Phoenix dactylifera: An update of its indigenous uses, phytochemistry and pharmacology

N Vyawahare, R Pujari, A Khsirsagar, D Ingawale, M Patil, V Kagathara

Abstract

Phoenix dactylifera L (Date palm) belonging to family Arecaceae, called ‘Nakhla’ and the ‘Tree of Life’ by the Arabs, is considered as one of the oldest cultivated fruit trees. It is believed to be indigenous to the countries around the Arabian Gulf. Many Middle Easterners believe that consumption of date fruits, particularly in the morning on an empty stomach, can reverse the actions of any toxic material that the subject may have been exposed to. Different parts of this plant are traditionally claimed to be used for the treatment of a broad spectrum of ailments including memory disturbances, fever, loss of consciousness and nervous disorders. There has been a tremendous interest in this plant as evidenced by the voluminous work in last few decades. Therefore, we aimed to compile an up to date and comprehensive review of Phoenix dactylifera that covers its traditional and folk medicine uses, phytochemistry and pharmacology including various preclinical and clinical studies.

INTRODUCTION

The role of traditional medicines in the solution of health problems is invaluable on a global level. Medicinal plants continue to provide valuable therapeutic agents, both in modern and in traditional medicine. With the associated side effects of the modern medicine, traditional medicines are gaining importance and are now being studied to find the scientific basis of their therapeutic actions. Research work on medicinal plants has intensified and information on these plants has been exchanged. This research will go a long way in the scientific exploration of medicinal plants for the benefit of man and is likely to decrease the dependence on synthetic drugs.

Phoenix dactylifera L. (date palm) a diploid with $2n = 36$, is a member of the monocot family Arecaceae classified as a dioecious tall evergreen tree. Date palms have been cultivated in the Middle East since at least 6000 BC. It is considered as native to countries around the Arabian Gulf. The Palm family is a symbol of prosperity and love to Muslims and its legend dates back to Judeo-Christian mythology. Date palm fruits have been an important component of the diet in most of the arid and semi-arid regions of the world. The various parts of this plant are widely used in traditional medicine for the treatment of various disorders which include memory disturbances, fever, inflammation, paralysis, loss of consciousness, nervous disorders. The fruits of Phoenix dactylifera are used as a detersive and astringent in intestinal troubles, treatment for sore throat, colds, bronchial asthma, to relieve fever, cystitis, gonorrhea, edema, liver and abdominal troubles and to counteract alcohol intoxication. It is also scientifically proved to possess a variety of pharmacological activities which indicate its usefulness in various kinds of diseases and disorders.

TAXONOMY


BOTANICAL DESCRIPTION

The date palm (Phoenix dactylifera) is dioecious, medium-sized tree with pinnate leaves containing about 150 leaflets having spines on the petiole. It consists of small yellowish flowers attached directly to the spikelets which develop into fruits. The fruits are known as dates. They are oval-cylindrical having single seed and range from bright red to bright yellow in colour when unripe, depending on variety.
PHYTOCHEMISTRY

Phytochemically the whole plant contains carbohydrates, alkaloids, steroids, flavonoids, vitamins and tannins. The phenolic profile of the plant revealed the presence of mainly cinnamic acids (ferulic, sinapic and coumaric acids and their derivatives, such as 5-o-caffeoylshikimic acid also called as dactyliferic acid), flavonoid glycosides (luteolin, methyl luteolin, quercetin, and methyl quercetin), flavonoids (catechin, epicatechin)\(^1\)\(^2\)\(^3\)\(^4\). Four free phenolic acids (protocatechuic acid, vanillic acid, syringic acid, and ferulic acid) and nine bound phenolic acids (gallic acid, protocatechuic acid, p-hydroxybenzoic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, and o-coumaric acid) were tentatively identified\(^5\)\(^6\). The Thin layer chromatography (TLC) analysis revealed the presence of steroids namely cholesterol, stigmasterol, campesterol and ß-sitosterol. Anthocyanins were detected only in fresh dates. The TLC analysis also showed that the major carotenoid pigment present in dates is lutein followed by ß-carotene\(^7\)\(^8\). Moreover the Gas liquid chromatography of the date seed oil revealed the presence of oleic, lauric, palmitic, Capric, myristic, myristoleic, palmitoleic, stearic, linoleic and linolenic acids. Dates contain at least six vitamins including a small amount of vitamin C, and vitamins B1 (thiamine), B2 (riboflavin), nicotinic acid (niacin) and vitamin A\(^9\). Enzymes such as phytase, invertase and peroxidase have been isolated in dates\(^10\). Presence of estrone has also been reported in the dried date seeds and pollens\(^20\).\(^21\). The date palm pollen grains showed the presence of ß-amirin, triterpenoids saponins and a crude gonadotropic substance\(^22\). Other isolated chemical constituents include ß-D glucan, heteroxylon, and galactomannans\(^23\)\(^24\)\(^25\).

BIOLOGICAL AND PHARMACOLOGICAL ACTIVITIES

Recently many pharmacological studies have been conducted on Phoenix dactylifera. A summary of the findings of these studies performed is presented below.

ANTIULCER ACTIVITY:

Pretreatment with date fruit ethanol and aqueous extracts at a dose of 4 ml/kg for 14 days markedly ameliorated the ulcer index, histological indices such as necrosis, haemorrhage, congestion and oedema in stomach sections and biochemical levels of some enzymes such as gastrin in plasma and mucin and histamine in gastric mucosae of ethanol-induced gastric ulceration in rats\(^26\). This lends support to the local folk medicinal claim that dates may be useful to humans with ulcers.

ANTICANCER ACTIVITY:

The polysaccharides (glucans) prepared from the date fruits
exhibited a dose dependent anticancer activity with an optimum activity at a dose of 1 mg/kg in tumour induced by subcutaneously transplanting allogenic solid Sarcoma-180 tumor cells into the right side of female CD1 mice. This research validated the traditional claim of date fruits to be used against various kinds of tumors.

**ANTI-DIARRHOEAL ACTIVITY:**
Phoenix dactylifera L spathe aqueous extract at doses of 3, 6 and 12 mg/kg produced a statistically significant reduction in both castor oil induced intestinal transit and frequency of diarrhoea in rats. These properties may explain the rational for the effective use of the plant as an anti diarrhoeal agent in traditional medicine.

**EFFECT ON GASTROINTESTINAL TRANSIT:**
Water and ethanolic extracts from date flesh and date pits at doses of 0.01, 0.02 and 0.04 ml/kg showed a dose dependent increase in the gastrointestinal transit time. While water extract from dialyzed date flesh extract induced a dose-dependent decrease the gastrointestinal transit time. The possible reason for this may be the method based extraction of particular component which could be valuable towards respective clinical conditions.

**HEPATOPROTECTIVE ACTIVITY:**
Pre and post treatment with aqueous extract of date flesh or pits significantly reduced CCl4 induced elevation in plasma activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), Alkaline phosphatase (ALP) enzymes and bilirubin concentration and ameliorated morphological and histological liver damage in rats. This study suggests that CCl4-induced liver damage in rats can be reversed by treatment of extracts from date flesh or pits. Moreover it can also be used prophylactically as a dymnamic liver support. In another study the date flesh or pit extracts not only normalised the elevated plasma activities of AST, ALT, ALP, lactate dehydrogenase (LDH), γ glutamyl transferase (γGT), enzymes and plasma concentration of bilirubin but also exhibited an enormous increase in the reduced serum levels of testosterone, alpha fetoprotein (AFP) and glucose in the thioacetamide induced chrotic rats. The extracts also showed significant reduction in oxidative stress evidenced by significant rise in the hepatic malonaldehyde (MDA) levels and decline in hepatic glutathione levels by normalising them. This data suggest that the daily oral consumption of an aqueous extract of the flesh of dates, and as a part of the daily diet ad libitum, was prophylactic to thioacetamide poisoning.

**ANTIMUTAGENIC ACTIVITY:**
Date fruit extract produced a dose-dependent inhibition of benzoyprene-induced mutagenecity on Salmonella tester strains TA-98 and TA-100 with metabolic activation. Extract from 3.6 mg/plate and 4.3 mg/plate was found required for 50% inhibition of His+ revertant formation in TA-98 and TA-100, respectively indicating potent antimutagenic activity.

**ANTIOXIDANT ACTIVITY:**
Phytochemicals from fruits have been shown to possess significant antioxidant capacities that may be associated with lower incidence and lower mortality rates of degenerative diseases in human. Various in vitro and in vivo antioxidant activites have been carried out on various extracts of different parts of Phoenix dactylifera. Studies conducted on antioxidant activity and phenolic content of various fruits of Phoenix dactylifera cultivated in Iran, Algeria and Bahrain demonstrated a linear relationship between antioxidant activity and the total phenolic content (TPC) of date fruit extract. Aqueous date extract was found to inhibit significantly the lipid peroxidation and protein oxidation and also exhibited a potent superoxide and hydroxyl radical scavenging activity in a dose-dependent manner in an in vitro study. Methanolic extract of Phoenix dactylifera seeds showed a significant increase in plasma levels of vitamin C, E and A, β-carotene and significant decrease in the elevated MDA levels due to the lipid peroxidation in adjuvant arthritis in rats. These findings suggests its possible use in diseases such as scurvy, ataxia and night blindness caused due to the deficiency of vitamins C, E and A respectively. Date seed oil was found to limit oxidative injuries induced by hydrogen peroxide in human skin organ culture which confirmed the potent free radical scavenging activity of the plant.

**EFFECT ON REPRODUCTIVE SYSTEM**
Oral administration of of date palm fruit suspensions at doses of 120 and 240 mg/kg improved the sperm count, motility, morphology, and DNA quality with a concomitant increase in the weights of testis and epididymis. Moreover, date extracts have been shown to increase sperm count in guinea pigs and to enhance spermatogenesis and increase the concentration of testosterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) in rats. This study suggests its usefulness in solving infertility problems in males. El-Desoky and his co-workers (1995) looked into the effect of date palm pollen grains
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(Phoenix dactylifera) on sexual hormonal balance, cholesterol, total lipids, total protein, albumin, globulin, and liver functions in control male and female rats, and castrated and ovariectomized rats. Their findings showed a decline in serum testosterone level; in control male rats, but a slight increase was detected in the castrated rats. Similarly, serum estradiol content was elevated in both control and ovariectomised rats. Progesterone level; however, decreased in control female rats, and was slightly increased in ovariectomized rats, with slight increase of serum FSH and LH in both normal and ovariectomised female rats. Pollen grains significantly increased serum globulin, total protein and total lipids in ovariectomized rats. Also serum ALP activity was increased in normal male rats. There was an increase in serum plasma glutamate pyruvate (GPT) activity in normal male, ovariectomized female and castrated rats, and similarly, glutamate oxaloacetate transaminase (GOT) activity was also increased in ovariectomized female and normal male rats. All these GPT and GOT values were still within the normal range in rats.

ANTIINFLAMMATORY ACTIVITY:
Oral administration of the methanolic and aqueous extracts of edible portion of Phoenix dactylifera fruits suppressed the swelling in the foot significantly by 67.8 and 61.3% respectively, while the methanolic extract of date seeds showed significant reduction by 35.5% in adjuvant arthritis in rats by mechanistically reducing ESR and plasma fibrinogen and normalizing the plasma level of antioxidants. Administration of the extracts also produced significant increase in body weight gain and food efficiency ratio.

ANTIVIRAL ACTIVITY
The crude acetone extracts of date palm pits at doses of 100 and 1000 µg/ml showed a rapid, strong and dose dependent ability to inhibit the infectivity of Pseudomonas phage ATCC 14209-B1 to Pseudomonas aeruginosa by binding to the phage, with minimum inhibitory concentration (MIC) of <10 µg/ml and completely prevented bacterial lysis, as evidenced by the presence of higher numbers of Pseudomonas aeruginosa cells surviving. These results suggest that the pit extract Phoenix dactylifera fruit could play an important role in controlling the replication of HIV-1 (Human Immuno Deficiency virus) by a novel mechanism of interaction with binding of the phage to the host bacterium and injection of its genome, which demonstrates its use in the treatment of AIDS (Aquired Immuno deficiency Syndrome) which has become a pandemic worldwide. Current treatment for HIV infection consists of highly active antiretroviral therapy which is associated with majority of side effects such as lipodystrophy, dyslipidaemia, diarrhoea, insulin resistance, an increase in cardiovascular risks and birth defects, so the Phoenix dactylifera can prove to be a novel drug for the treatment of AIDS without causing any side effects.

EFFECT ON HEMOLYTIC ACTIVITY OF
Phoenix dactylifera fruit extract at 5, 10 and 20% dilution when incubated with Streptococcus pyogenes for 24 h effectively slowed the growth of Streptococcus pyogenes to 30.8%, 64.7% and 88.5%, respectively. Date extract (DE) neutralised the hemolytic activity of the streptococcal exotoxin, streptolysin O and 96% inhibition was obtained at a very low concentration. (1:262144 DE dilution) 

EFFECT ON CISPLATIN-INDUCED GENOTOXICITY
Aqueous extract of pollen grains administered by oral route to mice at doses of 250 and 500 mg/kg significantly inhibited the cisplatin-induced genotoxicity. At histopathological level, a significant recovery of the testis histology was observed in animals administered with pollen grains prior to cisplatin treatment. Furthermore, administration of the pollens extract caused a decrease in epididymal sperms with tail abnormalities that would interfere with sperm motility, and the highest dose retained normal epididymal sperm number. These findings suggest the preventive role of the pollen grains against the chemotherapeutic-induced infertility in males.

ANTIHYPERTLIPIDEMIC ACTIVITY
In a study, Phoenix dactylifera fruit pulp was evaluated for its effect on the lipid metabolism in high cholesterol diet induced hypercholesterolemic hamsters wherein it significantly reduced the elevated levels of plasma lipids including cholesterol, triglycerides and low density lipoprotein (LDL) in the treated animals as compared to high cholesterol-diet supplemented animals indicating its possible beneficial effects in atherosclerosis development in humans. It also significantly reduced the total body, liver and kidney weights of the hamsters which were increased by the high cholesterol diet suggesting its possible use in the treatment of obesity which represents the most prevalent nutritional problem worldwide which in the long run predisposes to development of diabetes mellitus, hypertension, endometrial carcinoma, osteoarthritis, gall stones and cardiovascular diseases. In another report, the Phoenix dactylifera seed fibers (2.5%) supplemented with the basal diet significantly
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reduced the plasma triglyceride, LDL and total cholesterol levels and increased the high density lipoprotein (HDL) levels in the rats. This may be of particular importance in the light of the present evidence that the occurrence of coronary heart disease is strongly related to decreased HDL cholesterol concentration and increased LDL cholesterol concentrations. Another study evaluated the protective effects of Phoenix dactylifera pollen grains on liver and heart arteries in male rats fed with diet supplemented with different concentrations of date palm pollen grains (0.0%, 2.0% and 4.0%). In this study, the effects of Phoenix dactylifera pollen grains on liver function, lipid fractions of plasma, liver and brain, as well as fatty acid composition of liver lipids were investigated. The results exhibited significant reduction in plasma total cholesterol by 30.8% and 19.1%, total lipids by 39.6% and 39.86%, triglyceride by 6.9% and 41.8%, and low-density lipoprotein cholesterol by 54.7% and 21.8% in rats consumed modified diets containing 2.0% and 4.0% pollen grains of date palm, respectively. However, there was a significant (P<0.003) elevation in plasma HDL of treated rats compared to the control. Lipid fractions of liver and brain in treated rats were also significantly lowered as compared to the control. The liver function enzyme activities were significantly reduced in treated rats. The activities of liver enzymes namely GPT, GOT, LDH, ALP and γ-GT were significantly reduced in treated rats. The percentages of stearic acid, arachidic acid and lignoceric acid showed significant elevation in rats which consumed 2% and 4% pollen grains in the diets. This study showed that Phoenix dactylifera pollen grains play a role in lowering lipid fractions and protect the liver by maintenance of liver function enzyme activities.

NEPHROPROTECTIVE ACTIVITY

Al-Qarawi et al studied the effect of the extracts of the flesh and pits of Phoenix dactylifera on gentamicin induced nephrotoxicity in rats was investigated in which the significantly reduced the increase in plasma creatinine and urea concentrations induced by gentamycin nephrotoxicity and ameliorated the proximal tubular damage. Antioxidant components in the date (e.g., melatonin, vitamin E, and ascorbic acid) were suggested to be the basis of the nephroprotection.

CLINICAL STUDIES

Partysmart, a herbal formulation containing Phoenix dactylifera fruit powder as one of the ingredients was evaluated for its effect on blood and urinary levels of alcohol and acetaldehyde after alcohol ingestion and its safety as well as efficacy in the prevention of the alcohol-induced hangover symptoms in human volunteers in a prospective, randomised, double-blind, comparative, crossover phase III clinical trial. In this study, the formulation significantly reduced the mean hangover score along with the blood levels of alcohol and acetaldehyde without producing any clinically significant adverse effects providing a safe and effective novel herbal composition for the prevention of hangover syndromes and liver disorders in acute and chronic alcoholics.

A cosmeceutical composition containing alcoholic extract of Phoenix dactylifera fruit and seeds showed a significant wrinkles, toughness, fine lines, mottled hyperpigmentation, inflammatory papules and pustule, lesions, in the skins of various groups of patients suffering from different types of mucocutaneous skin disorders such as visible cheek nonhypertrophic actinic keratoses. rosacea, telangectasias, sebaceous hyperplasia, actinic/senile comedones, premalignant keratoses, acne vulgaris, extrinsic aging in controlled clinical studies indicating its ability to compensate the great need for new and effective treatment products for age and environmental insult related skin changes, disorders and diseases. Furthermore, kernel extract Phoenix dactylifera fruit with clinically proven anti-wrinkle efficacy and free radical scavenging properties is being included as an ingredient of D’Orientine™ S formulation which is used to protect the skin from environmental sources of aging and wrinkling.

A placebo-controlled clinical trial with 5% date pulp versus placebo in 10 patients was applied to the eyelid area twice daily for 5 weeks. A statistically significant reduction in wrinkle surface (27.6%) and wrinkle depth was achieved. Six of the participants said that visual improvement occurred. Moreover, Phoenix dactylifera is one of the ingredients of Epionce Renewal Eye Cream and Epionce Renewal Facial Cream which is applied to protect against signs of aging by the virtue of its antioxidant and soothing properties.

MEDICINAL APPLICATIONS OF

The water in which fresh dates are soaked for a while is a drink given to relieve alcohol intoxication. The milk in which clean and fresh dates are infused is a very nourishing and restorative drink to the children as well as adults especially during convalescence from fevers and smallpox. The sweet pulp of the date fruits is useful in dysentry. Date fruits are used as an ingredient in various aphrodisiacs and...
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tonic confections. They are also useful in asthma. Paste made from ground seeds of said to be applied for opacity of cornea and to the head to relieve headache and hemicrania. The smoke produced from burning of the date seeds in powder form is a useful fumigatory for piles. Some doctors advise dates as consumptives as they promote expectoration, soothe the chest and prevent constipation. Dried fruit pounded and mixed with almonds, quince seeds, pistachia nuts, spices and sugar forms a nutritious formulation. Seeds roasted and ground into powder make a beverage like coffee called “date coffee”. A fine paste of the seed of date fruit and the roots of Achyranthes aspera, applied to betel leaves like lime and made into small packets with clove, cardamom, catechu and betelnut powder is a popular antiperiodic remedy among Vaidyas for the prevention ofague which is preceded by severe shivering. A gum or juice obtained from the stem and named “laghi” (Khajurnidaru) is used as a demulscent, diuretic and referigerant in genitourinary affections The liquid distillate obtained from spathe of Phoenix dactylifera locally known as Maa Al-liqah or Maa Al-Tiltal, water of the spathe is believed to have certain medical uses as it relieves abdominal gases and pain especially after heavy meal and claimed to have anti-spasmodic activity. The flower of the plant is used as a purgative. The pollen grains of date palm have been used in Egyptian local practice to improve fertility in women.

CONCLUSION

In this systematic review, the pharmacological studies conducted on Phoenix dactylifera indicate the immense potential of this plant in the treatment of conditions such as diarrhoea, gastric ulcer, skin disorders, cardiovascular disorder, inflammatory ailments including liver and kidney disorders, microbial and viral infections, cancer, etc. Several studies indicate that consumption of fruits and vegetables is associated with reduced risk of several chronic diseases. Regarding dates the studies indicate that this fruit has important antioxidant activity due to the presence of water-soluble compounds with potent free radical-scavenging effects, such as phenolic compounds that may be associated with lower incidence and lower mortality rates of degenerative diseases in human. In spite of all these activities very meager work has been carried out on the chemical, biochemical, pharmaceutical and pharmacological aspects of the plant and hence extensive investigation especially on its clinical efficacy is needed to exploit its therapeutic utility to combat diseases. As the global interest towards traditional medicines over the conventional treatment is increasing due to safe and well tolerated remedies provided by them for the chronic illness with lesser side effects this review targets Phoenix dactylifera as a potentially safe and effective plant that has important medicinal values and benefits.

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Author Information

Neeraj Vyawahare, Ph.D.
Department of Pharmacology, AISSMS College of Pharmacy

Rohini Pujari, M. Pharm.
Department of Pharmacology, AISSMS College of Pharmacy

Ajay Khsirsagar, M Pharm.
Department of Pharmacology, AISSMS College of Pharmacy

Deepa Ingawale, M Pharm.
Department of Pharmacology, AISSMS College of Pharmacy

Manoj Patil, M Pharm.
Department of Pharmacology, AISSMS College of Pharmacy

Virendra Kagathara, M Pharm.
Department of Pharmacology, AISSMS College of Pharmacy