Review Article

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A REVIEW ON THE PROSPEROUS PHYTOCHEMICAL AND PHARMACOLOGICAL EFFECTS OF *FICUS CARICA*

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Abstract: *Ficus Carica* Linn belongs to the family Moraceae. It is commonly known as Anjeer, which is a medium sized deciduous tree widely distributed in sub-tropical and tropical countries. It has been used as fruit and medicine for several centuries. Phytoconstituents like flavonoids, phenolics, fatty acis, proanthocyanidine, phytosteroles (campesterol, stigmasterol, sitosterol), xanthotoxin, psoralens, bergapten, xanthotoxol have been extracted from leaves and fruits, and peptides from latex. The fruit extract possess hypoglycemic, diuretic, antioxidant, immunity, hepetoprotective activities, latex has anthelmintic and anticarcinogenic activities. The present review on the phytochemistry and pharmacology of Ficus is an effort to give a detailed literature survey of its properties.

Keywords: *Ficus Carica*, Levosulpiride, Metocel K100lv, K4m, Wet Granulation

INTRODUCTION

Ficus:

In English the word "fig" means giving care about something. The word ficolin, which appears similar to *Ficus* and refers to a lectin like compound combining the first parts of the words for *fibrinogen* and *collagen.*

Ficus constituted one of the largest genera of medicinal plants with about 750 species of woody plants, trees and shrubs primarily occurring in subtropical and tropical regions throughout the world. The genus is remarkable for the large variation in the habits of its species[1]. The most important species of *Ficus* are *F. bengalensis, F. carica, F. racemosa and F. elastica*. *Ficus Carica*is commonly referred as "Fig". Various parts of the plant like bark, leaves, tender shoots, fruits, seeds, and latex are medicinally important. The fig is a very nourishing food and used in industrial products. It is rich in vitamins, mineral elements, water, and fats. Figs are one of the highest plant sources of calcium and fiber. According to USDA data for the Mission variety, dried figs are richest in fiber, copper, manganese, magnesium, potassium, calcium, and vitamin K, relative to human needs.[2]

The genus, *Ficus*, consists of over 800 species and is one of about 40 genera of the mulberry family, Moraceae. There is significant genetic diversity among different varieties of fig, which contain remarkable pharmacological activities and are of commercial importance.[3] Literature survey indicated that figs have been cultivated over 1100 years and these are among the earliest cultivated plants for human use.[33]

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***Various species of Ficus*[4]:**

Ficus altissima (council tree), *Ficus aspera* (clown fig), *Ficus auriculata*, *Ficus roxburghii*, *Ficus benghalensis* (Indian banyan), *Ficus benjamina* (weeping fig), *Ficus benjamina* 'Exotica', *Ficus benjamina* 'Comosa', *Ficus binnendykii* (narrow-leaf ficus), *Ficus Carica* (common edible fig), *Ficus celebinsis* (willow ficus), *Ficus deltoidea* (mistletoe fig) syn. *Ficus diversifolia*, *Ficus elastic* (Indian rubber tree), *Ficus elastic* 'Abidjan', *Ficus elastic* 'Asahi', *Ficus elastic* 'Decora', *Ficus elastic* 'Gold', *Ficus elastic* 'Schrijveriana', *Ficus lacor* (pakur tree), *Ficus lingua* (box-leaved fig) syn. *Ficus buxifolia*, *Ficus lyrata* (fiddle-leaf fig), *Ficus macrophylla* (Moreton Bay fig), *Ficus microcarpa* (Chinese banyan), *Ficus microcarpa*var. crassifolia (wax ficus), *Ficus microcarpa* 'Variegata', *Ficus pseudopalma* (Philippine fig), *Ficus pumila* (creeping fig) syn. *Ficus repens*, *Ficus religiosa* (bo tree or sacred fig), *Ficus rubiginosa* (Port Jackson fig or rusty fig), *Ficus rubiginosa* 'Variegata' Ficus sagittata, *Ficus radicans* (Variegata), *Ficus saussureana*, syn. *Ficus dawei*, *Ficus stricta*, *Ficus subulata*, syn. *Ficus salicifolia, Ficus tikoua* (Waipahu fig).

Taxonomy:

Taxonomically it is classified as Kingdom- *plantae,* Sub-kingdom *tracheobionta,* Super division *spermatophyte,* Division *magnoliphyta,* Class *maghnoliosida,* Subclass *hamamelididae,* Order *urticales,* Family *moraceae,* Genus *Ficus,* Species *carica.*

Plant Discription:

It is monoecious, deciduous or large shrub, growing to a height of 6.9–10 metres (23–33 feet), with

smooth grey bark. Its fragrant leaves are 12–25 centimetres (4.7–9.8 inches) long and 10–18 centimetres (3.9–7.1 inches) across, and deeply lobed with three or five lobes. The complex inflorescence consists of a hollow fleshy structure called the syconium, which is lined with numerous unisexual flowers. The flower itself is not visible outwardly, as it blooms inside the infructescence. Although commonly referred to as a fruit, the fig is actually the infructescence or scion of the tree, known as a false fruit or multiple fruit, in which the flowers and seeds are borne. It is a hollow-ended stem containing many flowers. The small orifice (ostiole) visible on the middle of the fruit is a narrow passage, which allows the specialized fig wasp to enter the fruit and pollinate the flower, where after the fruit grows seeds.[24]

The edible fruit consists of the mature syconium containing numerous one-seeded fruits (druplets). The fruit is 3–5 centimetres (1.2–2.0 in) long, with a green skin, sometimes ripening towards purple or brown. *Ficus Carica* has milky sap (laticifer). The sap of the fig's green parts is an irritant to human skin.

Chemical composition:

Stem: campesterol, hentriacontanol, stigmasterol, euphorbol and its hexacosanate, ingenol andtaraxerone.

Leaves: moisture, 67.6%; protein, 4.3%; fat, 1.7%; crude fiber, 4.7%; ash, 5.3%; N-free extract, 16.4%; pentosans, 3.6%; carotene, bergaptene, stigmasterol, sitosterol, and tyrosine. Ficusin, taraxasterol, betasitosterol, rutin, sapogenin, Calotropenyl acetate, lepeolacetate and oleanolic

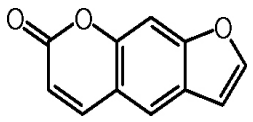
Latex: caoutchouc (2.4%), resin, albumin, cerin, sugarand malic acid, rennin, proteolytic enzymes, diastase, esterase, lipase, catalase, and peroxidase.

Seed: Dried seeds contain 30% of a fixed oil containing the fatty acids: oleic, 18.99%; linoleic, 33.72%; linolenic, 32.95%; palmitic, 5.23%; stearic, 2.1 8%; arachidic, 1.05%. It is edible oil and can be used as a lubricant.[25]

Phytochemical Properties:

Phytochemicals are the chemicals produced by plants. Literature survey indicated the presence of coumarins, flavonoids, sterols, triterpenoids, anthocyanins*etc*, in various parts of the plant. Dried seeds contain fixed oil containing the fatty acids *viz*oleic acid, linoleic acid, linolenic acid, palmitic acid, stearic acid, arachidic acid. Leaves contain bergapten, 4′,5′-dihydropsoralen, rutin, 24-methylenecycloartanol umbelliferone, marmesin, stigmasterol, β-sitosterol, ficusogenin, lupeol, psoralen ψ-taraxasterol ester and tyrosine moisture, protein, fat, crude fiber, ash, N-free extract, pentosans, carotene on a dry weight basis[31,32] . The latex contains 6-*O*-linoleyl-β-D-glucosyl-β-sitosterol, 6-*O*-Oleyl-β-D-glucosyl-β-sitosterol, 6-*O*-palmitoyl-β-D-glucosyl-β-sitosterol, caoutchouc, resin, albumin, cerin, sugar and malic acid, rennin, proteolytic enzymes, diastase, esterase, lipase, catalase, and peroxidase. Fruits contain cyanidin-3-*O*-glucoside, cyanidin-3-*O*rhamnoglucoside, saturated fat, cholesterol, sodium, insoluble sugars, protein, vitamin A, vitamin C, calcium, iron. Roots contain psoralen, bergapten.[5-9] Fig. shows the structures of phytochemical constituents present in *Ficus Carica* Linn.

Following are the chemical structures of few important compounds isolated from *Ficus Carica* Linn like paoralen (root) (1), umbelliferone (leaf) (2), lupeol (leaf) (3), guaiazulene (root) (4), xanthotoxin (leaf) (5), β-sitosterol (leaf) (6), O-Phenylphenol (fruit) (7), Guaiacol (root) (8), Dopamine (fruit) (9), Cadalene (leaf) (10), Angelicin (fruit) (11), Adrenalin (fruit) (12), Quercitin (leaf) (13), and raffinose (fruit) (14).[31]



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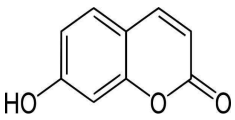

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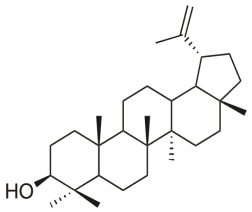

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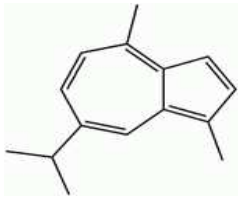

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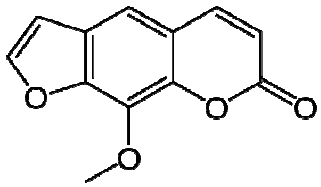

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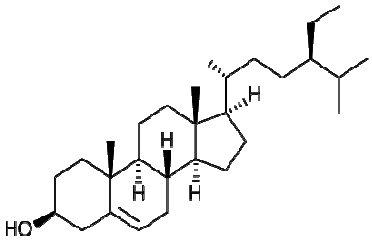

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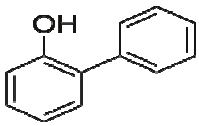

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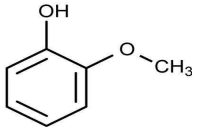

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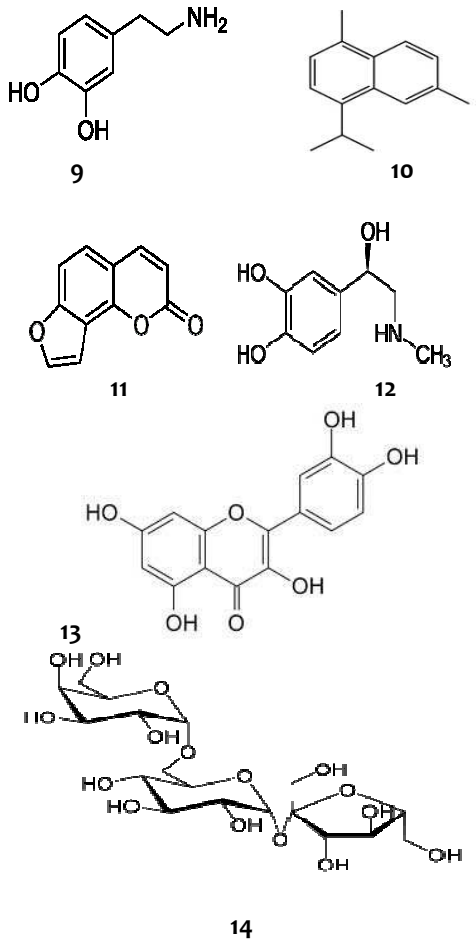

Traditional Uses:

Ficus Carica possesses many therapeutic uses. Its extract has been used for many centuries for external as well as internal uses. Fruits of *Ficus Carica* Linn. are used in leprosy, nose bleeding, antipyretic, aphrodisiac, lithontriptic, hair-nutritive, emollient, demulcent, laxative and in treatment of various inflammations, paralysis, liver diseases, chest pain, piles. Roots are used as tonic, leucoderma and ringworm infection. Latex is used as expectorant, diuretic, anthelmintic, anaemia. Leaves are used as antidiabetic, vermifuge, and contact dermatitis in human, phototoxicity in animals. Seeds are used as edible oil, lubricant.[10] Due to the iron-rich content of fig, it is ideal to include it in one's diet in anaemic condition. The burnt ash of the fig fruit is highly basic in nature and can be consumed a tea spoon before meals to counter hyperacidity. The fruit juice with honey is used to check haemorrhagia. In unani medicine anjeer is used as a mild laxative, expectorant and diuretic. Anjeer is used for the diseases in liver and spleen. The dry fruits of anjeer are a supplement food for diabetics[11]. Sweets in the markets with sugar free for diabetics contain ficuscarica. The paste of fruit is applied in swellings, tumours and inflammation for relieving pain.

Modern Uses:

Commercially, figs are peeled by immersion for 1min in boiling lye water or a boiling solution of sodium bicarbonate. In warm, humid climates, figs are generally eaten fresh and raw without peeling, and they are often served with cream and sugar. Peeled or unpeeled, the fruits may be cooked in various ways, as in pies, puddings, cakes, bread or other bakery products, or added to ice cream mix. Home owners preserve the whole fruits in sugar syrup or prepare them as jam, marmalade, or paste. Fig paste (with added wheat and corn flour, whey, syrup, oils and other ingredients) forms the filling for the bakery product. Other modern uses are as, poultice, eating, ointment, drink, gargle, simultaneously eating pickled figs, fumigation, rubbed externally, liniment, on sponge, enema, enema, skin application, ophthalmic *etc*[12]

Pharmacological Activity:

For many centuries, figs have been used in medicine, and this use was recorded in classical Middle Eastern and European medical writings. The placement of poultices of figs on tumors as treatment for abnormal swellings. Such swellings, according to reports of experts, could have been due to infection or, alternatively, cancer. Its pharmacological actions include antibacterial, antioxidant, anti-inflammatory, gastroprotective, antidiarrheal, vulnerary, antitumor, anticancer, antispasmodic, immunobalancing/ immunoharmonizing, and nutritive *par excellence*.

Nowadays we know that even single pure chemicals can exert pleiotropic effects (Having multiple effects) on genes. This means that the compound can induce or suppress a gene to transcribe proteins and that this effect can reverberate downward to affect multiple human organs and multiple physiological systems. If such a multiple or pleiotropic effect is possible from a pure chemical, how much more so, then, is the potential for multiple physiological targeting from a mixture of different compounds. The various extracts of the plant from different part showed many biological activities. Its fruit, root and leaves are used in the native system of medicine in different disorders such as metabolic, gastrointestinal, respiratory, inflammatory and cardiovascular disorders. *Ficus Carica* Linn., has been reported to exhibit antioxidant, anti-HSV, haemostatic, hypoglycemic and hypo-lipidemic activities.

Gentamicin induced nephrotoxicity:

Koreet et al. (2011) investigated the protective role of hydrochloric extract of *Ficuscarica* in gentamicin induced nephrotoxicity[13]. The rats were pre-fed experimental diets for 8 days and then received GM (100 mg/kg body weight/day) treatment for 8 days while still on diet. Serum parameters, oxidative stress

in rat kidney were analyzed. GM nephrotoxicity was recorded by increased serum creatinine and blood urea nitrogen. GM increased MDA level whereas decreased catalase, reduced glutathione. In contrast, HEFC alone increased CAT concentration, GSH content and decreased MDA level. HEFC supplementation ameliorated GM-induced specific metabolic alterations and oxidative damage due to its intrinsic biochemical/antioxidant properties.

Antidiabetic activity:

Stalin et al. (2012) evaluated the antidiabetic activity of methanolic leaf extract of *Ficuscarica* in Alloxan induced Diabetic rats[14]. Maximum reduction was observed on day 21. Gradual increase in body weight was also observed. MEFC 200 mg/kg exhibited maximum glucose lowering effect in diabetic rats. Metformin exhibited significant reduction in blood glucose levels at the end of the study when compared to diabetic control.

Perez *et al.* (1996) studied the hypoglycaemic effect of an aqueous extract of *Ficus Carica* leaves in streptozotocin-diabetic rats.[22] The extract induced a significant hypoglycaemic effect after either oral- or intraperitoneal (i.p.) administration. Results showed that *Ficus Carica* aqueous extract has a clear hypoglycaemic activity in treated versus non-treated diabetic rats. The mechanism involved in such an effect is not elucidated.

Antioxidant and Immunity activity:

Yang et al. (2009) investigated the antioxidative activities of water extract (WE) and crude hot-water soluble polysaccharide (PS) from *Ficus Carica*. fruit using various assays *in vitro*, including scavenging abilities on DPPH, superoxide and hydroxyl radicals and reducing power[15,30]. The immunity activities of PS were evaluated using the carbon clearance test and serum hemolysin analysis in mice. In addition, total phenolics and flavonoids contents were also determined. Both WE and PS have notable scavenging activities on DPPH with the EC50 values of 0.72 and 0.61 mg/ml, respectively. The PS showed higher scavenging activity than WE on superoxide radical (EC50, 0.95 mg/ml) and hydroxyl anion radical (scavenging rate 43.4% at concentration of 4 mg/ml). The PS (500 mg/kg) also has a significant increase in the clearance rate of carbon particles and serum hemolysin level of normal mice. The results indicate that both WE and PS might be applicable in healthy medicine and food industry.

Solomon et al. (2006) studied the potential health-promoting constituents of fig fruits, six commercial fig varieties differing in color (black, red, yellow, and green) were analyzed for total polyphenols, total flavonoids, antioxidant capacity, and amount and profile of anthocyanins[23]. Using reversed-phase liquid chromatography (RP-LC), various concentrations of anthocyanins but a similar profile was found in all varieties studied. Antioxidant capacity correlated well with the amounts of polyphenols and anthocyanins.

Diuretic Activity:

Sruthi et al. (2012) tested the ethanolic exract of *Ficus Carica* for diuretic activity in rats[16]. The parameters on individual rat were total urine volume, urine concentration of Na^+, K^+ and Cl^-. Ethanolic extract of *Ficus Carica* showed an increase in urine volume, cation and anion excretion. Based on the results, they concluded that *Ficus Carica* treatment produced marked diuresis.

Anticancer activity

Rubnov et al. (2001) reported a mixture of 6-*O*-acyl-β-D-glucosyl-β-sitosterols (where acyl moiety being primarily palmitoyl and linoleyl with minor amount of stearyl and oleyl) found in *Ficus Carica* Linn., resin as potent cytotoxic agents[17]. Both the natural and the synthetic compounds showed *in vitro* inhibitory effects on proliferation of various cancer cell lines.

Hypocholesterolaemic activity:

Canal et al. (2000) studied the hypo-cholesterolaemic effect of Ficus[18]. From the aqueous decoction of fig leaves, after treatment with Hydrochloride, centrifuging, treatment with sodium hydroxide and extraction with chloroform, the administration of the organic phase rats with streptozotocin induced diabetes led to a decline in the levels of total cholesterol and an decrease in the total cholesterol/HDL cholesterol ratio (with respect to the control group), together with a reduction of the hyperglycaemia.

Hepato protective activity:

Mujeeb et al. (2011) investigated the hepato protective activity of methanolic extract of *Ficus Carica* leaves in carbon tetrachloride induced hepatotoxicity in rats[19]. The degree of protection was measured by estimating biochemical parameters like serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), total protein (TP), total albumin (TA), alkaline phosphtase and the level of total serum bilirubin.

Mohan et al. (2007) evaluated the Hepato protective activity of *Ficus Carica* leaf extract on carbon tetrachloride induced hepatotoxicity[39]. The activity of extract was comparable to that of silymarin, a known Hepato protective.

Antiplatelet activity:

Richter et al. (2002) reported the antiplatelet activity of *Ficus Carica* Linn. Which was studied by taking the blood from normal human volunteers

reported to be free of medications for 1 week[20]. Platelet aggregation was induced with the agonists (adrenaline and ADP). The observed inhibitory effect of *Ficus Carica* Linn on adrenaline and ADP induced platelet aggregation at relatively lower doses (0.6 and 1.2mg/mL. An active principal (ficin) from this plant was shown to possess haemostatic effect through activation of factor X.

Anthelmintic activity:

Stepek et al. (2005) reported the anthelmintic efficacy of cysteine proteinases from fig (*Ficus Carica* Linn.) *in vitro*using the rodent gastrointestinal nematode *Heligmosomoides polygyrus*[21]. Within a 2 hour incubation period, cysteine proteinases, caused marked damage to the cuticle of *H. polygyrus* adult male and female worms, reflected in the loss of surface cuticular layers. The efficacy and mode of action make plant as potential candidates for a novel class of anthelmintics.

Immuno modulatory activity:

Patil et al. (2010) studied the Immuno modulatory activity of the ethanolic extract of *Ficus Carica* leaves[26]. The study was carried out by various hematological and serological tests. Administration of extract remarkably ameliorated both cellular and humoral antibody response. It was concluded that the extract possess immune modulatory activity.

Anti-inflammatory activity:

Patil et al. (2011) investigated the anti-inflammatory activity of *Ficus Carica* leaves[27]. The petroleum ether, chloroform and ethanol extract significantly reduced the carrageenan-induced paw edema in rats. These extracts showed a greater anti-inflammatory effect compared to standard drug Indomethacin.

Antimicrobial activity:

Aref et al. (2010) investigated the antimicrobial activity of *Ficus Carica* latex against resistant human pathogens[28-29]. The green fruit latex was collected. The antimicrobial activity of the extracts was evaluated and based respectively on the inhibition zone using the disc diffusion assay, minimal inhibition concentration (MIC) for bacterial testing and the method by calculating inhibition percentage (I%) for fungi inhibiting activities. The methanolic extract showed no activity against bacteria while ethyl acetate extract had inhibitory action on dividing bacteria.

Jeong et al. (2009) investigated the antimicrobial activity of methanol (MeOH) extract of figs against oral bacteria[35]. The MeOH extract showed a strong antibacterial activity against oral bacteria.

Balestra et al. (2009) studied the effect of *Ficus Carica* extract on tomato bacterial pathogens[38]. The extract was found useful in protecting pathogen attack in tomatoes.

Antispasmodic activity:

Gilani *et al*. (2008) reported that the ethanolic extract of the fruit of the plant (*Ficus Carica* Linn.) showed significant spasmolytic effect by using rabbit jejunum preperations[34]. The data obtained in this study indicated that the fig possessed spasmolytic effect mediated possibly through K+ATP channel activation.

Anti-pyretic activity:

Patil et al. (2010) evaluated the anti-pyretic effect of an ethanol extract of leaves, of *Ficus Carica* Linn. at normal body temperature and yeast-induced pyrexia, in albino rats[36]. The ethanol extract of *Ficus Carica*, at doses of 100, 200 and 300 mg/kg body wt. p.o., showed significant dose-dependent reduction in normal body temperature and yeast-provoked elevated temperature. The anti-pyretic effect of the ethanol extract of *Ficus Carica* was comparable to that of Paracetamol (150 mg/kg body wt., p.o.), a standard anti-pyretic agent.

Anti-Angiogenic activity:

Mostafaie et al. (2010) investigated the anti-angiogenic and anti-proliferative potentials of *Ficus Carica* latex extract using human umbilical vein endothelial cells (HUVECs)[37]. The results clearly indicated that latex extracts of *Ficus Carica* contain strong anti-angiogenic and anti-proliferative activities.

Hypotriglyceridaemic activity:

Pérez et al. (1999) investigated the hypolipidaemic effect of an intraperitoneal (i./p.) administration of a *Ficus Carica* leaf decoction[40]. The plasma total cholesterol levels, which were not modified, showed no significant differences in relation to baseline levels in the presence or absence of *Ficus Carica* treatment either. The clearly positive results indicated the presence in the fig leaf decoction of a compound or compounds that influence lipid catabolism.

Free Radical Scavenging Activity:

Yang et al. (2010) designed the method to study the ultrasonic-assisted extraction of total flavonoids from the leaves of *Ficus Carica Linn.,* and their scavenging activities against hydroxyl and superoxide anion free radicals[41]. The optimum conditions for extracting total flavonoids from the leaves of *Ficus Carica Linn.* Were found to be: ethanol concentration 40%, material-to-liquid ratio 1:60 (g/mL), extraction temperature 60°C and length of ultrasonic treatment of 50min. Under these optimum conditions, the extraction efficiency of total flavonoids reached as high as 25.04mg/g. The total flavonoids extract from the leaves had marked scavenging effects on both hydroxyl and superoxide

anion free radicals in a concentration-dependent fashion.

CONCLUSION

The present study shows the plant description, traditional uses, modern uses, phytocostituents and pharmacological activities of *Ficus Carica* Linn. The plant contains coumarins, flavonoids, sterols, triterpenoids, anthocyanins *etc*, in various parts of it. It has hepatoprotective, antidiabetic, antiplatelet, anthelmintic, hypocholesterolaemic, anticancer, diuretic, antioxidant and immunity activities.

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