutritional anemia, kidney, skin issues, ulcers, stomach aches, dysentery and liver diseases as well as anticancer and anti-inflammatory properties (5, 21). Acne, eczema, warts and papillomatosis were treated with latex in traditional Turkish medicine (22). A stomachic decoction can be made from the leaves. To alleviate the pain and swelling of piles, the leaves can be put in a steam bath of boiling water (23). The latex of the fig fruit is used in alternative medicine to treat viral infections of the skin like warts (24). We provide a historical context of the traditional use of *F. carica* for the development of evidence -based medicine. Many species in this genus are used in alternative medicine. Examining the criticism leveled at these species, considering what is now known about their anticancer activity is vital because it has the potential to bring conventional wisdom and evidence-based research closer together (Fig. 1).

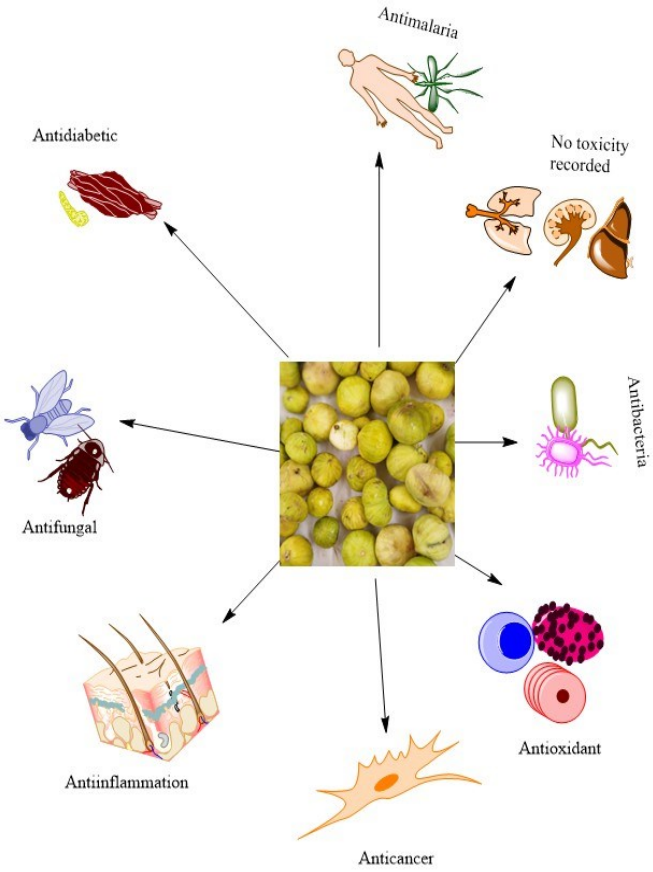

Fig. 1. Diseases treated with *Ficus carica.*

Biological activity

Antioxidant

Recently, health and food science researchers as well as medical professionals have developed an increased interest in the topic of antioxidants (25). Oxidative stress typically displays a failure of the physiological system to detoxify reactive intermediates and free radicals, leading to systemic symptoms of reactive oxygen species (25). The normal redox state of cells is destroyed by free radicals, which in turn can lead to harmful effects via the creation of peroxides by damaging DNA, proteins and lipids (26). *Ficus carica* extract is a potential source of free radical scavenging antioxidants due to the greater antioxidant activity of its various bioactive components (Table 1). The antioxidant power of fig plant was tested using a variety of solvents (Table 1). Extracts and chemical constituents have a variety of physiological effects on plants. Some of

them are advantageous to human health as well since they can function as antioxidants in a variety of ways, including as reducing agents, hydrogen donors, free radical scavengers, singlet oxygen quenchers and so on (Table 1).

The ability of a sample, such as a plant extract, to scavenge the stable 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical is a common metric for gauging its free radical scavenging efficacy. The extract exhibited the greatest ability to scavenge free radicals, with IC_{50} values of 13.6 µg GAE/mL for DPPH free radicals and 4.5 µg GAE/mL for 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) free radicals, respectively. The EC_{50} value for the overall antioxidant activity was 39 µg GAE/mL in the phosphomolybdenum assay (1). The scavenging of DPPH free radicals (1.45 mg/mL), the ratio of Beta-carotene to linoleic acid (1.56 mg/mL) and the reducing power of the essential oil (1.92 mg/mL) were all in the moderate range (2). The fruit's ethanolic extract had significantly ($p< 0.05$) higher activity than all other extracts and plant parts. The IC_{50} values the ethanolic extract of the fruit were found to be 134.44 µg/mL. (26). The maximum antioxidant activity was discovered in fruit latex, as measured by ferric reducing antioxidant power (FRAP) assay (1 mg/mL is equivalent to 179 mmol Fe^{2+}) and $ABTS^{+}$ (1 mg/mL is comparable to 0.2 µM Trolox) (22). El-Keurt sample ethanolic extract chelated greater than 88.1% of the DPPH radical with an IC_{50} = 0.0782 mg/g. The acetonic extract of the Ain Farès sample showed the highest percentage of FRAP complex inhibition (IC_{50} = 1179 mg/g) when compared to the other solvents tested (27). The ethanol extract at a dosage of 1000 µg/mL exhibited an inhibition rate of 62.99 µg/mL (28).

The water extract had an IC_{50} of 1.45 mg/mL and the methanol extract had an IC_{50} of 1.83 mg/mL for DPPH radical scavenging activity and ABTS radical scavenging activity. However, even at the decreased concentration, the ferric reducing power remained the same (29). Az (dark peel variety) aqueous extract has stronger antioxidant power (0.492 mg/mL) than Ta (light peel variety) aqueous extract (0.658 mg/mL). According to the findings, fig seeds extracted with 50% (v/v) aqueous methanol had the greatest FRAP (8504 mg $FeSO_4$/kg DM) and DPPH (41.6%) values (30). Fresh figs had the highest levels of antioxidant activity (21.3%, 1.2% TE/100 g fresh weight (fw) in the DPPH assay and 55.5%, 1% TE/100 g fw in the FRAP assay) (31). After 5 days, there was no correlation between the levels of polyphenolics and flavonoids and the antioxidant activity. Mice that were given the extracts had their body weight, immune organ index, immune injury, healing time, cytokine production, immune organ histopathology and gut microbiota all enhanced (32). The ability of *F. carica* to neutralize DPPH radicals was lower (20.54%) than that of ABTS radicals (68.98%) (33). The results showed that at 1 mg/mL, the extract had a scavenging ability of 75.7% against DPPH, indicating significant antioxidant activity (34). IC_{50} values of 7.9 and 13.4 µg/mL for antioxidant activity were determined for the leaves and fruit respectively (35).

According to the findings, the cultivar ABR latex has the greatest ORAC (450.30 µmol TE/g) (36). El-Keurt sample ethanolic extract chelated greater than 88.1%, 0.03% of the DPPH radical with an IC_{50} = 0.0782 mg/g (27). The IC_{50} values for inhibiting DPPH free radicals were as follows: pulp = 83.918 > peel = 41.846 > leaf = 17.407 µg/mL. The methanolic extract of the leaves exhibited the greatest potential (37). Compared to the gold standard vitamin C (IC_{50}=0.03 mg/mL), winter essential oil has the highest antioxidant activity (IC_{50}=0.04), followed by autumn (0.06 mg/mL) and summer (0.0646 mg/mL) (38). Essential oils bound nitric oxide and had a strong scavenging effect, with IC_{50} values of 0.032, 0.033 and 0.045 mg/mL for winter-extracted, autumn-recovered and summer-obtained oils, respectively (38). Numerous phenolic compounds (Fig. 2), including phenolic acids like ferulic acid and flavonoids like rutin, quercetin and luteolin as well as furanocoumarins like psoralen and bergapten and phytosterols like taraxasterol have been extracted from fig leaves and are thought to have pharmacological effects (39). The antioxidant power is due to phenolic and flavonoid levels. Phenolic compounds' ability to act as hydrogen donors is largely thought to be responsible for their ability to suppress radical scavenging (40). The published activity data indicates that antioxidant-rich plant extracts or isolated chemicals aid in the prevention of illness. Therefore, it is crucial to comprehend how antioxidants interact with the free radicals in *F. carica*.

Anti-inflammatory

The immune system's defensive reaction to foreign or internal non-infectious substances is what causes inflammation. The management of inflammatory diseases is a crucial topic that needs further attention. The World Health Organization (WHO) has identified the chronic inflammation and the diseases it causes as a serious global health concern (41). In light of these factors and the importance of using natural therapies and avoiding anti-inflammatory drugs' negative side effects, an experiment was conducted to test the ability of various fig extracts to reduce inflammatory reactions (Table 1). The maximum activity against the enzyme was (29.38%) at a concentration of 50 µg/mL (33). The data showed that the cultivar ABR latex has the most potent anti-inflammatory properties (IC_{50} 533 µg/mL) (36). Nitric oxide (NO) generation was significantly inhibited by prenylated isoflavone derivatives, with IC_{50} values ranging from 0.89 to 8.49 M, which is equivalent to the positive control (hydrocortisone) (42). Ficin, a novel enzyme isolated from fig latex was found to decrease the phosphorylation of I/NF- in LPS-stimulated RAW264 cells and reduce the production of NO and iNOS proteins. Inhibiting IL-6 receptor-associated MAPK and STAT3 activation, ficinolone has anti-inflammatory effects (43). We argue that more research is required in light of these justifications. Inhibiting inflammatory cytokines and mediators, *Ficus carica* may have additive effects. Supporting these findings and revealing more outcomes relevant to this study, however, will require *in vivo* clinical investigations.

Table 1. Profile of documented biological studies.

Sl No.	Activity	Method	Parts	Solvent	Concentrations	Reference
1	Antioxidant	DPPH, FRAP	Pulp	Distilled water, 80% methanol, 70% ethanol and 50% acetone	Not mentioned	(27)
		DPPH	Leaves	Ethanol	125, 250, 500, 750, 1000 µg/mL	(28)
		DPPH, Beta-carotene to linoleic acid, FRAP	Leaves (essential oil)	Not mentioned	Not mentioned	(2)
		DPPH, ABTS, FRAP	Leaves	Methanol, aqueous	2.5 to 0.004 mg/mL	(29)
		DPPH, FRAP	Seed	100% acetone, 100% methanol, 100% ethanol, 50% (v/v) aqueous acetone, 50% (v/v) aqueous methanol and 50% (v/v) aqueous ethanol	Not mentioned	(30)
		DPPH, FRAP	Fruits	Ethanol	0.1 to 0.15 mL	(31)
		DPPH, ABTS, phosphomolybdenum	Latex	Not mentioned	0.1 mL	(1)
		In vivo	Fruits	Not mentioned	Not mentioned	(32)
		DPPH	Leaves	Ethanol	(0-1 mg/mL)	(34)
		DPPH	Leaves, Fruit	Methanol	Not mentioned	(35)
		ORAC	Latex	Not mentioned	Not mentioned	(36)
		DPPH, FRAP	Not mentioned	Not mentioned	Not mentioned	(27)
		DPPH	Leaf, stembark, fruit	Hexane, ethyl acetate, ethanol, aqueous	100–500 µg/mL	(26)
		ABTS, FRAP	Fruit (latex)	Methanol	Not mentioned	(22)
		DPPH	Peel, pulp, and leaves	Methanol	Not mentioned	(37)
		DPPH, TAC, Nitric oxide chelating activity	Stems barks essential oil	Not mentioned	Not mentioned	(38)
2	Anti-inflammatory	Xanthine oxidase inhibition	Not mentioned	Not mentioned	Not mentioned	(33)
		Not mentioned	Fruits	Not mentioned	Not mentioned	(42)
		Xanthine oxidase test	Latex	Not mentioned	Not mentioned	(36)
3	Antibacterial	Microplates, disc diffusion	Pulp	Distilled water, 80% methanol, 70% ethanol and 50% acetone	1.17 to 150 µg/mL	(27)
		Disc diffusion	Fruit seed oil	Not mentioned	Not mentioned	(45)
		Agar overlay bioautography	Leaves	Not mentioned	Not mentioned	(46)
		Agar well diffusion	Leaves	Ethanol-water	Not mentioned	(3)
		Agar welldiffusion method	Leaves	Ethanol	200 and 500 mg/mL	(28)
		Not mentioned	Fruits	Not mentioned	Not mentioned	(14)
		Disc diffusion	Leaves (essential oil)	Not mentioned	10 µL	(2)
		Not mentioned	Leaves	Ethanol	Not mentioned	(17)
		Disc diffusion	Leaves	Methanol	25, 50, 100 mg/mL	(47)
		Disc diffusion, agar well diffusion	Leaves	Hexane	Not mentioned	(48)
		Microdilution broth method	Leaves	Methanol, aqueous	0.156 to 2.5 mg/mL	(29)
		Disc diffusion, ager well diffusion		Ethanol, methanol, aqueous	330, 500 and 1000 mg	(4)
		Not mentioned	Leaves	Aqueous, ethanol	Not mentioned	(49)
		Disc diffusion	Fruits	Methanol	Not mentioned	(50)
		Not mentioned	Leaves	Ethanol	200, 500 µg/mL	(51)
		Cup-cut agar method	Leaves, stem	Not mentioned	Not mentioned	(52)
		MIC	Leaves (AgNPs)	Not mentioned	Not mentioned	(53)
		Ager well diffusion	Root, stem, leaves, fruit	Methanol	Not mentioned	(54)
		Disc diffusion	Leaves	Aqueous	10, 20 and 30 mg/ mL	(55)
		Not mentioned	Not mentioned	Methanol, aqueous	0.5 µL (62.5 µg), 1 µL (125 µg), 5 µL (625 µg) and 10 µL (1250 µg)	(56)
		MTT	Endophytic fungi	Not mentioned	Not mentioned	(57)

		Disc diffusion	Fruit seed oil	Not mentioned	Not mentioned	(45)
		Disc diffusion	Leaf (essential oil)	Not mentioned	10 µL	(2)
		Microdilution broth method	Leaves	Methanol, aqueous	0.156 to 2.5 mg/mL	(29)
4	Antifungal	Ager well diffusion	Leaves	Ethanol, chloroform	Not mentioned	(60)
		MIC	Leaves (AgNPs)	Not mentioned	Not mentioned	(53)
		Ager well diffusion	Root, stem, leaves, fruit	Methanol	Not mentioned	(54)
		Disc diffusion	Leaves	Aqueous, methanol	10, 20 and 30 mg/ mL	(55)
		In vitro, in vivo	Leaves	Ethyl alcohol	0.1–2 mg/mL	(61)
5	Anti-parasitic	*In vivo*	Fruits	Cream	Cream twice a day for two weeks	(62)
		In vivo	Latex	Not mentioned	5% gel	(63)
		α-glucosidase and α-amylase	Leaves	Methanol, aqueous	0.1-2 mg/mL, 24 mg/kg/day	(29)
		Not mentioned	Peels	Methanol	10 mg/mL	(64)
		Not mentioned	Fruit, leaves, stembark	Hexane, ethyl acetate, ethanol, aqueous	100–500 µg/mL	(26)
		In vivo	Leaves	Ethanol	Not mentioned	(65)
		In vivo	Leaves	Dichloromethane	500 and 1000 mg/ kg	(66)
		In vivo	Leaf, bud	Not mentioned	200 mg/kg body weight	(67)
		Alpha-amylase Inhibition	Stems barks essential oil	Not mentioned	24, 48, 95 µg/mL	(38)
6	Antidiabetic	*In vivo*	Not mentioned	Not mentioned	300, 600 mg/kg g	(68)
		In vivo	Leaves	Ethyl acetate extract	250, 500 mg/kg	(69)
		In vivo	Leaves	Ethanol	Not mentioned	(70)
		In vivo	Leaves	Methanol	100, 200 mg/kg BW, daily for 5 weeks	(71)
		Not mentioned	Fruit (latex)	Methanol	Not mentioned	(22)
		Not mentioned	Pulp, peel and leaf	Methanol	Not mentioned	(37)
		In vivo	Liraglutide and nano extracts	Not mentioned	0.02 mg/kg BW/ day	(72)
		In vivo	Leaves	Not mentioned	2 g/kg	(73)
		Not mentioned	Peels	Methanol	10, 25 mg/mL	(64)
7	Anti-Cholinesterases	Not mentioned	Latex	Not mentioned	Not mentioned	(36)
		Not mentioned	Fruit, leaves, stembark	Hexane, ethyl acetate, ethanol, aqueous	100–500 µg/mL	(26)

		3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT)	Leaves	Hexane	250, 500, 750, and 1000 µg/mL	(48)
		XTT colorimetric assay	Leaves	Methanol, aqueous	1 mg/mL	(29)
		Not mentioned	Leaves	Not mentioned	Not mentioned	(74)
		Sulfo Rhodamine-B stain (SRB)	Not mentioned	Not mentioned	12.5–100 µg GAE/mL	(1)
		MTT	Not mentioned	Ethanol	Not mentioned	(33)
		Not mentioned	Leaves	Ethanol	5000, 2500, 1250, 625, 312.5 and 156 mg/mL	(34)
		MTT	Fruits	Not mentioned	3.9–500 µL/mL	(75)
		MTT	Peel, pulp, leaves, whole fruit, latex	Not mentioned	Not mentioned	(76)
		MTT	Methanol	Leaves, fruits	2000, 1000, 800, 400, 200, 100, 50, 25, 12, 5, 6, 3 µg/mL	(35)
		MTT	Not mentioned	Latex	0.1, 0.25, 0.5, 1%	(77)
8	Anticancer	*In vivo*	Ethanol	Fruits	Not mentioned	(78)
			Endophytes	Not mentioned	Not mentioned	(79)
		MTT	Fruits	Not mentioned	Not mentioned	(42)
		Not mentioned	Latex	Not mentioned	Not mentioned	(80)
		Not mentioned	Latex	Not mentioned	Not mentioned	(16)
		MTT	Leaves	Not mentioned	Not mentioned	(81)
		Not mentioned	Latex	Not mentioned	Not mentioned	(36)
		MTT	Latex	Not mentioned	Not mentioned	(82)
		MTT	Latex	Petroleum ether	0.125, 0.25, 0.5, 1 µg/mL	(83)
		MTT	Leaves	Methanol	150, 250, 350, 450, 550, 650, 750, 850 µg /mL	(84)
		MTT	Fruits (essential oil)	Hexane, aqueous	Not mentioned	(85)
		MTT	Latex	Not mentioned	Not mentioned	(86)
		In vivo	Leaves	Not mentioned	Not mentioned	(87)
		Not mentioned	Leaves	Methanol, aqueous	Not mentioned	(88)
9	Cytotoxicity	Sulfo Rhodamine-B stain (SRB)	Not mentioned	Not mentioned	12.5–100 µg GAE/mL	(1)
		In vivo	Not mentioned	Not mentioned	2000 mg/kg AgNPs,	(75)
		In vivo	Latex	Not mentioned	25–30 g	(86)

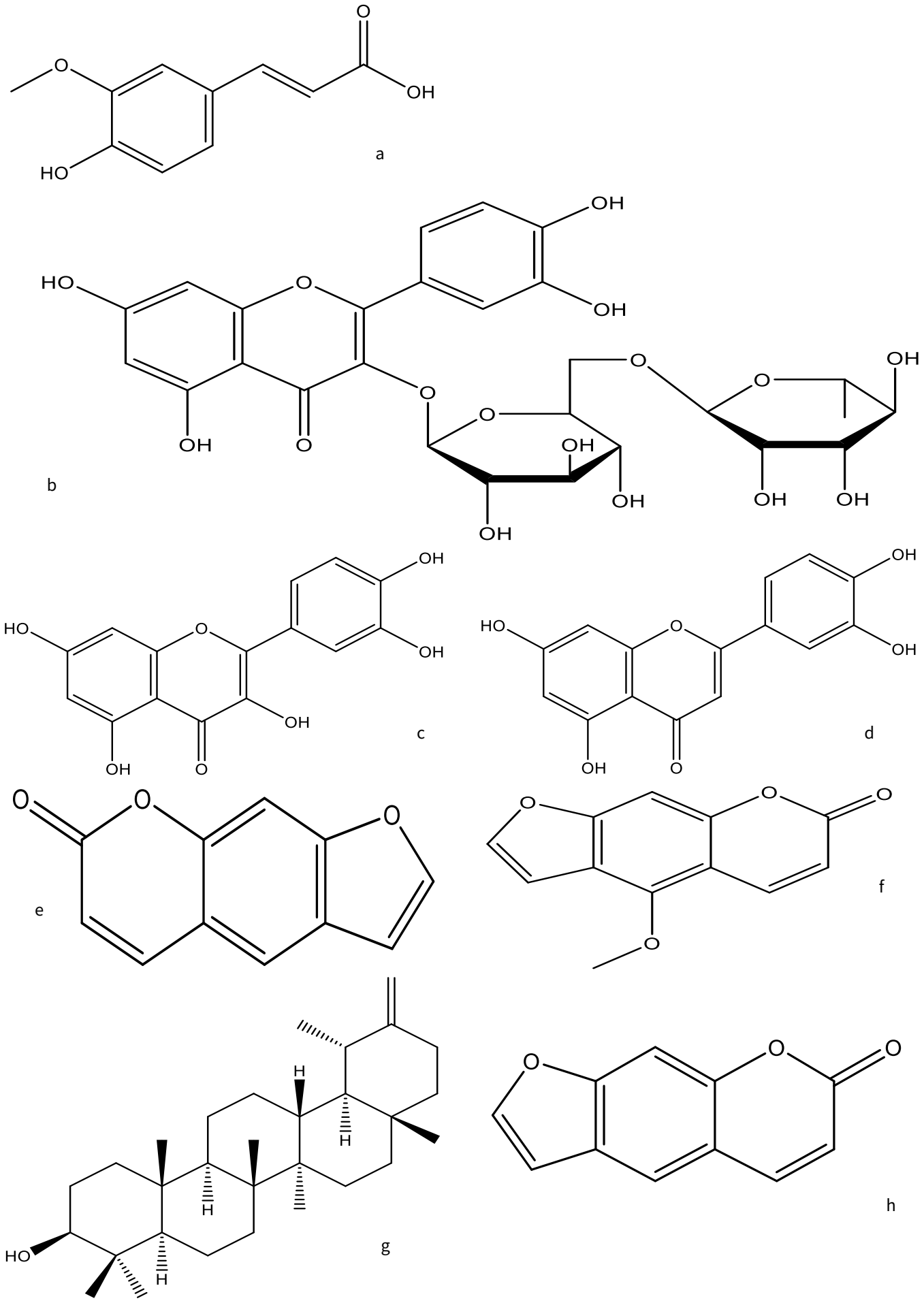

Fig. 2. Some of the compounds responsible for the biological activity. (a) Ferulic acid (b) Rutin (c) Quercetin (d) Luteolin (e) Psoralen (f) Bergapten (g) Taraxasterol and (h) Ficusin

Antibacterial

People and the various microorganisms that spread disease and sickness are still at odds. Pathogenic bacteria have become increasingly sophisticated in their ability to withstand antimicrobials as their prevalence has grown. Because multidrug-resistant microbes have contributed to a dramatic rise in the mortality toll from infectious illnesses, new antimicrobial agents and antibiotics are urgently needed (25). Man must consequently constantly search for other treatments. According to the early screening assays described in the following paper, components of *Ficus carica* may be employed as alternative treatment agents for a variety of bacterial strains. High antibacterial activity was defined as an inhibitory zone that was 14 mm or larger (including the diameter of the disc) (44).

With minimum inhibitory concentration (MIC) values ranging from 4.75 mg/mL to 38 mg/mL, essential oil had the greatest effectiveness against all microorganisms tested (2). The extract was highly effective in killing off several distinct types of bacteria (Table 1). Samples showed no inhibitory effect on *Escherichia coli*, while extracts made from many samples using 75% ethanol and 75% methanol showed only little activity (3). The methanolic extract of the El-Keurt variety significantly inhibited the activity of *Enterobacter cloacae* at 2.34 mg/mL of the extract, as determined by the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) (14). The extract's antibacterial effect was inhibited by both Gram-positive (methicillin-resistant *Staphylococcus aureus*: 10.4 mm inhibition zone diameter) and Gram-negative (*E. coli*: 13.25 mm inhibition zone diameter) bacteria (17). The inhibition zones of *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Streptococcus pneumoniae* were all smaller than 9.75 mm, 8.69 mm and 8.56 mm, indicating that they were less vulnerable to the extract (17). For gram-positive *S. saprophyticus* and *S. aureus*, the minimum inhibitory concentration of the aqueous extract was 133 mg/mL, while the minimum bactericidal concentration was 200 mg/mL (4).

The least bactericidal concentration (MIC) for *Citrobacter freundii* was 1.171 µg/mL, whereas the MIC for *Listeria innocua* was larger than 75 µg/mL, with *Enterococcus* and *Vibrio cholera* having a MIC equivalent to 300 µg/mL (27). Antibacterial activity carried out in ethanol extract of leaves at concentrations of 200 and 500 mg/mL against the selected bacterial strains revealed that it was effective. *K. pneumonia* was inhibited at 18 and 28 mm, *E. coli* at 20 and 26 mm, *S. aureus* at 24 and 26 mm and *P aeruginosa* at 22 and 28 mm (28). Activity of the methanolic extract was low against most bacteria but moderate against *E. coli* (0.625 mg/mL) and *S. aureus* (0.156 mg/mL). Moreover, while the aqueous extract was moderately effective against *S. aureus* (0.625 mg/mL), it was significantly less effective against the other microorganisms (29). Maximum inhibitory zone of 10 mm was observed for *Listeria monocytogenes* when treated with extract (29). The seed oil had the highest inhibition zone of 35 mm against *E. coli* (45). In the bio-autography experiment, inhibited *S. aureus* at a concentration with zones of inhibition ranging from 11 mm to 22 mm (46).

The extract of 'Blanquette' cultivar leaves showed strong activity against Gram positive bacteria (*P. aeruginosa* with 9. 25 mm in diameter as inhibition zone) at 100 mg/mL, followed by 8.75, and 8 mm at 50 and 25 mg/mL respectively. It also worked well against *S. aureus*, which recorded 8.25 mm at 50 mg/mL, 7.75 mm, 7.12 mm and 100 mg/mL (47). At the highest dose examined (100 mg/mL), no bacterial activity of the n-hexane extracts was found (48). The ethanolic extract exhibited *S. aureus* at 23 mm (49). Only Gram-positive bacteria (*B. subtilis* and *B. cereus*) were inhibited by the extracts (zone of inhibition 3.14 mm, MIC 8-10 mg/mL) (50). Activity of the extract was demonstrated against the test bacteria. Inhibitions of 18 and 28 mm were seen against *K. pneumonia*, 20 and 26 mm against *E. coli*, 24 and 26 mm against *S. aureus* and 22 and 28 mm against *P. aeruginosa* (28). The methanol extract of the stem component showed the greatest zone of inhibition against *S. aureus* (27 mm, $p>0.05$), while the methanol extract of the leaf showed the greatest zone of inhibition against *K. pneumoniae* (6 mm, $p>0.05$). Stem extracts from methanol were more effective at inhibiting *S. aureus* (27 mm, $p>0.05$) than leaf extracts (15 0.06 mm, $p>0.05$) (51).

The study indicated that the MIC values for *S. aureus*, *S. pyogenes*, *E. coli* and *P. aeruginosa* were 0.225, 0.056 and 0.112 mg/L respectively, when treated with Silver nanoparticles (AgNPs) (52). The average methanolic extract had an inhibition zone of 63 mm, while the average chloroform extract had an inhibition zone of 56 mm. The leaf extract is far more potent than the others in both methanolic and chloroform extractions (53). When exposed to chloroform extract of leaves (34 mm), *S. aureus* showed extreme sensitivity (53). With *S. aureus*, the greatest inhibition zone was measured at 25 mm at a concentration of 30 mg/mL (54). *S. aureus* showed the highest susceptibility to the water extract, with a concentration of 1 µL containing 125 µg (55). The 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) testing method demonstrated that the isolated endophytic fungus from the root had antibacterial activity, with a MIC value of 31.25 µg/mL and a cell death % of 62.29 % against *S. aureus* (56). Meanwhile, at a MIC of 500 µg/mL, the endophytic fungi isolated from the stem antibacterial active, causing 79.28% cell death (56). Their broad, extensive antibacterial activity may result from the combined polyphenolic effects of dried figs and extra virgin olive oils (57).

It is well established that certain chemical classes are biologically active and linked to their biological effects (12). The chemical makeup of the essential oil (EO) related to its antibacterial efficacy, suggesting that the EO's action may be linked to the high level of ficusin (Fig. 3). In addition, our EO contains several additional chemicals that have antibacterial properties. These include benzyl alcohol, bergapten and caryophyllene oxide (2). Flavonoids, steroids, saponins and/or tannins may all play a role in the antibacterial activity of leaf extract (17). Some

Ficus spp. members, modes of action suggest that an antibacterial agent may have more than one cellular target in addition to its principal site of action (58). Molecular interactions with proteins may involve non-specific forces including hydrophobic effects and hydrogen bonding, in addition to covalent bond formation, according to their theory. Antimicrobial activity may thus be associated with their capacity to render inactive microbial adhesins, enzymes, cell envelope transport proteins etc (58). The adhesion of the extract to the cell wall and membrane, the extract's penetration inside the cell and harm to intracellular organelles (Fig. 3), the extract's induction of cellular toxicity and oxidative stress caused by the production of reactive oxygen species (ROS) and free radicals and the extract's modulation of cellular signalling are the 4 well-defined mechanisms linked to the antimicrobial action of the plant extract. To improve the antibacterial activity of these extracts, it is essential to identify and purify the phenolic components in fig tree leaf extracts.

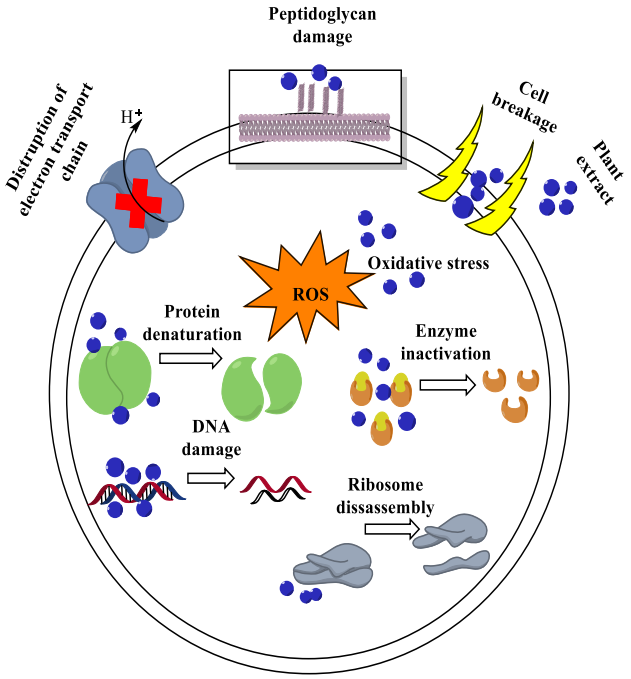

Fig. 3. Mechanism of action of *Ficus carica* part extract on bacteria.

Antifungal

Infectious infections are a leading cause of death and disability worldwide, especially in poorer regions (88). The continuous rise of microbes resistant to traditional antimicrobials has encouraged pharmaceutical companies to explore novel antimicrobial medications in recent years. When looking for new antifungals, it is important to prioritize those that come from plants. MIC values for inhibiting *Candida* species ranged from 4.75 mg/mL to 9.5 mg/mL (2). Methanol and water both have little action (≥ 2.5 mg/mL) against *Candida albicans* (29). The seed oil inhibited the growth of *C. albicans* and *Aspergillus flavus* at 25 and 30 mm respectively (46). The study indicated that the MIC value for AgNPs against *C. albicans* was 0.450 mg/L, meaning that they were effective at lower doses (52). Methanolic leaf extract (34 mm) was extremely effective against *Aspergillus niger* (53). *A. niger* at 1.5% and methanol extract recorded the highest percentage mycelial growth inhibition zones (33.53%), whereas *A. flavus* at 20% and methanol extract recorded the lowest % mycelial growth inhibition (22.22%) (54). Chloroform extract only demonstrated suppression on *Penicillium cyclopium* growth at 10.33 mm, while ethanol extract showed growth of all examined microorganisms (8–8.47 mm) (59). The current investigation found that even trace amounts of AITC were sufficient to halt the growth of *Penicillium expansum*. The *in vivo* regular visual checks revealed that the AITC-treated inoculation figs had a considerably lower proportion of rot than the control group (89). First and foremost, our investigation showed that the fruits were antifungal. This analysis corroborated the ethno botanical studies demonstrating the traditional medicinal potential of plant parts. The following studies report that when tested against human, animal and other fungal strains, all extracts showed substantial suppression of growth at a high inhibition zone.

Antiparasitic

Millions of natural products, with nearly unlimited structural diversity, are derived from higher plants. Many of these molecules perform useful biological processes and serve a variety of other purposes as well. Parasitic illnesses are a leading cause of illness and death worldwide and pose a serious threat to public health (88). Drug resistance, drug residues and unpleasant side effects are some of the problems that can arise when resorting to chemical treatments to combat parasites (88). Studying potential options for treatment is essential. The extracts were found to have an IC_{50} of 1.2 mg/mL when tested against promastigotes. Furthermore, *in vivo* experiment results showed that mice administered with the extract considerably reduced the mean size of lesions by 3.65 mm^2 (60). The randomized, placebo-controlled experiment showed that the novel drug was more effective than Hydrocortisone 1.0% ($p<0.05$) in reducing the SCORAD index, pruritus and intensity scores, while the placebo had no effect (61). Lesions in the group of mice given 5% *Ficus carica* gel were smaller on average than those in the control group, but when comparing groups treated with daily therapy alone, there was no statistically significant difference ($p> 0.05$). Using larger doses of *F. carica* latex for longer durations may increase its effectiveness against CL (62). All trials looked at, however, showed that the plant was effective against the parasites they used. Interestingly, the antiparasitic effects of the extract varied depending on both their chemical composition and the nature of the promastigote species. Similarly, the antiparasitic activity of the extracts varied depending on the promastigote species they were used against. These capacities of the extracts disrupt cell membranes and cause cell death in specific cell types suggests how they work (25). One such targeted technique that promotes apoptosis in parasites is interaction with the mitochondrial membrane.

Antidiabetic

People with diabetes mellitus are affected by this serious global health issue in both developed and developing nations (90). It is anticipated that this ailment will impact 25% of the world's population. Diabetes is defined by

improper glucose metabolism, which is exacerbated by low blood insulin levels (90). The search for novel treatments continues. The maximum alpha-amylase and alpha-glucosidase activities (IC_{50}=195.20 µg/mL and 6.9 µg/mL respectively) were discovered in the latex portion of fruit (22). The *Ficus carica* fruit ethanolic extract had substantially higher ($p< 0.05$) IC_{50} values for pancreatic lipase activity (230.475 µg/mL) than other plant extracts and fractions. The ethanolic extract of fruit showed significantly ($p< 0.05$) greater activity than other extracts (26). The ethanolic extract of fruit had IC_{50} values for inhibiting alpha glucosidase (255.57 µg/mL) and alpha amylase (315.89 µg/mL) (26). It was found that the water extract was more effective at inhibiting -glucosidase and -amylase enzyme activity (69.56% and 69.08%) than the methanol extract (64.93% and 67.32%), but that both extracts showed promise as inhibitors of these enzymes when compared to the standard antidiabetic drug acarbose (57.56% and 58.4%) at the same concentration (2 mg/mL) (29).

The AGH cultivar's latex contained more caffeic acid and showed more -glucosidase inhibitory activity (53.1%) than the ELB cultivar's latex did (36). The leaf extract had the strongest anti-amylase activity out of the 3 sections tested (IC_{50} value of pulp = 1.237 > peel = 0.899 leaf = 0.896 µg/mL) (38). Essential oils collected in summer (24.58), autumn (35.75) and winter (38.15) have respective IC_{50} values of 24.58, 35.85 and 38.15 µg/mL against –amylase (39). With an IC_{50} of 16.82 µg/mL, these numbers indicate a potent antidiabetic action, like that of acarbose (39). Inhibitory actions against -glucosidase were observed in all extracts. Only the BN extract revealed an IC_{50} higher than 3 mg/mL, while the AZ extract was the most effective (63). In comparison to the control group, the treatment group that received 40 mg, 60 mg and 80 mg doses of fig leaf ethanol extract had significantly lower blood glucose levels ($p<0.05$). The results were significantly different from the positive group ($p<0.05$) (64). The extract reduces blood glucose, improves blood lipids and promotes pancreatic -cell recovery. Meanwhile, 3,4-dihydropsoralen, umbelliferone and 7-hydroxyl-6-methylcoumarin were recovered from dichloromethane extract in addition to psoralen. In HepG2 cells, psoralen and umbelliferone increased glucose absorption (65). The data showed that exposure to alloxan results in hyperglycemia, elevated levels of liver and kidney biomarkers, decreased levels of antioxidative enzymes and triggered lipid peroxidation. All pharmacological changes brought on by alloxan have, however, been mitigated by therapy with extracts of *F. carica* leaves and buds and especially their combination (66).

The positive group (44.3%), the 300 mg/kg group (35.2%), the 600 mg/kg group (35.8%) and the 100 mg/kg group (17.3%) all saw decreases in blood sugar compared to the control group. Compared to the 100 mg/kg dose (17.3%) and the 300 mg/kg dose (29.0%), the 600 mg/kg variation dose (35.2%) gives the biggest blood sugar reduction, which is close to positive group (44.3%) (67). Effects on glucose, total cholesterol, triglycerides, body weight and hepatic glycogen levels were statistically significant ($p<0.005$) when using extracts at 250 and 500 mg/kg (68). Blood sugar levels in male spreague Dawley rats treated with ethanol extract were shown to decline more than those in rats treated with persimmon extract following the identical streptozotocin induction protocol (69). Glucose, lipid profile, kidney and liver enzyme levels were all considerably lowered after oral administration of the extracts at doses of 100 and 200 mg/kg (70). By reducing body weight, serum glucose, cholesterol, TG, LDL and VLDL while enhancing HDL protective properties, the extract showed promise in controlling obesity linked T2DM (91). Liraglutide and nano extracts considerably decreased ($p< 0.001$) the increased lipid profiles and blood glucose levels in the diabetic group (Group 2) (71).

The expression levels of apoptosis-related proteins such as FasL, caspase8, Bax/Bcl-2, Cyt-C, caspase-3, p-AMPK and p-JNK were lowered after administration of the extract and pancreatic tissue injury was dramatically improved in type 1 diabetic mice (72). Based on the data, it appeared that the extracts' anthocyanin content was principally responsible for their inhibitory actions against -glucosidase (63). This was due in large part to the several phenolics (rutin, luteolin, quercetin and chlorogenic acid) found in significant concentrations by UPLCMS (36). The crude extract and compounds of *F. carica* are likely to have hypoglycemic effects by preventing glucose absorption in the small intestine, increasing insulin secretion in the pancreas, which prevents glucose production in the liver or encouraging glucose uptake in peripheral tissues via glucose transporters (Fig. 4).

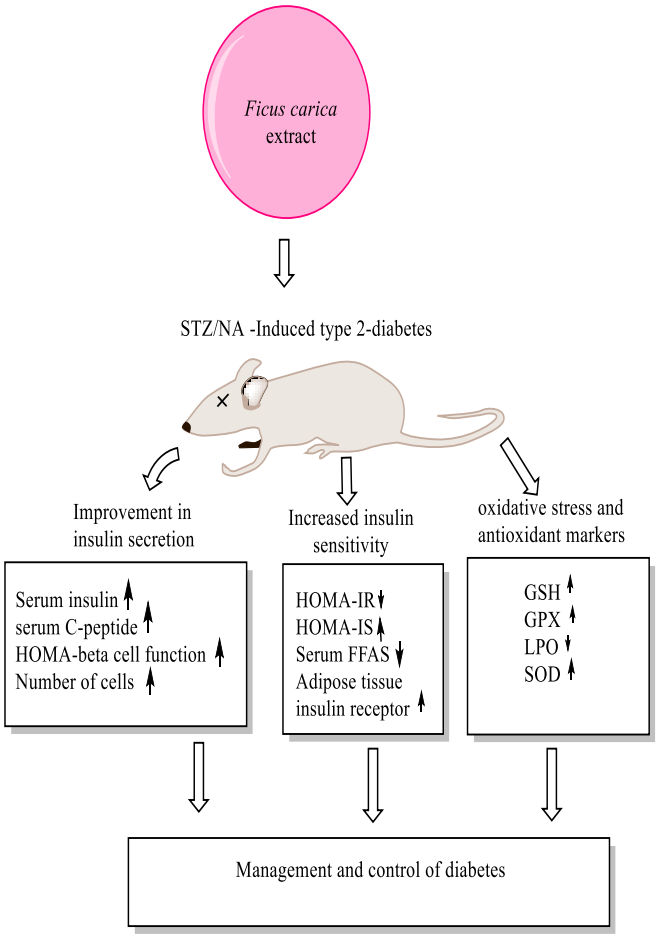

Fig. 4. Mechanism of action of *Ficus carica* extract on diabetes.

Anti-cholinesterases

Alzheimer's disease (AD) is characterized by a decline in brain acetylcholine (ACh) quantity, which manifests mostly in cognitive decline and behavioral disturbances in the elderly (92). The reduction of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) activity can make up for the loss of acetylcholine (ACh) label, as was discovered by the mechanistic approach to AD (92). Natural anti-cholinesterases are safer for avoiding illness progression. In terms of pancreatic lipase IC_{50} values (230.475 µg/mL), the *Ficus carica* fruit ethanolic extract had substantially higher activity ($p< 0.05$) than other plant extracts and fractions (26). The highest levels of acetylcholinesterase and tyrosinase enzyme inhibition (64.65% and 58.88% respectively) were observed in this extract (36). Due to the lack of AChE and BChE inhibitory action at 10 mg/mL, larger concentrations (25 mg/mL) were attempted. At this dose, the inhibition of AChE and BChE was quite mild. AZ extract showed the highest inhibitory action (IC_{50} values of 1.92 and 1.63 mg/mL for AChE and BChE respectively) out of all the tested compounds (63). These findings may shed light on how fig functions as an anti-cholinesterase drug in the treatment of mental health issues.

Anticancer

There have been numerous attempts to develop chemotherapy medications that are successful, yet selectivity and toxicity issues persist (35). The toxicity of contemporary chemotherapy and the resistance of cancer cells to anticancer drugs have prompted research into other forms of treatment and preventative measures (35). The use of plant-based remedies could be an option. There has been prior research into the potential of plants as an anticancer agent. The extract showed moderate activity against HepG2 and HCT116 cancer cell lines with IC_{50} values of 32.25 and 38.75 µg/mL respectively and significant potent cytotoxic activity ($p< 0.01$) against MCF-7 with IC_{50} concentration of 25.30 µg/mL after 48 h of incubation. Furthermore, it had no effect on HL-60 or A549 cancer cells (1). The latex showed dose-dependent anticellular growth effects. Moreover, latex treatment significantly enhanced apoptosis in FaDu cells, as evidenced by an increase in the expression of Bax (a proapoptotic protein) and a decrease in the expression of Bcl-2 (an anti-apoptotic factor) (16). The growth of MDA-MB-231 cells was considerably ($p>0.05$) and dose-dependently (IC_{50}=0.081 mg/mL) suppressed when the methanol extract was used. However, the water extract caused a modest decrease in cell viability at a concentration of 1 mg/mL (IC_{50}>1 mg/mL; $p>0.05$) (29).

At the concentrations used, *Ficus carica* had no effect (33). All chosen cell lines were effectively inhibited by the extract, demonstrating its potent anticancer effects. Both Hep2 and HepG2 cells were significantly inhibited by the extract, with percentages ranging from 80.7% to 66.9% (34). The IC_{50} values for the leaves and fruit of *F. carica* were greater than 653 µg/mL and greater than 2000 µg/mL respectively. Flow cytometry revealed that the Huh7it apoptosis and necrosis rates in leaf extracts were significantly greater than those in fruit extracts (35). Based on its cytotoxic action, the latex from the ABR cultivar was most effective against the HepG2 and MCF7 cell lines associated with hepatocellular carcinoma, whereas the latex from the AGH cultivar was found to be more effective against the HepG2 and HCT116 cell lines associated with colorectal cancer. The fibroblastic CCD45 SK cell line, on the other hand, was most sensitive to the cytotoxic effects of ELB extract (36). The IC_{50} values for compounds 1-16 against a panel of human cancer cell lines ranged from 0.18 to 18.76 µM, indicating that these compounds demonstrated potent antiproliferative effects *in vitro* (42). At 1000 µg/mL, the cytotoxic effect of the n-hexane extract was about 100% and this effect was dose-dependent. Two fig cultivars' n-hexane extracts exhibited similar cytotoxic effects regardless of extraction method ($p>0.05$) (49). 50% lethal concentration = 4.4 g mL^{-1} for aurosperone D and 3.0 g mL^{-1} for asperpyrone D in human cervical cancer cells. Strong antiproliferative effects were seen with both aurosperone D and asperpyrone D against human immortal erythroleukaemia cells 562 as well as human umbilical vein endothelial cells (IC_{50} values of 5.3 and 4.7 µg/mL for aurosperone D and asperpyrone D respectively) (73).

Asperazine was found to have moderate cytotoxicity (CC50=18.4 µg/mL) against HeLa cell lines and moderate antiproliferative effects (GI50=31.5 µg/mL) against human umbilical vein endothelial cell (HUVEC) and K-562 cell lines. Asperazine A, on the other hand, was only slightly effective as a cytotoxin against HeLa cell lines (CC50=34.6 µg/ mL) and as a cytostain against HUVEC and K-562 cell lines (GI50=40.7 and 50.2 µg/mL respectively) (93). After 48 h, cell lines were examined with varied concentrations of AgNPs. The half-maximal cytotoxic dose (LD50) of AgNPs was determined to be 12.411mg, while the LD_{50} determined for cell lines treated with fruit extract was 139.04 mg (74). After 48 h of treatment, the extracts of *F. carica* peel, pulp, leaves, entire fruit and latex significantly inhibited the proliferation of HCT-116 (IC_{50} values 239, 343, 177, 299 and 206 µg/mL) and HT-29 cells (IC_{50} values 207, 249, 230, 261 and 182 µg/mL) (75). After 24 h of treatment, the latex extract from the leaves decreased cell proliferation. At all three-time intervals (24, 48 and 72 h), compared to the untreated control, the cell viability of the treated cells was significantly ($p< 0.05$) lower. However, the viability trends depend on the dose and the duration (76). In 2 pancreatic cancer (PaCa) cell lines, the extract caused cell viability inhibition and apoptotic cell death in a dose- and time-dependent manner (77). The extract successfully prevented PaCa cells from migrating, metastasizing, invading and forming colonies. All endophytic strains were found to have antiproliferative effects against HUVEC and K-562, with GI_{50} values ranging from 4.75 to 13.75 µg/mL and to be cytotoxic toward HeLa, with CC_{50} values ranging from 8.25 to 18.75 µg/mL (78). Apoptosis-inducing gene expression levels went raised (94).

In addition, the treated cells showed cell cycle arrest during the S phase, as evidenced by an elevated % of S phase and altered expression of cyclin-dependent kinases. Cell motility, a prerequisite for metastasis, was

also reduced in treated cells (94). Alcohol-precipitated fraction of fig fruit latex (Affl) treatment dramatically reduced tumor growth in A549 xenograft mice, generated no visible injury to normal animal organs (liver or kidney) and decreased the proliferation, migration, invasion and clonogenesis of NSCLC cells (79). Antioxidant function and cytotoxic inhibitory activity of pectin against HepG2 and A549 cells showed a robust dose-dependent behavior (95). Cell viability and morphological alterations in the RD cell line were discovered to be dose-dependently affected by the extract. The anticancer impact of doxorubicin-HCl and decarbazine-based chemotherapy, Photosense-mediated photodynamic therapy (PDT) and chemo-PDT (tri-combination) was found to be enhanced by pre-incubation with the extract (CI <1) (80). Compared to other cell lines, the extract was most effective against the K562 line (IC_{50} value 234 µg/mL) and least effective against Hela cells (IC_{50}, >1000 µg/mL) (81). Rapid growth and invasion of HPV -positive cervical cancer-transformed cells are inhibited by the extract and the expression of the HPV oncoproteins E6, E7 as well as p16, is markedly down regulated (82). 3T3-L1 adipocytes had their transcriptional pathway of adipogenesis and insulin sensitivity was reduced by the treatment. Gene expression for PPAR ($p<0.05$), C/EBP ($p<0.05$), Leptin ($p<0.0001$), adiponectin ($p<0.05$) and GLUT4 ($p<0.01$) was all significantly reduced by 80 µg/mL (96). Methanolic extract inhibited B16F10 cell growth in a time- and dose-dependent fashion. The extract was found to cause chromatin condensation and fragmentation, as seen by AO/PI staining and by DAPI, which demonstrated an increase in apoptotic cells in treated groups (83). Both the essential oil extracted with water and the one extracted with hexane had IC_{50} values of 40% v/v in the cytotoxicity test. Cell cycle arrest in S phase decreased ROS production (86).

The IC_{50} value of the chloroform fraction was 0.219 and 0.748 mg/mL for the HepG2 and NIH cell lines respectively, making it the most effective fraction (85). Compounds unique to each extract explained the variation in antitumor efficacy (35). According to reports, the mechanism of action involves elevated intracellular ROS levels that might cause cell death (97). Vascular endothelial growth factor (VEGF), a prominent pro-angiogenic growth factor involved in the angiogenesis process and its receptors were both markedly down-regulated, with the latter being a concentration-dependent phenomenon. Basic fibroblast growth factor (bFGF), another pro-angiogenic growth factor, secretion was unaffected (20). The *F. carica* extract was discovered to function by causing an increase in intracellular ROS, which aided in the extract's ability to trigger apoptosis (77). The ROS scavenger NAC reduced this, indicating that ROS generation aided in the anticancer properties of the extract (77). The anticancer effects of *F. carica* leaf extracts were similar to those of two of the active components, bergapten and psoralen (Fig. 2), suggesting that these two components may play major roles in the anticancer actions of *F. carica* leaves (94). Research into the molecular basis of AFFL's effects showed that it stimulated Caspase-3 and Caspase-9 cleavage, inhibited Bcl-2 activity and induced apoptosis in tumor cells, hence increasing Caspase-1 expression (79).

Hepatotoxicity

The liver is one of the body's biggest organs and the primary location of metabolic and excretory activity (98). Damage to this organ, which plays a crucial role in the elimination of both naturally occurring and artificially introduced toxins, can have far-reaching effects on a person's health (98). Serum urea, creatinine, Hcy and kidney Hyp, lipid peroxidation, as well as kidney GSH, NO and TAC, are all significantly elevated while kidney GSH, NO and TAC are significantly decreased in CisPt-induced AKI in rats compared to control rats. Renal function was improved with efficient ROS scavenging capacity after treatment with Au-NPs and fig extract, especially at a ratio of (3:2). The severity of AKI was also reduced (87). Hepatoprotective effects have been shown in limited research.

Cytotoxicity

Many people use medicinal herbs, particularly in developing countries. They are so well-liked in the neighbourhood because they are affordable and conveniently accessible. Because herbal medicines are all natural, people around the world feel they are risk-free. The evidence, however, appears to support the opposite. If handled improperly, they can be very harmful. The safety of plant extracts must therefore be established. The enormous range of chemicals present in medicinal plants, all of which have advantageous biological effects, has been shown in several studies. At doses up to 100 µg/mL, none of the extracts tested were harmful to the human normal melanocyte HFB4 cell line (1). Oral administration of AgNPs is not associated with any adverse toxic effects in experimental animals (74). No fatalities were seen after a single dose of 2 g/kg of fraction was given. The chloroform fraction was found to contain lupeol acetate and lupeol palmitate, as determined by phytochemical analysis (85). At the concentrations used in this study, the cytotoxic effect is not hazardous. This finding is dose dependent. Cytotoxic effects are not observed at concentrations lower than or like what would be obtained by dissolving 5 drops in half a glass of water (approximately 250 L in 100 mL corresponds to 0.25% v/v). Concentrations between 0.5% and 1% v/v, however, are associated with a noticeable decline in vitality (87). The results of this investigation indicate that extracts from all parts of *Ficus carica* are nontoxic. Toxicological testing of individual chemicals is the cornerstone of any pharmaceutical or herbal composition.

Conclusion

It has been demonstrated that a variety of medicinal plants and the compounds derived from them have pharmacological and neurotherapeutic effects. We require a thorough understanding of the pharmacological effects of medicinal plants to more effectively coordinate the numerous on-going and future studies aimed at treating a wide range of human illnesses. This study reviewed the

information that was available regarding the pharmacological and therapeutic effects of *Ficus carica.* According to the review, *in vitro* and *in vivo* animal models have both been used to study the anticancer, antibacterial and antidiabetic effects of *F. carica*. Additional carefully designed clinical trials must be conducted to confirm the preclinical findings because the safety and efficacy in humans have not yet been fully vetted. One cannot overestimate the significance of establishing a safe dose standard. More research involving biologists, pharmacologists and medical doctors is needed to determine the constituents of *F. carica*, determine their biological activity, determine whether they are safe and effective for human use and ultimately gain Food and Drug Administration approval.

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