IOSR Journal Of Pharmacy *www.iosrphr.org*
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 7, Issue 3 Version. 1 (March 2017), PP. 33-48

Nutritional and pharmacological importance of *Ficus carica* - A review

Prof Dr Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, Thi qar University, Iraq.

Abstract:- The preliminary phytocemical analysis showed that the fruits of *Ficus carica* contained alkaloids, tannins, glycosides, flavanoids, saponins, coumarins, sterols, terpenes carbohydrates, phenols, essential oil, volatile oil, proteins and minerals. The previous pharmacological studies revealed that *Ficus carica* possessed antibacterial, antiviral, antiparasitic, antioxidant, anticancer, antimutagene, anti-angiogenic, antiinflammatory, antipyretic, antidiabetic, antiplatelet, reproductive, endocrine, immunological, dermatological, hypolipidemic, nootropic, antispasmodic, antidiarrheal, anti- warts, nephro- and hepato- protective effects. The current paper reviewed the chemical constituents, nutritional and pharmacological importance of *Ficus carica.*

Keywords: *Nutrition, pharmacology, constituents, Ficus carica*

I-INTRODUCTION:

During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world [1]**.** Plants generally produce many secondary metabolites which were constituted an important source of many pharmaceutical drugs [2-50]. Preliminary phytocemical analysis showed that the fruits of *Ficus carica* contained alkaloids, tannins, glycosides, flavanoids, saponins, coumarins, sterols, terpenes carbohydrates, phenols, essential oil, volatile oil, proteins and minerals. The previous pharmacological studies revealed that *Ficus carica* possessed antibacterial, antiviral, antiparasitic, antioxidant, anticancer, antimutagene, anti-angiogenic, antiinflammatory, antipyretic, antidiabetic, antiplatelet, reproductive, endocrine, immunological, dermatological, hypolipidemic, nootropic, antispasmodic, antidiarrheal, anti- warts, nephro- and hepato- protective effects. This review will shed light on the chemical constituents, nutritional and pharmacological importance of *Ficus carica.*

Synonyms:
Caprificus insectifera Gasp., *Caprificus leucocarpa* Gasp., *Caprificus oblongata* Gasp., *Caprificus pedunculata* (Miq.) Gasp., *Caprificus rugosa* (Miq.) Gasp., *Caprificus sphaerocarpa* Gasp., *Ficus albescens* Miq., *Ficus burdigalensis* Poit. & Turpin, *Ficus caprificus* Risso, *Ficus carica* var. caprificus Risso, *Ficus carica* var. domestica Czern. & Rav., *Ficus carica* var. riparium Hausskn., *Ficus colchica* Grossh., *Ficus colombra* Gasp., *Ficus communis* Lam., *Ficus deliciosa* Gasp., *Ficus dottata* Gasp., *Ficus hypoleuca* Gasp., *Ficus hyrcana* Grossh., *Ficus kopetdagensis* Pachom., *Ficus latifolia* Salisb., *Ficus leucocarpa* Gasp., *Ficus macrocarpa* Gasp., *Ficus neapolitana* Miq., *Ficus pachycarpa* Gasp., *Ficus pedunculata* Miq., *Ficus polymorpha* Gasp., *Ficus praecox* Gasp., *Ficus regina* Miq., *Ficus rugosa* Miq. and *Ficus silvestris* Risso [51].

Faxonomic classification:
Kingdom: Plantae, **Subkingdom**: Viridiplantae, **Infrakingdom**: Streptophyta, **Superdivision**: Embryophyta, **Division**: Tracheophyta, **Subdivision**: Spermatophytina, **Class**: Magnoliopsida, **Superorder**: Rosanae, **Order**: Rosales, **Family**: Moraceae, **Genus***: Ficus*, **Species**: *Ficus carica* [52].

Common names:
Arabic: teen; **Chinese:** wu hua guo, **English:** common fig, fig**; French:** carique**,** figuier commun; **German:** echte Feige, Essfeige, Feigenbaum; **India**: anjir; **Italian:** fico; **Korean:** muhwagwanamu ; **Portuguese:** figueira, figo, figueira-comum, figueira-da-europa , figueira-do-reino; **Spanish:** higo, higuera común; **Swedish:** fikon**,** getfikon [53]**.**

Distribution:
It was native to Africa, Asia and Europe, it was distributed in **Africa**: (Algeria, Morocco, Tunisia and Egypt); **Asia: (**Azerbaijan, Tajikistan, Turkmenistan, Afghanistan, Pakistan, Iran; Iraq, Palestine, Jordan, Lebanon, Syria and Turkey); **Europe**: (Greece, Italy and Spain); **Australia**: (Australia and Zealand); **Northern America:** United States and **Southern America:** Ecuador. Now, it was widely cultivated in tropical and subtropical areas [53].

Description:

A large shrub to small deciduous tree, 5-9 m tall with several spreading branches from a short, rough trunk. Bark smooth, grey or dull white, young twigs glabrous or softly hairy. Leaves with glabrous to tomentose up to 12 cm long grooved petiole; lamina variable in shape and size, broadly ovate to nearly orbicular, (4-) 5-15 (-20) cm long, (3.5-) 5-15 (-18) cm broad, undivided or obscurely palmatifid to mostly palmatipartite, lobes spathulate with entire to apically few-dentate margin, 5-costate at the cordate base, margins undulate-dentate or dentate-crenate, acute to ± obtuse, scabrous above, densely soft hairy beneath especially on nerves, lateral nerves 6-8 (-9) pairs, intercostals ascending-parallel; stipules ovate-lanceolate, 10-12 mm long, hairy to glabrescent Hypanthodia axillary solitary or paired, borne on upto 3 cm long peduncles, pyriform to globose, 1.5-2 cm in diameter, subsessile to sessile, subtended by 3, broadly deltoid basal bracts, apical orifice closed by 4-5, broadly deltoid, ciliate imbricate bracts. Male flowers: sepals usually 4, united, lobes lanceolate; stamens 4, filaments long with oval, exserted anthers. Female flowers: pedicellate, sepals 4, lobes lanceolate-oblong: ovary with lateral style, stigma entire or 2-fid. Figs usually pyriform-obovoid, 2-5 (-8) cm in diameter, glabrous or shortly hispid, yellowish to brownish violet [54-55].

Traditional uses:

Ficus carica was emollient, demulcent, cooling, laxative and nutritive. The edible fruits of *Ficus carica* were traditionally used for treatment of hemorrhoids, insect stings, gout, ulcers, and skin infections such as warts and viruses. Fruits were usually recommended for people suffering from constipation, nutrient for pregnant women and for mental and physical exhaustion. They were considered as antipyretic, tonic, purgative, alexiteric, aphrodisiac, lithontriptic, anti-inflammatory, expectorant, diuretic, and used for treatment of pharyngitis, gastritis, bronchitis, irritative cough, weakness, paralysis, thirst, diseases of the liver and spleen, pain in the chest, to cures piles, to stimulate growth of hair, and for leprosy and nose bleeding. The root was used as tonic, for leucoderma and ringworm [56-60].

II-CHEMICAL CONSTITUENTS:

Preliminary phytocemical analysis showed that the fruits contained alkaloids, tannins, glycosides, flavanoids, saponins, coumarins, sterols, terpenes carbohydrates, phenols and proteins [61-63]. Total phenolics of fig fruits was 10.90 µg GAE/mg, total flavonoids 2.75 µg CE/ mg, crude alkaloid 9.6% /100g dry weight and saponins 0.59 g/100g dry weight [64]. The phenolic contents of five different fig cultivars (Šaraguja, Termenjača, Crnica, Bjelica and Bružetka bijela) were determined as 7.24 to 11.17 mg CAE/g of dry extract [65]. Nutritional analysis of *Ficus carica* leaves sowed that they contained: moisture: 65.90%, ash 5.30%, proteins 5.90%, lipids 0.81%, fiber 4.50% and carbohydrates 17.50% [66]. While, dried fig fruit contained: energy 317.78 Kcal/100g, total carbohydrate 73.50%, fat 0.56%, protein 4.67%, fiber 3.68%, moisture 16.63% and ash 4.65% [67]. Mineral concentration (µg/g) of Hungarian origin *Ficus carica* fructus and folium respectively: Al: 24.24±14.72 and 105.5±1.98, B: 50.44±11.28 and 130.1±5.29, Ba: 6.60±1.09 and 7.97±0.09, Ca: 6006±613 and 27611±152, Cd: 0.61±0.01 and 0.64±0.00, Co: 0.69±0.33 and 0.41±0.01, Cr: 1.34±0.49 and 1.25±0.07, Cu: 5.66±0.00 and 8.57±0.13, Fe: 41.62±3.47 and 182.6±3.06, K: 13892±415 and 16000±234, Mg: 1381±186 and 3565±174, Mn : 7.76±0.01 and 27.02±1.31, Mo: 0.54±0.17 and 0.84±0.09, Na: 88.49±10.83 and 136.6±7.9, Ni: 1.74±0.07 and 1.70±0.03, P: 1054±44 and 1285±31, Pb: <detection limit and 0.99±0.27, S: 536.1±7.5 and 1150±67, Si: 157.4±40.4 and 106.9±16.3, Sn: 1.24±0.51 and 0.72±0.21, Sr: 20.12±2.89 and 64.37±4.20, Ti: 1.03±0.66 and 3.43±0.24, V: 0.38±0.02 and 9.80±0.39 and Zn: 0.58±0.00 and 14.27±0.80. While, mineral concentration (µg/g) of Italian origin *Ficus carica* fructus and folium respectively: Al: 131.8±5.1 and 34.36±3.60, B: 84.57±4.30 and 66.50±4.37, Ba: 13.46±0.06 and 10.70±0.30, Ca : 27531±137 and 18623±712, Cd: 0.65±0.01 and 0.63±0.01, Co: 0.41±0.01 and 0.39±0.01, Cr: 2.46±0.31 and 1.44±0.40, Cu: 4.84±0.21 and 4.21±0.00, Fe: 153.22±5.14 and 28.12±4.60, K: 24786±280 and 13902±879, Mg: 3519±70 and 2202±285, Mn: 22.69±0.61 and 5.06±0.82, Mo: 0.87±0.01 and 0.49±0.10, Na: 239.4±8.3 and 87.40±18.32, Ni: 1.44±0.19 and 0.73±0.01, P: 945.9±3.1 and 960.7±107.5, Pb: 1.12±0.17 and 2.90±2.66, S: 819.3±37.6 and 356.7±26.4, Si: 183.6±31.6 and 169.4±6.3, Sn: 0.91±0.22 and 1.49±0.49, Sr: 142.4±8.2 and 70.44±4.71, Ti: 4.70±0.38 and 0.66±0.33, V: 0.82±0.01 and 14.37±0.28, and Zn: 0.38±0.01 and 6.33±0.68 [68].The phenolics profiles of the leaves, pulps and peels of two white varieties of *Ficus carica* were determined by HPLC/DAD and HPLC/UV. All samples presented a similar phenolic profile composed of 3-O- and 5-O-caffeoylquinic acids, ferulic acid, quercetin-3-O-glucoside, quercetin-3-O-rutinoside, psoralen and bergapten [69]. Extracts of darker varieties showed higher contents of phenolics compared to lighter colored varieties. Fruit skins contributed most of the above phenolics compared to the fruit pulp. Antioxidant capacity correlated well with the amounts of polyphenols and anthocyanins (R^2 = 0.985 and 0.992, respectively). In the dark-colored Mission and the red Brown-Turkey varieties, the anthocyanin fraction contributed 36 and 28% of the total antioxidant capacity, respectively. C3R (cyanidin-3-O-rutinoside)

contributed 92% of the total antioxidant capacity of the anthocyanin fraction. Fruits of the Mission variety contained the highest levels of polyphenols, flavonoids, and anthocyanins and exhibited the highest antioxidant capacity [70].Six organic acids were identified in the fig leaves including: oxalic, citric, malic, quinic, shikimic, and fumaric acids [69].Ficins, cysteine endoproteolytic proteases were isolated from *Ficus carica* latex, these included ficins A, B, C, D1, D2 and E [71-72].Many volatile compounds were isolated from *Ficus carica* fructus included 2,3-butane-diol, tetramethyl-decane, trimethylundecane, octadecane, carvacrol, ß-Caryophyllene, caryophyllene-oxid and apiol [68].The volatile profile of fresh fruits (pulp and peel) and leaves of Portuguese *Ficus carica* white (Pingo de Mel and Branca Tradicional) and dark (Borrasota Tradicional, Verbera Preta and Preta Tradicional) varieties revealed the presence of fifty-nine compounds including (aldehydes, alcohols, ketones, esters, monoterpenes, sesquiterpenes, norisoprenoids). The highest diversity of compounds was found in leaves(40), followed by pulps (30) and peels (27), Pulps and peels were distinguished from leaves by their abundance of monoterpenes and aldehydes. All varieties presented a similar volatile profile, although some differences between white and dark varieties were noticed. The volatile compounds isolated from fresh fruits (pulp and peel) of *Ficus carica* were included Aldehydes: 3-Methyl-butanal, 2-Methyl-butanal, (E)-2-Pentenal, Hexanal, (E)-2-Hexenal; Alcohols: 1-Penten-3-ol, 3-Methyl-1-butanol, 2-Methyl-1-butanol, 1-Heptanol, Benzyl alcohol, (E)-2-Nonen-1-ol, Phenylethyl alcohol; Ketones: 3-Pentanone; Esters: Methyl butanoate, Methyl hexanoate, Hexyl acetate, Ethyl benzoate, Methyl salicylate; Monoterpenes: Limonene, Menthol; Sesquiterpenes: α-Cubenene, α –Guaiene, α –Ylangene, Copaene, β-Bourbonene, β –Elemene, α –Gurjunene, β –Caryophyllene, β –Cubebene, Alloaromadendrene, α –Caryophyllene, s-Muurolene, Germacrene D, (+)-Ledene, s-Elemene, s-Cadinene, a-Muurolene; Norisoprenoid: β –Cyclocitral; and Miscellaneous compounds: s-Nonalactone and Psoralen. On the other hand, sesquiterpenes constituted the main class of compounds in *Ficus carica* leaves, except for (Verbera Preta) variety, in which psoralens were the predominant compounds. Germacrene D, β caryophyllene and s-elemene were the major sesquiterpenes in leaves of all varieties [64].The compounds isolated from dried fig fruit extract were included Dimethyl Sulfoxide, 1,2-diethyl- Cyclooctane, 5-(hydroxymethyl)- 2-Furancarboxaldehyde, (1-methylethyl)- Cyclohexane, 1-Dodecene, Tetradecane, octyl-Cyclohexane, 1-Nonadecene, Hexadecane, Ethyl N-(2-methylphenyl) carbamate, N-[9-borabicyclo[3.3. 1]non-9-yl]-Propylamine, 8-Pentadecanone, 3-(m-aminobenzoyl) -2-methyl-Propionic acid, 1-Nonadecene, 1-Octadecene, Fluoroatropine, Isopropyl Myristate, 6,10,14-trimethyl 2-Pentadecanone, 1,1'-(1,4-butanediyl)bis-Cyclohexane, 8-Octadecanone, Ethyl ester Pentadecanoic acid, Hexadecyl-Oxirane, Methyl ester Hexadecanoic acid, Dibutyl phthalate, (E)- 5-Eicosene, Ethyl ester Hexadecanoic acid, Methyl ester Hexadecanoic acid, n-Hexadecanoic acid, Ethyl Cyclooctadecane, 10-Nonadecanone, Cyclohexadecane, Methyl ester 10,13-Octadecadienoic acid, (Z,Z,Z)- methyl ester -9,12,15-Octadecatrienoic acid, Methyl ester Octadecanoic acid, Oleic Acid, Linoleic acid ethyl ester, (Z,Z,Z)-ethyl ester 9,12,15-Octadecatrienoic acid, (E)- 5-Eicosene, Isoamyl laurate, Heptadecane, Oleic Acid, 16-Diepoxyhexadecane1, (Z)- 9-Octadecena, Z-5-Nonadecene, 2-hydroxy-1-(hydroxymethyl)ethyl ester Hexadecanoic acid, Diis ooctyl ester1,2-Benzenedicarboxylic acid, Ethyl ester, Nonadecanoic acid, 2,3-dihydroxypropyl ester-9-Octadecenoic acid, 9,12-Octadecadienoic acid, 2,6,10,15,19, 23 -hexamethyl-2,6,10,14,18,22-Tetracosahexaene, Eicosane, Gamma-Tocopherol, 9-Nonadecene, Octacosane, Vitamin E, Campesterol, Stigmasterol, Oxime, N-(2-trifluoromethylphenyl)- Pyridine- 3-carboxamide, Gamma-Sitosterol, 24(28)-dien-3-ol, (3beta24Z)- Stigmasta, Beta-Amyrin, 2 Naphthalene ,1,2,3,5,6,7,8,8a-octa hydro-1,8a-dimethyl-7-(1-methylethenyl), 5-Bromo-4-oxo-4,5,6,7-tetrahydrobenzofurazan, Acetate,(3beta)- Lanosta-8,24-dien-3-ol, 3alpha-12-Oleanen-3-yl acetate, Acetate,(3beta)- Lanosta-9(11),24-dien-3-ol and Acetate,(3beta,21beta)- A-Neogammacer- 22(29)-en-3-ol [64].

III-PHARMACOLOGICAL EFFECTS:

Antibacterial and antifungal effect:

The antimicrobial activity of methanol extract of figs was studied against oral bacteria [*Streptococcus mutans*(ATCC 25175), *Streptococcus sanguinis* (ATCC 10556), *Streptococcus sobrinus* (ATCC 27607), *Streptococcus ratti* (KCTC 3294), *Streptococcus criceti* (KCTC 3292), *Streptococcus anginosus* (ATCC 31412) and *Streptococcus gordonii* (ATCC 10558), *Aggregatibacter actinomycetem comitans* (ATCC 43717), *Fusobacterium nucleatum* (ATCC 51190), *Prevotella intermedia* (ATCC 49046) and *Porphyromonas gingivalis* (ATCC 33277)]. The methanolic extract showed (MICs: 0.156 to 5 mg/ml and MBCs: 0.313 to 5 mg/ml) against the tested oral bacteria. The combination of methanolic extract and ampicillin or gentamicin showed synergistic effect against oral bacteria [73]. The antibacterial effects of different polarities crude extract from the leaves of *Ficus carica* (250-2000 µg/ml) were studied against *Staphylococcus aureus*, *Escheichia coli* and *Pseudomonas* sp by agar disc diffusion method. The dried leaves were macerated in absolute ethanol and the crude extract was defatted with ethanol-water, then the defatted hydro alcoholic crude extract was extracted with hexane, chloroform and ethyl acetate. Hydroalcoholic crude extract and its derived fractions display

moderate antimicrobial potential against *Staphylococcus aureus*, *Escheichia coli* and *Pseudomonas* sp, in the range of 0%–13% [74]. Ethanolic leaf extract and latex of fig (*Ficus carica*) were investigated for their antimicrobial activity against six bacterial strains, two Gram positive (*Staphylococcus aureus* and *Streptococcus pyogenes*) and four Gram negative (*Klebsiella pneumonae*, *Pseudomonas aeruginosa*, *Salmonella typhi* and *Escherichia coli*), and three fungal strains (*Candida albicans*, *Fusarium oxysporum* and *Aspergillus nigar*), using agar well diffusion method for determination of inhibitory zone diameters (IZD). The ethanolic extract of leaves exhibited strong activity against *Staphylococcus aureus* (13 mm), *Salmonella typhi* (14 mm), and *Fusarium oxysporum* (16 mm), whereas The latex showed higher activity against *Staphylococcus aureus*, *Salmonella typhi* and *Streptococcus pyogenes* (15, 15 and 14mm respectively), and *Aspergillus nigar* (18 mm). *Klebsiella pneumonae* and *E. coli* seemed to be resistant to both extract which showed (8 and 9 mm) for leafe extracts and (11 and 10 mm) for ethanolic leaf extract and latex respectively [75]. Methanolic, hexanoïc, chloroformic and ethyl acetate extracts of *Ficus carica* latex were investigated for their *in vitro* antimicrobial proprieties against five bacteria species and seven strains of fungi. The methanolic extract had no effect against bacteria except against *Proteus mirabilis*, while the ethyl acetate extract showed inhibitory effect on the multiplication of five bacteria species (*Enterococcus fecalis, Citobacter freundei, Pseudomonas aeruginosa, Echerchia coli* and *Proteus mirabilis*). For yeasts, ethyl acetate and chlorophormic fractions showed a very strong inhibition (100%); methanolic fraction totally inhibited *Candida albicans* (100%) at a concentration of 500 microg/ml, but showed negative effect against *Cryptococcus neoformans*. *Microsporum canis* was strongly inhibited by methanolic extract (75%) and totally with ethyl acetate extract at a concentration of 750 microg/ml. Hexanoïc extract showed medium results [76].The antimicrobial effects of the methanol extract (40-60 µg/ml) of *Ficus carica* leaves were tested against *S. epidermidis, K. Pneumoniae, B. Subtilis, E. aerogens,* and *B. cereus.* The extract possessed antibacterial activity with MIC of 7, 3, 4, 6 and 3.5 µg/ml and MBC of 11, 6, 7, 11 and 8 µg/ml against *S. epidermidis, K. Pneumoniae, B. Subtilis, E. aerogens,* and *B. cereus* respectively [77]. The antimicrobial activity of methanol extract of fig leaves was investigated against methicillin- resistant *Staphylococcus aureus* (MRSA). MICs: 2.5 to 20 mg/ml and MBCs: 5 to 20 mg/ml were recorded for the methanol extract against MRSA isolates. The combination of the methanol extract and oxacillin or ampicillin showed reduction of growth ≥4-8-fold in all tested bacteria, which was considered to be synergistic. Furthermore, time-kill study revealed that a combination of methanol extract with oxacillin or ampicillin produced a more rapid decrease in the concentration of bacteria CFU/ml than methanol extract alone [78].
Two different extracts of *Ficus carica* fruits were evaluated against drug resistant human pathogens (*E.coli, Pseudomonas aeruginosa, Streptococcus sp., Enterobacter sp., Klebsiella pneumonia, S. typhi* and *S. paratyphi*).. The ethanol extracts was found to be more effective than methanol extract. The MIC values fell in the range of 0.94 to 30 µg/ml [79]. Hexane extract of *Ficus carica* latex was assayed for antibacterial activity against several Gram-positive and Gram-negative bacteria. A strong bactericidal effect was demonstrated. The most sensitive bacteria were *Staphylococcus saprophyticus* clinical isolate, and *Staphylococcus aureus* ATCC 25923, with MIC of 19 µg/ml [80].Antibacterial activity of fig fruit extract was investigated against *Proteus mirabilis* and three Gram positive (*Staphylococcus aureus, Staphylococcus epidermidis* and *Bacillus subtilis*) The dried fig extract inhibited only two isolates, *Bacillus subtilis* (16 mm, 100mg/ml) and *Proteus mirabilis* (18.5mm, 100mg/ml) [64].The crude extracts of *Ficus carica* was examined for their anti- quorum sensing properties. Anti- quorum sensing activity was measured by quantifying violacein production and swarming motility. Results revealed that all extracts possessed anti- quorum sensing ability. The dichloromethane extract exhibited the most pronounced inhibition of quorum sensing activity [81].
Ficus carica has also evaluated for antifungal activities. A low-molecular-weight protein, isolated from freshly collected latex of the *Ficus carica* was found to possess antifungal activity [82].

Antiviral effect:

The latex of Ficus possessed antiviral properties against some human viruses. The ability of *Ficus carica* latex to interfere with the infection of caprine herpesvirus-1 (CpHV-1) was investigated *in vitro*. *Ficus carica* latex was resuspended in culture media containing 1% ethanol and was tested for potential antiviral effects against CpHV-1. Titration of CpHV-1 in the presence or absence of *Ficus carica* latex was performed on monolayers of Madin Darby Bovine Kidney (MDBK) cells. Simultaneous addition of *Ficus carica* latex and CpHV-1 to monolayers of MDBK cells resulted in a significant reduction of CpHV-1 titres 3 days post-infection. Its effect was comparable to that achieved by acyclovir [83]. The methanolic, hexanic, ethyl acetate, hexane-ethyl acetate (v/v) and chloroformic extracts of *Ficus carica* latex were investigated *in vitro* for their antiviral potential activity against herpes simplex type 1 (HSV-1), echovirus type 11 (ECV-11) and adenovirus (ADV). The hexanic and hexane-ethyl acetate (v/v) extracts inhibited multiplication of viruses at concentrations of 78 µg/ml [84]. The anti-HSV effect of the water extract from the leaves of *Ficus carica* was investigated on Hep-2, BHK21 and PRK cells. The water extract from the leaves of *Ficus carica* possessed distinct anti-HSV-1 effect. The MTC was 0.5 mg/ml, TDO was 15 mg/ml, and TI was 30.0 mg/ml. It possessed low toxicity and directly killing-virus effect on HSV-1[85].

The efficacy of hexanic extracts of fig (*Ficus carica*) and olive (*Olea europaea*) fruit and also nano-selenium on the immunogenicity of the inactivated avian influenza virus subtype H9N2 was evaluated in broiler chickens. The results indicated that the prepared emulsions could elicit a little degree of immunity, but they could not inhibit the anamnestic response and infection [86].

Antiparasitic effect:

The aqueous and methanolic extracts were active against the earthworms *Pheretima posthuma* causing paralysis and death [87-88].Within a 2h incubation period, cysteine proteinases from fig (*Ficus carica*), caused marked damage to the cuticle of rodent gastrointestinal nematode *Heligmosomoides polygyrus* adult male and female worms, reflected in the loss of surface cuticular layers [89].The milky sap of *Ficus carica* was significantly toxic against early fourth-stage larvae of *Aedes aegypti* with a lethal concentration LC_{50} value of 10.2 mg/ml and an LC_{90} value of 42.3 mg/ml. Two furocoumarins, 5-methoxypsoralen and 8-methoxypsoralen, were isolated from the milky sap of *Ficus carica*, their LC_{50} values were 9.4 and 56.3 mg/ml, respectively [90].

Antioxidant effect:

The antioxidant activity and effects of *Ficus carica* leaves extract on ischemia/ reperfusion injuries were studied in isolated heart of rat. The treated groups received enriched solution with the extract (0.04, 0.2 and 1 mg/ml) during stabilization and reperfusion (after 30 min global ischemia), respectively. Cardiac arrhythmias were analyzed and TTC method was used for infarct size determination. The extract displayed antioxidant activity in the DPPH assay (RC_{50}=0.06666 mg/ml). Total phenolic content was 12.29 mg GAE/100 g dry sample, and the amount of flavonoids was calculated 40.729 mg/g. The extract decreased number of VEBs, incidence and duration of Rev VF with clear reduction in infarct size and infarct volume ($P<0.001$) [91]. The antioxidant activity of the extracts of five different fig cultivars (Šaraguja, Termenjača, Crnica, Bjelica and Bružetka bijela) were studied. The DPPH radical scavenging capacity was found to exhibit IC_{50} value for the extract concentration lower than 0.40 mg/ml for extract cultivars 'Crnica', while for others this capacity was higher than 0.60 mg/ml. Using the reducing power antioxidant test, higher antioxidant activity was determined for 'Bjelica' than in all other extracts [65].The antioxidative activities of water extract and crude hot-water soluble polysaccharide from *Ficus carica* fruit were investigated using various assays *in vitro*, including scavenging abilities on DPPH, superoxide and hydroxyl radicals and reducing power. Both water extract and crude hot-water soluble polysaccharide possessed notable scavenging activities on DPPH with the EC_{50} values of 0.72 and 0.61 mg/ml, respectively. The crude hot-water soluble polysaccharide showed higher scavenging activity than water extract on superoxide radical (EC_{50}, 0.95 mg/ml) and hydroxyl anion radical (scavenging rate 43.4%) at concentration of 4 mg/ml [92]. The free radical scavenging potential of Cyanidin-3-rhamnoglucoside, the major anthocyanin in fresh fig fruits, was evaluated in vitro using several free radical generators. Electron paramagnetic resonance was used to determine the scavenging properties of C3R toward superoxide radical anion O_2^{-}, hydroxyl radical OH, and singlet radical $^1O_2$. Cyanidin-3-rhamnoglucoside possessed dose-dependent antioxidant effects. It elevated the reduced glutathione concentration and the redox ratio (GSH/GSSG) in fibroblast cells in a dose-dependent manner. Moreover, Cyanidin-3-rhamnoglucoside reduced the induction of ROS by butathionine sulfoximine and elevated the redox ratio [93].

Cyanidin-3-rhamnoglucoside was also evaluated by various antioxidant assays *in vitro* and correlated with its protective effect to cultured NIH-3T3 fibroblast cells. In addition to its scavenging of reactive oxygen species (ROS), cyanidin-3-rhamnoglucoside showed a strong chelating activity toward the Fe^{2+} ion. Pretreatment with cyanidin-3-rhamnoglucoside inhibited proapoptotic processes that were initiated by the oxidation of lysosome membranes in fibroblast cells [94]. Methanol leaf extracts of *Ficus carica* (150 mg/kg) also showed antioxidant and hepatoprotective activity in hepatotoxicity induced in rats by carbon tetrachloride[95].

The methanol extracts of *Ficus carica* leaves were screened for *in vitro* antioxidant activities using 2,2-diphenyl- 1-picrylhydrazyl (DPPH). The extracts showed 4.111, 8.101 and 10.222 % scavenging inhibition at concentration of 10, 150 and 250 µg/ml respectively [77]. The different plant parts exhibited activity against DPPH and nitric oxide radicals in a concentration-dependent way. However, only the leaves extract presented capacity to scavenge superoxide radical, which appeared related with their phenolics content [69].The antioxidant potential of fig fruit extract was determined against ascorbic acid as percent inhibition of ABTS free radicals. The antioxidant activity (IC_{50} value) as was found to be 19.8 mg/ml. In FRAP assay, FRAP activity was found to be 60.48 in fig extract [64].The antioxidant activities of the *Ficus carica* was studied using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method. The extract of *Ficus carica* showed potent antioxidant activity comparable to standard Ginkgo biloba [96-97].An ethanol extract of fig branches and its ethyl acetate, hexane, butanol, and water fractions were examined for their abilities to scavenge free radicals. The results showed that the ethyl acetate fraction contained the largest amount of phenolic compounds and showed the highest free radical scavenging activity [56].

The antioxidant effects of different polarities crude extract from the leaves of *Ficus carica* were studied. The dried leaves were macerated in absolute ethanol and the crude extract was defatted with ethanol-water , then the defatted hydroalcoholic crude extract was extracted with hexane, chloroform and ethyl acetate. The antioxidant potential was determined against 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. The extracts possessed antioxidant activity in the order of hydroalcoholic > ethyl acetate > hexane > chloroform [74].

Anticancer effect:

The anticancer effect of *Ficus carica* tree latex was evaluated in human cancer cells. The *in vitro* effect of different doses of *Ficus carica* tree latex (2.5, 5 , and 10 mg/ml) on esophageal cancer cell line was evaluated after 72 hours by MTT assay. There was a significant anticancer effects in 10 mg/ml treatment of latex after 72 hours on esophageal cancer line (P: 0.025). Ten mg/ml was the optimum concentration in the inhibition of cell line growth [98].The anticancer properties of ethanolic extract of powder of *Ficus carica* (FC) fruits was studied using breast cancer cell lines (MCF7). The extract showed strong anti-cancer activities. At a concentration of 1000 µg/ml, 85.5 and 89 % inhibition were recorded after 24 and 48 hours, at a concentration of 1000 µg/ml, 85.5 and 89 % inhibition were recorded after 24 and 48 hours. While, at concentration of 500 µg/ml, the recorded inhibition were 76, 80.5 and 82.5 % after 24, 48 and 72 hours [96]. The effect of crude water extracts of *Ficus carica* upper parts was investigated on cell lines derived from different human tissue origins (Hep3b: Hepatocellular carcinoma; Hela: cervical epithelial cancer; and PC-3*:* prostate cancer). The results showed a concentration-dependent reduction in the final number of cancer cells in consequence to treatment. The plant extract possessed antiproliferation effect and cytotoxicity [99]. A mixture of 6-O-acyl-beta-D-glucosyl-beta-sitosterols, the acyl moeity being primarily palmitoyl and linoleyl with minor amounts of stearyl and oleyl, showed potent cytotoxicity. They showed *in vitro* inhibitory effects on proliferation of various cancer cell lines [100].Nine new tirucallane-type triterpenoids, ficutirucins A-I, were isolated from the fruit of *Ficus carica*, and were evaluated for their cytotoxic activities against three human cancer cell lines, MCF-7, HepG-2, and U2OS. Ficutirucins A, B, C, F,G and I exhibited moderate cytotoxic activities with IC_{50} values of 11.67 - 45.61 µM against one or more of the three cancer cell lines [101].The anti-proliferative activity of *Ficus carica* latex and the effect of the *Ficus carica* latex -temozolomide combination were studied in the T98G, U-138 MG, and U-87 MG Glioblastoma multiforme cell lines using the WST-1 assay. The mechanism of cell death was analyzed using Annexin-V/FITC and TUNEL assays, and the effect of *Ficus carica* latex on invasion was tested using the chick chorioallantoic membrane assay. To determine the effect of *Ficus carica* latex on Glioblastoma multiforme progression, the expression levels of 40 Glioblastoma multiforme associated miRNAs were analyzed in T98G cells using RT-qPCR. Results showed that *Ficus carica* latex causes cell death in Glioblastoma multiforme cells with different responses to *Ficus carica* latex - temozolomide combination, and this effect was synergistically increased in combination with temozolomide [102]. The aerial components of *Ficus carica* were examined to assess phototoxic activity on human melanoma cells. Leaves demonstrated the best antioxidant and anti-proliferative activity in comparison to bark and wood. In particular, leaves were shown to possess the highest anti-radical activity and inhibition of peroxidation, with IC_{50} values of 64 and 1.48 µg/ml respectively. The leaves had highest anti-proliferative activity with IC_{50} value of 3.92 µg/ml [103]. The latex obtained from the fruits of *Ficus carica* showed antiradical activity with an IC_{50} value of 0.05 mg/ml, while the latex obtained from the leaves showed the antiproliferative activity with an IC_{50} value of 1.5 µg/ml on the human tumor cell line A375 (melanoma) after irradiation at a specific UVA dose (1.08 J/cm^2) [104-105].

Antimutagene effect:

The extracts from fig brunches (*Ficus carica*) possessed antimutagene activity, it showed ability to decrease the frequency of spontaneous and gamma-rays induced chromosome aberrations in meristematic cells of *Vicia faba* and marrow cells of mice [106]. The plant extract also decreased the level of mutations induced by N-metil-N'-nitro-N-nitrozoguanidin in *Vicia faba* cells, chlorophyll mutations in *Arabidopsis thaliana* and NaF induced mutability in rat marrow cells [107].

Anti-angiogenic effect:

The anti-angiogenic and anti-proliferative potentials of *Ficus carica* latex extract were investigated using human umbilical vein endothelial cells (HUVECs). Different doses of latex extract were added to a three-dimensional culture of HUVEC in a collagen matrix. After 3-5 days of treatment, the anti-angiogenic effects of the extracts were monitored microscopically. For the anti-proliferation assay, different doses of the extracts were examined on HUVECs. The results indicated that latex extract inhibited proliferation and capillary tube formation of HUVECs in a dose-dependent manner at the range of 100-400 µg/ml. Furthermore, the extract was not cytotoxic up to 450 µg/ml as assessed by trypan blue and lactate dehydrogenase cytotoxicity assays [108].
The anti-angiogenic effects of the ethanol extract of *Ficus carica* leave was also investigated in human umbilical vein endothelial cells (HUVECs). The extract dose dependently inhibited the tube formation of

HUVECs. Furthermore, the extract significantly decreased mRNA expression levels of VEGF-A and Integrin β3 in HUVECs at 20 μg/ml concentration of the extract compared to untreated control cells ($P < 0.05$) [109].
The antiangiogenesis effect of Ficus carica leaves extract was investigated in an air pouch model of inflammation in rat. Inflammation was induced by injection of carrageenan into pouches. The extract was administered at 5, 25, and 50 mg/pouch, and then the volume of exudates, the cell number, TNFα, PGE2, and VEGF levels were measured. Angiogenesis of granulation tissues was determined by measuring hemoglobin content. Leukocyte accumulation and volume of exudate were significantly inhibited by the extract. It also significantly decreased the production of TNFα, PGE2, and VEGF, while angiogenesis was significantly inhibited by all administered doses [110].

Antiinflammatory and antipyretic effects:

An ethanol extract of fig branches and its ethyl acetate, hexane, butanol, and water fractions were examined for their abilities to inhibit inflammatory reactions. Every fraction of fig, particularly the ethanol extract and the ethyl acetate and hexane fractions, inhibited nitric oxide production in RAW264.7 cells. Tumor necrosis factor-α level also decreased significantly in all tested groups[56].The anti-inflammatory effect of petroleum ether, chloroform and ethanol extracts (300 and 600 mg/kg) of the leaves of *Ficus carica* was studied by carrageenan-induced rat paw edema and cotton pellet granuloma methods. The ethanolic extract 600mg/kg exhibited maximum anti-inflammatory effect, (75.90%) in acute inflammation and 71.66% reduction in granuloma weight in chronic study. The petroleum ether, chloroform and ethanol extracts also significantly reduced carrageenan-induced rat paw edema and cotton pellet granuloma method in rats [111].

The hydroalcoholic extract of fruit of *Ficus carica* was evaluated for anti-inflammatory activities in albino Wistar rat. In cotton wool granuloma technique, the hydroalcoholic extract of *Ficus carica* (250-750 mg, orally) inhibited the inflammatory effect on both phases of inflammation and the effect was dose related [112].
The antipyretic effect of an ethanol extract of leaves of *Ficus carica* was evaluated on normal body temperature and yeast-induced pyrexia, in albino rats. A yeast suspension (10 ml/kg bw) increased rectal temperature 19 hours after the subcutaneous injection. The ethanol extract of *Ficus carica*, at doses of 100, 200 and 300 mg/kg body wt. po, showed significant dose-dependent reduction in normal body temperature and yeast-provoked elevated temperature. The effect extended up to five hours after drug administration. The anti-pyretic effect of the ethanol extract of *Ficus carica* was comparable to that of paracetamol (150 mg/kg body wt., po.), a standard anti-pyretic agent [113].

Antidiabetic effect:

The hypoglycemic effect of a decoction of leaves of *Ficus carica*, as a supplement to breakfast, on diabetes control was studied in insulin-dependent diabetes mellitus patients. The patients were managed with their usual diabetes diet and their twice-daily insulin injection. During the first month, patients were given a decoction of leaves of *Ficus carica* and during the next month a non-sweet commercial tea. Post-prandial glycemia was significantly lower during supplementation with a decoction of leaves of *Ficus carica* 156.6 ± 75.9 mg/dl versus non-sweet commercial tea 293.7 ± 45.0 mg/dl ($P < 0.001$). Medium average capillary profiles were also lower in patients during *Ficus carica* therapy versus non-sweet commercial tea. Average insulin dose was 12% lower during *Ficus carica* therapy in the total group [114].The aqueous decoction of fig leaves was treated with HCI, centrifuged, treated with sodium hydroxide (NaOH) and extracted with chloroform, the administration of the organic phase to rats with streptozotocin-induced diabetes led to a decline in the levels of total cholesterol and decrease in the total cholesterol/HDL cholesterol ratio compared to control group, together with a reduction of the hyperglycaemia [115].

Nephro- and hepato- Protective effect:

Petroleum ether extract of dried leaves were tested for antihepatotoxic activity on rats treated with 50 mg/kg of rifampicin orally. There was significant reversal of biochemical (glutamic oxaloacetate transaminase, glutamic pyruvic transaminase, bilirubin), histological and functional changes (pentobarbitione sleeping time) induced by rifampicin in rats treated by petroleum ether extract [116]. The hepato-protective action of *Ficus carica* leaf ethanolic extract was evaluated in hepatotoxicity induced by carbon tetrachloride (CCl_4) in mice. Different doses of *Ficus carica* ethanol extract (200, 400 and 800 mg/kg) were given prior to intoxication with CCl_4. Levels of marker enzymes such as alanine aminotransferase and aspartate aminotransferase were increased significantly in CCl_4 treated mice. Pre-treatment with the plant extract and intoxicated with CCl_4, decreased activities of these enzymes. Furthermore, pre-treatment with the extract resulted in less pronounced destruction of the liver architecture with no fibrosis and moderate inflammation was observed compared with untreated group [117].The protective effect of hydroalcohalic extract of *Ficus carica* on gentamicin -induced renal proximal tubular damage was investigated in rats. The rats were pre-fed experimental diets for 8 days and then received gentamicin (100 mg/kg bw/day) treatment for 8 days, while still on diet. Serum parameters,

oxidative stress in rat kidney were analyzed. Gentamicin nephrotoxicity was confirmed by increased serum creatinine and blood urea nitrogen. Gentamicin increased MDA level whereas decreased catalase and reduced glutathione. While, hydroalcohalic extract of *Ficus carica* alone increased CAT concentration, GSH content and decreased MDA level. Hydroalcohalic extract of *Ficus carica* supplementation ameliorated gentamicin - induced specific metabolic alterations and oxidative damage due to its intrinsic biochemical/antioxidant properties [57].The effects of *Ficus carica* leaf extract was studied in renal oxidative stress induced by gentamicin in albino mice (400 mg/kg/day of the extract orally with gentamicin 200 mg/kg/day intraperitoneally for a period of 8 days). Gentamicin treatment increased serum urea and creatinine levels. *Ficus carica* leaf extract treated animals showed significant reduction in biochemical markers of kidney functions. The histopathological examination gave further confirmation to the biochemical results [118].

Reproductive and endocrine effects:

An aqueous ethanol extract of the dried fruits of *Ficus carica* was screened for *in vivo* aphrodisiac activity. Results reveal that on the 1st day of treatment all the treated groups showed increase copulatory sexual behavior and orientational activity in all the experimental animals. The prolonged treatments for all the treated groups were highly effective for increase the sexual libidity, as compared to the solvent control[62]. The protective effect of *Ficus carica* leaf extracts 200 mg/kg, was also studied on sperm parameters in mice intoxicated with formaldehyde. The results showed that formaldehyde significantly decreased gonadosomatic index and increased percentage of immotile sperm compared with control group. Disorganized and vacuolated seminiferous epithelium, spermatogenic arrest, and lumen filled with immature germ cells were also observed in the testes of mice intoxicated with formaldehyde. However, *Ficus carica* leaf extracts improved sperm count, nonprogressive motility of spermatozoa, and gonadosomatic index in formaldehyde-treated male mice. Moreover, seminiferous tubule with spermatogenic arrest was rarely seen [119].*Ficus carica* was evaluated for its ameliorative effect in the regulation of thyroidism in rat model. Male albino rats were treated orally with doses of 500, 250 and 125 mg/ Kg of ethanolic extract of *Ficus carica* leaf. Propylthiouracil (PTU) (10 mg/kg, sc) and Thyroxine (T4) (0.5 mg/kg, ip) were used as standards for anti thyroid and thyroid drug. The treatments were given between 9.00 and 10.00 h of the day to avoid circadian variation and continued for 21 days. T4 administration (0.5 mg/kg/d for 21 days, ip) increased the levels of serum T3 and T4, However, simultaneous administration of the *Ficus carica* leaf extract showed a potential in the regulation of thyroidism as estimated by relative potency of plant extract calculated in terms of percent increase or decreases in thyroid hormones. Phytochemical analyses revealed the presence of tyrosine in the leaf extract which was the precursor of T3 and T4 hormones [120].

Effect on memory:

The cognitive effects of hexane extract of *Ficus carica* leaves was investigated in normal and memory deficit mice. Hexane extracts of leaves of *Ficus carica* (100 and 200mg/kg) were administered to adult Swiss albino Wistar mice and the acquisition, retention and retrieval of spatial recognition memory was determined, by using Y-maze and rectangular maze models (interoceptive behavioral models). Scopolamine hydrobromide was used as the amnestic agent. The higher doses of the plant extract, exhibited a more nootropic potential. Maximum response was observed with the using of 200mg/kg of extract [121].

Hypolipidemic effect:

The hypolipidemic and preventive effects of *Ficus carica* leaf extract (50 or 100 mg/kg for 6 weeks) were studied in hyperlipidemia in high fat diet-induced obese male rats. *Ficus carica* leaf extract significantly lowered TG and IL-6 levels and elevated HDL cholesterol ($p < 0.05$). The effects of *Ficus carica* leaf extract on lipid parameters were more pronounced than those of the positive control pioglitazone. *Ficus carica* leaf extract significantly lowered atherogenic index and coronary risk index ($p < 0.01$) while it had no effect on adiponectin and leptin levels [122]. The leaves of *Ficus carica* were extracted using methanol, extract was dried and re-extracted by water: chloroform and water: petroleum ether. Effect of methanolic extracts and fractions on the secretion and cell content of cholesterol in HepG2 cells were studied. Extracts were added to the media in both basal and glucose stimulated conditions and incubated for 48h. While glucose significantly increased cholesterol secretion (17±0.76 mg/dl) *vs* basal condition (6.91±0.66 mg/dl), co-incubation with extracts reduced secretion of cholesterol in many concentrations of the stimulated condition [123].

Antispasmodic and antidiarrheal effects:

The aqueous-ethanolic extract of the ripe dried fruit of *Ficus carica* was studied for antispasmodic effect on the isolated rabbit jejunum preparations. The aqueous-ethanolic extract of the ripe dried fruit of *Ficus carica* (0.1-3.0 mg/ml) produced relaxation of spontaneous, and low K^+ (25 mM)-induced contractions with negligible effect on high K^+ (80 mM) similar to that caused by cromakalim [61]. The antidiarrheal activities of the ethanolic extracts of the leaves of *Ficus carica* was investigated in different of animal models (castor oil-

induced diarrhea, gastrointestinal motility test, prostaglandin E_2 (PGE_2)-induced enteropooling) in Wistar albino rats. The ethanolic extract of *Ficus carica* leaves showed significant inhibitory activities against castor oil-induced diarrhea and PGE2-induced enteropooling in rats at 400 and 600 mg/kg [124].

Antiplatelet effect and effect on clotting factors:

The aqueous-ethanolic extract of the ripe dried fruit of *Ficus carica* was studied for antiplatelet effect using *ex vivo* model of human platelets. The aqueous-ethanolic extract of the ripe dried fruit of *Ficus carica* (0.6 and 0.12 mg/ml) inhibited the adenosine 5'-diphosphate and adrenaline-induced human platelet aggregation [61].The proteases, ficin derived from *Ficus carica* shortened the activated partial thromboplastin time and the prothrombin time of normal plasmas and plasmas deficient in coagulation factors, except plasma deficient in factor X (FX), and generated activated FX (FXa) in defibrinated plasma. Chromatographic separation of ficin from *Ficus carica* yielded six proteolytic fractions with a different specificity towards FX. Two factor X activators with molecular masses of 23.2 and 23.5 kDa were identified, and their action was studied on purified human FX. Factor X was converted to activated FX beta by consecutive proteolytic cleavage in the heavy chain between Leu178 and Asp179, Arg187 and Gly188, and Arg194and Ile195 (FX numbering system) with concomitant release of a carboxy-terminal peptide. The cleavage pattern of FXa degradation products in the light chain was influenced by Ca^{2+} and Mn^{2+} [125].

Effect in constipation:

The effects of fig (*Ficus carica*) paste in constipation was studied in loperamide-induced constipation in a rat model. Fecal pellet number, weight and water content were increased in the fig-treated groups as compared to the control group. Increased intestinal transit length and reduced fecal pellet number in the distal colons were also recorded in fig-treated rats. Exercise and ileum tension was increased in the treated groups as compared to the control group [126]. A randomized, double-blind, placebo-controlled trial was carried out to investigate the efficacy of supplementation with *Ficus carica* paste in constipation. Subjects with functional constipation were orally supplemented with *Ficus carica* paste for 8 weeks. Primary outcomes (colon transit time) and secondary outcomes (questionnaire related to defecation) were compared before and after the 8-week intervention period. *Ficus carica* paste supplementation was associated with significant reduction in colon transit time and significant improvement in stool type and abdominal discomfort compared with the placebo. Blood parameters and clinical findings for organ toxicity remained within normal ranges [127].

Dermatological effects:

A prepare matrix type transdermal patches of tramadol HCl was prepared using various ratios of *Ficus carica* fruit mucilage and povidone. The prepared patches were examined for physicochemical characterization and *in vitro* drug permeation studies (using a Keshary-Chien diffusion cell across hairless Albino rat skin), skin irritation studies and accelerated stability studies. The formulated patches possessed satisfactory physicochemical properties, in vitro drug permeation and devoid of serious skin irritation. The selected formulation (F-5) was retained the characteristics even after the accelerated environmental conditions. The study concluded that *Ficus carica* fruit mucilage with povidone was a good combination for preparing transdermal patches [128].

Anti- warts effect:

A prospective, open right/left comparative anti- warts trial, of fig tree latex therapy vs. local standard of cryotherapy was carried out on twenty-five patients. The patients were instructed in self-application of fig tree latex to warts on one side of the body. The wart on the opposite side was treated using standard cryotherapy. A 6-month follow-up study was planned. In 11 (44%) of the 25 patients, complete resolution of fig tree latex-treated warts was observed. The remaining 14 patients (56%) had a complete cure following cryotherapy. Two patients had complete remission on both sides [129].

Effect on immunity:

The immunity activities of crude hot-water soluble polysaccharide from *Ficus carica* were evaluated using the carbon clearance test and serum hemolysin analysis in mice. The crude hot-water soluble polysaccharide (500 mg/kg) possessed a significant increase in the clearance rate of carbon particles and serum hemolysin level of normal mice [92].

Ficus carica polysaccharides effectively stimulate dendritic cells, partially through the dectin-1/Syk pathway, and promote their maturation, as shown by the up-regulation of CD40, CD80, CD86, and major histocompatibility complex II (MHCII). *Ficus carica* polysaccharides also enhanced the production of

cytokines by DCs, including IL-12, IFN-γ, IL-6, and IL-23. Moreover, *Ficus carica* polysaccharides -treated dendritic cells showed an enhanced capability to stimulate T cells and promote T cell proliferation [130].
The effect of *Ficus carica* polysaccharide supplementation with feed (at 0%, 0.1%, 0.5% and 1.0%) was investigated on genes Interleukin 1-β (IL-1β), tumor necrosis factor α (TNF-α) and heat shock protein 70 (HSP70) gene expression in blood, humoral innate immune parameters and resistant to *Flavobacterium columnare* of grass carp at weeks 1, 2 and 3. The results revealed that administration of *Ficus carica* polysaccharide significantly ($P<0.05$) up regulated IL-1β and TNF-α gene expression. HSP70 gene expression was significantly ($P<0.05$) lower in *Ficus carica* polysaccharide -fed fish at the end of trial. The serum total protein, albumin and globulin did not significantly increased in any diet on the first week whereas it was significantly enhanced in 0.5% and 1.0% supplementation diets on weeks 2 and 3 when compared to control. The serum complement C3 was significantly ($P<0.05$) increased on weeks 1 and 2 when compared to control. However, it significantly enhanced the serum lysozyme activity, bactericidal activity from weeks 1-2 as compared to control. Grass carp fed with *Ficus carica* polysaccharide showed remarkably higher resistance against *Flavobacterium columnare* (60% survival) compared to the control group (30% survival) [131].

Cholinesterase inhibitory effect:

The n-hexane, chloroform, acetone, methanol, n-butanol, and water extracts of the leaves of *Ficus carica* var. domestica were screened for their cholinesterase inhibitory effect. Cholinesterase inhibition against acetyl- (AChE) and butyrylcholinesterase (BChE) was measured by the spectrophotometric method at concentrations of 25, 50, and 100 microg/ml. Results revealed that the n-hexane and acetone extracts exerted a notable inhibition against both AChE (62.9 ±0.9% and 50.8 ±2.1%, respectively) and BChE (76.9 ± 2.2% and 45.6 ± 1.3%) respectively [132].

Effect on osteoclastogenesis:

The hexane soluble fraction of *Ficus carica* was potent inhibitor of osteoclastogenesis in RANKL-stimulated RAW264.7 cells, and in bone marrow-derived macrophages. Hexane soluble fraction exerted its inhibitory effects by suppression of p38 and NF-kappaB but activation of ERK. Hexane soluble fraction also significantly decreased the expression of NFATc1 and c-Fos, the master regulator of osteoclast differentiation [133].

Allergy and toxicity:

The irritant potential of total methanolic extract and five triterpenoids isolated from the leaves of *Ficus carica* were investigated by open mouse ear assay. Total methanolic extract, calotropenyl acetate, methyl maslinate and lupeol acetate showed potent and persistent irritant effects [134].Two arborists presented acutely with blistering eruptions affecting their forearms, hands, and fingers. The previous day, both men had pruned branches from a large fig tree. The following morning, both complained of a burning discomfort which rapidly evolved into erythema and bullae on skin that had been in direct contact with the tree branches. These symptoms gradually resolved over 4 to 6 weeks [135]. A patch test and histopathological study were conducted for patients with photo contact dermatitis from the fig tree to evaluate the mechanism underlying the photoreaction. Patch and photopatch testing with serial dilutions of two natural furocoumarins [5-methoxypsoralen and 8-methoxypsoralen (8-MOP)] contained in plant sap were performed in 47 patients. A synthetic furocoumarin, 4,5',8-trimethylpsoralen, was also tested. Histopathological analyses were made of some positive photoreactions. Positive photopatch tests reactions to 8-MOP were obtained in 12 of 47 patients, in 4 of them down to a concentration of 0.0001%. Patch tests and photopatch tests to the other two furocoumarins were negative. Histopathological findings on biopsies from positive photopatch tests to 8-MOP showed dermatitis [136].Psoralen and bergapten were the only significant photoactive compounds, present in appreciable quantities in the leaf and shoot sap of *Ficus carica* but were not detected in the fruit or its sap. These compounds were more concentrated in the leaf sap compared to the shoot sap. The photosensitization and skin reaction were induced primarily by psoralen. The response can follow contact with the leaf and shoot sap but not with the fruit sap, and was expected to occur more frequently from exposure to the leaf sap. The higher content of both photoactive compounds in spring and summer was partly responsible for the increased incidence of fig dermatitis during these seasons. Ingestion of the fruit does not cause photosensitization due to absence of photoactive furocoumarins [137].

Conclusion:

The current paper reviewed the chemical constituent, nutritional, pharmacological and therapeutic effects of *Ficus carica* as promising herbal drug because of its safety and effectiveness.

REFERENCES:

[1] Rossato SC, Leitao-Filho H and Gegossi A. Ethnobotany of Caicaras of the Atlantic forest coast (Brazil). Econ Bot 1999; 53: 387-395.
[2] Al-Snafi AE. The chemical constituents and therapeutic importance of *Cressa cretica*- A review . IOSR Journal of Pharmacy 2016; 6(6): 39-46.
[3] Al-Snafi AE. Medical importance of *Cichorium intybus* – A review IOSR Journal of Pharmacy 2016; 6(3): 41-56.
[4] Al-Snafi AE. The contents and pharmacological importance of *Corchorus capsularis*- A review. IOSR Journal of Pharmacy 2016; 6(6): 58-63.
[5] Al-Snafi AE. The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia*- A review. IOSR Journal of Pharmacy 2016; 6(6): 64-75.
[6] Al-Snafi AE. Chemical constituents and pharmacological effects of *Cynodon dactylon*- A review. IOSR Journal of Pharmacy 2016; 6(7): 17-31.
[7] Al-Snafi AE. A review on *Cyperus rotundus* A potential medicinal plant. IOSR Journal Of Pharmacy 2016; 6(7): 32-48.
[8] Al-Snafi AE. A review on chemical constituents and pharmacological activities of *Coriandrum sativum*. IOSR Journal of Pharmacy 2016; 6(7): 17-42.
[9] Al-Snafi AE. Pharmacology and toxicology of *Conium maculatum*- A review. The Pharmaceutical and Chemical Journal 2016; 3(2):136-142.
[10] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects (part 1). Asian Journal of Pharmaceutical Science & Technology 2015; 5(4): 271-284.
[11] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antiparasitic, antiprotozoal, molluscicidal and insecticidal activity (part 1). J of Pharmaceutical Biology 2015; 5(3): 203-217.
[12] Al-Snafi AE. *Eschscholzia californica*: A phytochemical and pharmacological review. Indo Am J P Sci 2017; 4(02): 257-263.
[13] Al-Snafi AE. Pharmacological and therapeutic importance of *Erigeron canadensis* (Syn: *Conyza canadensis*). Indo Am J P Sci 2017; 4(02): 248-256.
[14] Al-Snafi AE. Phytochemical constituents and medicinal properties of *Digitalis lanata* and *Digitalis purpurea* - A review. Indo Am J P Sci 2017; 4(02): 225-234.
[15] Al-Snafi AE. Therapeutic and biological activities of *Daphne mucronata* - A review. Indo Am J P Sci 2017; 4(02): 235-240.
[16] Al-Snafi AE. Medicinal plants with anticancer effects (part 2)- plant based review. Sch Acad J Pharm 2016; 5(5): 175-193.
[17] Al-Snafi AE. A review on *Erodium cicutarium*: A potential medicinal plant. Indo Am J P Sci 2017; 4(01): 110-116.
[18] Al-Snafi AE. Pharmacology of *Echinochloa crus-galli* - A review. Indo Am J P Sci 2017; 4(01): 117-122.
[19] Al-Snafi AE. The pharmacological potential of *Dactyloctenium aegyptium*- A review. Indo Am J P Sci 2017; 4(01): 153-159.
[20] Al-Snafi AE. Chemical constituents, pharmacological and therapeutic effects of *Eupatorium cannabinum*- A review. Indo Am J P Sci 2017; 4(01): 160-168.
[21] Al-Snafi AE. Nutritional and therapeutic importance of Daucus carota- A review. IOSR Journal of Pharmacy 2017; 7(2): 72-88.
[22] Al-Snafi AE. Chemical constituents and pharmacological effects of Dalbergia sissoo - A review. IOSR Journal of Pharmacy 2017; 7(2): 59-71.
[23] Al-Snafi AE. Medical importance of Datura fastuosa (syn: Datura metel) and Datura stramonium - A review. IOSR Journal of Pharmacy 2017; 7(2):43-58.
[24] Al-Snafi AE. A review on *Dodonaea viscosa*: A potential medicinal plant. IOSR Journal of Pharmacy 2017; 7(2): 10-21.
[25] Al-Snafi AE. The pharmacology and medical importance of *Dolichos lablab* (*Lablab purpureus*)- A review. IOSR Journal of Pharmacy 2017; 7(2): 22-30.
[26] Al-Snafi AE. Pharmacological and therapeutic importance of *Desmostachya bipinnata*- A review. Indo Am J P Sci 2017; 4(01): 60-66.
[27] Al-Snafi AE. Chemical constituents and pharmacological effects of *Eryngium creticum*- A review. Indo Am J P Sci 2017; 4(01): 67-73.
[28] Al-Snafi AE. The pharmacology of Equisetum arvense- A review. IOSR Journal of Pharmacy 2017; 7(2): 31-42.
[29] Al-Snafi AE. Antiparasitic, antiprotozoal, molluscicidal and insecticidal activity of medicinal plants (part 2) – plant based review. Sch Acad J Pharm 2016; 5(6): 194-207.

[30] Al-Snafi AE. Medicinal plants with antidiabetic effects (part 2): plant based review. IOSR Journal of Pharmacy 2016; 6(7): 49-61.
[31] Al-Snafi AE. Medicinal plants with antioxidant and free radical scavenging effects (part 2): plant based review. IOSR Journal Of Pharmacy 2016; 6(7): 62-82.
[32] Al-Snafi AE. Medicinal plants with antimicrobial activities (part 2): Plant based review**.** Sch Acad J Pharm 2016; 5(6): 208-239.
[33] Al-Snafi AE. Medicinal plants with cardiovascular effects (part 2): plant based review. IOSR Journal of Pharmacy 2016; 6(7): 43-62.
[34] Al-Snafi AE. Detoxification capacity and protective effects of medicinal plants (part 2): plant based review. IOSR Journal of Pharmacy 2016; 6(7): 63-84.
[35] Al-Snafi AE. Beneficial medicinal plants in digestive system disorders **(**part 2): plant based review. IOSR Journal of Pharmacy 2016; 6(7): 85-92.
[36] Al-Snafi AE. Immunological effects of medicinal plants: A review (part 2). Immun Endoc & Metab Agents in Med Chem 2016; 16(2): 100-121.
[37] Al-Snafi AE. Medicinal plants affected male and female fertility (part 1)- A review. IOSR Journal of Pharmacy 2016; 6(10): 11-26.
[38] Al-Snafi AE. Antiparasitic effects of medicinal plants (part 1)- A review. IOSR Journal of Pharmacy 2016; 6(10): 51-66.
[39] Al-Snafi AE. Antimicrobial effects of medicinal plants (part 3): plant based review IOSR Journal of Pharmacy 2016; 6(10): 67-92.
[40] Al-Snafi AE. Medicinal plants with central nervous effects (part 2): plant based review. IOSR Journal of Pharmacy 2016; 6(8): 52-75.
[41] Al-Snafi AE. Medicinal plants affected reproductive systems (part 2) - plant based review. Sch Acad J Pharm 2016; 5(5): 159-174.
[42] Al-Snafi AE. The pharmacological and toxicological effects of *Coronilla varia* and *Coronilla scorpioides*: A Review. The Pharmaceutical and Chemical Journal 2016, 3(2):105-114.
[43] Al-Snafi AE. The constituents and pharmacology of *Corchorus aestuans*: A review. The Pharmaceutical and Chemical Journal 2016; 3(4):208-214.
[44] Al-Snafi AE. The chemical constituents and pharmacological activities of *Cymbopagon schoenanthus*: A review. Chemistry Research Journal 2016; 1(5):53-61.
[45] Al-Snafi AE. Traditional uses, constituents and pharmacological effects of *Cuscuta planiflora* . The Pharmaceutical and Chemical Journal 2016; 3(4): 215-219.
[46] Al-Snafi AE. The constituents and pharmacology of *Cnicus benedictus*- A review. The Pharmaceutical and Chemical Journal 2016; 3(2):129-135.
[47] Al-Snafi AE. Medicinal importance of *Colchicum candidum*- A review. The Pharmaceutical and Chemical Journal 2016; 3(2):111-117.
[48] Al-Snafi AE. Nutritional value and pharmacological importance of citrus species grown in Iraq. IOSR Journal of Pharmacy 2016; 6(8): 76-108.
[49] Al-Snafi AE. Pharmacological activities of *Cotoneaster racemiflorus*- A review. The Pharmaceutical and Chemical Journal 2016; 3(2): 98-104.
[50] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their detoxification capacity and protective effects (part 1). Asian Journal of Pharmaceutical Science & Technology 2015; 5(4): 257-270.
[51] The plant list, a working list of all plant species, *Ficus carica*, http://www. theplantlist.org/tpl1.1/record/kew-2809827 .
[52] ITIS, *Ficus carica*, http://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic= TSN& search_value=19093
[53] U.S. National Plant Germplasm System, Taxon: *Ficus carica* L. https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?16801
[54] Flora of Pakistan, *Ficus carica* L., http://www.efloras.org/florataxon.aspx? Flora _id=5&taxon_id=200006351
[55] Flora of China, *Ficus carica*, www.efloras.org
[56] Park S, Han J, Im K, Whang WK and Min H. Antioxidative and anti-inflammatory activities of an ethanol extract from fig (*Ficus carica*) branches. Food Science and Biotechnology 2013; 22(4): 1071-1075.
[57] Kore KJ, Shete RV, Kale BN and Borade AS. Protective role of hydroalcoholic extract of *Ficus carica* in gentamicin induced nephrotoxicity in rats. Int J of Pharm & Life Sci (IJPLS) 2011; 2(8): 978-982.
[58] Nadkarni KM. Indian materia medica, Vol. 1. Popular Book Depot, Bombay-India, 1982: 545- 547 .
[59] Burkill IH. A Dictionary of the Economic Products of Malay Peninsular. Ministry of Agriculture, Malaysia 1935:1005–1006.
[60] Ponelope O. 100 Great natural remedies. Kyle Cathic Limited, NewYork, USA 1997:98-99.

[61] Gilani AH, Mehmood MH, Janbaz KH, Khan AU and Saeed SA. Ethnopharmacological studies on antispasmodic and antiplatelet activities of *Ficus carica*. J Ethnopharmacol 2008; 119(1):1-5.
[62] Palaniyappan V, Bommireddy EP, Gudipudi and YandamalaN. *In vivo* fertility enhancing activity (aphrodisiac) of *Ficus carica* fruit on male wistar rats. International Journal of Pharmacy and Pharmaceutical Sciences 2013; 5(2):516-518.
[63] Nebedum JO, Udeafor PC and Okeke CU. Comparative effects of ethanolic extracts of *Ficus carica* and *Mucuna pruriens* leaves on haematological parameters in albino rats. Biokemistri 2010; 22(2): 77-84.
[64] Oliveira AP, Silva LR, de Pinho PG, Valentão P, Silva BM, Pereira JA and Andrade PB. Volatile profiling of *Ficus carica* varieties by HS-SPME and GC–IT-MS. Food Chemistry 2010; 123: 548–557.
[65] Mujić I, Dudas S, Skutin HM, Perusic D, Zeković Z, Lepojević Z, Radojković M, Vidović S, Milošević S and Mesic EO. Determination of antioxidant properties of fig fruit extract (*Ficus carica* L.). ISHS Acta Horticulturae 940: XXVIII International Horticultural Congress on Science and Horticulture for People (IHC2010): International Symposium on the Challenge for a Sustainable Production, Protection and Consumption of Mediterranean Fruits and Nuts 2010.
[66] El-Shobaki FA, El-Bahay AM, Esmail RS, Abd El Megeid AA and Esmail NS. Effet of figs fruits (*Ficus carica* L.) and its leaves on hyperglycemia in alloxan diabetic rats. World Journal of Dairy and Food Sciences 2010; 5 (1): 47-57.
[67] Soni N, Mehta S, Satpathy G and Gupta RK. Estimation of nutritional, phytochemical, antioxidant and antibacterial activity of dried fig (*Ficus carica*). Journal of Pharmacognosy and Phytochemistry 2014; 3 (2): 158-165.
[68] Ficsor E, Szentmihályi K, Lemberkovics E, Blázovics A and Balázs A. Analysis of *Ficus carica* L. – volatile components and mineral contents. Eur Chem Bull 2013; 2(3): 126-129.
[69] Oliveira AP, Valentão P, Pereira JA, Silva BM, Tavares F and Andrade PB. *Ficus carica* L.: Metabolic and biological screening. Food Chem Toxicol 2009; 47(11):2841-2846.
[70] Solomon A, Golubowicz S, Yablowicz Z , Grossman S, Bergman M, Gottlieb HE, Altman A, Kerem Z and Flaishman MA. Antioxidant activities and anthocyanin content of fresh fruits of common fig (*Ficus carica* L.). J Agric Food Chem 2006; 54 (20): 7717–7723.
[71] Devaraj KB, Kumar PR and Prakash V. Purification, characterization, and solvent-induced thermal stabilization of ficin from *Ficus carica*. J Agric Food Chem 200; 56(23): 11417-11423.
[72] Baeyens-Volant D, Matagne A, El Mahyaoui R, Wattiez R and Azarkan M. A novel form of ficin from *Ficus carica* latex: Purification and characterization. Phytochemistry 2015; 117: 154-167.
[73] Jeong MR, Kim HY and Cha JD. Antimicrobial activity of methanol extract from *Ficus carica* leaves against oral bacteria. Journal of Bacteriology and Virology 2009; 39(2): 97-102.
[74] Weli AM, Al-Blushi AAM and Hossain MA. Evaluation of antioxidant and antimicrobial potential of different leaves crude extracts of Omani *Ficus carica* against food borne pathogenic bacteria. Asian Pac J Trop Dis 2015; 5(1): 13-16.
[75] Rashid KI and Mahdi NM. Antimicrobial activity of fig (*Ficus carica* Linn.) leaf extract as compared with latex extract against selected bacteria and fungi. Journal of Babylon University/Pure and Applied Sciences 2014; 5(22): 1620-1626.
[76] Aref HL, Salah KB, Chaumont JP, Fekih A, Aouni M and Said K. *In vitro* antimicrobial activity of four *Ficus carica* latex fractions against resistant human pathogens (antimicrobial activity of *Ficus carica* latex). Pak J Pharm Sci 2010; 23(1): 53-58.
[77] Ahmad J, khan I, Khan S and Iqbal D. Evaluation of Antioxidant and antimicrobial activity of *Ficus carica* leaves: an *In vitro* approach. J Plant Pathol Microb 2013; 4:157.
[78] Young-Soo L and Jeong-Dan C. Synergistic antibacterial activity of fig (*Ficus carica*) leaves extract against clinical isolates of methicillin-resistant *Staphylococcus aureus.* Kor J Microbiol Biotechnol 2010; 38(4): 405–413.
[79] Jasmine R, Manikandan K, Niveditha B, Thirupathi K and Manikandan G. Evaluation the efficiency of *Ficus carica* fruits against a few drug resistant bacterial patogenes. World Journal of Pharmacy and Pharmaceutical Sciences 2014; 3(2): 1394-1400.
[80] Lazreg-Aref H, Mars M, Fekih A, Aouni M and Said K. Chemical composition and antibacterial activity of a hexane extract of Tunisian caprifig latex from the unripe fruit of *Ficus carica*. Pharm Biol 2012; 50(4): 407-412.
[81] Sun S, Li H, Zhou W, Liu A and Zhu H. Bacterial quorum sensing inhibition activity of the traditional Chinese herbs, *Ficus carica* L. and *Perilla frutescens*. Chemotherapy 2014;60:379-383.
[82] Mavlonov GT, Ubaidullaeva KA, Rakhmanov MI, Abdurakhmonov IU and Abdukarimov A. Chitin-binding antifungal protein from *Ficus carica* latex. Chem Natural Comp 2008; 44: 216-219.
[83] Camero M, Marinaro M, Lovero A, Elia G, Losurdo M, Buonavoglia C and Tempesta M. *In vitro* antiviral activity of *Ficus carica* latex against caprine herpesvirus-1. Nat Prod Res 2014; 28(22): 2031-2035.

[84] Lazreg Aref H, Gaaliche B, Fekih A, Mars M, Aouni M, Pierre Chaumon J and Said K. In vitro cytotoxic and antiviral activities of *Ficus carica* latex extracts. Nat Prod Res 2011; 25(3): 310-319.
[85] Wang G, Wang H, Song Y, Jia C, Wang Z and Xu H. Studies on anti-HSV effect of *Ficus carica* leaves. Zhong Yao Cai 2004; 27(10): 754-756.
[86] Asl Najjari AH, Rajabi Z, Vasfi Marandi M and Dehghan G. The effect of the hexanic extracts of fig (*Ficus carica*) and olive (*Olea europaea*) fruit and nanoparticles of selenium on the immunogenicity of the inactivated avian influenza virus subtype H9N2. Vet Res Forum 2015; 8(6): 227-231.
[87] Chandra DS and Kashyap P. Comparative in-vitro anthelmintic activity of different parts of *Ficus carica*. International Journal of Herbal Drug Research 2011; 1: 8-10.
[88] Patil AP, Patil VR, Patil VR and Chaudhary RY. Anthelmintic and preliminary phytochemical screening of leaves of *Ficus carica* Linn againt intestinal helminthiasis. International Journal of Research in Ayurveda and Pharmacy 2010; 1(2): 601-605.
[89] Stepek G, Buttle DJ, Duce IR, Lowe A and Behnke JM. Assessment of the anthelmintic effect of natural plant cysteine proteinases against the gastrointestinal nematode, *Heligmosomoides polygyrus in vitro.* Parasitology 2005; 130(Pt 2): 203-211.
[90] Chung IM, Kim SJ, Yeo MA, Park SW and Moon HI. Immunotoxicity activity of natural furocoumarina from milky sap of *Ficus carica* against *Aedes aegypti* L. Immunopharmacol Immunotoxicol 2011; 33: 515–518.
[91] Allahyari S, Delazar A and Najafi M. Evaluation of general toxicity, anti-oxidant activity and effects of *Ficus carica* leaves extract on ischemia/reperfusion injuries in isolated heart of rat. Adv Pharm Bull 2014; 4(Suppl 2): 577-582.
[92] Yang XM, Yu W, Ou ZP, Ma HL, Liu WM and Ji XL. Antioxidant and immunity activity of water extract and crude polysaccharide from *Ficus carica* L. fruit. Plant Foods Hum Nutr 2009; 64(2): 167-173.
[93] Solomon A, Golubowicz S, Yablowicz Z, Bergman M, Grossman S, Altman A, Kerem Z and Flaishman MA. EPR Studies of O_2^-, OH, and $^1O_2$ scavenging and prevention of glutathione depletion in fibroblast cells by cyanidin-3-rhamnoglucoside isolated from fig (*Ficus carica* L.) fruits. J Agric Food Chem 2010; 58(12):7158-7165.
[94] Solomon A, Golubowicz S, Yablowicz Z, Bergman M, Grossman S, Altman A, Kerem Z and Flaishman MA. Protection of fibroblasts (NIH-3T3) against oxidative damage by cyanidin-3-rhamnoglucoside isolated from fig fruits (*Ficus carica* L.). J Agric Food Chem 2010; 58(11): 6660-6665.
[95] Singab AN, Ayoub NA, Ali EN and Mostafa NM. Antioxidant and hepatoprotective activities of Egyptian moraceous plants against carbon tetrachloride-induced oxidative stress and liver damage in rats. Pharm Biol 2010;48(11):1255-1264.
[96] Jasmine R, Manikandan K and Karthikeyan. Evaluating the antioxidant and anticancer property of *Ficus carica* fruits. African Journal of Biotechnology 2015;14(7):634-641.
[97] Ali H, Monga J, Gupta L, Manigauha A, Trivedi VB, Ahi J. Antioxidant potential of *Ficus carica* by the DPPH free radical method: *In vitro* analysis. Oriental Journal of Chemistry 2009; 25(1): 257-260.
[98] Hashemi SA and Abediankenari S. Suppressive effect of fig (*Ficus carica*) latex on esophageal cancer cell proliferation. Scientific Journal of the Faculty of Medicine in Niš 2013; 30(2): 93-96.
[99] Al Owini SH. A Study on the effect of some plant extracts on certain malignant cell lines *in vitro.* MSc thesis, Department of Biology, Faculty of science, Islamic University – Gaza 2006.
[100] Rubnov S, Kashman Y, Rabinowitz R, Schlesinger M and Mechoulam R. Suppressors of cancer cell proliferation from fig (*Ficus carica*) resin: isolation and structure elucidation. J Nat Prod 2001; 64(7): 993-996.
[101] Jing L, Zhang YM, Luo JG and Kong LY. Tirucallane-type triterpenoids from the fruit of Ficus carica and their cytotoxic activity. Chem Pharm Bull (Tokyo) 2015; 63(3): 237-243.
[102] Tezcan G, Tunca B, Bekar A, Yalcin M, Sahin S, Budak F, Cecener G, Egeli U, Demir C, Guvenc G, Yilmaz G, Erkan LG, Malyer H, Taskapilioglu MO, Evrensel T and Bilir A. *Ficus carica* latex prevents invasion through induction of let-7d expression in GBM cell lines. Cell Mol Neurobiol 2015; 35(2): 175-187.
[103] Conforti F, Menichini G, Zanfini L, Tundis R, Statti GA, Provenzano E, Menichini F, Somma F and Alfano C. Evaluation of phototoxic potential of aerial components of the fig tree against human melanoma. Cell Prolif 2012;45(3):279-285.
[104] Menichini G, Alfano C, Provenzano E, Marrelli M, Statti GA, Somma F, Menichini F and Conforti F. Fig latex (*Ficus carica* L. cultivar Dottato) in combination with UV irradiation decreases the viability of A375 melanoma cells *in vitro*. Anticancer Agents Med Chem 2012; 12(8): 959-965.

[105] Marrelli M, Menichini F, Statti GA, Bonesi M, Duez P, Menichini F and Conforti F. Changes in the phenolic and lipophilic composition, in the enzyme inhibition and antiproliferative activity of *Ficus carica* L. cultivar Dottato fruits during maturation. Food Chem Toxicol 2012; 50(3-4):726-733.
[106] Agabeĭli RA, Kasimova TE and Alekperov UK. Antimutagenic activity of plant extracts from Armoracia rusticana, *Ficus carica* and *Zea mays* and peroxidase in eukaryotic cells. Tsitol Genet 2004; 38(2): 40-45.
[107] Agabeĭli RA and Kasimova TE. Antimutagenic activity of *Armoracia rusticana*, Zea mays and *Ficus carica* plant extracts and their mixture. Tsitol Genet 2005; 39(3): 75-79.
[108] Mostafaie A, Mansouri K, Norooznezhad AH and Mohammadi-Motlagh HR. Anti-angiogenic activity of *Ficus carica* latex extract on human umbilical vein endothelial cells. Cell Journal (Yakhteh) 2011; 12(4): 525-528.
[109] Ghambarali Z, Bidmeshkipouri A, Akrami H, Azadbakht M and Rabzia A. Ethanolic extract of *Ficus carica* leave suppresses angiogenesis by regulating VEGF-A and Integrin β3 mRNA expression in human umbilical vein endothelial cells. Indian J Physiol Pharmacol 2014; 58(4): 407-415.
[110] Eteraf-Oskouei T, Allahyari S, Akbarzadeh-Atashkhosrow A, Delazar A, Pashaii M, Gan SH and Najafi M. Methanolic extract of *Ficus carica* Linn. leaves exerts antiangiogenesis effects based on the rat air pouch model of inflammation. Evid Based Complement Alternat Med 2015; doi: 10.1155/2015/760405.
[111] Patil VV and Patil VR. Evaluation of anti-inflammatory activity of *Ficus carica* Linn. leaves. Indian Journal of Natural Products and Resources 2011; 2(2): 151-155.
[112] Singh S, Tomar A and Chandel HS. Anti-inflammatory effect of hydroalcoholic extract of fruit of *Ficus carica* . Int J Drug Res Tech 2012; 2 (6): 440-445.
[113] Patil VV, Bhangale SC and Patil VR. Evaluation of anti-pyretic potential of *Ficus carica* leaves. International Journal of Pharmaceutical Sciences Review and Research 2010; 2(2): 48-50.
[114] Serraclara A, Hawkins F, Pérez C, Domínguez E, Campillo JE and Torres MD. Hypoglycemic action of an oral fig-leaf decoction in type-I diabetic patients. Diabetes Res Clin Pract 1998; 39(1): 19-22.
[115] Canal JR, Torres MD, Romero A and Pérez C. A chloroform extract obtained from a decoction of *Ficus carica* leaves improves the cholesterolaemic status of rats with streptozotocin-induced diabetes. Acta Physiol Hung 2000; 87(1): 71-76.
[116] Gond NY and Khadabadi SS. Hepatoprotective activity of *Ficus carica* leaf extract on rifampicin-induced hepatic damage in rats. Indian J Pharm Sci 2008; 70(3): 364-366.
[117] Aghel N, Kalantari H and Rezazadeh S. Hepatoprotective effect of *Ficus carica* leaf extract on mice intoxicated with carbon tetrachloride. Iranian Journal of Pharmac Res 2011; 10 (1): 63-68.
[118] Ghaffar A, Tahir M, Lone KP, Faisal B and Latif W. The effect of *Ficus carica* L. (ANJIR) leaf extract on gentamicin induced nephrotoxicity in adult male albino mice. J Ayub Med Coll Abbottabad 2015; 27(2): 398-401.
[119] Naghdi M, Maghbool M, Seifalah-Zade M, Mahaldashtian M, Makoolati Z, Kouhpayeh SA, Ghasemi A and Fereydouni N. Effects of common fig (*Ficus carica*) leaf extracts on sperm parameters and testis of mice intoxicated with formaldehyde. Evid Based Complement Alternat Med 2016; doi: 10.1155/2016/2539127.
[120] Vasundhara S, Gupta D, Saraf R and Shubhini A. *Ficus carica* leaf extract in regulation of thyroidism using ELISA technique. Asian Journal of Pharmaceutical & Clinical Research 2012; 5(2): 44-48.
[121] Vasundhara S, Hafsa A and Rajiv G. Memory enhancement of *Ficus carica* leaves in hexane extract on interoceptive behavioral models. Asian J Pharm Clin Res 2013; 6(Suppl 3): 109-113.
[122] Joerin L, Kauschka M, Bonnländer B, Pischel I, Benedek B and Butterweck V. *Ficus carica* leaf extract modulates the lipid profile of rats fed with a high-fat diet through an increase of HDL-C. Phytother Res 2014; 28(2): 261-267.
[123] Fatemi A, Rasouli A and Asadi F. Effect of fig (*Ficus carica*) leaf extract on the secretion and content of cholesterol in Hepg2 cell. American Journal of Animal and Veterinary Sciences 2007; 2 (4): 104-107.
[124] Patil VV, Bhangale SC, Chaudhari KP, Kakade RT, Thakare VM, Bonde CG and Patil VR. Evaluation of the antidiarrheal activity of the plant extracts of Ficus species. Zhong Xi Yi Jie He Xue Bao 2012; 10(3): 347-352.
[125] Richter G, Schwarz HP, Dorner F and Turecek PL. Activation and inactivation of human factor X by proteases derived from *Ficus carica*. Br J Haematol 2002; 119(4): 1042-1051.
[126] Lee HY, Kim JH, Jeung HW, Lee CU, Kim DS, Li B, Lee GH, Sung MS, Ha KC, Back HI, Kim SY, Park SH, Oh MR, Kim MG, Jeon JY, Im YJ, Hwang MH, So BO, Shin SJ, Yoo WH, Kim HR, Chae HJ and Chae SW. Effects of *Ficus carica* paste on loperamide-induced constipation in rats. Food Chem Toxicol 2012; 50(3-4): 895-902.
[127] Baek HI, Ha KC, Kim HM, Choi EK, Park EO, Park BH, Yang HJ, Kim MJ, Kang HJ and Chae SW. Randomized, double-blind, placebo-controlled trial of *Ficus carica* paste for the management of functional constipation. Asia Pac J Clin Nutr 2016; 25(3): 487-496.

[128] Ahad HA, Ishaq BM, Shaik M and Bandagisa F. Designing and characterizing of tramadol hydrochloride transdermal patches prepared with *Ficus carica* fruit mucilage and povidone. Pak J Pharm Sci 2016; 29(3): 945-951.
[129] Bohlooli S, Mohebipoor A, Mohammadi S, Kouhnavard M and Pashapoor S. Comparative study of fig tree efficacy in the treatment of common warts (Verruca vulgaris) vs. cryotherapy. Int J Dermatol 2007; 46(5): 524-526.
[130] Tian J, Zhang Y, Yang X, Rui K, Tang X, Ma J, Chen J, Xu H, Lu L and Wang S. *Ficus carica* polysaccharides promote the maturation and function of dendritic cells. Int J Mol Sci 2014; 15(7): 12469-1279.
[131] Yang X, Guo JL, Ye JY, Zhang YX and Wang W. The effects of *Ficus carica* polysaccharide on immune response and expression of some immune-related genes in grass carp, *Ctenopharyngodon idella*. Fish Shellfish Immunol 2015;42(1):132-137.
[132] Orhan IE, Ustün O and Sener B. Estimation of cholinesterase inhibitory and antioxidant effects of the leaf extracts of Anatolian *Ficus carica* var. domestica and their total phenol and flavonoid contents. Nat Prod Commun 2011; 6(3): 375-378.
[133] Park YR, Eun JS, Choi HJ, Nepal M, Kim DK, Seo SY, Li R, Moon WS, Cho NP, Cho SD, Bae TS, Kim BI and Soh Y. Hexane-soluble fraction of the common fig, *Ficus carica*, inhibits osteoclast differentiation in murine bone marrow-derived macrophages and RAW 264.7 cells. Korean J Physiol Pharmacol 2009;13(6):417-424.
[134] Saeed MA and Sabir AW. Irritant potential of triterpenoids from *Ficus carica* leaves. Fitoterapia 2002; 73(5): 417-420.
[135] Derraik JG and Rademaker M. Phytophotodermatitis caused by contact with a fig tree (*Ficus carica*). N Z Med J 2007; 120(1259): U2658.
[136] Bonamonte D, Foti C, Lionetti N, Rigano L and Angelini G. Photoallergic contact dermatitis to 8-methoxypsoralen in *Ficus carica*. Contact Dermatitis 2010; 62(6): 343-348.
[137] Zaynoun ST, Aftimos BG, Abi Ali L, Tenekjian KK, Khalidi U and Kurban AK. *Ficus carica*; isolation and quantification of the photoactive components. Contact Dermatitis 1984; 11(1): 21-25.