

**REVIEW ARTICLE** 



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

Abdulrahman Mahmoud Dogara⁺, Harmand A. Hama& Dogan Ozdemir

Biology Education Department, Tishk International University, Erbil, Iraq

\*Email: abdulrahman.mahmud@tiu.edu.ig; abdouljj@yahoo.com

# 

#### **ARTICLE HISTORY**

Received: 14 November 2023 Accepted: 12 March 2024

Available online Version 1.0:09 April 2024 Version 2.0:14 April 2024



#### Additional information

**Peer review:** Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

**Reprints & permissions information** is available at https://horizonepublishing.com/ journals/index.php/PST/open\_access\_policy

**Publisher's Note**: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc See https://horizonepublishing.com/journals/ index.php/PST/indexing\_abstracting

**Copyright**: © The Author(s). This is an openaccess article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited (https://creativecommons.org/licenses/ by/4.0/)

#### **CITE THIS ARTICLE**

Dogara AM, Hama HA, Ozdemir D. Taxonomy, traditional uses and biological activity of *Ficus carica* L. (Moraceae): A review. Plant Science Today. 2024; 11(2): 385–400. https:/ doi.org/10.14719/pst.3085

## 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).

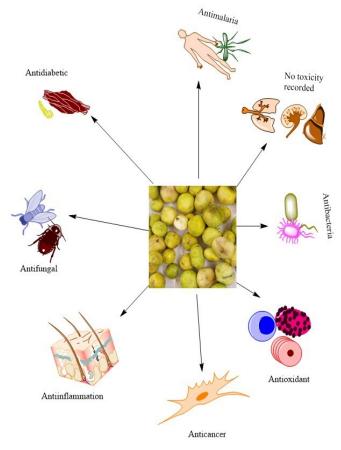


Fig. 1. Diseases treated with Ficus carica.

# **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<sub>50</sub> 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<sub>50</sub> 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  $\mu$ g/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 Fe2+) 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<sub>50</sub> = 0.0782 mg/g. The acetonic extract of the Ain Farès sample showed the highest percentage of FRAP complex inhibition  $(IC_{50} = 1179 \text{ mg/g})$  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<sub>50</sub> of 1.45 mg/mL and the methanol extract had an IC<sub>50</sub> 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<sub>4</sub>/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<sub>50</sub> 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  $IC_{50} = 0.0782 \text{ mg/g}$  (27). The  $IC_{50}$ values for inhibiting DPPH free radicals were as follows:  $pulp = 83.918 > peel = 41.846 > leaf = 17.407 \mu g/mL$ . The methanolic extract of the leaves exhibited the greatest potential (37). Compared to the gold standard vitamin C (IC<sub>50</sub>=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<sub>50</sub> values of 0.032, 0.033 and 0.045 mg/mL for winterextracted, 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 antiinflammatory 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  $\mu$ g/mL (33). The data showed that the cultivar ABR latex has the most potent anti-inflammatory properties (IC<sub>50</sub> 533 µg/mL) (36). Nitric oxide (NO) generation was significantly inhibited by prenylated isoflavone derivatives, with IC<sub>50</sub> 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	Referenc
		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 100% acetone, 100%	2.5 to 0.004 mg/mL	(29)
		DPPH, FRAP	Seed	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)
1	Antioxidant	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)
	Anti- inflammatory	Xanthine oxidase inhibition	Not mentioned	Not mentioned	Not mentioned	(33)
2		Not mentioned	Fruits	Not mentioned	Not mentioned	(42)
		Xanthine oxidase test	Latex	Not mentioned	Not mentioned	(36)
		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)
3	Antibacterial	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 0.5 ul (62 5 ug) 1	(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)

https://plantsciencetoday.online

		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	Ethanol, chloroform Leaves		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
6	Antidiabetic	Alpha-amylase Inhibition	Stems barks essential oil	Not mentioned	24, 48, 95 μg/mL	(38
		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)
		МТТ	Not mentioned	Ethanol	Not mentioned	(33)
		Not mentioned	Leaves	Ethanol	5000, 2500, 1250, 625, 312.5 and 156 mg/mL	(34)
		МТТ	Fruits	Not mentioned	3.9–500 µL/mL	(75)
8		МТТ	Peel, pulp, leaves, whole fruit, latex	Not mentioned	Not mentioned	(76)
		МТТ	Methanol	Leaves, fruits	2000, 1000, 800, 400, 200, 100, 50, 25, 12, 5, 6, 3 μg/mL	(35)
		МТТ	Not mentioned	Latex	0.1, 0.25, 0.5, 1%	(77)
	Anticancer	In vivo	Ethanol	Fruits	Not mentioned	(78)
			Endophytes	Not mentioned	Not mentioned	(79)
		МТТ	Fruits	Not mentioned	Not mentioned	(42)
		Not mentioned	Latex	Not mentioned	Not mentioned	(80)
		Not mentioned	Latex	Not mentioned	Not mentioned	(16)
		МТТ	Leaves	Not mentioned	Not mentioned	(81)
		Not mentioned	Latex	Not mentioned	Not mentioned	(36)
		МТТ	Latex	Not mentioned	Not mentioned	(82)
		МТТ	Latex	Petroleum ether	0.125, 0.25, 0.5, 1 μg/mL	(83)
		МТТ	Leaves	Methanol	150, 250, 350, 450, 550, 650, 750, 850 μg /mL	(84)
		МТТ	Fruits (essential oil)	Hexane, aqueous	Not mentioned	(85)
		МТТ	Latex	Not mentioned	Not mentioned	(86)
		In vivo	Leaves	Not mentioned	Not mentioned	(87)
9	Cytotoxicity	Not mentioned	Leaves	Methanol, aqueous	Not mentioned	(88)
		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)

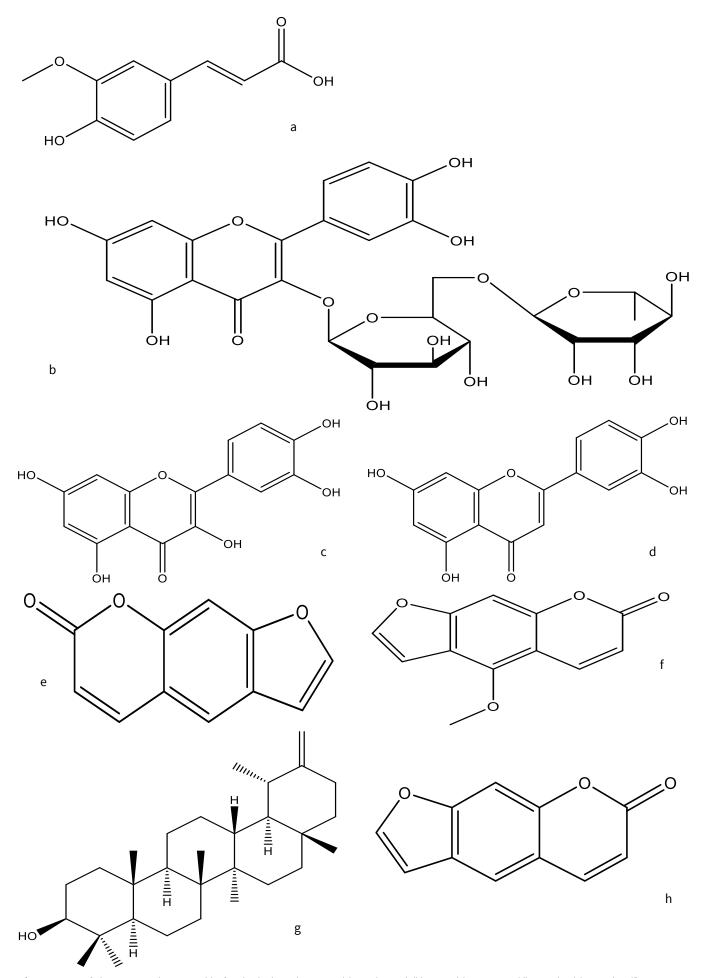


Fig. 2. Some of the compounds responsible for the biological activity. (a) Ferulic acid (b) Rutin (c) Quercetin (d) Luteolin (e) Psoralen (f) Bergapten (g) Taraxasterol and (h) Ficusin

#### 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  $\mu$ L containing 125  $\mu$ g (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.

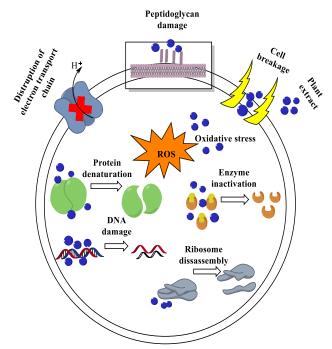


Fig. 3. Mechanism of action of Ficus carica part extract on bacteria.

## 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 ( $\geq$ 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<sup>2</sup> (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<sub>50</sub> 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<sub>50</sub> values for inhibiting alpha glucosidase (255.57 µg/mL) and alpha amylase (315.89  $\mu$ g/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  $\mu$ g/mL) (38). Essential oils collected in summer (24.58), autumn (35.75) and winter (38.15) have respective IC<sub>50</sub> values of 24.58, 35.85 and 38.15 µg/mL against -amylase (39). With an IC<sub>50</sub> of 16.82  $\mu$ g/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<sub>50</sub> 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

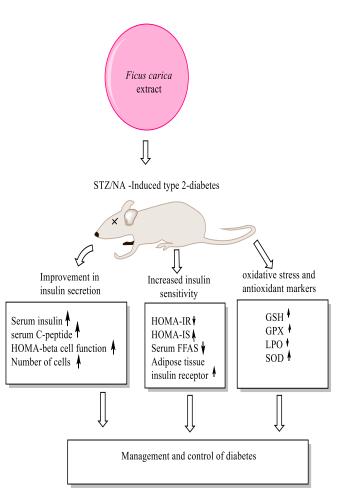


Fig. 4. Mechanism of action of Ficus carica extract on diabetes.

or encouraging glucose uptake in peripheral tissues via glucose transporters (Fig. 4).

#### Anti-cholinesterases

Alzheimer's disease (AD) is characterized by a decline in brain acetylcholine (ACh) guantity, 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 anticholinesterases are safer for avoiding illness progression. In terms of pancreatic lipase IC<sub>50</sub> values (230.475  $\mu$ g/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 guite mild. AZ extract showed the highest inhibitory action (IC<sub>50</sub> 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<sub>50</sub> values of 32.25 and 38.75 µg/mL respectively and significant potent cytotoxic activity (p<0.01) against MCF-7 with IC<sub>50</sub> 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 dosedependently (IC<sub>50</sub>=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<sub>50</sub>>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<sub>50</sub> 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<sub>50</sub> 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<sup>-1</sup> for aurosperone D and 3.0 g mL<sup>-1</sup> 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 (IC50 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<sub>50</sub> 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<sub>50</sub> values 239, 343, 177, 299 and 206 µg/mL) and HT-29 cells (IC<sub>50</sub> 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<sub>50</sub> values ranging from 4.75 to 13.75 µg/mL and to be cytotoxic toward HeLa, with CC₅₀ 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 (tricombination) 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  $(IC_{50}, >1000 \ \mu g/mL)$  (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 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<sub>50</sub> values of 40% v/v in the cytotoxicity test. Cell cycle arrest in S phase decreased ROS production (86).

The IC<sub>50</sub> 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 proangiogenic growth factor involved in the angiogenesis process and its receptors were both markedly downregulated, with the latter being a concentrationdependent 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.

# References

- Abdel-Aty AM, Hamed MB, Salama WH, Ali MM, Fahmy AS, Mohamed SA. *Ficus carica, Ficus sycomorus* and *Euphorbia tirucalli* latex extracts: Phytochemical screening, antioxidant and cytotoxic properties. Biocatalysis and Agricultural Biotechnology. 2019. https://doi.org/10.1016/ j.bcab.2019.101199
- Nafis A, Kasrati A, Jamali CA, Samri SE, Mezrioui N. Antioxidative effect and first evidence of synergistic antimicrobial effects of *Ficus carica* (L.) leaf essential oil with conventional antibiotics. Journal of Essential Oil Bearing Plants. 2019;22(5):1289-98. https://doi.org/10.1080/0972060X.2019.1684386
- Radwan S, Handal G, Rimawi F, Hanania M. Seasonal variations in antioxidant activity, total flavonoids content, total phenolic content, antimicrobial activity and some bioactive components of *Ficus carica* L. in Palestine. International Journal of PharmTech Research. 2020;13(04):329-40. http:// dx.doi.org/10.20902/IJPTR.2019.120404
- Jabbari S, Firoozabad MSM. Antimicrobial effect of *Ficus carica* on nosocomial bacterial infections. Avicenna Journal of Pharmaceutical Research. 2021;2(2):73-78. 10.34172/ ajpr.2021.14
- George TT, Oyenihi AB, Oyenihi OR, Obilana AO. Composition and health-promoting effects of fig (*Ficus carica*) extracts. In book: Fig (*Ficus carica*): Production, Processing and Properties. Springer. 2023; p. 561-78. https://doi.org/10.1007/978-3-031-16493-4\_25
- Mawa S, Husain K, Jantan I. *Ficus carica* L. (Moraceae): Phytochemistry, traditional uses and biological activities. Evidence-Based Complementary and Alternative Medicine. 2013;2013. https://doi.org/10.1155/2013/974256
- Badgujar SB, Patel VV, Bandivdekar AH, Mahajan RT. Traditional uses, phytochemistry and pharmacology of *Ficus carica*: A review. Pharmaceutical Biology. 2014;52(11):1487-503. https:// doi.org/10.3109/13880209.2014.892515
- Bouyahya A, Bensaid M, Bakri Y, Dakka N. Phytochemistry and ethnopharmacology of *Ficus carica*. International Journal of Biochemistry Research and Review. 2016;14:1-12. https:// doi.org/10.9734/IJBCRR/2016/29029
- 9. Salehi B, Prakash Mishra A, Nigam M, Karazhan N, Shukla I, Kiełtyka-Dadasiewicz A. Ficus plants: State of the art from a phytochemical, pharmacological and toxicological perspective.

Phytotherapy Research. 2021;35(3):1187-217. https:// doi.org/10.1002/ptr.6884

- Li Z, Yang Y, Liu M, Zhang C, Shao J, Hou X. A comprehensive review on phytochemistry, bioactivities, toxicity studies and clinical studies on *Ficus carica* Linn. leaves. Biomedicine and Pharmacotherapy. 2021;137:111393. https://doi.org/10.1016/ j.biopha.2021.111393
- Morovati MR, Ghanbari-Movahed M, Barton EM, Farzaei MH, Bishayee A. A systematic review on potential anticancer activities of *Ficus carica* L. with focus on cellular and molecular mechanisms. Phytomedicine. 2022:154333. https:// doi.org/10.1016/j.phymed.2022.154333
- El-Beltagi HS, Mohamed HI, Abdelazeem AS, Youssef R, Safwat G. GC-MS analysis, antioxidant, antimicrobial and anticancer activities of extracts from *Ficus sycomorus* fruits and leaves. Contribution to Journal. 2019. https://doi.org/10.15835/ nbha47211405
- Keskin D, Ceyhan Guvensen N, Zorlu Z, Ugur A. Phytochemical analysis and antimicrobial activity of different extracts of fig leaves (*Ficus carica* L.) from West Anatolia against some pathogenic microorganisms. Journal of Pure and Applied Microbiology. 2012;6(3):1105-10.
- Souhila B, Asma B, Boumediene M, Aicha TT. Antimicrobial activity of dried fig (*Ficus carica* L.) extracts from the region of Mascara (Western Algeria) on *Enterobacter cloacae* identified by MALDI-TOF/MS. European Journal of Biological Research. 2021;11(2):234-41. http://dx.doi.org/10.5281/zenodo.4641370
- Weli AM, Al-Blushi AAM, Hossain MA. Evaluation of antioxidant and antimicrobial potential of different leaves crude extracts of Omani *Ficus carica* against food borne pathogenic bacteria. Asian Pacific Journal of Tropical Disease. 2015;5(1):13-16. https://doi.org/10.1016/S2222-1808(14)60619-8
- Shin B-S, Lee SA, Moon SM, Han S-H, Hwang EJ, Kim SG. Latex of *Ficus carica* L. induces apoptosis through caspase and Bcl-2 family in FaDu human hypopharynx squamous carcinoma cells. International Journal of Oral Biology. 2017;183-90. https:// doi.org/10.11620/IJOB.2017.42.4.183
- Tkachenko H, Buyun L, Osadowski Z, Honcharenko V, Prokopiv A. Antimicrobial screening of the ethanolic leaves extract of *Ficus carica* L. (Moraceae)– An ancient fruit plant. Plant Introduction. 2017;73:78-87. https://doi.org/10.5281/ zenodo.2283589
- Shahinuzzaman M, Yaakob Z, Anuar FH, Akhtar P, Kadir N, Hasan AM. *In vitro* antioxidant activity of *Ficus carica* L. latex from 18 different cultivars. Scientific Reports. 2020;10(1):10852. https://doi.org/10.1038/s41598-020-67765-1
- Lansky EP, Paavilainen HM, Pawlus AD, Newman RA. *Ficus* spp. (Fig): Ethnobotany and potential as anticancer and antiinflammatory agents. Journal of Ethnopharmacology. 2008;119 (2):195-213. https://doi.org/10.1016/j.jep.2008.06.025
- Pawlus A, Cartwright C, Vijjeswarapu M, Liu Z, Woltering E, Newman R. Anti-angiogenic activity from the fruit latex of *Ficus carica* (Fig). Planta Medica. 2008;74(09):PA97. https:// doi.org/10.1055/s-0028-1084095
- Canal J, Torres MD, Romero A, Pérez C. A chloroform extract obtained from a decoction of *Ficus carica* leaves improves the cholesterolaemic status of rats with streptozotocin-induced diabetes. Acta Physiologica Hungarica. 2000;87(1):71-76. https://doi.org/10.1556/aphysiol.87.2000.1.8
- Paşayeva L, Özalp B, Fatullayev H. Potential enzyme inhibitory properties of extracts and fractions from fruit latex of *Ficus carica* based on inhibition of α-amylase and α-glucosidase. Journal of Food Measurement and Characterization. 2020;14:2819-27. https://doi.org/10.1007/s11694-020-00527-9

- 23. Patil VV, Patil VR. Evaluation of anti-inflammatory activity of *Ficus carica* Linn. leaves. Indian Journal of Natural Product. 2011;2(2):151-55.
- Lazreg Aref H, Gaaliche B, Fekih A, Mars M, Aouni M, Pierre Chaumon J. *In vitro* cytotoxic and antiviral activities of *Ficus carica* latex extracts. Natural Product Research. 2011;25(3):310-19. https://doi.org/10.1080/14786419.2010.528758
- Dogara AM. Biological activity and chemical composition of Detarium microcarpum Guill. and Perr—A systematic review. Advances in Pharmacological and Pharmaceutical Sciences. 2022;2022. https://doi.org/10.1155/2022/7219401
- Mopuri R, Ganjayi M, Meriga B, Koorbanally NA, Islam MS. The effects of *Ficus carica* on the activity of enzymes related to metabolic syndrome. Journal of Food and Drug Analysis. 2018;26(1):201-10. https://doi.org/10.1016/j.jfda.2017.03.001
- Benmaghnia S, Meddah B, Tir-touil A, Hernández JAG. Phytochemical analysis, antioxidant and antimicrobial activities of three samples of dried figs (*Ficus carica* L.) from the region of Mascara. Journal of Microbiology, Biotechnology and Food Sciences. 2021;2021:208-15. 10.15414/jmbfs.2019.9.2.208-215
- Begum HA, Hamayun M, Rauf M, Gul H, Ali K, Khan W. Antimicrobial, antioxidant, phytochemical and pharmacognostic study of the leaf powder of *Ficus carica* L.. Pure and Applied Biology (PAB). 2020;9(1):999-1008. http:// dx.doi.org/10.19045/bspab.2020.90105
- Ergül M, Ergül M, Eruygur N, Mehmet A, Esra U. *In vitro* evaluation of the chemical composition and various biological activities of *Ficus carica* leaf extracts. Turkish Journal of Pharmaceutical Sciences. 2019;16(4):401. 10.4274/ tjps.galenos.2018.70037
- Nakilcioğlu-Taş E, Ötleş S. Influence of extraction solvents on the polyphenol contents, compositions and antioxidant capacities of fig (*Ficus carica* L.) seeds. Anais da Academia Brasileira de Ciências. 2021;93. https://doi.org/10.1590/0001-3765202120190526
- Petkova N, Ivanov I, Denev P. Changes in phytochemical compounds and antioxidant potential of fresh, frozen and processed figs (*Ficus carica* L.). International Food Research Journal. 2019;26(6):1881-88.
- Zhao J, Gong L, Wu L, She S, Liao Y, Zheng H. Immunomodulatory effects of fermented fig (*Ficus carica* L.) fruit extracts on cyclophosphamide-treated mice. Journal of Functional Foods. 2020;75:104219. https://doi.org/10.1016/ j.jff.2020.104219
- Amessis-Ouchemoukh N, Ouchemoukh S, Meziant N, Idiri Y, Hernanz D, Stinco CM. Bioactive metabolites involved in the antioxidant, anticancer and anticalpain activities of *Ficus carica* L., *Ceratonia siliqua* L. and *Quercus ilex* L. extracts. Industrial Crops and Products. 2017;95:6-17. https://doi.org/10.1016/ j.indcrop.2016.10.007
- Abdel-Rahman R, Ghoneimy E, Abdel-Wahab A, Eldeeb N, Salem M, Salama E. The therapeutic effects of *Ficus carica* extract as antioxidant and anticancer agent. South African Journal of Botany. 2021;141:273-77. https://doi.org/10.1016/ j.sajb.2021.04.019
- Purnamasari R, Winarni D, Permanasari AA, Agustina E, Hayaza S, Darmanto W. Anticancer activity of methanol extract of *Ficus carica* leaves and fruits against proliferation, apoptosis and necrosis in Huh7it cells. Cancer Informatics. 2019;18:1176935119842576. https:// doi.org/10.1177/1176935119842576
- Yahiaoui S, Kati DE, Ali LM, El Cheikh K, Morére A, Menut C. Assessment of antioxidant, antiproliferative, anti-inflammatory and enzyme inhibition activities and UPLC-MS phenolic determination of *Ficus carica* latex. Industrial Crops and Products. 2022;178:114629. https://doi.org/10.1016/

j.indcrop.2022.114629

- Ara I, Naqvi SH, Rehman N, Qureshi MM. Comparative antioxidative and antidiabetic activities of *Ficus Carica* pulp, peel and leaf and their correlation with phytochemical contents. Pharm Res. 2020;4(2):000197. https:// doi.org/10.23880/oajpr-1600197
- ElAchaouia YI, Fakhfakh J, Adhar M, Affes M, Tounsi S, Allouche N. Determination of chemical composition, antioxidant, antibacterial and antidiabetic activities during maturation of *Ficus carica* stems and barks essential oils. Chemistry Africa. 2023;1-11. https://doi.org/10.1007/s42250-023-00600-y
- Jeong MR, Kim HY, Cha JD. Antimicrobial activity of methanol extract from *Ficus carica* leaves against oral bacteria. Journal of Bacteriology and Virology. 2009;39(2):97-102. https:// doi.org/10.4167/jbv.2009.39.2.97
- Soltana H, Tekaya M, Amri Z, El-Gharbi S, Nakbi A, Harzallah A. Characterization of fig achenes' oil of *Ficus carica* grown in Tunisia. Food Chemistry. 2016;196:1125-30. https:// doi.org/10.1016/j.foodchem.2015.10.053
- Ginwala R, Bhavsar R, Chigbu DGI, Jain P, Khan ZK. Potential role of flavonoids in treating chronic inflammatory diseases with a special focus on the anti-inflammatory activity of apigenin. Antioxidants. 2019;8(2):35. https://doi.org/10.3390/ antiox8020035
- Liu Y-P, Guo J-M, Yan G, Zhang M-M, Zhang W-H, Qiang L. Antiinflammatory and antiproliferative prenylated isoflavone derivatives from the fruits of *Ficus carica*. Journal of Agricultural and Food Chemistry. 2019;67(17):4817-23. https:// doi.org/10.1021/acs.jafc.9b00865
- Cho UM, Choi DH, Yoo DS, Park SJ, Hwang HS. Inhibitory effect of ficin derived from fig latex on inflammation and melanin production in skin cells. Biotechnology and Bioprocess Engineering. 2019;24:288-97. https://doi.org/10.1007/s12257-019-0010-0
- Debib A, Tir-Touil A, Mothana R, Meddah B, Sonnet P. Phenolic content, antioxidant and antimicrobial activities of two fruit varieties of Algerian *Ficus carica* L.. Journal of Food Biochemistry. 2014;38(2):207-15. https://doi.org/10.1111/ jfbc.12039
- Duman E, Şimşek M, Özcan MM. Monitoring of composition and antimicrobial activity of fig (*Ficus carica* L.) fruit and seed oil. Journal of Agroalimentary Processes and Technologies. 2018;24 (2):75-80.
- Barolo MI, Castelli MV, López SN. Antimicrobial properties and biotransforming ability of fungal endophytes from *Ficus carica* L. (Moraceae). Mycology. 2023;14(2):108-32. https:// doi.org/10.1080/21501203.2023.2175500
- Belattar H, Himour S, Yahia A. Pytochemical screening and evaluation antimicrobial activity of the methanol extract of *Ficus carica*. Revista Mexicana De Ciencias Agrícolas. 2021;12 (1):1-9. https://doi.org/10.29312/remexca.v12i1.2435
- Boyacioglu O, Kara B, Can H, Yerci TN, Yilmaz S, Boyacioglu SO. Leaf hexane extracts of two Turkish fig (*Ficus carica* L.) cultivars show cytotoxic effects on a human prostate cancer cell line. Agriculture and Food Sciences Research. 2019;6(1):66-70. https://doi.org/10.20448/journal.512.2019.61.66.70
- Mennane Z, Tabet Z, Aabid T, Souhaila T, Emrani A, Abrini J. Ethnobotanical study of fig tree (*Ficus carica* L.) and olive (*Olea europaea* L.) from Tetouan Province in Morocco and study their antimicrobial activity. E3S Web of Conferences. EDP Sciences. 2021. https://doi.org/10.1051/e3sconf/202131901091
- Shahbazi Y. Antibacterial and antioxidant properties of methanolic extracts of apple (*Malus pumila*), grape (*Vitis vinifera*), pomegranate (*Punica granatum L.*) and common fig

(Ficus carica L.) fruits. Pharmaceutical Sciences. 2017;23(4):308-15. 10.15171/PS.2017.4551

- Doro B, Garsa S, Abusua F, Elmarbet N, Shaban M. *In vitro* antibacterial activity of *Ficus carica* L. (Moraceae) from Libya. Journal of Complementary and Alternative Medical Research. 2018;5(3):1-8. https://doi.org/10.9734/JOCAMR/2018/40820
- Acay H. Biosynthesis and characterization of silver nanoparticles using fig (*Ficus carica*) leaves: A potential antimicrobial activity. Applied Ecology and Environmental Research. 2019;17:13793-802. http://dx.doi.org/10.15666/ aeer/1706\_1379313802
- Akhter S, Rafique T, Naseer M, Sadiq R, Ali Q, Zikrea A. Antibacterial and antifungal activity of *Ficus carica* plant extract. Journal of Pharmaceutical Research International. 2021;33 (18):1-9. http://dx.doi.org/10.9734/JPRI/2021/v33i1831311
- Yousef NS, El-Ghandour AA, El-Shershaby SS. Antimicrobial activity of fig and olive leaves extracts. Journal of Food and Dairy Sciences. 2019;10(12):503-08. 10.21608/JFDS.2019.71369
- 55. Abbas SN, Jamshed K, Nasir SB. Antimicrobial activities of methanolic and aqueous extracts of *Nigella sativa* and *Ficus carica*. Biologia (Pakistan). 2019;65(1):101-12.
- 56. Rimbawan F, Pinus Jumaryatno AF. Isolation endophytic fungi from *Ficus carica* L. as antibiotic producer against *Staphylococcus aureus*. Proceedings of International Conference on Technology and Social Science. 2018. https://conf.ejikei.org/ICTSS2018/proceedings/materials/proc\_files/A037/ CameraReadyManuscript\_ICTSS2018\_GS\_A037.pdf
- Debib A, Tir-Touil M, Meddah B, Hamaidi-Chergui F, Menadi S, Alsayadi M. Evaluation of antimicrobial and antioxidant activities of oily macerates of Algerian dried figs (*Ficus carica* L.). International Food Research Journal. 2018;25(1):351-56.
- Tkachenko H, Buyun L, Terech-Majewska E, Osadowski Z. In vitro antimicrobial activity of ethanolic extracts obtained from Ficus spp. leaves against the fish pathogen Aeromonas hydrophila. Fisheries and Aquatic Life. 2016;24(4):219-30. https://doi.org/10.1515/aopf-2016-0019
- Desta W, Shumbahri M, Gebrehiwot S. Application of *Ficus carica* L. and *Solanum incanum* L. extracts in coagulation of milk: The case of traditional practice in Ab'ala area, Afar regional state, Ethiopia. Biochemistry Research International. 2020;2020:1-7. https://doi.org/10.1155/2020/9874949
- Siyadatpanah A, Mirzaei F, Hossain R, Islam MT, Fatemi M, Norouzi R. Anti-parasitic activity of the Olea europaea and Ficus carica on Leishmania major: New insight into the antileishmanial agents. Biologia. 2022;77(7):1795-803. https:// doi.org/10.1007/s11756-022-01066-y
- Abbasi S, Kamalinejad M, Babaie D, Shams S, Sadr Z, Gheysari M. A new topical treatment of atopic dermatitis in pediatric patients based on *Ficus carica* L. (Fig): A randomized, placebo-controlled clinical trial. Complementary Therapies in Medicine. 2017;35:85-91. https://doi.org/10.1016/j.ctim.2017.10.003
- Pouryousef A, Eslami E, Shahriarirad S, Zoghi S, Emami M, Cheraghi MR. Effects of topical gel formulation of *Ficus carica* latex on *Cutaneous leishmaniasis* induced by Leishmania major in BALB/c mice. BMC Research Notes. 2021;14(1):199. https:// doi.org/10.1186/s13104-021-05614-8
- 63. Meziant L, Bachir-bey M, Bensouici C, Saci F, Boutiche M, Louaileche H. Assessment of inhibitory properties of flavonoidrich fig (*Ficus carica* L.) peel extracts against tyrosinase, αglucosidase, urease and cholinesterases enzymes and relationship with antioxidant activity. European Journal of Integrative Medicine. 2021;43:101272. https://doi.org/10.1016/ j.eujim.2020.101272
- 64. Kurniawan MF, Yusuf FA. The possible antidiabetic effect of *Ficus carica* L. tablet on alloxaninduced diabetes model in rats. Open

Access Macedonian Journal of Medical Sciences. 2021;9(A):727-34. https://doi.org/10.3889/oamjms.2021.6609.

- Lin L, Zhang Y. Chemical constituents and antidiabetic activity of dichloromethane extract from *Ficus carica* leaves. Diabetes, Metabolic Syndrome and Obesity. 2023:979-91. https:// doi.org/10.2147/DMSO.S405150
- 66. El Ghouizi A, Ousaaid D, Laaroussi H, Bakour M, Aboulghazi A, Soutien RS. *Ficus carica* (Linn.) leaf and bud extracts and their combination attenuates type-1 diabetes and its complications via the inhibition of oxidative stress. Foods. 2023;12(4):759. https://doi.org/10.3390/foods12040759.
- Priyoherianto A, Saputra ME, Ikhda C, Hamidah N. The antidiabetic activity of *Ficus carica* folium in *Mus musculus*. 2018;17:44-47. https://doi.org/10.9790/0853-1704094448
- Stephen Irudayaraj S, Christudas S, Antony S, Duraipandiyan V, Naif Abdullah AD, Ignacimuthu S. Protective effects of *Ficus carica* leaves on glucose and lipids levels, carbohydrate metabolism enzymes and β-cells in type 2 diabetic rats. Pharmaceutical Biology. 2017;55(1):1074-81. https:// doi.org/10.1080/13880209.2017.1279671
- Oktarina Y, Mulyani S. The difference in the activity of ethanol extracts of leaves of anti diabetic tin (*Ficus carica* L.) leaf, rambutan (*Nephelium lappaceum*) and Persimmon (Diospyros Ft L) on the white mancit on streptozotocin induced. Caring: Indonesian Journal of Nursing Science. 2019;1(1):49-55. https:// doi.org/10.32734/ijns.v1i1.1172.
- Ramadan S, Hegab AM, Al-Awthan YS, Al-Duais MA, Tayel AA, Al-Saman MA. Comparison of the efficiency of *Lepidium sativum*, *Ficus carica* and *Punica granatum* methanolic extracts in relieving hyperglycemia and hyperlipidemia of streptozotocininduced diabetic rats. Journal of Diabetes Research. 2021;2021. https://doi.org/10.1155/2021/6018835.
- Alalwani AD, Hummdi LA, Qahl SH. Effect of nano extracts of Olea europaea leaves, Ficus carica and liraglutide in lipidemic liver of type 2 diabetic rat model. Saudi Journal of Biological Sciences. 2022;29(7):103333. https://doi.org/10.1016/ j.sjbs.2022.103333
- Zhang Y, Li Y, Ma P, Chen J, Xie W. *Ficus carica* leaves extract inhibited pancreatic β-cell apoptosis by inhibiting AMPK/JNK/ caspase-3 signaling pathway and antioxidation. Biomedicine and Pharmacotherapy. 2020;122:109689. https:// doi.org/10.1016/j.biopha.2019.109689
- Alqahtani AM, Attia G. Bioactive metabolites of Aspergillus neoniger, an endophyte of the medicinal plant Ficus carica. Indian Journal of Pharmaceutical Sciences. 2021;83(1):101-09. https://doi.org/10.36468/pharmaceutical-sciences.755
- Jacob SJP, Prasad VS, Sivasankar S, Muralidharan P. Biosynthesis of silver nanoparticles using dried fruit extract of *Ficus carica*- Screening for its anticancer activity and toxicity in animal models. Food and Chemical Toxicology. 2017;109:951-56. https://doi.org/10.1016/j.fct.2017.03.066
- Soltana H, Pinon A, Limami Y, Zaid Y, Khalki L, Zaid N. Antitumoral activity of *Ficus carica* L. on colorectal cancer cell lines. Cellular and Molecular Biology. 2019;65(6):6-11. https:// doi.org/10.14715/cmb/2019.65.6.2
- AlGhalban FM, Khan AA, Khattak MNK. Comparative anticancer activities of *Ficus carica* and *Ficus salicifolia* latex in MDA-MB-231 cells. Saudi Journal of Biological Sciences. 2021;28(6):3225-34. https://doi.org/10.1016/j.sjbs.2021.02.061
- Ou A, Zhao X, Lu Z. Autophagy is involved in *Ficus carica* fruit extract-induced anti-tumor effects on pancreatic cancer. Biomedicine and Pharmacotherapy. 2022;150:112966. https:// doi.org/10.1016/j.biopha.2022.112966
- 78. Abdou R, Mojally M, Attia GH. Investigation of bioactivities of endophytes of *Ficus carica* L. Family Moraceae. Bulletin of the

National Research Centre. 2021;45:1-7. https://doi.org/10.1186/ s42269-021-00505-1

- Baohong L, Zhongyuan L, Ying T, Beibei Y, Wenting N, Yiming Y. Latex derived from *Ficus carica* L. inhibited the growth of NSCLC by regulating the caspase/gasdermin/AKT signaling pathway. Food and Function. 2023;14(4):2239-48. DOIhttps:// doi.org/10.1039/D2FO02284B
- Aziz B, Khurshid A, Mahmood R, Khan JA, Javaid S, Alam M. Study of synergistic effects of *Ficus carica* leaves extract mediated chemo-photodynamic therapy on rhabdomyosarcoma cells. Photodiagnosis and Photodynamic Therapy. 2021;36:102565. https://doi.org/10.1016/ j.pdpdt.2021.102565
- Azami H, Malek-Hosseini S, Taghi MM, Zareinejad M, Amirghofran Z. Antitumor activity and immunomodulatory effects of *Ficus carica* latex. Journal of Shahid Sadoughi University of Medical Sciences. 2020. https://doi.org/10.18502/ ssu.v28i12.5776
- Ghanbari A, Le Gresley A, Naughton D, Kuhnert N, Sirbu D, Ashrafi GH. Biological activities of *Ficus carica* latex for potential therapeutics in Human Papilloma Virus (HPV) related cervical cancers. Scientific Reports. 2019;9(1):1013. https:// doi.org/10.1038/s41598-018-37665-6
- Sadeghizade M, Baharara J, Salek F, Amini E. Assessment the effect of *Ficus carica* leaf extract on B16F10 melanoma cancer cells: The roles of p53, Caspase-3 and Caspase-9 on induction of intrinsic apoptosis cascade. Jundishapur Journal of Natural Pharmaceutical Products. 2022;17(2). https://doi.org/10.5812/ jjnpp.117429
- Kalefa NK, Al-Shawi AA. The essential oils isolated from the fruit of *Ficus carica* induced reactive oxygen species and apoptosis of human liver cancer cells. Egyptian Journal of Chemistry. 2023;66(2):257-65. https://doi.org/10.21608/ EJCHEM.2022.136132.5995
- Jeivad F, Yassa N, Ostad SN, Hassannejad Z, Gheshlaghi GH, Sabzevari O. *Ficus carica* L. latex: Possible chemo-preventive, apoptotic activity and safety assessment. Iranian Journal of Pharmaceutical Research: IJPR. 2020;19(3):231. https:// doi.org/10.22037/ijpr.2020.1101151
- El-Sayed SM, El-Naggar ME, Hussein J, Medhat D, El-Banna M. Effect of *Ficus carica* L. leaves extract loaded gold nanoparticles against cisplatin-induced acute kidney injury. Colloids and Surfaces B: Biointerfaces. 2019;184:110465. https:// doi.org/10.1016/j.colsurfb.2019.110465
- Di Vito M, Gentile M, Mattarelli P, Barbanti L, Micheli L, Mazzuca C. Phytocomplex influences antimicrobial and health properties of concentrated glycerine macerates. Antibiotics. 2020;9 (12):858. https://doi.org/10.3390/antibiotics9120858
- Abdulrahman MD, Zakariya AM, Hama HA, Hamad SW, Al-Rawi SS, Bradosty SW. Ethnopharmacology, biological evaluation and chemical composition of *Ziziphus spina*-christi (L.) Desf.: A review. Advances in Pharmacological and Pharmaceutical Sciences. 2022;2022. https://doi.org/10.1155/2022/4495688

- Calvo P, Blanco M, Rodríguez M, Serradilla M, Sánchez F. In vitro and in vivo antifungal activity of allyl isothiocyanate (AITC) against *Penicillium expansum* in figs (*Ficus carica* L.). VI International Symposium on Fig. 2019;1310. https:// doi.org/10.17660/ActaHortic.2021.1310.42
- Dogara AM, Hamad SW, Hama HA, Bradosty SW, Kayfi S, Al-Rawi SS. Biological evaluation of *Garcinia kola* Heckel. Advances in Pharmacological and Pharmaceutical Sciences. 2022;2022. https://doi.org/10.1155/2022/3837965
- 91. Arafa E-SA, Hassan W, Murtaza G, Buabeid MA. *Ficus carica* and *Sizigium cumini* regulate glucose and lipid parameters in high-fat diet and streptozocin-induced rats. Journal of Diabetes Research. 2020;2020. https://doi.org/10.1155/2020/6745873
- Dalai MK, Bhadra S, Chaudhary SK, Bandyopadhyay A, Mukherjee PK. Anti-cholinesterase activity of the standardized extract of *Syzygium aromaticum* L. Pharmacognosy Magazine. 2014;10(Suppl 2):S276. https://doi.org/10.4103/0973-1296.133275
- Abdou R, Alqahtani AM, Attia GH. Anticancer natural products from Aspergillus neoniger, an endophyte of Ficus carica. Bulletin of the National Research Centre. 2021;45(1):1-6. https:// doi.org/10.1186/s42269-021-00536-8
- 94. Zhang Y, Wan Y, Huo B, Li B, Jin Y, Hu X. Extracts and components of *Ficus carica* leaves suppress survival, cell cycle and migration of triple-negative breast cancer MDA-MB-231 cells. OncoTargets and Therapy. 2018:4377-86. https:// doi.org/10.2147/OTT.S171601
- 95. Gharibzahedi SMT, Smith B, Guo Y. Ultrasound-microwave assisted extraction of pectin from fig (*Ficus carica* L.) skin: Optimization, characterization and bioactivity. Carbohydrate Polymers. 2019;222:114992. https://doi.org/10.1016/ j.carbpol.2019.114992
- Pucci M, Mandrone M, Chiocchio I, Sweeney EM, Tirelli E, Uberti D. Different seasonal collections of *Ficus carica* L. leaves diversely modulate lipid metabolism and adipogenesis in 3T3-L1 adipocytes. Nutrients. 2022;14(14):2833. https://doi.org/10.3390/nu14142833
- 97. Zhou J-l, Huang XY, Qiu HC, Gan RZ, Zhou H, Zhu HQ. SSPH I, a novel anti-cancer saponin, inhibits autophagy and induces apoptosis via ROS accumulation and ERK1/2 signaling pathway in hepatocellular carcinoma cells. OncoTargets and Therapy. 2020;13:5979. https://doi.org/10.2147/OTT.S253234
- Abou Seif HS. Physiological changes due to hepatotoxicity and the protective role of some medicinal plants. Beni-suef University Journal of Basic and Applied Sciences. 2016;5(2):134-46. https://doi.org/10.1016/j.bjbas.2016.03.004