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REVIEW ARTICLE

**Traditional uses, phytochemistry and pharmacology of *Ficus carica*:
A review**Shamkant B. Badgujar^{1,2}, Vainav V. Patel¹, Atmaram H. Bandivdekar¹, and Raghunath T. Mahajan²

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Abstract

Context: *Ficus carica* Linn (Moraceae) has been used in traditional medicine for a wide range of ailments related to digestive, endocrine, reproductive, and respiratory systems. Additionally, it is also used in gastrointestinal tract and urinary tract infection.

Objective: This review gathers the fragmented information available in the literature regarding morphology, ethnomedicinal applications, phytochemistry, pharmacology, and toxicology of *Ficus carica*. It also explores the therapeutic potential of *Ficus carica* in the field of ethnopharmacology.

Materials and methods: All the available information on *Ficus carica* was compiled from electronic databases such as Academic Journals, Ethnobotany, Google Scholar, PubMed, Science Direct, Web of Science, and library search.

Results: Worldwide ethnomedicinal uses of *Ficus carica* have been recorded which have been used traditionally for more than 40 types of disorders. Phytochemical research has led to the isolation of primary as well as secondary metabolites, plant pigment, and enzymes (protease, oxidase, and amylase). Fresh plant materials, crude extracts, and isolated components of *Ficus carica* have shown a wide spectrum of biological (pharmacological) activities.

Conclusion: *Ficus carica* has emerged as a good source of traditional medicine for the treatment of various ailments such as anemia, cancer, diabetes, leprosy, liver diseases, paralysis, skin diseases, and ulcers. It is a promising candidate in pharmaceutical biology for the development/formulation of new drugs and future clinical uses.

Keywords

Biological activities, ethnomedicine, fig

History

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Introduction

The genus *Ficus* (Moraceae) constitutes one of the largest genera of angiosperms with more than 800 species of trees, epiphytes, and shrubs in the tropical and sub-tropical regions worldwide (Singh et al., 2011). It is one of the 40 genera of the mulberry family, Moraceae. The Asian–Australasian region is the richest and most diverse containing about 500 *Ficus* species. In contrast, the *Ficus* in Africa and the Neotropics are fewer, with approximately 110 and 130 species, respectively. About half of the *Ficus* species are monoecious and the rest are functionally dioecious (Berg, 2003). Many *Ficus* species consist of numerous varieties, significant genetic diversity, and outstanding pharmacological activities that are of remarkable commercial importance (Woodland, 1997).

Ficus carica Linn is the most popular member of the genus *Ficus*, and it is known by more than 135 names (Table 1).

Although it is native to Sub-Himalayan tract, Bengal, and central India, it has been extensively cultivated worldwide. *Ficus carica* is a temperate species, native to southwest Asia and the Mediterranean region (from Afghanistan to Portugal) and has been widely cultivated from ancient times for its fruits (nutritional value), also referred to as figs. Figs have considerable cultural importance throughout the tropics, both as objects of worship and for their many practical uses. This plant also invites attention of the researchers worldwide for its biological activities. The therapeutic utilities of *Ficus carica* have been indicated in the traditional systems of medicine such as Ayurveda, Unani, and Siddha (Prasad et al., 2006). It has been used to cure disorders of the endocrine system (diabetes), respiratory system (liver diseases, asthma, and cough), gastrointestinal tract (ulcer and vomiting), reproductive system (menstruation pain), and infectious diseases (skin disease, scabies, and gonorrhoea). Continuous research is in progress to validate its traditional medicinal uses, and it is also described in detail in the present article. Some of the earlier published reviews of this plant include pharmacological activities (Chawla et al., 2012; Joseph & Raj, 2011; Patil & Patil, 2011a), but few of them appear in all three reviews. Additionally, Chawla et al. (2012) described the spectroscopic data of 15 phytochemicals.

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Table 1. Vernacular names of *Ficus carica* Linn.

Region/language/ system of medicine	Name
English	Common fig tree, Fig
Hindi	Anjeer, Anjir, Tin
Sanskrit	Angira, Anjeer, Anjir, Anjira, Phalgu, Rajodumbara, Udumvara
Eastern India	Doomoor, Angir, Dumur, Dumar, Udumbara
Western India	Anjir, Anjeer, Angir
Southern India	Anjeera, Anjoora, Anjooram, Anjura, Anjuru, Appira, Cevvatti, Chikappatti, Cimaiyatti, Madipatu, Manchi Medi, Manjimedhi, Shima-Atti, Shimayatti, Simaatti, Simayatti, Simeyam, Simmeatti, Tacaiyatti, Tenatti, Tenatti, Teneyatti, Theneyatthi, Utumparam
Northern India	Fagari
Urdu	Poast, Darakht Anjir, Anjir Zard
Unani	Anjir
Arabic	Anjir, Teen, Teen barchomi, Ten
Brazil	Figo, Figueira, Figueira-Da-Europa
Portuguese	Figueira-Do-Reino
Burmese	Thaphan, Thinbaw, Thapan
Chinese	Mo Fa Guo, Wu Hua Guo
Cook Islanda	Suke
Croatian	Smokva, Smokvencia, Smokvina
Czech	Smokvon
Danish	Almindelig Figen, Figen
Dutch	Echte Vijboom, Gewone Vijgeboom, Vijg
Eastonian	Harilik, Viigipuu
Eucador	Higo
Finnish	Viikuna
French	Caprifiguiet, Carique, Figue, Figuier, Figue Commune
German	Echte Feige, Echter Feigenbaum, Essfeige, Feige, Feigenbaum
Hungarian	Fugea
Italian	Fic, Fico, Fico Comune
Iran	Anjeer
Japanese	Ichijiku
Korean	Mu Hwa Gwa, Mu Hwa Gwa Na Mu
Macedonian	Smoka
Malaysia	Anjir
Mangarevan	Pika
Marshallse	Wojke, Piik
Nepalese	Anjiir
Norwegian	Fiken
Pakistan	Faag, Anjeer, Injir, Baghi, Inzar, Anzar, Anjir
Palestinian	Fig
Persian	Anjir, anjeer
Palauan	Uosech
Polish	Figowiec
Russian	Inzir
Samoan	Mati
Serbian	Smoka, Smokovnica, Smokva
Solvascina	Figa, Figovec, Figovina
Solvencina	Figonik
Spanish	Breva, Higo, Hibuera comun
Swedish	Fikon, fikontrad
Tongarevan	Monamona
Taomotuan	Tute
Turkey	Incir, Yemis
Vietnamese	Qua Va, Vo Hoa Qua

Source: Nadkarni (1982), Kirtikar and Basu (1995), Khare (2007), and Lin (2012).

Common vernacular names, propagation, economic importance, primary and secondary metabolites, enzyme profile, nutritive value, traditional as well as allied applications and toxicological studies have not appeared in earlier reviews.

Hence, emphasis is being placed on the areas of the most recent interest and those which have not been reported in previous reports.

Taxonomy

Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Order: Urticales, Family: Moraceae, Genus: *Ficus*, Species: *carica*.

Botanical description

Ficus carica (Figure 1A) is usually a 15–20 ft tall deciduous tree, with numerous spreading branches and trunk rarely more than 7 ft in diameter. The latex of the plant is milky white and mainly contains ficin, i.e., protein hydrolytic enzyme (Badgujar, 2011). The root system in the plant is typically shallow and spreading. The species name *carica* means having papaya-like leaves. Figs (Figure 1B) are axillary on leafy branchlets, paired or solitary, and usually pear shaped. The matured “fig” has a tough peel (pure green, green suffused with brown, brown or purple), often cracking upon ripeness, and exposing the pulp beneath (Figure 1C). Flowers are seen in receptacles; arise from the axils of old leaves. The upper part of receptacle is occupied by female flowers and the lower part by male flowers. The ripen receptacle, saikonium, contains a large number of small whitish seeds. Seeds may be large, medium, small, or minute and range in number from 30 to 1600 per fruit. The edible seeds are numerous and generally hollow, unless pollinated. Pollinated seeds provide the characteristic nutty taste of dried figs. The interior portion is a white, inner ring containing a seed mass bound with jelly-like flesh. The leaves of the plant are bright green (Figure 1D), single, alternate, and large (usually up to 1 ft in length). They are more or less deeply lobed with 1–5 sinuses, rough hairy on the upper surface and soft hairy on the underside (Figure 1E). The bark is smooth (Figure 1F). The outer bark is silvery gray or ash-colored, exfoliated with irregular rounded flakes. The middle bark sections appear as brownish or light reddish brown in color. The inner part consists of the layers of light yellowish or orange brown colored granular tissue.

Propagation

Ficus carica has been cultivated for a long time worldwide for its edible fruit. It can be propagated by seeds or by vegetative methods. The main varieties cultivated are “Vasilika”, “Smyrneika”, “Vardika”, “Vazanata”, “Kadota”, “Napolitana negra”, “Progontto Blanco”, and “Gentile Bianco”. The main method of propagation is by hardwood cuttings. Vigorous 1-year shoot or 2- to 3-year old wood are successfully used for vegetative propagation. Cutting should be prepared well before bud break and their basal ends should be allowed to form callus for about 10 d at 24 °C in a humid environment. Cuttings should be taken in the nursery for one or two seasons and then transplanted to their permanent location (Bajaj, 1991).

Seed propagation is used only for breeding new cultivars. The small seeds can be easily germinated in well-prepared soil. Fertile seeds should be separated from sterile ones by floating them in water. One-year-old branches can be

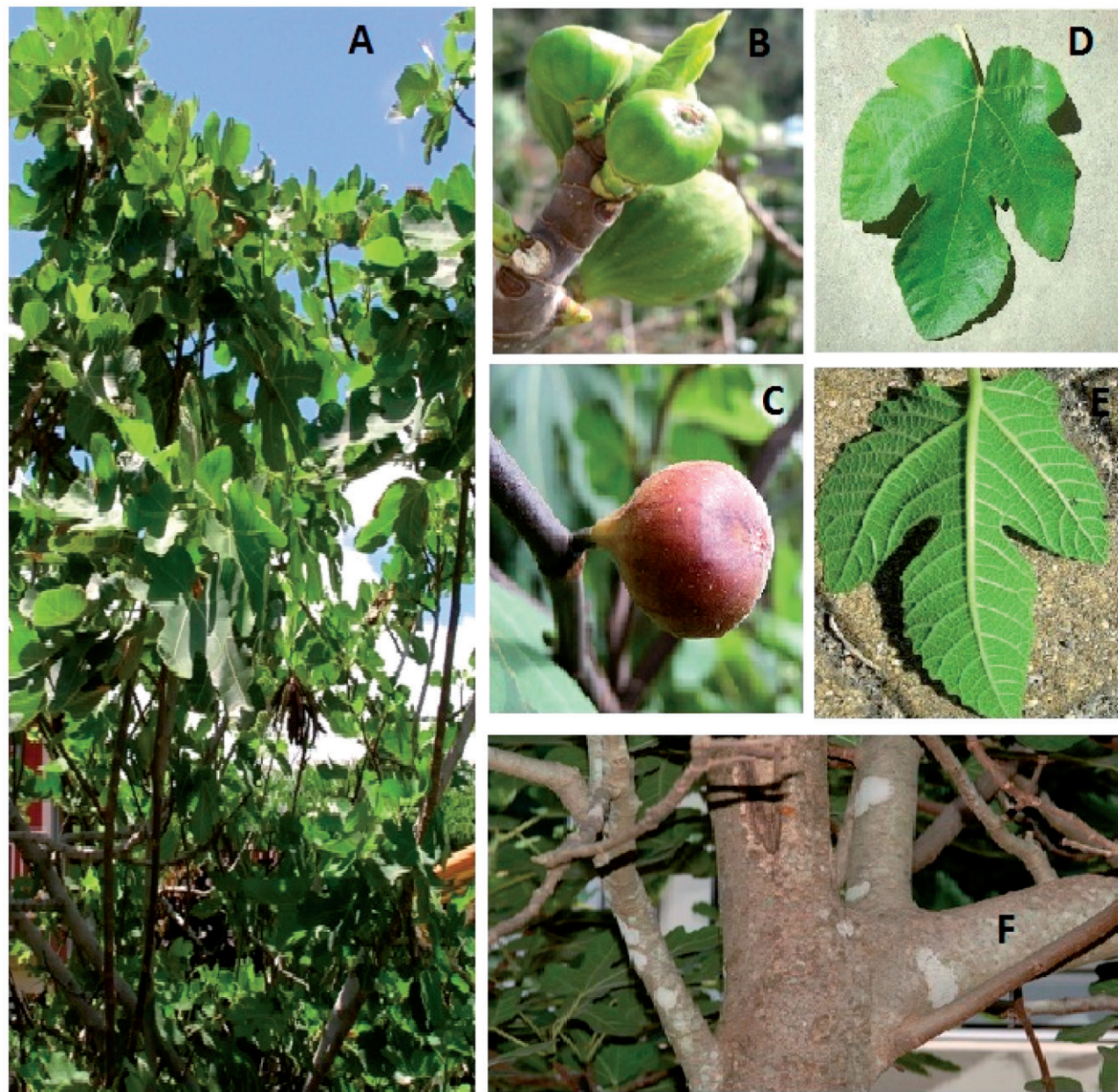


Figure 1. *Ficus carica* Linn (A) *Ficus carica* tree, (B) unripe figs, (C) ripe figs, (D) upper surface of dark green leaf, (E) lower surface of dark green leaf, and (F) stem-bark.

air-layered in early spring in order to obtain rooted plants by mid-summer (Hartmann & Kester, 1983).

Ornamental *Ficus* are usually air-layered or propagated by cuttings. Cuttings are usually air-leaf buds, taken either from the mid-stem or from the vegetative apex. The best seasons are late winter and spring. The latex flowing out of the cutting dries within 24 h. Cuttings are basally treated with plant hormones. This layer method is used when large plants are quickly required (Bajaj, 1991).

Economic importance

Fresh and dry fig (fruit) has been popularly consumed as a dietary food material since the beginning of civilization. Fig syrup (10–20 ml) is used as a remedy for mild constipation (Khare, 2007). Leaves are traditionally used as fodder for domestic animals. The plant latex is used as a curdling

agent in the production of extremely well-known milk product like cheese by several indigenous communities. The wood is used for hoops, garlands, and for ornamental purposes also.

Phytochemistry

Phytochemical research carried out on *Ficus carica* has led to the isolation of phytosterols, anthocyanins, amino acids, organic acid, fatty acids, phenolic components, hydrocarbons, aliphatic alcohols, volatile components, and few other classes of secondary metabolites from its different parts (Figure 2). Mostly these phytochemicals are found in latex followed by leaves, fruit, and root (Table 2).

Some of the phytoconstituents of *Ficus carica* are used in the production of sunscreen and coloring agents (Chawla et al., 2012). In addition to these, *Ficus carica* are also has

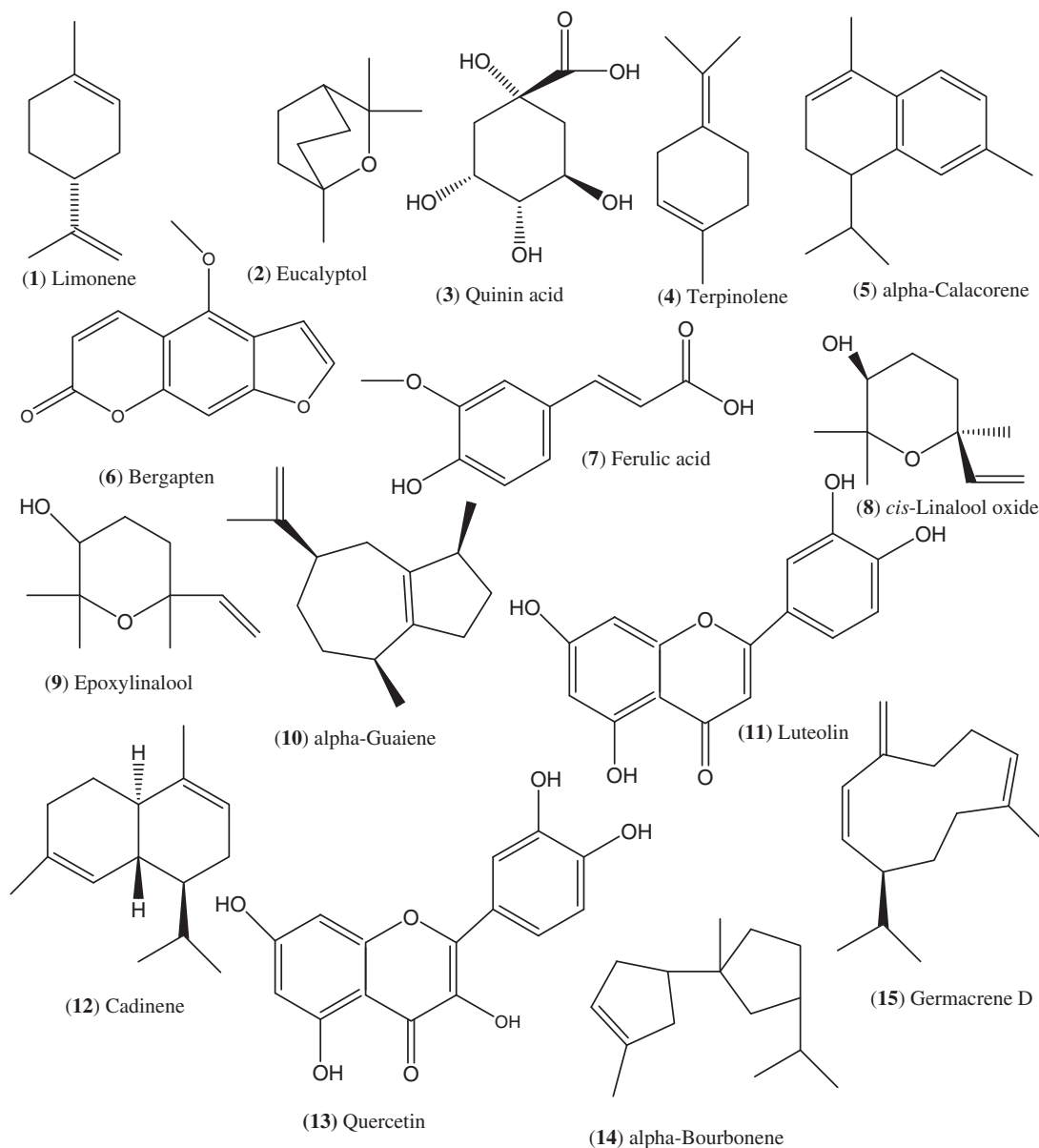


Figure 2. Chemical structures of compounds from *Ficus carica*.

remarkable pharmacological properties such as antioxidant, anticancer, cytotoxic, anti-inflammatory, and hypolipidemic activities (Table 3).

Organic acids

Organic acid profile of fig leaves is composed by six organic acids: oxalic, citric, malic, quinic, shikimic, and fumaric acids (Oliveira et al., 2009). In pulps and peels, quinic acid was absent. Quinic and shikimic acids were reported first time in *Ficus carica* by Shiraishi et al. (1996). Quantity of quinic acid is high, i.e., 10 502 mg/kg of leaf extract followed by malic, citric, oxalic, shikimic, and fumaric acids (8704, 2280, 155, 142, and 23 mg/kg of extract, respectively).

Amino acids

The amino acid profile of *Ficus carica* latex was identified by high-performance liquid chromatography coupled to ultraviolet–visible spectroscopy (HPLC/UV-vis). It revealed the

presence of 13 compounds, comprising five essential amino acids (leucine, tryptophan, phenylalanine, lysine, and histidine) and eight non-essential amino acids (asparagine, alanine, glutamine, serine, glycine, ornithine, tyrosine, and cysteine). Tryptophan, cysteine, and tyrosine are found in higher quantities relative to the other amino acids (Oliveira et al., 2010).

Fatty acids

The fatty acid profile of *Ficus carica* latex was determined by gas chromatography ion trap mass spectrometry (GC-ITMS). It revealed the presence of 14 major detectable fatty acids. These acids are identified as myristic, pentadecylic, palmitic, margaric, *cis*-10-heptadecenoic, stearic, oleic, elaidic, linoleic, arachidic, heneicosylic, behenic, tricosylic, and lignoceric. Their quantity is reported as 0.56, 1.35, 28.94, 0.66, 0.10, 8.62, 5.54, 0.35, 14.59, 91.29, 0.77, 26.43, 1.25, and 1.90 mg/kg of latex tissue, respectively (Oliveira

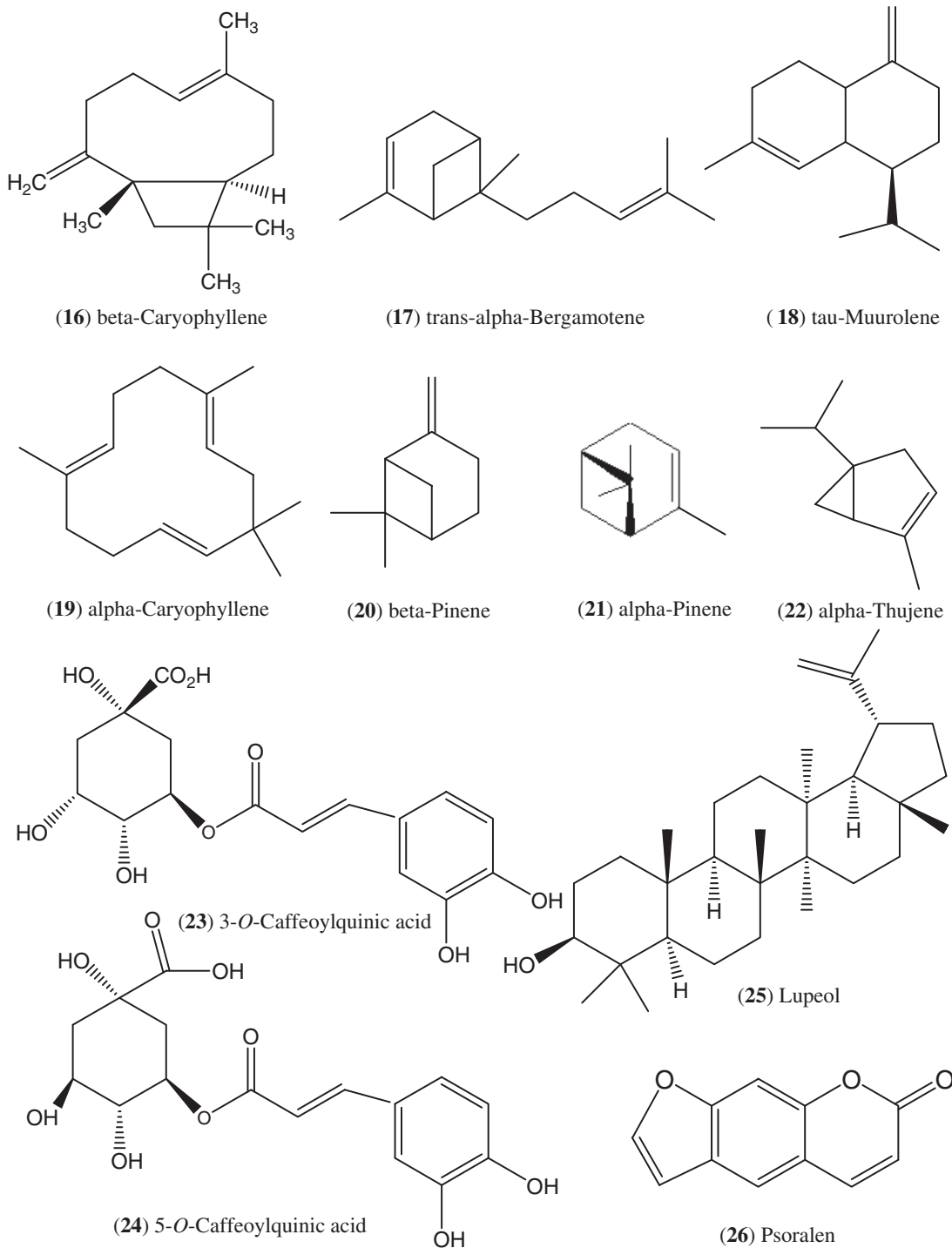


Figure 2. Continued.

et al., 2010). Palmitic, arachidic, and behenic acids are the major fatty acids (21.4, 44.1, and 13.1% of total fatty acid content, respectively). Latex is essentially constituted by saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acid with the quantity of 161.77, 5.89, and 14.59 mg/kg of latex, respectively (Oliveira et al., 2010). Few of them were also accounted from dried fig fruit with the help of gas chromatography. Linolenic acid was the most predominant fatty acid (53.1%) in dried fig fruit, followed by linoleic acid (21.1%), palmitic acid (13.8%), and oleic acid (9.8%) (Jeong & Lachance, 2001).

Flavonoids

The main free flavonoid (non-glycosylated) in *Ficus carica* was found to be luteolin, which was also discovered to be the main free flavonoid in *Pistacia lentiscus* Linn (Anacardiaceae) locally named as Mastic tree. Luteolin (5,7,3',4'-tetrahydroxy-flavone) turned out to be the major flavonoid in the *Ficus* leaf, with a slightly higher flavonoid content than quercetin, i.e., 3,5,7,3',4'-pentahydroxy-flavone (680 and 630 mg/kg extract, respectively). Another flavonoid identified in the *Ficus*, although in a smaller amount,

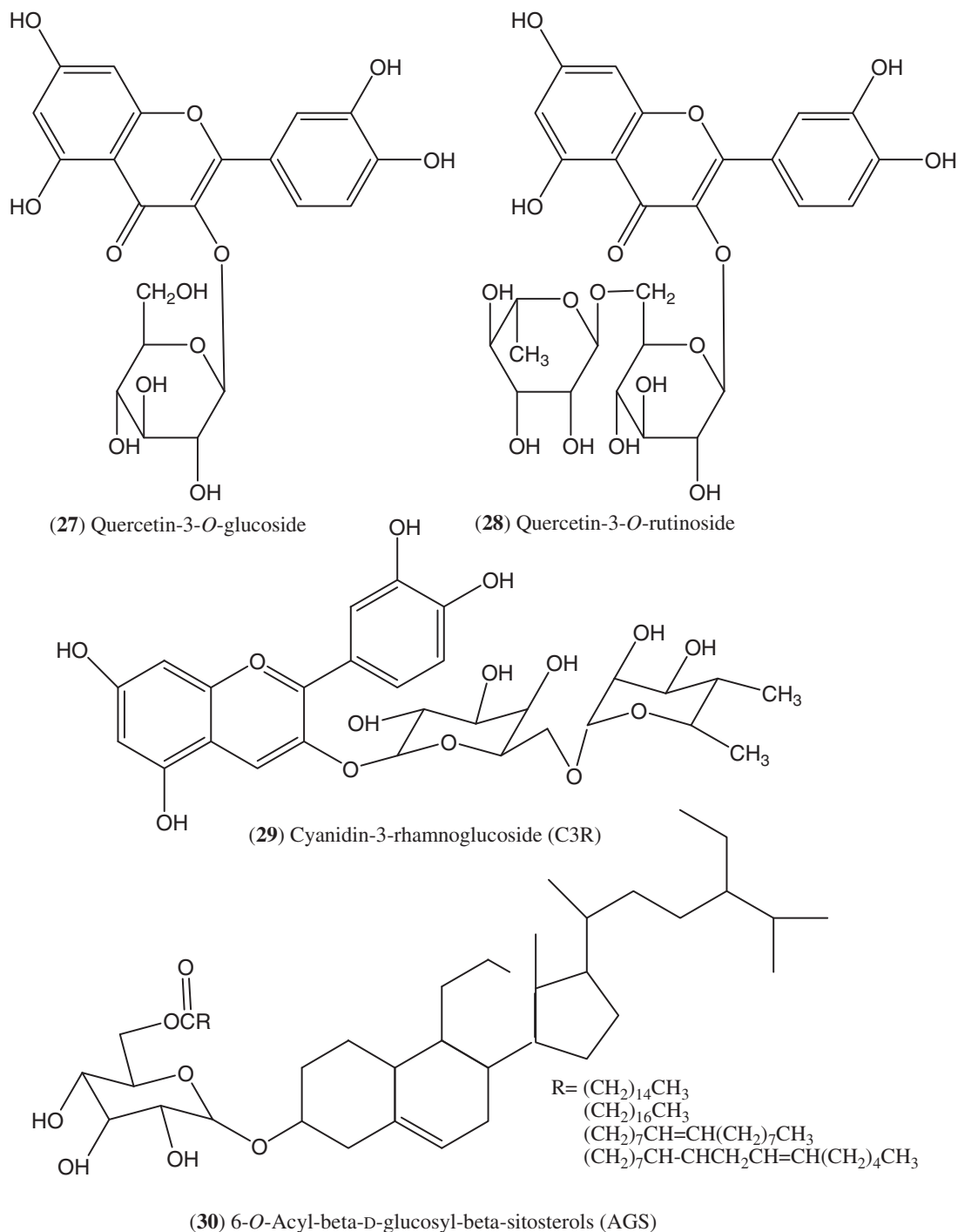


Figure 2. Continued.

i.e., 17 mg/kg extract, is biochanin A, i.e. 5,7-dihydroxy-4'-methoxy-isoflavone, present mainly as a free aglycone (Vaya & Mahmood, 2006).

Luteolin (C₁₅H₁₀O₆) is believed to have the potential to play a significant role in health, as it is considered to exhibit broad-ranging anti-inflammatory benefits (Jang et al., 2008), as well as anticarcinogenic, antimicrobial, antioxidant, and immunomodulatory effects. Cancer, hypertension, inflammation, and many other conditions have been treated with luteolin-rich food in traditional medicine (Lin et al., 2008). Quercetin (C₁₅H₁₀O₇), a chemical similar to the glycoside rutin, is a unique flavonoid that has been extensively studied

by researchers around the world, starting with the discovery of both vitamin C and flavonoids by Albert Szent-Gyorgyi who received the Nobel Prize in 1937 for research in this area. Quercetin is frequently used therapeutically in allergic conditions, including asthma and hay fever, eczema, and hives. Additional clinical uses include treatment of gout, pancreatitis and prostatitis, which are also, in part, inflammatory conditions. The common link is its ability to mediate production and manufacture of pro-inflammatory compounds. However, its uses also may be important in cancer therapeutics. Quercetin is a recognized antioxidant and has been studied for its gastro-protective effects, inhibition of

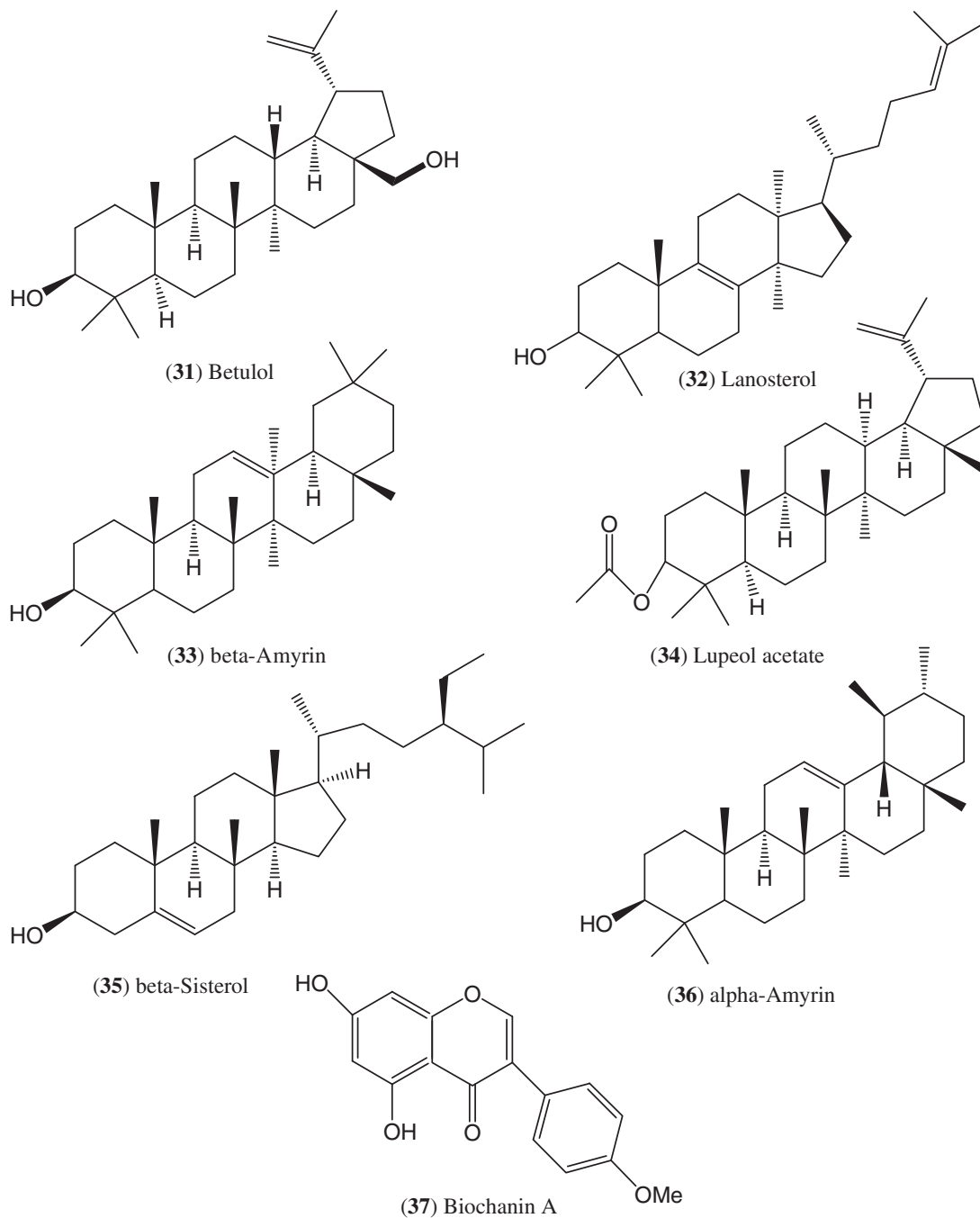


Figure 2. Continued.

carcinogenicity either alone or in combination with chemotherapeutic agents, reducing risk of cataract (Murray, 1996). Biochanin-A is a phytoestrogen that has been shown to have a chemopreventive role in cancer (Medjakovic & Jungbauer, 2008). This role may involve its effect on cell-death signaling pathways, which could prevent the proliferation of tumor cells.

Phenolic compounds

Phenolic compounds are ubiquitously distributed in fruits, where they exert specific functions and are very important for sensory properties, i.e., flavor and color. Moreover, phenolic compounds have become popular among scientists and consumers for their health-promoting properties, mainly for

their antioxidant property (Caro & Piga, 2008). The phenolic profile of fig leaves is composed by seven phenolic compounds, namely 3-CQA [3-*O*-caffeoylquinic acid], 5-CQA [5-*O*-caffeoylquinic acid], Q-3-Glu [quercetin 3-*O*-glucoside], Q-3-rut [quercetin 3-*O*-rutinoside], ferulic acid, psoralen, and bergapten (Oliveira et al., 2009).

Phytosterols

Phytosterols are cholesterol-like molecules found in most plant foods, with the highest concentrations occurring in vegetable oils. They are absorbed only in trace amounts but inhibit the absorption of intestinal cholesterol, including recirculating endogenous biliary cholesterol, a key step in cholesterol elimination (Ostlund, 2002). These compounds

Table 2. Occurrence of phytoconstituents in different parts of *Ficus carica*.

S. no.	Plant part	Type	Examples	Reference
1	Leaves	Flavonoid	Quercetin, luteolin, biochanin-A, luteolin-6C-hexose-8C-pentose, apigenin rutinoside, Kaempferol rutinoside, Quercetin rutinoside, Quercetin glucoside, Quercetin acetylglucoside	Vaya and Mahmood (2006) and Vallejo et al. (2012)
2	Latex	Phytosterols	Betulol, lupeol, lanosterol, lupeol acetate, β -amyirin, β -sisterol and, α -amyirin	Oliveira et al. (2010)
3	Fruit	Anthocyanin	Cyanidin-3-rhamnoglucoside, cyanidin-3-glucoside, cyanidin-3,5-diglucoside, cyanidin-3-rutinoside, pelargonidin-3-glucoside, cyanidin 3-rutinoside dimmer, (epi)catechin-(4 \rightarrow 8)-cyanidin 3-glucoside, (epi)catechin-(4 \rightarrow 8)-cyanidin 3-rutinoside, cyanidin 3,5-diglucoside, (epi)catechin-(4 \rightarrow 8)-cyanidin 3-rutinoside, (epi)catechin-(4 \rightarrow 8)-pelargonidin 3-rutinoside, (epi)catechin-(4 \rightarrow 8)-pelargonidin 3-rutinoside, carboxypyranocyanidin 3-rutinoside, cyanidin 3-malonylglucosyl-5-glucoside, Pelargonidin 3-glucoside, pelargonidin 3-rutinoside, peonidin 3-rutinoside and cyanidin 3-malonylglucoside	Solomon et al. (2006), Dueñas et al. (2008), and Yemiş et al. (2012)
4	Leaves	Organic acids	Oxalic, citric, malic, quinic, shikimic and fumaric acids	Oliveira et al. (2009)
5	Latex	Fatty acids	Myristic acid, pentadecylic acid, palmitic acid, margaric acid, <i>cis</i> -10 heptadecenoic acid, stearic acid, oleic acid, elaidic acid, linoleic acid, arachidic acid, heneicosylic acid, behenic acid, tricosylic acid and lignoceric acid	Oliveira et al. (2010)
6	Latex	Amino acids	Leucine, tryptophan, phenylalanine, lysine, histidine, asparagine, alanine, glutamine, serine, glycine, ornithine, tyrosine, cysteine	Oliveira et al. (2010)
7	Leaves	Phenolic compounds	3-CQA (3-O-caffeoylquinic acid), 5-CQA (5-O-caffeoylquinic acid), Q-3-Glu (quercetin 3-O-glucoside), Q-3-rut (quercetin 3-O-rutinoside), ferulic acid, psoralen, bergapten, pyrogallol, phenol, 3-5-dimethoxy, coumaric, phenolphtelin, pinocembrine, chysin, galangin, protocetchol, vinallin, cinnamic, quercetin and pinostrobin	Oliveira et al. (2009) and El-Shobaki et al. (2010)
8	Latex	Volatile compounds	Pentanal, hexanal, heptanal, benzaldehyde and octanal 7, 1-butanol-3-methyl, 1-butanol-2-methyl, 1-pentanol, 1-hexanol, 1-heptanol, phenylethyl alcohol, phenylpropyl alcohol; 6-methyl-5-hepten-2-one; monopterpenes α -thujene, α -pinene, β -pinene, limonene, terpinolene, eucalyptol, <i>cis</i> -linalool oxide, linalool and epoxylinool; sesquiterpenes α -guaiene, α -bourbonene, β -caryophyllene, <i>trans</i> - α -bergamotene, α -caryophyllene, τ -muurolene, germacrene D, cadinene and α -calacorene	Oliveira et al. (2010)
9	Latex	Sterols	6-O-Acyl- β -D-glucosyl- β -sitosterols	Rubnov et al. (2001)
10	Leaves	Triterpenoids	Bauerenol, calotropenyl acetate, lupeol acetate, methyl maslinate and oleanolic acid	Saeed and Sabir (2002)

Table 3. Pharmacological activities of some phytoconstituents reported in different parts of *Ficus carica*.

S. no.	Part used	Type	Examples	Pharmacological activity/uses
1	Leaf	Coumarin	4',5'-Dihydropsoalene, umbelliferone, marmesin, bergapten	Sunscreen agent, cytotoxic, photosensitizer
2	Fruit	Coumarin	Umbelliferone, scopoletin	Anticancer, anemia, antioxidant
3	Leaf	Flavonoid	Rutin	Anticancer, coloring agent
4	Fruit	Alkaloid	Quinines	Antimalarial
5	Leaf	Sterol	Bauerenol, 24-methylenecycloartanol, ψ -taraxasterol ester, lupeol	Anticancer, antiprotozoal, chemopreventive, anti-inflammatory
6	Leaf	Triterpenoid	Ficusogenin	Anticancer, anti-inflammatory
7	Leaf, root	Coumarin	Psoralen	Sunscreen, tanning activator
8	Leaf, root	Sterol	β -Sitosterol	Hypolipidemic
9	Fruit	Anthocyanin	Cyanidin-3-O-glucoside, cyanidin-3-O-rhamnoglucoside	Antioxidant and radical scavenging actions
10	Latex	Triterpenoid	6-O-Linoleyl- β -D-glucosyl- β -sitosterol, 6-O-Oleyl- β -D-glucosyl- β -sitosterol, 6-O-palmitoyl- β -D-glucosyl- β -sitosterol	Hypolipidemic
11	Fruit	Hydrocarbon	Stilbenes	Antioxidant, hemoptysis, antiseptic

are involved in important cellular processes, such as the regulation of membrane fluidity, adaptation of membranes to temperature (Bouvier et al., 2005), and also participation in cellular differentiation and proliferation (Piironen

et al., 2000). GC-ITMS identified seven phytosterols from the extract of *Ficus carica* latex. They are quantified with the help of high-performance liquid chromatography coupled to diode array detection (HPLC-DAD). The quantity of betulol,

lupeol, lanosterol, lupeol acetate, β -amyirin, β -sisterol, and α -amyirin phytosterols was 327, 2827, 2634, 1989, 1197, 10564, and 76 mg/kg of plant latex, respectively. Thus, β -sitosterol is the compound present in highest quantities (ca. 54%) and α -amyirin is the minor one, i.e., ca. 0.4% (Shiraishi et al., 1996).

Volatile compounds

A total of 31 volatile compounds have been identified from the latex of *Ficus carica* with the help of headspace solid-phase microextraction/gas chromatography-ion trap mass spectrometry analysis (HS-PME/GCIT-MS). These are namely aldehydes (pentanal, hexanal, heptanal, benzaldehyde, and octanal); alcohols (1-butanol-3-methyl, 1-butanol-2-methyl, 1-pentanol, 1-hexanol, 1-heptanol, phenylethyl alcohol, and phenylpropyl alcohol); ketone (6-methyl-5-hepten-2-one); monoterpenes (α -thujene, α -pinene, β -pinene, limonene, terpinolene, eucalyptol, *cis*-linalool oxide, linalool, and epoxylinool); sesquiterpenes (α -guaiene, α -bourbonene, β -caryophyllene, *trans*- α -bergamotene, α -caryophyllene, τ -muurolene, germacrene D, cadinene, and α -calacorene) (Shiraishi et al., 1996).

Anthocyanin

Solomon et al. (2006) detected a new anthocyanin pigment from fig. With the help of proton and carbon NMR spectroscopy, they elucidated the structure of new anthocyanin named cyanidin-3-rhamnoglucoside designated as C3R. It is a well-established fact that plant origin secondary metabolites is well recognized for their medicinal values and health-promoting properties. Solomon et al. (2010) investigated the antioxidant properties of C3R. This compound inhibits the lipid peroxidation by producing peroxy radicals and malondialdehyde in a dose-dependent manner. In addition to this, scavenging on reactive oxygen species, C3R showed a strong chelating activity toward the Fe^{2+} ion. The high antioxidant potential, with several modes of action of purified C3R, may contribute to health benefits by the consumption of fresh fig fruits.

Enzyme profile of latex

The latex of this plant is a rich source of hydrolytic enzymes. Ten proteolytic enzyme components have been reported from the latex (Sgariberi et al., 1964). Two proteolytic enzyme components are characterized and designated as C and D components (Kramer & Whitaker, 1969). Ficin S is an example of a sugar containing proteinase that has been well characterized from *Ficus* latex (Sugiura & Sasaki, 1974). *Ficus* latex is also reported to consist of several other enzymes namely rennin, protease, diastase, esterase, lipase, catalase, and peroxidase (Khare, 2004). Devaraj and his coworkers (2008) isolated and characterized the cysteine protease from latex. In 2009, two independent studies demonstrated rennet-like milk clotting protease activity of latex (Badgujar & Mahajan, 2009a; Nouani et al., 2009). Recently, Bidhi and Kahli amylases have been characterized from latex (Aref et al., 2011a). In addition, the latex of this plant has been reported to contain significant quantities of antioxidant

enzymes such as polyphenol oxidase, catalase, peroxidase, superoxide dismutase, glutathione-S-transferase, glutathione peroxidase, and glutathione reductase (Hossein & Ilghar, 2011; Vijayakumari et al., 2012). Some known salient features of proteases, oxidase, and amylase of *Ficus carica* are summarized in Table 4.

In addition to this, Stepek and coworkers (2005) described anthelmintic efficacy of cysteine protease of fig using rodent gastrointestinal nematode. An active principle of *Ficus carica*, i.e., ficin was remarkably reported for its hemostatic activity through activation of blood clotting factor X (Richter et al., 2002). The efficacy and mode of action make as plant protease(s) as a potential candidate for novel class of antiplatelet agent.

Nutritive value

Ficus carica is widely grown for its edible fruit. These are sweet and succulent; a fully ripe specimen is an exquisite fruit that almost literally melts in the mouth. The fruit is often dried for later use and this dried fruit is a major item of commerce. Figs are one of the highest plant sources of calcium and fiber. According to USDA data for the Mission variety, dried figs are richer in fiber, copper, manganese, magnesium, potassium, calcium, and vitamin K, relative to human needs. They have smaller amounts of many other nutrients. On a weight basis, figs contain more calcium (132.5 mg/100 g) as compared with apples (7.14 mg/100 g), bananas (3.88 mg/100 g), dates (25.0 mg/100 g), grapes (10.86 mg/100 g), orange (40.25 mg/100 g), prunes (18.0 mg/100 g), raisins (40.0 mg/100 g), and strawberries (14.01 mg/100 g). According to Pasman et al. (1997), the average energy intake decreased significantly after the supplementation of fiber-rich food. A recent study has shown that the addition of a soluble fiber supplement to the dietary food material could aid in weight loss. Thus, figs and their soluble fiber may be of help in weight reduction, because figs provide more fiber (12.21 g/100 g) than all the above-mentioned common fruits (Vinson, 1999). Phenolics are an important constituent of fruit quality because of their contribution to the taste, color, and nutritional properties of fruit. Amongst phenolics analyzed in the fruit of this plant, rutin (28.7 mg/100 g) is found in highest quantity (Veberic et al., 2008), followed by (+)-catechin (4.03 mg/100 g), chlorogenic acid (1.71 mg/100 g), (–)-epicatechin (0.97 mg/100 g), gallic acid (0.38 mg/100 g), and finally, syringic acid (0.10 mg/100 g). Thus, as a typical, seasonal fresh fruit, figs are an important constituent of the regional diet.

Traditional and contemporary uses

Ficus carica has been extensively used in traditional medicine for a wide range of ailments. Its bark, fruit, leaves, roots, and latex are medicinally used in different forms. Also, it is used in combination with another medicinal plant, *Laurus nobilis* Linn (Lauraceae) traditionally known as *Paathri* and together with natural foods such as honey and milk (Idolo et al., 2010; Manjula et al., 2011). In addition, in Mediterranean countries, the fig is so widely used both fresh and dried that it is called “the poor man’s food”. In Unani medicine, *Ficus carica* is used as a mild laxative, expectorant, diuretic; also in

Table 4. Some reported salient features of enzymes of *Ficus carica*.

Salient features		1	2	3	4	5	6	7	8	9	10	11
EC 3.4.4.12	4.8	9.1	8.0	60	Cysteine and mercaptoethanol	HgCl ₂ and p-chloromercuribenzoate	nr ^a	Glyco protease	nr ^a	nr ^a	nr ^a	Sugiura and Sasaki (1974)
EC 3.4.22.3	nr ^a	nr ^a	7.0	nr ^a	nr ^a	nr ^a	23.1	Cysteine protease	nr ^a	nr ^a	nr ^a	Devaraj et al. (2008)
nr ^a	nr ^a	nr ^a	5.0	81	CaCl ₂	nr ^a	nr ^a	Milk clotting protease	nr ^a	nr ^a	nr ^a	Nouani et al. (2009)
nr ^a	4.58	nr ^a	6.5	50	Cysteine	HgCl ₂	23	Cysteine protease	nr ^a	nr ^a	nr ^a	Badgujar (2011)
nr ^a	nr ^a	nr ^a	6.5	45	Fe ⁺⁺ and Cu ⁺⁺	Mg ⁺⁺ and EDTA	nr ^a	Bidhi amylase	nr ^a	nr ^a	nr ^a	Aref et al. (2011a)
nr ^a	nr ^a	nr ^a	7.0	45	Mg ⁺⁺ and Ca ⁺⁺	nr ^a	nr ^a	Kahlil amylase	nr ^a	nr ^a	nr ^a	Aref et al. (2011a)
nr ^a	nr ^a	nr ^a	nr ^a	40	nr ^a	Ascorbic acid and L-cysteine	nr ^a	Copper containing oxidase enzyme	nr ^a	nr ^a	nr ^a	Hosseini and Ighar (2011)

1: Nomenclature; 2: sugar content (%); 3: pl; 4: optimum pH; 5: optimum temperature (°C); 6: activator; 7: inhibitor; 8: molecular weight; 9: type of enzymes; 10: N-terminal sequence; 11: reference; ^anr: not reported.

treatment of diseases of liver and spleen as deobstruent and anti-inflammatory agent. In ethnomedicine, fruits are used in leprosy and nose bleeding, and are used as antipyretic, aphrodisiac, lithontriptic, hair-nutritive, emollient, demulcent, laxative, and in the treatment of various inflammations, paralysis, liver diseases, chest pain, and piles. Roots are used as tonic in the treatment of leucoderma and ringworm infection. Latex is used as expectorant, diuretic, anthelmintic and anemia. Leaves are used as antidiabetic, vermifuge, and contact dermatitis in humans, phototoxicity in animals. Seeds are used as edible oil and lubricant (Kirtikar & Basu, 1995). Traditional and contemporary uses of *Ficus carica* including, Ayurvedic, Unani, and reports of different ethnobotanical survey, are shown in Table 5.

Pharmacological reports

Antipyretic

The significant antipyretic effect of an ethanol extract of *Ficus carica* was demonstrated in a study (Patil et al., 2010a), where this extract was effective at dose of 100, 200, and 300 mg/kg in reducing normal body temperature. Furthermore, the effect extended up to 5 h after drug administration when compared with that of paracetamol (150 mg/kg.), a standard antipyretic agent.

Anti-inflammatory

Petroleum ether (PEE), chloroform (CE), and ethanol (EE) extracts of *Ficus carica* leaves are reported for anti-inflammatory activity against carrageenan-induced rat paw edema. The EE exhibits greater anti-inflammatory effect than PEE and CE of *Ficus carica* as compared with the standard drug, indomethacin (Patil & Patil, 2011b).

Antispasmodic and antiplatelet

The aqueous ethanol extract (AEE) of *Ficus carica* fruit was studied for antispasmodic effect on rabbit jejunum preparations and for antiplatelet effect using *ex vivo* model of human platelets. When AEE is tested in isolated rabbit jejunum, it produced relaxation in a spontaneous way. AEE also inhibits the adenosine 5'-diphosphate and adrenaline-induced human platelet aggregation. This study exhibits the remarkable spasmolytic property in the ripe dried fruit of *Ficus carica* along with antiplatelet activity that provides sound pharmacological basis for its medicinal use in the gut motility and inflammatory disorders (Gilani et al., 2008).

Anthelmintic

As per WHO, only a few drugs are frequently used in the treatment of helminthes in human beings. Anthelmintics from the natural sources may play a key role in the treatment of parasite infections. Anthelmintic activity of aqueous, petroleum ether, chloroform, and methanol extract of leaves of *Ficus carica* was investigated against *Pheritima posthuma* in comparison with mebendazole as a standard drug (Patil et al., 2010b). This type of activity is also reported in different members of *Ficus*, i.e., *Ficus benghalensis* Linn and *Ficus racemosa* Linn (Chandrashekhar & Latha, 2008).

Table 5. Traditional and contemporary applications of *Ficus carica*.

S. no.	Ailment/use	Part/preparation used	Locality	Reference
1	Abdominal pain	Decoction with dried fruits and unpeeled almond	Abruzzo, Italy	Idolo et al. (2010)
2	Antihelmentic	Fruits are used a tonic	Gilgit, Pakistan	Khan and Khatoon (2007)
3	Antiseptic for urinary tract	Latex Decoction made with 0.5 l water, 5 dried fruits, 4 <i>Laurus nobilis</i> leaves and a peeled apple	Peshawar, Pakistan Abruzzo, Italy	Zabihullah et al. (2006) Idolo et al. (2010)
4	Anorexia	Bark, leaves and latex	Pakistan	Marwat et al. (2009)
5	Anemia	Fruit	Khuzestan, Iran	Ramazani et al. (2010)
6	Ascites	Fruit	Khuzestan, Iran	Ramazani et al. (2010)
7	Bee sting	Latex soothes the bee sting by simply rubbing on the skin	Buner, Pakistan	Badgujar (2011)
8	Blood deficiency	Leaves	South-eastern Nigeria	Nebedum et al. (2010)
9	Boils	Fruit extraction	Istanbul, Turkey	Gülay and Neriman (2006)
10	Bone treatment	Bark	India	Kirtikar and Basu (1995)
11	Bronchitis	Aqueous infusion of fresh leaf tender is taken orally as a drink	Ecuador	Tene et al. (2007)
12	Burn and Emollient	Fruit and latex	Nablus, Palestine	Jaradat (2005)
13	Cardiac troubles	Fruits are used a tonic	Gilgit, Pakistan	Khan and Khatoon (2007)
14	Corns	Latex	Istanbul, Turkey	Gülay and Neriman (2006)
15	Constipation	Juice extracted from fruit is taken orally	Jodhpur, India	Prajapati et al. (2007)
16	Cough	Decoction of fruit with honey Fruit and latex Decoction of boiled fruits is taken orally	Abruzzo, Italy Nablus, Palestine Northern and central Oman	Idolo et al. (2010) Jaradat (2005) Ghazanfar and Al-Abahi (1993)
17	Diabetes	Decoction of leaves	Islamabad, Pakistan	Khan et al. (2011)
18	Drink (Tea)	Dry fruit powder is used in tea recipes, as nutritional one	Turkey	İsmet et al. (2010)
19	Earache	Leaf juice with honey	Nepal	Kunwar and Bussmann (2006)
20	Eye vision problem	Powder of dry fruits and sugar is taken orally with water twice a day	Abbottabad, Pakistan	Abbasi et al. (2010)
21	Expectorant	Fruit	Northern Pakistan	Afzal et al. (2009)
22	Fever	Dried fruits	Bangladesh	Khanom et al. (2000)
23	Food	Fruit Dried fruit to sweeten decoction Leaves are fodder for goats The unripe fruit and young growth are cooked and eaten as vegetable	Shangla, Pakistan Abruzzo, Italy Buner, Pakistan Rawalpindi, Pakistan	Ibrar et al. (2007) Idolo et al. (2010) Badgujar (2011) Husain et al. (2008)
24	Fuel	Wood	Buner, Pakistan	Badgujar (2011)
25	Hemorrhoids	Leaves	Istanbul, Turkey	Gülay and Neriman (2006)
26	Hepatitis	Decoction of fruit	Istanbul, Turkey	Gülay and Neriman (2006)
27	Inflammation	Bark	Khuzestan, Iran	Ramazani et al. (2010)
28	Intestinal pain	Bark	Pakistan	Marwat et al. (2009)
29	Jaundice	20 ml of leaf juice mixed with a cup of goat milk is administered early in the morning one a day for 3 d	Andhra Pradesh, India	Manjula et al. (2011)
30	Kidney stone	Fruit and latex Bark and leaves Fruit	Nablus, Palestine Pakistan Northern Pakistan	Jaradat (2005) Marwat et al. (2009) Afzal et al. (2009)
31	Laxative	Leaves and latex Fruit juice is taken orally	Buner, Pakistan Jodhpur, India	Zaman et al. (2011) Prajapati et al. (2007)
32	Leucoderma	Root	Maharashtra, India	Kalaskar et al. (2010)
33	Liver diseases	Fruit	Northern Pakistan	Afzal et al. (2009)
34	Menstruation pain and Sedative	Aqueous infusion of fresh leaf tender is taken orally as a drink	Ecuador	Tene et al. (2007)
35	Mouth cavity diseases	Dried fruits	Abbottabad, Pakistan	Qureshi et al. (2008)
36	Paralysis	Dried fruit	Bangladesh	Khanom et al. (2000)
37	Piles and chronic ulcer	Fruit juice and latex	Rawalpindi, Pakistan	Husain et al. (2008)
38	Regulates blood stream	Decoction made with dried fruits, lemon peel and <i>Laurus nobilis</i> leaves	Abruzzo, Italy	Idolo et al. (2010)
39	Skin disease	Fruit and latex Stem latex Fruit and latex	Nablus, Palestine Gilgit, Pakistan Nablus, Palestine	Jaradat (2005) Khan and Khatoon (2007) Jaradat (2005)
40	Stomach cancer	Leafy latex	Sari, Iran	Hashemi et al. (2011)

(continued)

Table 5. Continued

S. no.	Ailment/use	Part/preparation used	Locality	Reference
41	Wart	Milky latex is applied externally	Alasehir, Turkey Izmir, Turkey Jodhpur, India Istanbul, Turkey	Ugulu (2011) Ugulu et al. (2009) Prajapati et al. (2007) Gülay and Neriman (2006)
42	Weakness	Fruit juice Single dry fruit is deep in water for a night. This fruit is consumed at morning for 15 d	Kashmir, Pakistan Maharashtra, India	Ishtiaq et al. (2007) Patil et al. (2011)
43	Wound	Fruit and latex	Nablus, Palestine	Jaradat (2005)

Hepatoprotective

The methanol extract of the leaves of *Ficus carica* was evaluated for hepatoprotective activity in CCl₄-induced liver damage in a rat model. The extract of 500 mg/kg (oral dose) exhibited a significant protective effect reflected by lowering the serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total serum bilirubin, and malondialdehyde equivalent, an index of lipid peroxidation of the liver (Krishna et al., 2007). Significant reversal of biochemical, histological, and functional changes was induced by petroleum ether extract treatment in rifampicin-treated rats, indicating promising hepatoprotective activity (Gond & Khadabadi, 2008). Hepatoprotective activity was also reported in the leaf extracts of *Ficus racemosa* Linn and *Ficus hispida* Linn. f. possess significant hepatoprotective activity against carbon tetrachloride- and paracetamol-induced hepatotoxicity in rats, respectively.

Anticonstipation effect

Constipation is one of the most common gastrointestinal complaints worldwide. This study examined the effects of fig paste for the treatment of loperamide-induced constipation in a rat model. For this purpose, animals were divided into one normal control group and four experimental groups (0, 1, 6, and 30 g/kg). Loperamide (2 mg/kg, twice per day) was injected intraperitoneally to induce constipation in the four experimental groups. Fig paste was administered for 4 weeks to assess its anticonstipation effects. In progress, fecal pellet number, weight, and water content were increased in the fig-treated groups as compared with the control group. Reductions in body weight and increased intestinal transit length were observed in the fig-treated groups. Fecal pellet number was reduced in the distal colons of the fig-treated rats. Exercise and ileum tension increased in the experimental groups as compared with the control group. Constipation was decreased when the fig fruit was fed to rats (Lee et al., 2012). Furthermore, a clinical study (Kim et al., 2010) showed that fig fruit supplementation improved symptoms in patients suffering from functional constipation. This randomized controlled study of 20 female patients with functional constipation demonstrated that supplementation with fig fruit increased the number of bowel movements, reduced defecation time, and improved the abdominal pain. Thus, fig supplementation may be a useful therapeutic and preventive strategy for chronic constipation.

Hypoglycemic

The hypoglycemic effect of an aqueous extract of leaves has been demonstrated in streptozotocin-induced diabetic rats (Perez et al., 1996), where weight loss was prevented in these animals. Additionally, treatment resulted in an increase in the survival index that correlated with increased plasma insulin levels. A similar activity has also been reported for the fruit of *Ficus carica* (El-Shobaki et al., 2010).

Hypocholesterolemic activity

The leaves of fig have hypocholesterolemic activity. Chloroform extract is prepared from the aqueous decoction of fig leaves. It causes decline in the levels of total cholesterol and decrease in the total cholesterol/HDL cholesterol ratio, together with a reduction of the hyperglycemia. In addition to this, the cell content of cholesterol in HepG2 cells appreciates the reduction of blood cholesterol level in streptozotocin-induced diabetic rats (Canal et al., 2000).

Hypolipidimic activity

Further hypolipidimic study in the animal model is extended by Asadi and coworkers (2006). The fig tree leaves (fig tree leaf extract (FTE)) were reported to decrease hepatic TG (triglyceride) content and secretion of TG and cholesterol from the liver. Furthermore, the hepatic TG content and TG secretion values from the liver significantly decreased with slight increase of the FTE dose. This result suggests that the leaf extract could be a beneficial supplement to modulate TG and cholesterol secretion from the liver (Asadi et al., 2006).

Anticancer effect

Bioactive compounds like 6-*O*-acyl-β-D-glucosyl-β-sitosterols, i.e., AGS (acyl moiety: palmitoyl, linoleyl, stearyl, and oleyl) were isolated from fig latex. Palmitoyl derivative of AGS acts as the most potent inhibitor for various cancer cell lines as compared with linoleyl, stearyl, and oleyl derivatives. AGS is reported for *in vitro* inhibition of DG-75, Jurkat, and DU-145 cancer cell lines. Thus, AGS is the most potent anticancer agent (Rubnov et al., 2001).

Cytotoxicity

The cytotoxicity of fruit and leaf extracts as well as latex of *Ficus carica* was evaluated using HeLa cell lines. Plant latex and different extracts (ethanol, ethyl acetate, and dichloromethane) could reduce the viability of HeLa cell lines at low

concentrations. The approximate IC_{50} values of ethanol, ethyl acetate, and dichloromethane extracts of the leaves and fruits are 10, 13, 12 $\mu\text{g/ml}$ and 12, 12, 11.5 $\mu\text{g/ml}$, respectively, and for latex 17 $\mu\text{g/ml}$. Thus, fig containing active principles may be responsible for cytotoxicity (Khodarahmi et al., 2011).

Antiviral

Five extracts (methanol, hexanic, ethyl acetate, hexane-ethyl acetate, and chloroformic) of *Ficus carica* were tested for antiviral and cytotoxic effects. All the above-mentioned extracts did not exhibit any cytotoxic effect on Vero cells (Aref et al., 2011b). *In vitro* antiviral potential activity was studied by observing cytopathic effect against herpes simplex type 1 (HSV-1), echovirus type 11 (ECV-11), and adenovirus (ADV). The hexanic and hexane-ethyl acetate extracts inhibited multiplication of viruses at concentrations of 78 $\mu\text{g/ml}$. These two extracts are the most potent candidates for herbal medicines used in the therapy of viral infectious diseases such as herpes virus, echovirus, and adenovirus. Thus Aref and coworkers (2011a,b) concluded that activities namely antiviral and cytotoxicity were not correlated with each other.

Antimutagenic

Antimutagenic action of plant extracts of *Armoracia rusticana*, *Ficus carica*, *Zea mays* and their mixture on environmental xenobiotics has been investigated. The plant extracts and their mixture decreased the level of mutations induced by *N*-methyl-*N'*-nitro-*N*-nitrozo-guanidin (MNNG) in *Vicia faba* cells, chlorophyll mutations in *Arabidopsis thaliana*, and NaF-induced mutability in rat marrow cells. The plant extracts and their mixture demonstrate the ability to decrease the genotoxicity of environmental mutagens (Agabeili & Kasimova, 2005).

Anti-angiogenic activity

Ali Mostafaie et al. (2011) investigated the anti-angiogenic and anti-proliferative potentials of *Ficus carica* latex extract using human umbilical vein endothelial cells (HUVECs). The results clearly indicated that latex extracts of *Ficus carica* contain strong anti-angiogenic and anti-proliferative activities. Therefore, latex extract could be an ideal candidate as a potential agent for the prevention of angiogenesis in cancer and other chronic disorders.

Erythropoietic effect

Lohar et al. (2009) reported about the erythropoietic activities of some medicinal plants found in India: *Aegel marmelos* L. (Rutaceae), *Asparagus recemosus* Willd (Liliaceae), *Boerhavia diffusa* L. (Nyctaginaceae), *Carissa congesta* Wt. (Apocynaceae), *Eugenia jambolana* Lam (Myrtaceae), *Ficus carica* L. (Moraceae), *Phoenix sylvestris* L. (Palmae), *Phyllanthus emblica* L. (Euphorbiaceae), *Spinaca oleracean* L. (Chenopodiaceae), and *Vitis vinifera* L. (Vitaceae) on Wistar albino rats. Fruit, leaf, and root extracts of these plants were prepared and fed to experimental rat model for seven consecutive days to evaluate their effects on the

hematological parameters such as red blood cells count (RBC count) and hemoglobin (Hb%). In the test, animals showed augmentation as compared with the controlled group of rats. Rats fed with fruit extracts of *Aegel marmelos*, *Carissa congesta*, *Eugenia jambolana*, *Ficus carica*, *Phoenix sylvestris*, *Phyllanthus emblica*, and *Vitis vinifera* separately showed increase in their hematological parameters. Obtained results indicate that most of the plant extracts boost synthesis of hemoglobin and formation of RBCs in the descending order: *Phyllanthus emblica*, *Spinaca oleracean*, *Ficus carica*, *Phoenix sylvestris*, *Boerhavia diffusa*, *Aegel marmelos*, *Vitis vinifera*, *Eugenia jambolana*, *Asparagus recemosus*, and *Carissa congesta*.

Haemostatic effect

Richter et al. (2002) found that ficin (mixture of proteases) present in latex of *Ficus carica* possessed the significant hemostatic effect by shortening the activated partial thromboplastin time and the prothrombin time. This showed that the hemostatic potency of *Ficus* proteases was based on the activation of human coagulation factor X.

Antimicrobial activities

Antibacterial activity of methanol extract of *Ficus carica* leaves exhibits strong antibacterial activity against *Streptococcus gordonii*, *Streptococcus anginosus*, *Prevotella intermedia*, *Aggregatibacter actinomycetemcomitans*, and *Porphyromonas gingivalis* (MIC, 0.156–0.625 mg/ml; MBC, 0.313–0.625 mg/ml), while *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus sanguinis*, and *Streptococcus criceti* appeared to be less sensitive (MIC, 2.5–10 mg/ml; MBC, 2.5–10 mg/ml). Thus, figs could be employed as a natural antibacterial agent in oral care recipes against pathogenic bacteria of oral cavity (Jeong et al., 2009).

With the help of advanced tool and technologies, i.e., mass spectroscopy and amino acid sequencer, an antifungal protein was characterized from the latex of *Ficus carica*. The seven N-terminal amino acid sequence of low molecular weight (6481 Dalton) protein is RPdffLE, i.e., Arg–Pro–Asp–Phe–Phe–Leu–Glu (Mavlonov et al., 2008). Very recently, chlorophormic, ethyl acetate, methanol, and hexanoic extracts of latex were investigated for antifungal activity against *Aspergillus fumigates*, *Trichophyton rubrum*, *Trichophyton soudanense*, *Microsporium canis*, *Scopulariopsis brevicaulis*, *Candida albicans*, and *Cryptococcus neoformans*. The methanol fraction is the most suitable antifungal agent against *C. albicans*. Ethyl acetate, methanol, and hexanoic extracts strongly inhibit the growth of *M. canis* (Aref et al., 2010).

Antioxidant activity

Vinson et al. (1999) reported significant antioxidant activity in dried fruits of *Ficus carica*. Dried figs are *in vitro* antioxidants after human consumption. These findings suggest that dried fruits should be a greater part of the diet as they are dense in phenol antioxidants and nutrients most probably fiber.

Free radical scavenging activity

Yang et al. (2009) designed the method to study the ultrasonic assisted extraction of total flavonoids from the fruit of *Ficus carica* and their scavenging activities against hydroxyl and superoxide anion free radicals (Chawla et al., 2012). The optimum conditions for extracting total flavonoids from the leaves of *Ficus carica* were found to be the following: ethanol concentration 40%, material-to-liquid ratio 1:60 (g/ml), extraction temperature 60 °C, and length of ultrasonic treatment of 50 min. Under these optimum conditions, the extraction efficiency of total flavonoids reached as high as 25.04 mg/g. The total flavonoid extract from the leaves had marked scavenging effects on both hydroxyl and superoxide anion free radicals in a concentration-dependent fashion.

Immunostimulant

The immunomodulatory effect of ethanol extract of the leaves of *Ficus carica* was studied in mice. This study was carried out with the help of various hematological and serological tests. Administration of extract remarkably ameliorated both cellular and humoral antibody response. Thus, the ethanol extract of the leaves of *Ficus carica* possess promising immunostimulant properties (Patil et al., 2010c).

Antiwarts activity

A prospective, open right/left comparative trial of fig tree latex therapy versus local standard of cryotherapy was carried out on 25 patients with common warts (*Verruca vulgaris*). It was found that fig tree latex therapy was marginally less effective than cryotherapy. Adverse effects were observed only in cryotreated warts. Fig tree latex therapy of warts offers several beneficial effects including short duration therapy, no reports of any side effects, ease-of-use, patient compliance, and a low recurrence rate (Bohlooli et al., 2007).

Irritant potential

The irritant potential of methanol extract and five newly isolated tripterpenoids (bauerenol, calotropenyl acetate, lupeol acetate, methyl maslinate, and oleanolic acid) of *Ficus carica* reported with the help of a open mouse ear assay method. Total methanol extract, calotropenyl acetate, methyl maslinate, and lupeol acetate showed potent and persistent irritant effects as compared with other triterpenoids of *Ficus carica* (Saeed & Sabir, 2002).

Environmental application

Endophytic fungus

Four compounds were isolated from the culture of *Alternaria* sp. FL25, an endophytic fungus of *Ficus carica*. On the basis of spectroscopic data (MS, ¹H-NMR, and ¹³C-NMR), the four compounds were identified as fumitremorgin B, fumitremorgin C, helvolic acid, and cyclo-(Phe-Ser). These compounds exhibit significant growth inhibition activity against tested phytopathogenic fungi, namely *Alternaria brassicae*, *Botrytis cinerea*, *Fusarium oxysporum* f. sp. *niveum*, *Alternaria alternata*, *Fusarium oxysporum* f. sp. *cucumerinum*,

Colletotrichum gloeosporioides, *Phytophthora capsici*, *Valsa mali*, *Fusarium oxysporum* f. sp. *Fragariae*, and *Fusarium graminearum* (Chengliang & Yangmin, 2010). The ethyl acetate extract of endophytic *Aspergillus* sp. isolated from *Ficus carica* showed significant antimicrobial activity against *Pseudomonas aeruginosa*. Instrumental analysis like UV-Visible, TLC, IR, and HPLC indicated the presence of phenol groups and amine groups in the antimicrobial compound of endophytes of *Ficus carica* (Prabavathy & Nachiyar, 2011). Thus, these potent natural products of endophytes of *Ficus carica* could be utilized in antibiotics preparation in near future.

Larvicidal activity

The milky sap of *Ficus carica* was found to be significant toxic action against early fourth-stage larvae of *Aedes aegypti* with a lethal concentration LC₅₀ value of 10.2 µg/ml and an LC₉₀ value of 42.3 µg/ml (Chung et al., 2011). Two natural furocoumarins, namely 5-methoxypsoralen and 8-methoxypsoralen, were isolated from the milky sap of *Ficus carica*. The LC₅₀ value of 5-methoxypsoralen and 8-methoxypsoralen were 9.4 and 56.3 µg/ml, respectively.

Nematicidal activity

Recently, nematicidal activity of the latex of *Ficus carica* was evaluated against root knot nematode named *Meloidogyne incognita* using okra as a host plant (Badgujar & Mahajan, 2009b). Furthermore, a bioactive compound called psoralen has been well characterized from the methanol extract of the leaf of *Ficus carica*. It is a type of benzopyrone (coumarin) that shows potent nematicidal activity against several nematodes such as *Bursaphelenchus xylophilus*, *Panagrellus redivivus*, and *Caenorhabditis elegans* (Liu et al., 2011).

Bio-control agent

Biological control of parasites in organic farming is based on naturally occurring compounds and antagonists. Bacterial diseases are a serious problem in greenhouse and in open field on different plants. Amongst them, *Pseudomonas syringae* pv. *syringae*, *Pseudomonas viridiflava* and *Pseudomonas syringae* pv. *tomato* are particularly dangerous on kiwifruit and tomato plants, respectively. At present, to control these bacterial pathogens, especially in organic agriculture, few effective strategies could be adopted. Copper treatments and appropriate agronomical practices are suggested (Varvaro et al., 2001). Aqueous extracts from *Allium sativum* and *Ficus carica* fruits reduce the survival and the damages (disease incidence and disease severity) caused by bacterial pathogens of kiwifruit (*Pseudomonas syringae* pv. *syringae*, *Pseudomonas viridiflava*) and of tomato (*Pseudomonas syringae* pv. *tomato*) plants. *In vitro* tests, both vegetal extracts, show antimicrobial activity against these bacterial strains utilized at different concentrations (Balestra et al., 2008, 2009).

Toxicology

The long history of ethnomedicinal application, with no reports of any serious side effect, suggests that *Ficus carica*

could be considered as safe. In most of the toxicity experiments which were carried out on *Ficus carica*, no sign of toxicity was observed. In acute toxicity studies carried out on albino mice, the ethanol, chloroform, and petroleum ether extract of *Ficus carica* were found to be safe at a dose of 5000 mg/kg of body weight (Patil & Patil, 2011b). Very recently, the acute toxicity of ethanol extract of *Ficus carica* fruit was studied according to OECD guideline number 423. This extract was not lethal to the rats even at 2000 mg/kg body weight (Sruthi et al., 2012). The overall toxicity studies carried out on *Ficus carica* accounts for its safety at the recommended therapeutic doses.

Conclusion

An extensive literature survey revealed that *Ficus carica* is a sacred and important medicinal plant used for the ethnomedicinal treatment of anemia, bronchitis, constipation, diabetes, fever (jaundice), hemorrhoids, inflammation, liver disorders, infectious diseases, and many more throughout the world. Pharmacological studies carried out on the fresh plant materials, crude extracts, and isolated components of *Ficus carica* provide an experimental support for its numerous traditional uses. Recent studies have been focused on evaluating the antibacterial, anticancer, antifungal, antihelminthic, anti-inflammatory, antimutagenic, antipyretic, antispasmodic and antiplatelet, antiviral, cytotoxicity, hepatoprotective, hypoglycemic, hypolipidemic, and immunostimulant activities. Most of the mentioned pharmacological studies were aimed at validating its traditional uses. It has been found that some of its traditional uses have been extensively explored by several research groups, like anti-inflammatory and antimicrobial activities. However, no experimental evidence available substantiate its traditional use in wound healing, hematic disorders, cardiac disorders, and sexual disorders (menstruation pain), which need further experimental evidence.

Different parts of *Ficus carica* have been employed in the treatment of some ailments in varied geographical locations, like for kidney stone treatment; its fruit and latex are prescribed in Nablus, Palestine, whereas fruit and leaves are recommended in Pakistan. Similarly, in the recipe of wart medicine, its milky latex is applied externally in Jodhpur (India) and Alasehir (Turkey) while fruit juice is used in Kashmir. The explanation for such a practice warrants further phytochemical and pharmacological studies.

The majority of the pharmacological studies that have been carried out on *Ficus carica* were conducted using crude extracts. Thus, it is difficult to reproduce the outcomes of these studies and to locate the precise bioactive metabolite. Hence, there is a need for phytochemical standardization and identification of potent bioactive candidates. Phytochemical research carried out on *Ficus carica* has led to the isolation of few classes of plant metabolites. However, the vast traditional use and proven pharmacological activities of *Ficus carica* indicate that an immense scope still exists for its phytochemical exploration.

As being a dietary supplement, parts of *Ficus carica* contain essential amino acids (like leucine, tryptophan, phenylalanine, lysine, and histidine), vitamins (like vitamin

A, vitamin C, thiamine, riboflavine, and niacin), dietary fiber, minerals (like sodium, potassium, and calcium) and carbohydrate. Thus, it could be explored for a variety of normal body functions and growth.

In this review, 22 biological activities of *Ficus carica* are described. However, the potent bioactive secondary metabolite for anticancer, haemostatic effect, antifungal activity, scavenging effect, and irritant potential is described by earlier researchers of this field. There are a number of research papers appeared in the literature indicating relevant chemical characterization of flavonoids, phytosterols, anthocyanins, phenolic compounds, sterols, and volatile compounds. They failed to recognize the referred biological activities. Therefore, there is a vast scope for establishing a relation between given phytoconstituents and biological activities. The outcome of the future research in the above-mentioned areas will provide a convincing support for the future clinical uses of *Ficus carica* in modern medicine.

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Declaration of interest

Authors declare no conflict of interest.

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