

REVIEW

***Ajwa* Date (*Phoenix dactylifera*): An Emerging Plant in Pharmacological Research**

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Abstract: Date Fruits are consumed in Arab areas for a long time as a part of essential diet. *Phoenix dactylifera* belongs to family Arecaceae and its leaves, barks, pits, fruits and pollens have anticancer, antioxidant, hepatoprotective, antidiabetic, antihypertensive, antiulcerative, anti-inflammatory, antiproliferative, antimutagenic, antidiarrheal, antibacterial, antifungal and antiviral potential. Besides these, Dates also increase level of estrogen, testosterone, RBCs, Hb, PCV, reticulocytes and platelet counts. It can also cure lead induced hemotoxicity, side effects of methylprednisolone, male and female infertility. It has also cerebroprotective, neuroprotective and haemopoietic activity. *Phoenix dactylifera* can be used for number of complications if further evaluated and isolated. The present paper is an overview of pharmacological properties of *Phoenix dactylifera* reported in literature.

Keywords: *Phoenix dactylifera*, palm dates, dates, arecaceae, Ajwa, pharmacological properties.

INTRODUCTION

The emergence of resistance and tolerance to the existing drugs has created a decreased efficacy of these drugs in use. This problem has been tried to be overcome by increasing the drug delivery to the target site by the use of polymers (Khalid *et al.*, 2009; Hussain *et al.*, 2011) or through nanotechnology (Naz *et al.*, 2012; Ehsan *et al.*, 2012), synthesis of new drugs, either by the use of proteomics (Qadir, 2011; Qadir and Malik, 2011), or synthesis from lactic acid bacteria (Masood *et al.*, 2011), or marine microorganisms (Javed *et al.*, 2011). However, now a days, the trend is being changed from synthetic drugs to the natural drugs either from plants or microbes to control the diseases. The natural products are constantly being screened for their possible pharmacological value particularly for their anti-inflammatory (Qadir, 2009), hypotensive (Qadir, 2010), hepatoprotective (Ahmad *et al.*, 2012; Ali *et al.*, 2013), hypoglycaemic (Nisa *et al.*, 2009; Qadir and Malik, 2010), amoebicidal (Asif and Qadir, 2011), anti-fertility, cytotoxic, antimicrobial (Amin *et al.*, 2012), spasmolytic, bronchodilator (Janbaz *et al.*, 2013a), antioxidant (Janbaz *et al.*, 2012), anti-diarrheal (Janbaz *et al.*, 2013b) and anti-Parkinsonism properties. Arecaceae family also known as Palm family has 4000 species distributed over 200 genera. Date, coconut and African palm oil is major crops from this family. Genus *Phoenix* has 12 species and among them 5 are edible including *Phoenix dactylifera*. There are almost 3000 cultivators of Palm family all over the world (Rieger and Basra, 2006). Date palm is native to North

Africa and Persian Gulf regions but its exact origin is uncertain. Top ten producer of *Phoenix dactylifera* are Iraq, Egypt, Saudi Arabia, Tunisia, Algeria, UAE, Oman, Libya Arab Jamahiriya, Pakistan, Sudan, Europe, and USA (Lim, 2012). Taxonomical Position of *Phoenix dactylifera* is given in table 1.

Phytochemical Analysis

Phytochemical analysis of whole plant shows carbohydrates, alkaloids, steroids, flavonoids, vitamins and tannins. The phenolic profile of the plant revealed the presence of mainly cinnamic acids, flavonoid glycosides, flavanols. The Thin layer chromatography (TLC) analysis showed the presence of steroids namely cholesterol, stigmasterol, campesterol and α -sitosterol. While fresh dates contain Anthocyanins (Vembu *et al.*, 2012). Dates are rich source nutrients as carbohydrates (44-88%), Dietary fibers (6.4-11.5%), fats (0.2-0.5%) and proteins (2.3-5.6%). Dates also contain fatty acids e.g. Palmitoleic acid, Oleic, Linoleic and Linolenic acid. There are 23 types of amino acids in date's proteins and some of them are not present in nutritious fruits like bananas, oranges and apples. Besides this vitamin A, B₁, B₂ and nicotinic acid are also constituents of dates (Abdu, 2011).

Antioxidant and Hepatoprotective

Free radicals cause many oxidative damages in body and lead to Carcinogenesis, Mutagenesis, aging, atherosclerosis, neuro-degenerative diseases and stress induced depression. Free radicals attack on proteins, lipids and nucleic acid in Biological systems and cause said complications that lead to decline in quality of life.

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Phoenix dactylifera is famous for its use in jaundice and in women before and after delivery in traditional medicine. Date's syrups can replace honey by 75 % because of its main constitute "Sugar". In vitro studies proved that *Phoenix dactylifera* has antioxidant and antimutagenic properties. Palm date syrup was tested on 25 New Zealand rabbits for its hepatoprotective effects in which hepatotoxicity were induced by carbon tetrachloride. In this study mainly ALT and AST level were tested by the enzymatic kits while NADH disappearance was also measured by spectrophotometry from the blood taken from heart. NADH disappearance is actually directly proportional to activity of ALT and AST. This study shows significant reduction of ALT and AST levels. Interesting thing in this study was that three kinds of syrups were used Saudi, Iraqi and Rotab (Yameni) and reduction in enzyme levels was different with these three varieties. Researchers concluded that hepatoprotective activity is dependent upon the total phenolic contents and flavonoids in *Phoenix dactylifera*. Among them variety Rotab has strongest antioxidant and hepatoprotective effects and this is due to high total phenolic contents and high flavonoids in Rotab. Iraqi syrup has lowest hepatoprotective and antioxidant properties due to low phenolic contents and flavonoids. This study strongly suggests the use of *Phoenix dactylifera* as dietary habit for better health (Shoabi ZA *et al.*, 2012).

Table 1: Taxonomical Position of *Phoenix dactylifera*

Kingdome	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Liliopsida
Subclass	Arecidae
Order	Arecales
Family	Arecaceae
Genus	<i>Phoenix</i>
Species	<i>Phoenix dactylifera</i> L.

In another study flesh of *Phoenix dactylifera* was used to determine its hepatoprotective potential in rabbits. In this study 60 New Zealand rabbits were used in six groups (10/group). Hepatotoxicity was induced by CCl₄ and the levels of AST, ALT, IgM, IgG and IgA were seen after treatment with water extract. Rabbit's livers were also homogenized for the estimation of malondialdehyde (MDA) and (Glutathione) GSH as a biomarker of lipid peroxidation and antioxidative stress respectively. In this study water extract of *Phoenix dactylifera* caused significant ameliorations of AST and ALT. During hepatotoxicity lipid peroxidation products (MDA) increases and endogenous antioxidant (GSH) decreases. Pretreatment with extract ameliorates increased and decreased level of MDA and GSH respectively. Elevated level of IgM, IgG and IgA (near to control level) indicate potent antioxidant property of *Phoenix dactylifera* as

hepatotoxicity decreased the level of these proteins especially IgG. This study also suggests proposed mechanisms of action of *Phoenix dactylifera* in hepatoprotectivity. One is that Beta-Sitosterol in *Phoenix dactylifera* is responsible for protective effects, second flavonoids in *Phoenix dactylifera* inhibit Cytochrome P450 aromatase that favors liver regeneration and thirdly ascorbic acid contents of *Phoenix dactylifera* play an important in liver protection. This study significantly shows CCl₄ induced hepatotoxicity can be ameliorated by aqueous flesh extract of *Phoenix dactylifera* (El-Gazzar *et al.*, 2009).

Ajwa date as functional food is proved by another study using 28 wistar rats in which Orchoatoxin A was used to induce hepatotoxicity. In this 4 weeks study the effect of aqueous extract of flesh of *Phoenix dactylifera* was determined in affected rats by analyzing the levels of ALT, total bilirubin and by examining the liver tissues. Extract showed strong antioxidant activity with significant results. Levels of bilirubin and ALT were markedly lower as compared to control group. While normal tissues were seen under the microscope after treatment with *Phoenix dactylifera* aqueous extract. Many histological alterations were enormously reduced after extract application as compared to rats treated with Orchoatoxin A. It can be concluded from this study that *Phoenix dactylifera* may boost antioxidant enzyme that provides protection to hepatocytes against oxidative stress (Abdu, 2011).

Table 2: Compounds detected in *P. dactylifera* extracts by column chromatography (Abbas and Ateya, 2011).

n-Hexane Fraction: Clionasterol acetate, β- Sitosterol acetate, β-Sitosterol caproate, Cerotic acid, Lignoceric acid, Behenic acid, β- Sitosterol, Cholesterol, Estrone, Estradiol
Ethyl Acetate Fraction: Isorhamnetin-3-O-glucoside, Apigenin, Luteolin-7-O-glucoside, Naringin, Rutin

In another study carried out on 60 albino rats in which hepatotoxicity were induced by thioacetamide that cause liver cirrhosis through its hepatotoxin metabolite thioacetamide S-oxide. In this study hepatoprotective effect of Ascorbic acid was also studied with *Phoenix dactylifera*. When these rats were treated with aqueous extract of *Phoenix dactylifera* made from flesh, there were marked improvement in liver health. Biochemical investigators in this study were glucose, ALT, AST, bilirubin, ALP, LDH, gamma glutamyl transferase, serum alpha fetoprotein, serum testosterone and reduced levels of GSH. Interesting thing in this study is its comprehensiveness as large numbers of parameter were examined. These parameters which showed marked increase except GSH and Glucose (both were decreased) in cirrhotic rats when treated with aqueous extract gave

Table 3: Phytochemical Analysis of Different parts of *Phoenix dactylifera* plant (Al-Daihan and Bhat, 2012)

	Carbohydrates	Alkaloids	Steroids	Saponins	Flavonoids	Tannins
Leaf	P	P	P	A	A	P
Fruit	P	P	P	P	P	P
Seed	P	P	P	A	A	A
Bark	P	P	A	A	P	P

P: Present, A: Absent

excellent results vary from highly significant to very highly significant. Hypogonadism which is a complication in cirrhosis of liver can be treated with *Phoenix dactylifera* extract. This study suggests *Phoenix dactylifera* as a safe and effective plant for medicinal purposes (Ahmed *et al.*, 2008).

Extracts date's pits and date's flesh were applied on male wistar rats. Hepatotoxic agent used in this study was CCl₄. Hepatoprotective effect was calculated by formula of Singh *et al.* Blood samples at 29th day of treatment were collected from inner canthus and were assayed for the levels of ALT, AST, ALP and bilirubin. Liver morphology was assessed by the observer who was blinded to the treatment. Levels of ALP, AST, ALP and bilirubin were significantly reduced in both post and pre treatment animals. After calculating value of percentage protection from the Singh *et al.* formula it was clear that both extracts have hepatoprotective activity in CCl₄ induced hepatotoxic animals. Proposed mechanism of action of *Phoenix dactylifera* in this study is presence of phenols and flavonoids. This study suggests that *Phoenix dactylifera* is inexpensive and effective prophylactic or/and treatment for liver injury (Al-Qarawi *et al.*, 2004).

When antioxidant effect of seeds of *Phoenix dactylifera* was studied in immature female albino rats by comparing with standard antioxidant D, L alpha tocopherol then results suggested highest antioxidant activity of D, L alpha tocopherol (92%) followed by non polar (57.8%) and then polar (53.9%) extracts of seeds of *Phoenix dactylifera* (Ammar *et al.*, 2009).

In another study 14 varieties of dates (Shahani, Khasuei,, Sayer, Zahedi, Shekar, Shahabi, Kabkab, Khenizi, Maktub, Kabkab dalaki2, Shahabi 2, Majul, Gofar and Lasht) were tested for their antioxidant activities by extracting their phenolic contents of seeds in five extracts [Water, methanol: water (50:50, v/v), methanol, dimethyl sulfoxide (DMSO) and water: methanol: acetone: formic acid (20:40:40:0.1)]. These varieties were collected from Iran. Antioxidant study was determined by Ferric Reducing Ability Plasma (FRAP) method. Phenolic contents were also determined from each extract. DMSO extract in this study show highest antioxidant activity as well as highest phenolic contents while water and Water: Methanol extract had lowest activity. This study

demonstrate direct proportional of phenolic contents with antioxidant activity (Ardekani *et al.*, 2010).

Phoenix dactylifera has potential role to protect cellular damage caused by oxidative stress generated by free radicals production in body (Pujari *et al.*, 2011). Some varieties of *Phoenix dactylifera* are rich source of dietary fibers so they can be included in formulation of fiber and group of antioxidant food (Mrabet *et al.*, 2012).

Ingestion of dimethoate (organophosphate insecticides) causes hepatotoxicity in rats and pretreatment of these rats with fruit extract of *Phoenix dactylifera* cause prevention against oxidative damage to hepatocytes (Saafi *et al.*, 2011). Khalas variety of *Phoenix dactylifera* in Oman has highest antioxidant activity than other varieties (Al-Farsi *et al.*, 2005). Among different varieties Rotab syrup of *Phoenix dactylifera* has highest antioxidant potential followed by Saudi syrup then Iraqi Syrup (Al-Mamary *et al.*, 2011)

Male Infertility and Testicular Dysfunction

Use of herbal medicines for improvement of sexual life is improving day by day in developing countries. *Phoenix dactylifera* pollens can increase level of testosterone in cirrhotic patients thus improve sexual quality of life (Ahmed *et al.*, 2008). In a study 50 Sprague-Dawley rats were feed on *Phoenix dactylifera* pollen suspension for 35 days. Investigating parameters were blood and serum samples and morphology of testis, epididymis, seminal vesicle and prostate was determined under microscope. After treatment it was seen that after treatment sperm parameters e.g. motility, count and morphology improved especially with dose 120 mg/kg. *Phoenix dactylifera* pollen suspension has also cause reduction in DNA denaturation especially with high doses. Weight of testis and epididymus also increased during this study while there was little affect of *Phoenix dactylifera* pollens on prostate and seminal vesicle or histology of reproductive tissues. It has also reported that dates contain estradiol and flavonoids that increase sperm health thus improving male reproductive activity. *Phoenix dactylifera* also has gonadotrophin like effects may be due to steroidal components. Thus pollens of *Phoenix dactylifera* can be used to treat male infertility problems (Bahmanpour *et al.*, 2006).

Table 4: MICs of Different Extracts against *S. pyogenes*

Extracts	MIC (mg/ml)
Methanol Leaves Extract	1.33
Methanol Pits Extract	1.15
Acetone Leaves Extract	1.6
Acetone Pits extract	1.4

Table 5: Nutrients in different varieties of *Phoenix dactylifera*

Macro-Nutrients	Calcium, Phosphorous, Sodium, Sodium, Magnesium
Micro-Nutrients	Iron, Zinc, Copper, Manganese, Cobalt, Molybdenum, Aluminum, Arsenic, Barium, Cadmium, Chromium, Nickle, Lead, Strontium, Venadium

Benefits of *Phoenix dactylifera* for male infertility were also tested in another study by examining the effects of pollen extract on testicular dysfunction induced by cadmium which has gonadotoxic and spermiotoxic potential. Cadmium causes reduction in weight of sex organs, testosterone hormone, epididymal sperm count and their motility as well as testicular deformity and DNA damage that leads of infertility. When these affected rats were treated with *Phoenix dactylifera* pollen suspension then there was improvement in sperm characteristics as well as in testicular morphology. *Phoenix dactylifera* pollen suspension when given with cadmium to rats, provide protective effects against these complications that lead to infertility. *Phoenix dactylifera* pollens also protects from testicular damage. Suspension also increases testosterone and estrogen level (Saddiq and Bawazir, 2010). This study suggests that *Phoenix dactylifera* may be useful to resolve problems related to male infertility (Waffa *et al.*, 2012).

Female infertility and hormone levels

Women have three estrogenic hormones as Estradiol, Estrone and Estriol, among them estradiol is most potent hormone of reproductive age and estrone is a hormone in menopausal women. It has also been reported that estrone is present in Egyptian palm pollens. First determination of estradiol and estriol was carried out during a study in which extract of pollen grains of date palm was subjected to column chromatography. N-Hexane and Ethyl Acetate fractions of pollen extracts were examined that demonstrated 10 and 5 compounds respectively including estradiol and Estrone. Compounds shown by each fraction is given in table 1.

In this study estriol presence in dates was first determined by using HPLC. This study also supports strong antioxidant activity of *Phoenix dactylifera* pollen extract.

This a first study that demonstrate phytochemical analysis of *Phoenix dactylifera*. We can conclude from this study that *Phoenix dactylifera* can also be used for Female infertility due to hormonal deficiency (Abbas and Ateya, 2011). Estradiol like activity of *Phoenix dactylifera* was also determined by another study in which 24 immature white female albino rats were used in which polar (methanol and anhydrous methanol) and non polar (petroleum ether and ether) extract of seeds of *Phoenix dactylifera* was used to study its effects on uterine weight and degree of opening of vagina. The effects of these two extracts were compared with estradiol. After investigating it was seen that estradiol has maximum effects on said parameters followed by polar extract while non polar extract has lowest effect. Results of this study suggest that both extracts have estrogen like activity in rats but at different degrees. Interestingly this study also proved the safety of both extracts because acute toxicity studies was also conducted on adult male and female albino mice (Ammar *et al.*, 2009). *Phoenix dactylifera* can also be used for treatment of menopause as it contains estrogen (Hassan *et al.*, 2012).

Anti-diabetic activity

Anti diabetic activity of *Phoenix dactylifera* was tested on male wistar rats by inducing diabetes with alloxan. Ethanolic leaf extract of *Phoenix dactylifera* was used in this study and phytochemical analysis of extract was also carried out that shows presence of flavonoids, Saponins, Steroids and phenols while tannins, alkaloids and terpenoids were absent in the extract. Results of this study demonstrate significant antihyperglycemic and antilipaemic effects. This study also demonstrates mechanism of action of extract similar to hypoglycemic sulphonylureas (Mard *et al.*, 2010; Patel *et al.*, 2012). Date fruit aqueous extract when examined on streptozocin induced diabetic rats then results demonstrated that *Phoenix dactylifera* has potential to prevent diabetes hazards and cause improvement in diabetic neuropathy (Zangiabadi *et al.*, 2011).

Anti-Cancer and Antimutagenesis activity

It has been proved with many studies that foods having antioxidant activity can treat cancer and cardiovascular problems thus increasing life by 60%. In a study anticancer and antimutogenesis effects of *Phoenix dactylifera* were tested on *Salmonella typhimurium* by using vital capacity test and Ames test. Rat liver extract of *Phoenix dactylifera* pollen grains was applied on the bacterium and prevention percent was determined. Results of this study displayed anticancer and antimutagenesis activity of *Phoenix dactylifera* pollen grains (Gita *et al.*, 2011). Another study also showed that fruit extract of *Phoenix dactylifera* has potent antimutogenic activity and this study also demonstrate free radical scavenger like activity of fruit extract of *Phoenix dactylifera* (Vayalil, 2002).

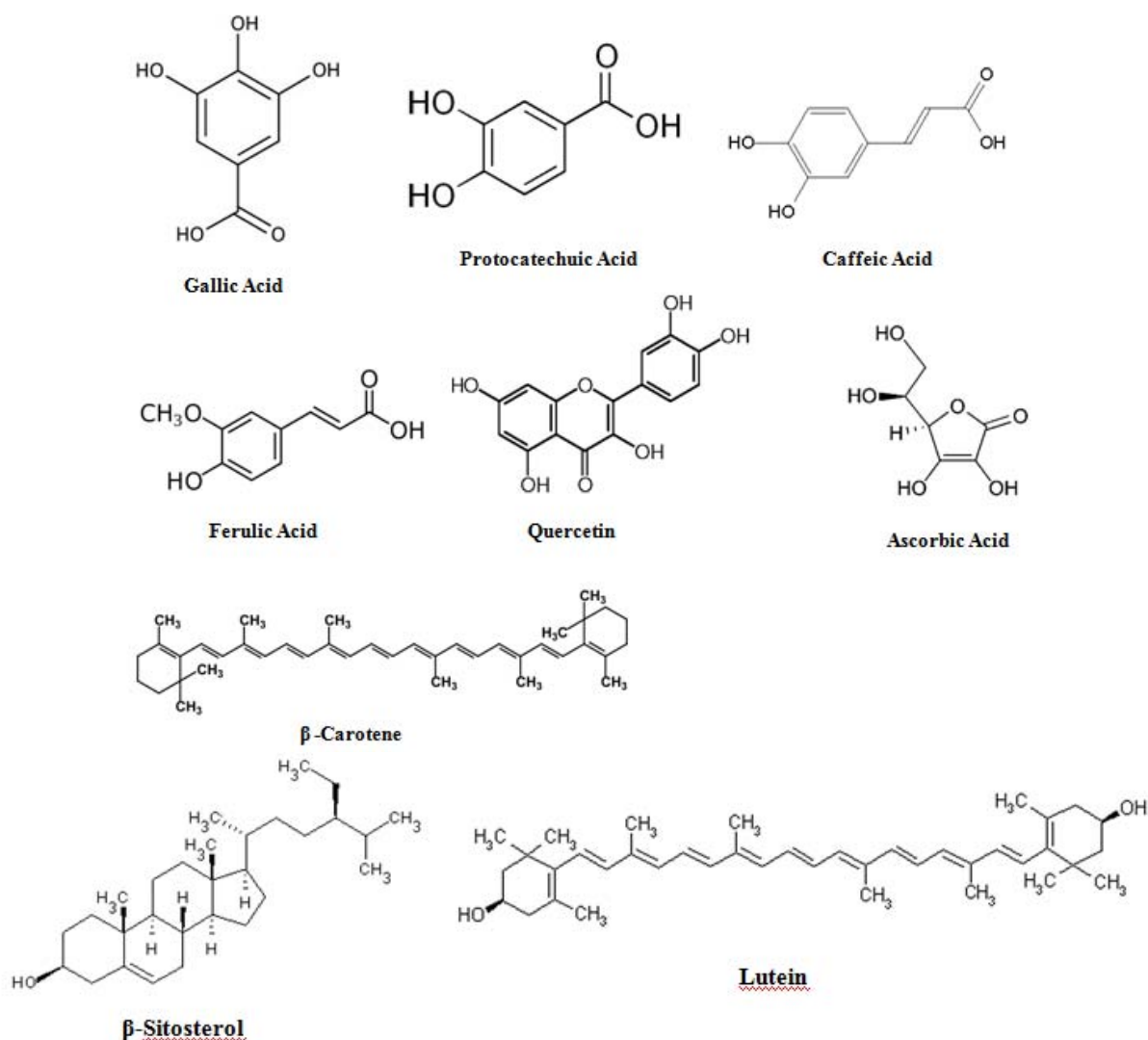


Fig. 1: Phytochemical constituents of *Phoenix dactylifera* (Vyawahare *et al.*, 2012).

In another study Glucan (a polysaccharide) was isolated from the Libyan dates and its anticancer study reveals that Glucan has potent antitumor activity may be due to (1-3) β -D-Glucan linkages. This was first study performed on dates for its anticancer activity (Ishurd and Kennedy, 2005).

Anticancer activity of *Phoenix dactylifera* has also been reported by Biglari *et al.* This study demonstrates anticancer potential of *Phoenix dactylifera* fruits for lymphoma (Biglari *et al.*, 2011).

Antidiarrheal Activity

Aqueous extract of *Phoenix dactylifera* can also be used for the treatment of Diarrhea which has been proved by a study in which same extract significantly reduced mean number of defecation when compared to control saline group. *Phoenix dactylifera* can reduce severity of diarrhea

in dose dependent way. In this study diarrhea was induced by castor oil (Kumar *et al.*, 2010; Al-Taher, 2008).

Anti Inflammatory and Anti Proliferative Activity

When pollen suspension and extract was administered in experimentally induced atypical prostatic hyperplasia (APH) in rats then results demonstrated protective effects of suspension as well as extract in APH induced rats. They cause modulation in cytokine expression and/or upregulation in autocrine/paracrine receptors (Elberry *et al.*, 2011). Hot water fruit extract of *Phoenix dactylifera* can also stimulate cellular immune system in mice (Karasawa *et al.*, 2011).

Treatment of Lead induced Haematotoxicity

Lead ingestion causes reduction in hematocrit, RBC, WBC, hemoglobin concentration, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration,

and lymphocyte and monocyte count; and cause increase in neutrophil count. In a study 40 rats (Grouped in four) were used among them haemotoxicity in blood was induced by 1 % lead acetate in 20 rats. After treatment with ethanolic extract of fruit of *Phoenix dactylifera* all the adverse effects induced by lead were prevented. So this study strongly suggests that extract of *Phoenix dactylifera* is good for blood's health and avoids lead induced haematotoxicity (Wahab *et al.*, 2010).

Haemopoietic Activity

Phoenix dactylifera besides of having different pharmacological activities also has Haemopoietic activity that was confirmed by a study in which 50 rats were grouped in 10 groups. They were subjected to aqueous and methanolic extract of fruits of *Phoenix dactylifera*. Results of this study revealed that level of RBC, Hb, PCV, reticulocytes and platelets count increased in dose dependent manner after administration of both extract. This increase levels show significant difference from control group. Total and differential count of WBCs and bone marrow examination did not differ significantly from control group. This study suggests that *Phoenix dactylifera* has haemopoietic activity in wistar rats (Onuh *et al.*, 2012).

Cerebroprotective and neuroprotective activity

Cerebroprotective effects of date seed extract was examined on male rats suffering from cerebral ischemia. According to this study seed extract significantly reduce neuronal damage. Ultrastructures of cortical neurons were also preserved by treatment with seed extract. Improvement in fall out latency time was also seen in group who was treated with seed extract. There was also reduction in oxidative stress in brain and restoration of antioxidative enzymes. Besides these benefits *Phoenix dactylifera* seed extract also attenuates muscle weakness that shows protective effect against ischemic reperfusion damage. This cerebroprotective effect of *Phoenix dactylifera* may be due to its antioxidant activity. This study suggests that *Phoenix dactylifera* use can be beneficial to manage brain ischemia (Kalantaripour *et al.*, 2012).

Another study also confirms neuroprotective effect of fruits of *Phoenix dactylifera* after applying to mice in which ischemia was induced by bilateral common carotid artery occlusion. Results of this strongly demonstrate that due to antioxidative properties *Phoenix dactylifera* is a neuroprotective agent and this activity is dedicated to presence polyphenolic compounds like flavonoids, plant sterols and ascorbic acid (Pujari *et al.*, 2011).

Antihypertensive

Phoenix dactylifera is also used in south east morocco as traditional treatment for hypertension (Tahraoui *et al.*, 2007).

Gastroprotective Activity

In a study ethanol induced gastric ulcer in rats was treated with aqueous and ethanolic extracts of fruits and pits of *Phoenix dactylifera*. Levels of histamine and gastrin that had been raised due to ulcer induced by ethanol were normalize mainly by fruit extracts and by pits extracts to some extent. Results showed that these extracts can reduce severity of ulcer and ethanolic undialyzed extract is most effective for this purpose as compared to others. This study also suggests that this gastroprotective activity of *Phoenix dactylifera* is may be due to its antioxidant potential (Al-Qarawi *et al.*, 2005). Gastric emptying can be increased by ingestion of water and ethanolic extracts of fruits of *Phoenix dactylifera* (Al-Qarawi *et al.*, 2003).

Antibacterial Activity

Antibacterial activity of *Phoenix dactylifera* was determined by Sooad and Ramesa by using leaf, seed, fruit and bark of plant. Three extracts (aqueous, methanol and acetone) were tested against standard gram positive (*S. aureus*, *S. pyogenes*) and gram negative strain (*E. coli*, *P. aeruginosa*) and antibacterial activity was measured by disc diffusion method through zone of inhibition and standard drug used was Kanamycin. Results demonstrated that all parts of plant have antibacterial potential in all extracts. Aqueous extracts were less antimicrobial than methanol and acetone. On other hand fruit and leaf extracts had better antibacterial activity than seed and bark. Acetone fruit extract and methanol leaf extract has highest activity against *S. aureus* and *E. coli* respectively. But all the extracts were less effective than standard Kanamycin. This study also give comprehensive phytochemical profile of *Phoenix dactylifera* plant as described in table 3. This study suggests that leaf and fruit are effective antibacterial than seed and bark. Effectiveness of methanol and acetone extract is due to their ability to extract wide range of constitutes than water and these suggests methanol a better and suitable solvent for antimicrobial studies. As fruit part has highest antibacterial activity except *E. coli* and it is due to presence of maximum constituents in it. Antibacterial activity of *Phoenix dactylifera* is may be due to its constituents as alkaloids, flavonoids and tannins have been reported to have antibacterial properties. In this study Pits of *Phoenix dactylifera* have activity against gram negative bacteria (Al-Daihan and Bhat, 2012).

Antibacterial activity of seed and pits of *Phoenix dactylifera* was also determined in another study by measuring MIC of water, methanol and acetone extracts of pits and seeds against 7 pathogenic bacteria e.g. *E. coli*, *S. aureus*, *S. subtilis*, *S. pyogenes*, *P. aeruginosa*, *E. faecalis*, and *S. flexeneri*. In this study three varieties of dates were used Barhee, Sukri and Rothana. Methanol and acetone extracts of leaf and pits of all three varieties have good antibacterial activity against *B. subtilis* and *S. pyogenene*. Growth of *E. faecalis* is not inhibited by any

extract of any variety. Order of antibacterial effectiveness is given as (Except *E. faecalis*) of Barhee variety: Doxycyclin > Methanol Pits extract > methanol Pits extracts > Methanol leaves extract > Acetone Leaves extracts > Water extracts Results of this study shows that *S. pyogenes* strain are most sensitive than any other strain while *P. aeruginosa* is resistant to aqueous extract of pits and leaves. While in Sukri variety methanol extracts have better antibacterial activity than others and its order of antibacterial activity is: *S. pyogenes* > *B. subtilis* > *S. aureus* > *E. coli* > *P. aeruginosa* > *S. flexeneri*.

Similarly order of antibacterial activity of Rothna variety with Methanol pits extract is: *S. pyogenes* > *B. subtilis* > *S. aureus* > *E. coli* > *P. aeruginosa* > *S. flexeneri*. As most sensitive strain for all varieties is *S. pyogenes* of MIC of this strain was determined after preparing its methanol and acetone extracts of leaves and pits.

This study also suggests that antimicrobial activity of this plant might be due to chemicals present in it (Perveen K et al., 2012).

It has been also proved that pits are more effective than other antibiotics and it is due to difference in resistance of bacteria. Methanolic pits extract of *Phoenix dactylifera* has also activity against *E. coli* and *K. pneumonia* (Saddiq and Bawazir, 2010).

Antifungal activity

Antifungal activity of leaves and pits of *Phoenix dactylifera* was determined by Bokhari and Perveen (2012). They tested water; methanol and acetone extract of leaves and pits on seven pathogenic fungi *F. oxysporum*, *Fusarium sp.*, *F. solani*, *A. flavus*, *A. alternata*, *Alternaria sp.* and *Trichoderma sp.* by agar well diffusion and agar dilution method. Two varieties of dates Barhee and Rothna were tested against test fungi. Water extracts of both varieties showed no effect on growth of tested fungi. Strong antifungal activity was seen with methanol pits and leaves extract against *A. alternata*. Poor to negligible antifungal activity was seen with all extracts against *A. flavus*. Methanolic extracts of both varieties showed good activity against all fungi except *A. flavus*. Order of activity according to zone of inhibition against almost all fungi is given below: Methanolic pits extract > Methanolic Leaves extract > Acetone pits extract > Acetone leaves extract Results of this study strongly demonstrate that two varieties of *Phoenix dactylifera* extracts have antifungal properties. Difference in degree of inhibition of fungi growth may be due to phytochemicals present in two varieties (Bokhari and Perveen, 2012). Antifungal activity of *Phoenix dactylifera* has also confirmed by another study in which dichloromethanolic extract has best antifungal activity (Boulenouar et al., 2011).

Antiviral Activity

Jassim and Naji (2007) studied antiviral activity of acetone pits extract of *Phoenix dactylifera* against lytic pseudomonas phage using *Pseudomonas aeruginosa* as host cell. According to results extract showed antiviral activity with MIC <10ug/ml for *Pseudomonas* phage. It was also found that extract strongly inhibit infectivity of *pseudomonas* phage. The decimal reduction time, concentration exponent and phage inactivation kinetics were determined that strongly agree with antiviral potential of *Phoenix dactylifera*. Inhibition of infectivity of phage and bacterial lysis with *Phoenix dactylifera* pits extract shows that *Phoenix dactylifera* may be an inexpensive way to protect from viral infections and further studies on *Phoenix dactylifera* may open some ways for HIV treatment (Jassim and Naji, 2007).

Obesity

Aqueous extract of *Phoenix dactylifera* can reduce obesity while further studies are required for its clinical use (Vembu et al., 2012).

Effects of reducing side effects of methylprednisolon

Treatment with methylprednisolon causes decrease in Noradrenalin, Dopamine and GABA while 2 weeks administrations of pits cause maximal increase in these neurotransmitters. Administration of methylprednisolon and pits of *Phoenix dactylifera* cause increase level of testosterone serum. So results of this study demonstrate that pits of *Phoenix dactylifera* can be used for male infertility as well as to minimize the adverse effects of methylprednisolon (Saddiq and Bawazir, 2010).

As excipient

Dried Fruit powder of *Phoenix dactylifera* can also be used as binder in tablet manufacturing as it shows good flow properties and compressibility. In a study in which powder of fruits of *Phoenix dactylifera* were used as binder in paracetamol tablet formulation it has been proved that powder of fruits of *Phoenix dactylifera* is better than acacia and tragacanth in all aspects (Ngwuluka et al., 2010).

Nutritional value of Phoenix dactylifera

Nutritional elements of *Phoenix dactylifera* are given below determined by a study Habib and Ibrahim (2012).

As shown by table *Phoenix dactylifera* can be a good source of minerals and elements and can be used in deficiency states (Habib and Ibrahim, 2011).

Anti-nutritional factors

As we know that dates are rich source of nutrients but some nutrients in dates may cause serious complications if taken in large quantities. A study was conducted 2011 in which nutritional concentration of 21 varieties of *Phoenix dactylifera* in Pakistan was determined in which total

oxalate, phytate and tannin contents were determined by specified procedures. Consumption of tannins in large doses can cause bowel, stomach and kidney irritation, GIT pain, liver damage, mineral and iron deficiency. Phytates and oxalates also cause mineral deficiency is extensive users. Calcium oxalate being insoluble can cause kidney stone. Though all varieties of dates have nutritional values but some of them may cause serious hazards to life by their extensive or regular use. Results of this study suggests that dates in general and especially four varieties (Aseel, Dhakki, Hallavi, Dora) are at safe corner of use and should be included in regular diet without any hazards (Nadeem *et al.*, 2011).

Effects on cytokine in allergic rhinitis

Palm date immunotherapy causes increase levels of serum and nasal IL-10 in allergic rhinitis patients (Boghdadi *et al.*, 2012).

Effects on labor parameter and delivery outcomes in pregnancy

A prospective study was carried out on 69 pregnant women to check the effect of *Phoenix dactylifera* on labor and delivery parameters. Consumption of date fruits were 6 per day for 4 weeks and control group was non-consumer of dates. Results of this study significantly showed that need of labor induction or augmentation is less in date fruit users as compared to control and delivery outcomes are though favorable but non-significant (Al-Kuran *et al.*, 2011).

CONCLUSION

Reported Pharmacological activities of *Phoenix dactylifera* support its traditional use in different diseases and also confirm its importance in Islamic teachings. The consumption of dates has positive effects on human health both for men and women and results of these findings suggests that it can also be a useful commercial drug after identification and isolation of active components that will assist in the treatment of cardiac, gastric and neuronal diseases.

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