

FICUS CARICA AND ITS CONSTITUENTS ROLE IN MANAGEMENT OF DISEASESARSHAD H RAHMANI*¹, YOUSEF H ALDEBASI²¹Department of Medical Laboratories, College of Applied Medical Sciences, Qassim University, Saudi Arabia. ²Department of Optometry, College of Applied Medical Sciences, Qassim University, Saudi Arabia. Email: rehmani.arshad@gmail.com

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ABSTRACT

Alternative medicines or formulation based on natural sources are good option in diseases cure and prevention. *Ficus carica* is member of Moraceae family and its health management properties have been mentioned in religious books and traditional medicines. It holds various constituents including phenolic compounds, minerals and vitamins and such ingredient shows role in disease cure. Studies based on *in vivo* and *in vitro* reported that figs fruits, stem, leaves, and latex have health management effect through antioxidant, anti-inflammatory effects, antimicrobial, anticarcinogenic, and anti-inflammatory effects. Moreover, an inverse correlation between figs use and development of disease has been noticed. Despite its implications in disease management, little is known about their mechanism of action. In this review, efforts are made based on *in vivo* and *in vitro* studies to illuminate the role of *F. carica* leaves and fruits in the prevention of diseases.

Keywords: *Ficus carica*, Antioxidant, Anti-inflammatory effect, Health management.© 2017 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2017.v10i6.17832>**INTRODUCTION**

Medicinal plants and their constituents have been extensively used as health promoting effect. Epidemiological studies have proven that natural product has disease cure potentiality through modulation of physiological and biological activities. Medicinal plants and its constituents have confirmed their role in diseases prevention and treatment [1,2]. In this vista, *Ficus carica* and its ingredients have confirmed diseases preventive ability.

F. carica is generally known as fig, and it is a small deciduous tree native to Asia Minor, Persia, Syria and the Mediterranean region [3]. *Ficus* is a member of Moraceae family which cover one of the chief genera of angiosperms with approximately 800 species of trees, shrubs, hemiepiphytes, climbers, and creepers in the tropics and subtropics [4]. A country such as Turkey, Egypt, Morocco, Spain, Greece, California, Italy, and Brazil are chief producers and also in hot, dry summers and mild winters countries [5]. Its health beneficial effect has been mentioned in religious books including Bible and Quran. In sura al-Teen of Quraan, the medicinal benefit is discussed as "I swear by the fig and the Olive" (Sura no. 95 verse no. 1). Moreover, its health promoting effect has mentioned as Hazrat Abu Darda (Radiallaho Anho) narrates Prophet Mohammad (Peace Be Upon Him) said, "Eat fig, it cure the piles and is useful in rheumatism" [6]. Leaves of figs traditionally used in the management of diseases such as vitiligo, diabetes, coughs, asthma, constipation, and gingivitis [3,7]. Moreover, roots used in the treatment of leukoderma and ringworms and fruits also shows role as antipyretic, purgative, aphrodisiac properties, and have shown to be valuable in inflammations and paralysis [8,9]. A study has summarized the various activities of *F. carica* [10], and another previous studies reported that latex and its derivatives have been revealed to suppress the growth of transplanted and spontaneous tumors [11,12]. In this review, we focused the health beneficial effects of as antioxidant, anti-inflammatory effects, and antimicrobial, anticarcinogenic, and anti-inflammatory effects.

BOTANICAL DESCRIPTION OF F. CARICA

Fig (*F. carica* L.) is one of the traditional Mediterranean species belongs to family of Moraceae. Tree of *F. carica* L is generally tall as 15-20 ft that has numerous spreading branches and a trunk more than 7 ft in

diameter [13]. Its leaves are long with multi-lobes. *Ficus* cover one of the major genera of angiosperms with approximately 800 species of trees, shrubs, hemiepiphytes, climbers, and creepers in the tropics and subtropics worldwide [4]. Detailed botanical information is discussed below [14].

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

INGREDIENTS OF F. CARICA

F. carica contains various valuable constituents in fruits and leaves (Table 1). The majority species of *F. carica* hold constituents such as phenolic compounds, organic acids, and volatile compounds [15,16]. Fruits constitute various valuable ingredients including cyanidin-3-O-glucoside, cyanidin-3-Orhamnoglucoside, saturated fat, cholesterol, and sodium, insoluble sugars, protein, vitamin A, vitamin C, calcium, iron [17]. The study based on phytochemical analysis confirmed that the aqueous extract of ripe dried fruit contain alkaloids, flavonoids, coumarins, saponins, and terpenes [18,19]. The leaves have been reported to have furanocoumarins including psoralen, bergapten, xanthotoxin [20] and triterpenes such as calotropenyl acetate and lupeol acetate [21]. The other valuable ingredients are phenolics, anthocyanins, fructose, glucose, and sucrose were identified from the figs [22] and the previous finding reported that fruit has phytosterols [23].

ROLE OF F. CARICA IN DISEASES PREVENTION

F. carica hold various constituents and ingredients shows pivotal role in the disease management (Table 2) and its role is explained as.

Antioxidant activity

Medicinal plants and their ingredients show therapeutics role in diseases cure and prevention due to the rich source of antioxidant [24]. In this regards, *F. carica* shows health promoting effect due to the

Table 1: Chief ingredients of *F. carica*

Parts of <i>F. carica</i>	Constituents	References
Fruits	Cyanidin-3-O-glucoside, cyanidin-3-Orhamnoglucoside, saturated fat, cholesterol, sodium, insoluble sugars, protein, vitamin A, vitamin C, calcium, iron	[18]
Ripe dried fruit	Alkaloids, flavonoids, coumarins, saponins, and terpenes	[19,20]
Dried seeds	Fixed oil including fatty acids	[15]
Leaves	Furanocoumarins including psoralen, bergapten, xanthotoxin, triterpenes such as calotropenyl acetate and lupeol acetate	[21,22]
Leaves	3-O- and 5-O-caffeoylquinic acids, ferulic acid, quercetin-3-O-glucoside, quercetin-3-O-rutinoside and psoralen	[15]

F. carica: *Ficus carica*

Table 2: Pharmacological activity of different parts of *F. carica*

Plants parts	Pharmacological activities	Finding/outcome of the study	References
Fruits	Antioxidative	Extract showed effective scavenging activities	[26]
Branches	Antioxidant and anti-inflammatory	Study finding demonstrated that branches of figs possessed pharmacological activity and might be useful for developing antioxidant or anti-inflammatory agents	[27]
Leaves	Anti-inflammatory	Study result confirmed that extract showed anti-inflammatory effect, that was 75.90% in acute inflammation and in chronic study it was 71.66% reduction in granuloma weight	[28]
Leaves	Anti-pyretic	Extract showed significant dose-dependent reduction in normal body temperature	[31]
Latex	Anticancer	Inhibition of growth of stomach cancer cell line was noticed	[30]
Latex	Anticancer	Latex and its derivatives have been revealed to suppress the growth of transplanted and spontaneous tumors	[11,12]
Fig latex	Anticancer	6-O-acyl-beta-D-glucosyl-beta-sitosterols showed inhibitory effects on proliferation of cancer cell lines	[32]
Stem bark	Anti-diabetic	Extract showed significant protection and lowered the blood glucose levels to normal	[35]
Leaves	Anti-diabetic	Aqueous extract showed hypoglycemic activity in treated versus non-treated diabetic rats	[36]
Leaves	Hepato-protective	Leaves extract demonstrated important hepatoprotection dose-dependent manner	[38]
Latex	Antibacterial	Ethyl acetate extract showed inhibition effect on the multiplication of bacteria species and for the opportunist pathogenic yeasts	[43]
Latex extract	Anti-angiogenic	Results of the study confirmed that latex extract could inhibit proliferation and capillary tube	[46]
Leaves	Anti-angiogenic	Finding observed that the extract dose dependently inhibited the tube formation of HUVECs	[47]
Latex	Antiviral	Simultaneous addition of F-latex and CpHV-1 to monolayers of MDBK cells resulted in a significant reduction of CpHV-1 titers	[45]
Fruits	Antispasmodic	Study results showed the presence of spasmolytic activity in the ripe dried fruit mediated through the activation of K ⁺ ATP channels	[49]
Leaves	Immunomodulatory	Administration of extract remarkably ameliorated both cellular and humoral antibody response	[50]
Latex	Anthelmintic	Results of the study confirmed that latex administered in was effective in the removal of <i>S. obvelata</i>	[51]
Leaves	Anti-nematicidal	Finding result confirmed leaf extract showed the strongest nematicidal activity	[52]
Leaves	Sperm parameters	Leaf extracts improved sperm count, non-progressive motility of spermatozoa, and gonadosomatic index	[55]
Fruits	Nephroactivity protective	HEFC supplementation ameliorated GM-induced specific metabolic alterations and oxidative damage due to its intrinsic biochemical/antioxidant properties	[60]
Leaves	Inhibitor of osteoclastogenesis	Study results showed that hexane soluble fraction is a potent inhibitor of osteoclastogenesis	[61]
Leaves	Effect on ischemia/reperfusion injuries	Leaf extract decreased number of VEBs, incidence and duration of rev VF with clear reduction in infarct size and infarct volume	[62]

VF: Ventricular fibrillation, VEBs: Ventricular ectopic beats, HUVEs: Human umbilical vein endothelial cells, *F. carica*: *Ficus carica*

rich source of antioxidant. A study was performed to determine the antioxidant activity, and results of the study revealed that antioxidant activity was found to be very good [25]. Antioxidative activities of water extract and crude hot-water soluble polysaccharide (PS) from fruit was investigated and finding confirmed that both water extract and crude hot-water soluble PS showed prominent scavenging activities with the effective concentration values of 0.72 and 0.61 mg/ml, respectively [26]. Furthermore, The PS also showed a significant increase in the clearance rate of carbon particles and serum hemolysin level of normal mice [26].

Another study was carried out based on preparation of ethanol extract and its ethyl acetate, hexane, butanol, and water fractions and examined for scavenge free radicals potentiality. Results data revealed that the ethyl acetate fraction hold the largest amount of phenolic compounds and showed the highest free radical scavenging activity [27].

Anti-inflammatory effect

Inflammation is a natural response of body against microorganism and toxic materials. Various medicinal plants have proven their role as anti-

inflammatory agent without any severe side effect. Experiment was performed based on different types extract of fig branches to examine abilities to scavenge free radicals and inhibit inflammatory reactions. Finding of the study revealed that the ethyl acetate fraction contained the largest amount of phenolic compounds and showed the highest free radical scavenging activity. Furthermore, all fraction of fig, especially ethanol extract and the ethyl acetate and hexane fractions inhibited nitric oxide production in RAW264.7 cells [27]. Another experiment was performed to check the effect of anti-inflammatory activity of leaves through different types of extract. Finding of the study demonstrated that ethanolic extract showed maximum anti-inflammatory effect that was 75.90% in acute inflammation and in chronic study showed 71.66% reduction in granuloma weight [28]. Furthermore, extract such as petroleum ether, chloroform, and ethanol showed significantly reduced edema [28].

Antipyretic effect

Commonly used antipyretic drugs are toxic to liver cells and cause complications. Antipyretic effect of ethanol extract of leaves was evaluated and extract at doses of 100, 200, and 300 mg/kg body wt. showed significant dose-dependent reduction in normal body temperature and yeast-provoked elevated temperature [29].

Anti-cancer activity

F. carica shows role as antitumor through inhibitory effects on proliferation of various cancer cell lines. A study was carried out to check the anticancer effect of latex in different concentration and finding showed that 5 mg/ml concentration had the greatest effect in inhibition of stomach cancer cell line growth [30]. Another study reported that latex and its derivatives have been showed to suppress the growth of transplanted and spontaneous tumors [11,12]. Cytotoxicity of fruit and leaf extracts as well as the latex on HeLa cell line was examined and results showed that latex and different extracts could reduce the viability of HeLa cells at concentrations as low as 2 µg/mL in a dose-dependent manner [31]. A mixture of 6-O-acyl-beta-D-glucosyl-beta-sitosterols was isolated as an effective cytotoxic agent from fig latex and result confirmed *in vitro* inhibitory effects on proliferation of various cancer cell lines [32]. Antiproliferative activity of *F. carica* (fig) latex (FCL) and the effect of the FCL-temozolomide (TMZ) combination were examined in the cell lines such as T98G, U-138 MG, and U-87 MG glioblastoma multiforme (GBM) and data of the results showed latex FCL causes cell death in GBM cells with different responses to TMZ, and this effect is synergistically increased in combination with TMZ [33]. Anticancer effect of fig tree latex on human cancer cells was evaluated and results confirmed that there was a significant change in 10 mg/ml treatment of latex after 72 hrs on esophageal cancer line and 10 mg/ml was the optimum concentration in the inhibition of cell line growth [34].

Antidiabetic activity

Experiment-based studies have shown that *F. carica* and its extract have antidiabetic activity. Antidiabetic effect of methanolic extract of stem bark was carried out and finding confirmed that extract showed significant protection and lowered the blood glucose levels to normal [35]. Another study was performed to evaluate the hypoglycemic effect of an aqueous extract of leaves. Findings of the study showed that extract has a clear hypoglycemic activity in treated versus non-treated diabetic rats [36].

Hepatoprotective effect

Liver-related diseases are major health problem worldwide and associated with considerable morbidity and mortality. Products based on plants or natural products are popular in the treatment of liver diseases. Experiment was performed on leaves extract and antihepatotoxic activity was tested with 50 mg/kg of rifampicin. Results of the study confirmed that there was significant reversal of biochemical, histological and functional changes, shows potential hepatoprotective activity [37]. Other study was carried out on ethanolic extract leaves to check the hepatoprotective activity and results showed that extract demonstrated significant hepatoprotection dose-

dependent manner [38]. Another study finding confirmed that stem extract treatment prior to methanol intoxication has noteworthy role in protecting animals from hepatic oxidative damage [39]. Hepatoprotective role of latex against lead acetate-induced oxidative stress was evaluated. Outcome of the study revealed that latex noticeably attenuated the prior lead-induced biochemical alterations in serum and liver tissues and histological as well as cellular changes [40].

Hypolipidemic effect

The study was performed on extract from leaves, could be used to decrease hepatic triglyceride (TG) content and secretion of TG and cholesterol (TC) from the liver. Livers with high abdominal fat pad ratios were extracted, sliced, and cultured with increasing concentrations of extract, insulin and both of them. Whereas insulin considerably increased TG secretion, TG content and TC secretion) higher than the basal levels, when full-time equivalent was added these effects were drastically reduced to the basal levels in a concentration-dependent manner [41].

Antimicrobial effect

The worldwide emergence of multi-drug resistant bacteria is increasingly and limiting the effectiveness of drugs and significantly causing failure of treatment [42]. However, there is an urgent need to investigate an alternative source with established antimicrobial activity to overcome such problem. Experiment was performed based on different extract of latex to investigate antimicrobial properties against bacteria species and strains of fungi. Finding of the study confirmed that methanolic extract had no effect against bacteria except for *Proteus mirabilis* [43]. Furthermore, ethyl acetate extract showed inhibition effect on the multiplication of five bacteria species and for the opportunist pathogenic yeasts, ethyl acetate and chlorophormic fractions showed strong inhibition [43]. Another study was carried out to investigate the antimicrobial activity of methanol extract against oral bacteria and results revealed that extract showed a strong antibacterial activity against oral bacteria [44]. The extract was screened for antibacterial activity and outcome of study demonstrated that zone of inhibition against *P. mirabilis* and *Bacillus subtilis* [24]. Another experiment was made to confirm the ability of latex to interfere with the infection of caprine herpesvirus-1 *in vitro*. Finding demonstrated that simultaneous addition of latex and CpHV-1 to monolayers kidney cells resulted in a noteworthy reduction of CpHV-1 titers 3 days post-infection and this effect was comparable to that induced by acyclovir [45].

Anti-angiogenic effect

Anti-angiogenic and anti-proliferative activity of latex extract was investigated using human umbilical vein endothelial cells (HUVECs). Results of the study confirmed that extract could inhibit proliferation and capillary tube [46]. Other study was carried out to evaluate the anti-angiogenic effects base on HUVECs and finding observed that the extract inhibited the tube formation of HUVECs [47]. Anti-angiogenesis effect of leaves extract in an air pouch model of inflammation was evaluated. Result revealed that the extract had significant antioxidant activity with total phenolic content of 11.70 mg gallic acid equivalents/100 g dry sample [48]. Furthermore, it significantly decreased the production of tumor necrosis factor- α , prostaglandin E₂, and vascular endothelial growth factor, whereas angiogenesis was significantly inhibited through all administered doses [48].

Antispasmodic activity

An experiment was performed based on aqueous-ethanolic extract to study the antispasmodic effect. Outcome of the finding showed the presence of spasmolytic activity in the ripe dried fruit possibly mediated through the activation of K⁺ ATP channels [49].

Immunomodulatory effect

Immunomodulatory effect was evaluated and results of the study confirmed that administration of extract remarkably ameliorated both cellular and humoral antibody response [50].

Anthelmintic activity

Anthelmintic activity of the latex was examined and results confirmed that administered in doses of 3 ml/kg/day was capable in the removal of *Syphacia obvelata* (41.7%) [51].

Nematicidal activity

The methanol extracts from forty plant species were screened to evaluate the nematicidal activity against *Bursaphelenchus xylophilus*, *Panagrellus redivivus*, and *Caenorhabditis elegans* nematodes. Outcome of the study confirmed that leaf extract showed the strongest nematicidal activity causing 74.3%, 96.2%, and 98.4% mortality, respectively [52].

Effect on Alzheimer's disease

Experiment was made to evaluate the effect of dietary supplementation with 4% figs on the memory, anxiety, and learning skills and study results showed that Tg mice fed with control diet without figs showed significant memory deficits, increased anxiety-related behavior, and motor coordination compared to the wild-type control mice fed same diet, and Tg mice fed on 4% fig diet supplementation [53]. Another study was made to examine the beneficial effects of dietary supplements containing pomegranate, figs, or the dates on suppressing inflammatory cytokines. Finding confirmed that increased levels of inflammatory cytokines and eotaxin activity were decreased by administration of the diet supplements [54].

Effect on sperm parameters

Experiment was made based to investigate effect of leaf extracts in sperm parameters and testis intoxicated and results of the study showed that extracts improved sperm count, non-progressive motility of spermatozoa, and gonadosomatic index in treated testes [55]. Earlier study concluded that ethanolic extract showed the aphrodisiac activity and this action was dose dependent [56].

Nephroprotective effect

Medicinal plant or product from the natural source has confirmed role as nephroprotective. Earlier finding has proven nephroprotective effect of *Mimosa pudica* root, *Phyllanthus acidus* leaves and *Carica papaya* [57-59]. Protective effect of hydroalcoholic extract on GM-induced renal proximal tubular damage was evaluated and results revealed extract alone increased catalase concentration, glutathione content and decreased malondialdehyde level [60]. Furthermore, extract supplementation ameliorated GM-induced specific metabolic alterations and oxidative damage [60].

Effect on osteoclastogenesis

Another study results showed that hexane soluble fraction of the fig is a potent inhibitor of osteoclastogenesis in RANKL-stimulated RAW264.7 cells and in bone marrow-derived macrophages [61].

Effect on ischemia/reperfusion injuries

Experiment was made to evaluate antioxidant activity and leaves extract effect on ischemia/reperfusion injuries. Outcome of the study revealed that extract showed antioxidant activity and extract decreased number of ventricular ectopic beats, incidence and duration of Rev ventricular fibrillation with clear reduction in infarct size as well as infarct volume [62].

CONCLUSION

Treatment based on allopath is expensive and also shows adverse complications either in short term or long term. Popularity of alternative medicine and natural products is increasing worldwide due to inexpensive and health promoting activities. In this vista, *F. carica* Linn generally known as Fig is a small deciduous tree and it holds wide-ranging diseases management activities due to a rich source of antioxidant activity. Experimentation based on different types of extract has confirmed their role in diseases cure. Detailed study based on animal model and clinical trials should be conducted to know the safe dose and mode of action in health management.

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