Date Palm against Human Infertility

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Contributor: Jameel Al-Khayri , Jose Manuel Lorenzo , , Summar A. Naqvi , Mohammed Alaghbari , Muhammad Faisal Manzoor , Rana Muhammad Aadil

Due to its antioxidant potential, dates are considered a functional treatment for reducing the risks of infertility. In males, the date palm has a potent effect on the reproductive parameters including hormonal levels and seminal vesicle parameters as well as sperm motility, count, and viability; whereas, in females, it shows a convincing effect on reproductive parameters including oogenesis process, strengthening of oocytes, regulation of hormones, strengthening of pregnancy, reduction of the need for labor augmentation, and postpartum hemorrhage prevention.

date palm | human infertility | natural remedies | fertility enhancers

1. Introduction

Infertility is defined as the inability of any couple having a pregnancy within 12 months of sexual intercourse after the use of protection measures [1]. In developing countries, more than 186 million women suffer from infertility disorders [2]. A considerable percentage of men who suffer from sexual dysfunctions experience harm to their subjective quality of life [3]. Furthermore, infertility rates are higher in other parts of the world, such as Eastern and Central Europe, Sub-Saharan Africa, Central, and South Asia, where they might exceed 30% [2].

The term infertility and subfertility are used conversely. In primary infertility, a woman is not diagnosed with a clinical pregnancy and meets the criteria to be stated as infertile, whereas secondary infertility applies to the condition when a woman is diagnosed with a clinical pregnancy previously but is currently unable to establish a clinical pregnancy [4][5]. A study was conducted in 2010–2012 on 15,000 men and women in England, which stated that 12.5% of the women and 10.1% of the men experienced primary infertility [6]. In Pakistan, infertility prevalence is 22% with primary infertility comprising 4% of the total infertility cases [1].

The extensive use of the date palm as a botanical and medicinal plant demonstrates its relevance to human health. Additionally, clinical trials have explained several benefits regarding date palm [7]. Pakistan is one of the major producers of date fruits in the world [8]. Moreover, the date palm has been used throughout history to treat endocrine and reproductive system disorders [9].

2. Causes of Infertility in Female

According to the Center for Disease Control, female infertility can be caused by defective ovulation, transport (ovum and sperm), and implantation (zygote). Several known causes for female infertility are premature ovarian insufficiency, polycystic ovarian syndrome (PCOS), and endometriosis (a condition in which endometrial tissue grows on ovaries, the bowel, and the tissue lining of the pelvis) [10]. Abdominal surgeries cause scar tissue to develop that may alter the movement of the ovaries, fallopian tubes, and uterus. Like defective ovulation and transport, defective implantation may also lead to infertility through the congenital anomaly and fibroid formation.

Additionally, uterine flatulence is a form of complex dystemperament, which can trigger female infertility [11]. Poor lifestyle choices, such as eating patterns, stress, drinking, smoking, and obesity, can affect the general health and reproductive competence of a person and have been reported to significantly reduce the chances of pregnancy in women [12].

3. Date Palm: Nutritional Profile

The date is known for its rich source of macro-and micronutrients. Natural antioxidants such as phenolic acids, flavonoids, and tannins, are abundant in dates [13]. Major sugar constituents (Glucose and fructose), amino acids (glutamine and aspartic acid) are present in various date cultivars. Moreover, large amounts of essential amino acids are present whereas histidine was also present in the lowest concentration [14]. **Table 1** shows the nutrient profile of the date palm.

Table 1. The nutrient profile of the date palm.

Main Group	Nutritional Profile	Reference
Vitamins	Vit A, Vit E, Vit C, Vit B1, B2, B3, B6, B7, B9, Carotenoids (such as lutein, β-cryptoxanthin, and β-carotene)	[15][16][17][18]
Minerals	Al, Ca, Cu, Fe, K, Mg, Mn, P, Sr and Zn, Se, Mb, Co, Si	[18][19][20]
Phytochemicals	Flavonoids (isorhamnetin, apigenin, lutein, and naringin), and phenolic compounds (caffeic acid, gallic acid, catechin, coumaric acid, chlorogenic acid, and quercetin), tannins and anthocyanins, rutin	[21][22]
Protein	Amino acids (aspartic acid, threonine, glutamine, proline, glycine, alanine, Valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, Histidine, lysine, arginine, and serine)	[23]
Fatty acid	Unsaturated fatty acids (oleic, linoleic, and Linolenic acids) Saturated fatty acids (palmitic, linoleic, myristic acids)	[18][24][25]
Carbohydrates	Soluble sugars, dietary fiber	[26]

Aluminium: Al; Calcium: Ca; Copper: Cu; Iron: Fe; Potassium: K; Mmagnesium: Mg; Manganese: Mn; Phosphorus: P; Strontium: Sr; Zinc: Zn; Selenium: Se; Molybdenum: Mb; Cobalt: Co; Silicon: Si.

The major constituents of date pollen are amino acids including glutamine, proline, glycine, leucine, tyrosine, phenylalanine, aspartic acid, threonine histidine, lysine, arginine, methionine, isoleucine, serine, alanine, and Valine [27]. Furthermore, pollen is a rich source of important vitamins, especially vitamin B (Thiamine, riboflavin, biotin, folic acid) and vitamin A [28][29][30]. The pollen also contains considerable levels of vitamins C and E. DPP also contains minerals such as Zn, selenium, Fe, molybdenum, Cu, Mn, cobalt, and fatty acids, including, linoleic, myristic, and palmitic acids [30]. In DPP extracts, significant amounts of rutin, flavonoids (lutein, naringin, isorhamnetin, and apigenin), and phenolic compounds (chlorogenic acid, catechin, gallic acid, quercetin, coumaric acid, caffeic acid) were identified [31].

On average, date leaves contained 4.8% crude protein, 31.9% crude fiber (neutral detergent fiber at 81.5%, acid detergent fiber at 59.8%, and lignin at 14.6%), and 12.9% ash (average Ca content of about 7 g/kg and P about 1 g/kg) on a dry weight basis [32]. Seeds had a low concentration of protein and lipid but contain dietary fiber and ash content. The seed has a very low sugar content, compared to the high sugar content in the date pulp. Date palm seeds are rich sources of many minerals, K content was highest, followed by sulfur, P, Ca, Mg, and sodium (descending order), while in trace minerals, the highest selenium content is followed by Fe, silicone, Zn, Cu, Mn, Sr, and Al in descending order.

4. Date Palm Fruit, Pollen, and Seed: A Remedy against Infertility

The date, an economical and natural food source, is an important nutritional fruit in various regions. Dates were used for both dietary and phytomedicinal purposes against several health disorders, such as infertility. Date fruit contains simple sugars that are a readily accessible energy source, strengthen uterine muscles, and provide energy to the mother during labor. This section describes the health-promoting properties of bioactive components present in date palm attributed towards the betterment of fertility (**Figure 1**).

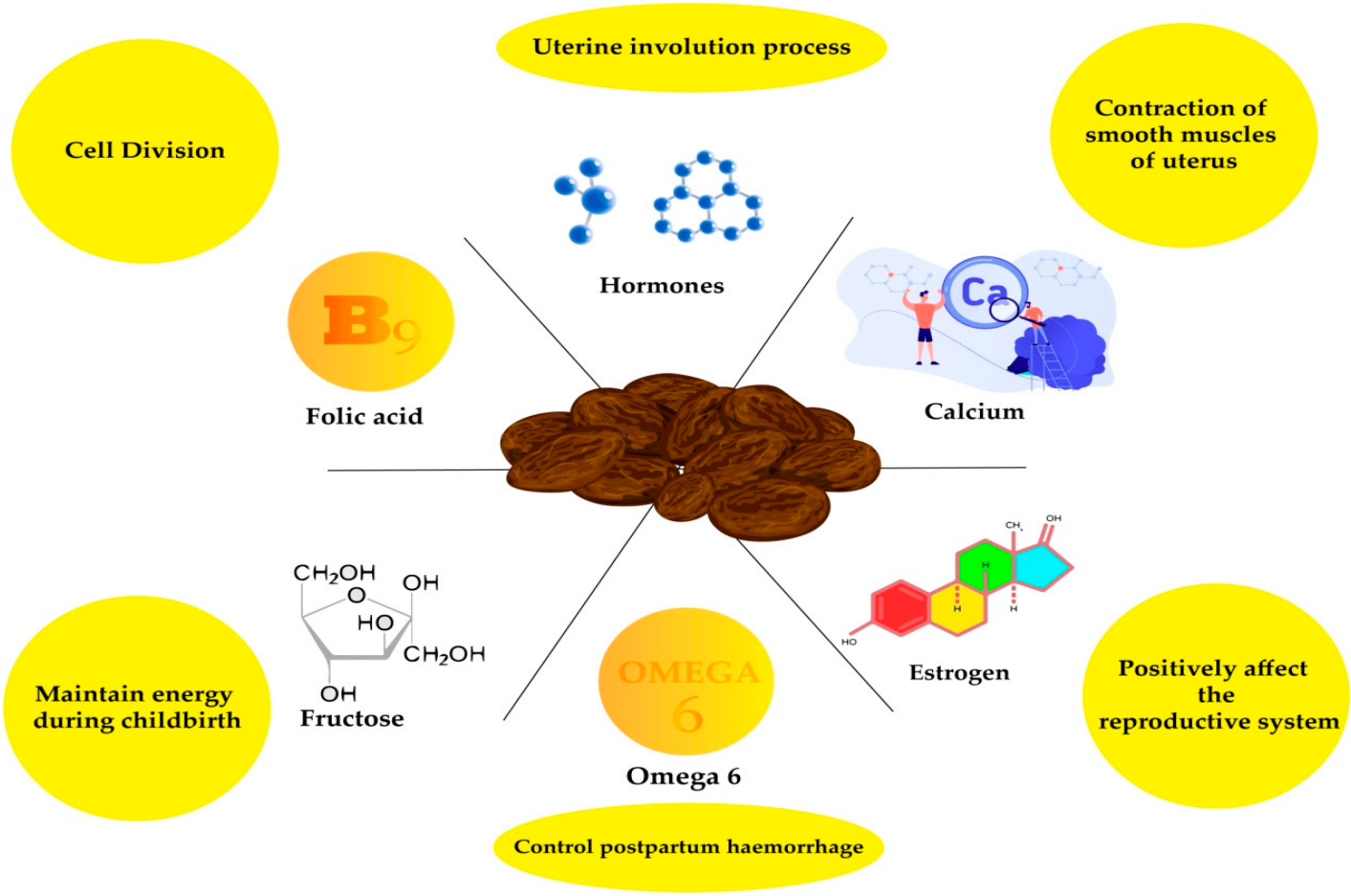

Figure 1. How date palm positively affects different parameters of fertility.

Moreover, early Egyptians and Chinese people used DPP as a rejuvenating medicinal agent and it is currently used as a dietary supplement globally [33]. The aphrodisiac effect of DPP might be attributed to the presence of estrogen hormones. Date palm have a role in fertility improvement and sexual reproduction (**Figure 2**). Additionally, DPP can be used in the treatment of sexual incapacity and weakness in the Arab world and may cause a substantial rise in testosterone levels in oligoasthenozoospermic patients and follicle-stimulating hormone (FSH) levels in azoospermic patients [34].

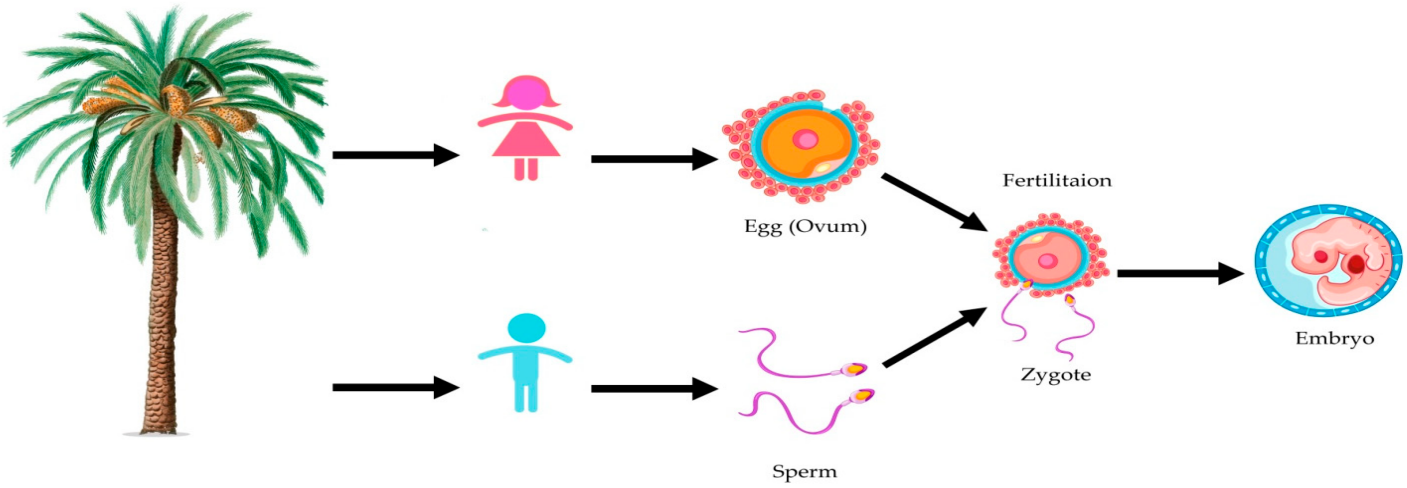

Figure 2. Illustration of the effect of date palm on sexual reproduction.

Furthermore, frequent oral administration of date palm pits caused a substantial increase in the concentration of mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hemoglobin, whereas the total protein, alanine aminotransferase, and creatinine decreased significantly. Date seeds also have the potential to improve the testosterone level, serum biochemical values, and antioxidant status in testis [35]. Thus, date and other parts (DPP and seed) have wide therapeutic potential as a natural remedy against infertility in males and females.

Various studies have been conducted that have shown the effect of the date palm parts on male fertility parameters. [36] designed a study to examine the effect of DPP andAstragalus ovinus (A. ovinus) extracts on fertility factors in male rats. Date seed significantly increased body weight gain. the summary of the date and its different parts improving male fertility.

[37], testicular dysfunction-induced rats (n= 48) were studied. Oral administration of DPP results in rejuvenation of sperm counts, motility, sex organs weight, and testosterone level that were reduced by inducing cadmium chloride (CdCl2). DPP treatment also restored the reduced glutathione, catalase (CAT), and superoxide dismutase (SOD). DPP treatment improved the reproductive damage and destructive effects of Cd on oxidative stress, spermatogenesis, and testis [38].

[39] carried out a study to determine the effect of DPP and seed extract of date palm on Cd-induced male albino rats (n= 36). Remarkable improvement was observed in luteinizing hormone (LH), aromatase enzyme, follicle-stimulating hormone (FSH), sperm quality, testosterone, estradiol (E2), total antioxidant capacity (TAC), xanthine oxidase (XO), glutathione, malondialdehyde (MDA), CAT, and SOD. DPP or date palm seed reduced the risk of Cd-linked infertility. [37] reported that DPP caused a significant enhancement in estradiol levels and sperm parameters in addition to a remarkable protective effect against testicular dysfunction induced by cadmium chloride.

[40] performed a study on rats, which recommended that the intake of 5 and 10% of DPP extracts might be beneficial for diabetic-induced male infertility. [41] carried out a study to explain the effect of DPP extract in streptozotocin-induced male diabetic rats (n= 30) and found that DPP improved FSH LH and testosterone levels

and may protect the testis structure. In another study, the effect of date pit powder was observed on the rejuvenation of reproductive functions in male diabetic rats. Their findings proved that the supplementation of date pit powder brings out a remarkable improvement in body weight, glycemic state, lipid profile, serum testosterone level, SOD activity, and sperm characteristics [42].

Another study was aimed to assess the effects of bee pollen (BP) and DPP suspensions (100 mg/kg body weight/day for 4 weeks) on streptozotocin-induced diabetic male Wistar rats. The results implicated that BP and DPP showed an antihyperglycemic effect through the normalization of testicular histological destructive changes, pituitary testicular axis dysfunction, and also showed improvement in the anti-oxidant system [15].

[36] performed a study to examine the effect of DPP (ethanolic extract) on thyroid-induced male infertile rats that resulted in the restoration of genital sex organs weight, serum LH, FSH, T, sperm count, and motility due to induced hyper- and hypothyroidism. [16] to examine the effect of DPP extract on testicular dysfunction of thyroid-disorder-induced male infertile rats. Supplementation of DPP extract to normal rats augmented serum levels of LH, sperm count, and motility as well as testicular antioxidant status. Additionally, it was proved that DPP extract caused a remarkable improvement in hyper- or hypothyroidism-induced sex hormones, testicular dysfunction, testicular marker enzyme activities, and sperm qualities [17].

It is worth highlighting that date palm and its constituents have a significant effect on female fertility parameters. [18] to check the effect of lyophilized extract (500 mg/kg) of date pits and plasma estradiol concentration (2 mg/kg) on the uterine rate of female rats. The polar fraction of the lyophilized extract greatly decreased the concentration of plasma estradiol. Furthermore, pollen extracts showed significant improvement in antral follicles and other sex hormones in female Balb/c mice [19].

There is a positive impact on maternal outcomes (both the first and third stages of labor) and as well as fetal health factors. Findings showed that date consumption reduces the need for labor augmentation but does not expedite the onset of labor [20]. [21] conducted a study to show the effect of date fruit on female labor parameters and delivery outcomes In the date fruit group, cervical dilation was also significantly increased, the requirement of oxytocin/protein was 28%, there was a higher rate of spontaneous labor, and the latent phase of the first stage of labor was shorter, as compared to the non-date fruit group.

Moreover, another study was carried out to identify the effect of eating dates and drinking water during labor versus Intravenous (IV) fluids on labor and neonatal outcomes. The results of the study showed a significantly shorter median duration of the second and third stages of labor among the study group compared to the control group with no significant harm regarding the mode of delivery and neonatal outcomes [22]. [23] carried out a study to determine the effect of date palm syrup on labor pain in nulliparous women (n= 80). Date palm syrup significantly lowered labor pain and starting impact occurred late by the usage of palm syrup, but it has a long relief effect.

Royani et al. [24] conducted a study to evaluate the potential effect of Ajwa dates on the prevention of preeclampsia threats in pregnant women. Findings have shown that the daily intake of 7 Ajwa dates has a remarkable impact to

decrease the Roll-over-Test (ROT) and Mean arterial pressure (MAP) in pregnant women at the risk of developing preeclampsia, thereby helping to prevent preeclampsia from developing.

Another aspect attributed to date palm is the prevention of postpartum hemorrhage [25] carried out a study that aimed to determine the effect of date fruit in nulliparous women (n= 100) on the amount and duration of postpartum bleeding. The results indicated that the date fruit was not effective in reducing the number of bleeding days. Another study was designed to elucidate the effectiveness of dates on postpartum hemorrhage Findings clearly highlighted that date was more effective than the infusion of oxytocin on postpartum hemorrhage [26].

[43] conducted a study to check the effect of date fruit on a postpartum hemorrhage. Results manifested that the mean of blood loss in the date group was significantly less than the oxytocin group in the entire three hours after delivery. From 37 weeks of gestation to delivery, the treatment group was given 7–9 dates/day. Findings showed that there were no major variations in estimating blood loss in the type of delivery and course of labor.

[44] conducted a study to determine the effect of DPP suspension on adult female rats exposed to lead acetate. Results showed that oral administration of a protective dose of DPP suspension (150 mg/kg body weight) could lead to a re-balancing of the harmful effects. Another study was carried out to compare the effect of ethanol extract of date palm fruit and propolis on fertility in female mice. It was observed that ethanol extract of Khalal date fruit dose can increase the number of ovarian follicles higher than propolis [45].

A study was conducted to investigate the effect of date fruit on the reproductive process of female rats. Moreover, concomitant supplementation of barley and date fruit to the hypercholesterolemic mice group revealed remarkable improvement in ovarian function and structure [46]. **Table 2** shows the summary of date palm and its constituents improving female fertility parameters.

Table 5. The summary of date palm and its constituents improving female fertility parameters.

Date and Date Products	Subjects	Target	Material and Method	Active Component	Result	References
Date fruit	154 Nulliparous women	The onset of labour and the need for induction	Date consumer (77) and Date control group (77) Intake (7 dates/day)	–	No significant difference in the onset of spontaneous labour. Date consumption reduces the need for labour augmentation but does not expedite the onset of labour	[47]
Date fruit	Females	Labour parameter and delivery outcomes	Date fruit group: 69 women for 4 weeks per	–	In the date fruit group, cervical dilation was significantly	[48]

Date and Date Products	Subjects	Target	Material and Method	Active Component	Result	References
			day before labour Non-date fruit group: 45 Intake (6 dates/day for 4 weeks)		increased, there was a higher rate of spontaneous labour and the latent phase of the first stage of labour was shorter 28% of women in this group required the use of protein or oxytocin compared with 43% in the non-date fruit group	
Date fruit	Nulliparous women (18–35 years) who were in their 37–38th week of pregnancy	Duration of labour	Control group Date consuming group (70–76 g dates daily for from the 37th week of pregnancy)	Tannins	There was no significant difference between the average length of the active phase of labour in the two groups	[49]
Date fruit	Pregnant women	Onset and progression of labour	89 participants Control group: (31 women) Date consuming group: 26 women (7 dates/day) Dates + water consuming group: 32 women (7 dates + 250 mL)	–	Significant positive impact on maternal outcomes on both the first and third stage of labour and fetal well-being factors No significant difference between the date fruit consumer and their counterparts regarding cervical dilation, the regularity of uterine contraction, and maternal progression factors	[50]
Date fruit	Pregnant women	Postpartum Haemorrhage	Group 1 (50 g oral deglet Noor dates Group 2 (10 units of Intramuscular oxytocin)	Serotonin	In the whole three hours after delivery, the blood loss means in date group was significantly less than the oxytocin group	[51]

Date and Date Products	Subjects	Target	Material and Method	Active Component	Result	References
Date fruit	Pregnant women	Bleeding, length of labour, type of labour	Total of 60 Treated Group (30) consumed 7–9 dates per day since 37th-week gestation Control group (30)	–	The result of the study about the length of labour showed that there was an effect of data consumption on the length of labour with a value of $p = 0.000$	[52]
Date fruit	Pregnant women	Preeclampsia	40 Pregnant women were randomly assigned to Control group (10) Intervention group (30) Intake (7 dates/day for a week)	–	Daily consumption of 7 Ajwa date Has a remarkable potential to decrease MAP and ROT in pregnant women at risk of developing preeclampsia and thus prevent from preeclampsia	[53]
DPP	Female reproductive study	Reproductive System	Intake (100 and 200 mg/kg)	Flavonoid, Alkaloid, and Estradiol	The use of DPP suspension during gestation and lactation increase oogenesis significantly	[54]
DPP	Adult female Albino rats exposed to lead acetate	Ovarian function and fertility	Total = 404 (4 groups) Control Group (orally 1 mL distilled water) T1 was given orally 150 mg/kg BW. DPP (0.5 mL) T2 was given orally 10 mg/kg BW. Lead acetate 1 mL T3 was given oral administration of both DPP 150 mg/kg	–	Oral administration of DPP with a protective dose of 150 mg/kg BW lead to rebalancing the harmful effect of lead acetate in female rats	[55]

Date and Date Products	Subjects	Target	Material and Method	Active Component	Result	References
			BW and 10 mg/kg BW. lead acetate All animals were treated via gavages needles for 6 weeks			
Date palm syrup	Nulliparous Women	Labour pain	Total = 80 Control Group: Water Palm Syrup Group: Consumed pulp-free syrup added in 150 mL water	–	Date palm syrup significantly reduces labour pain. Findings showed that starting impact occurred late in palm syrup usage, but it has a long relief effect	[56]
Probiotic fermented milk, Sukkary date fruit extract, and their mixture	Mature late pregnant Najdi ewes	Neonatal traits Hematological Parameters	Total = 20 Group 1 (control) Group 2 (50 mL date extract every other day for the last 8th week of pregnancy Group 3 (50 mL of probiotic fermented cow's milk for the same period Group 4 (50 mL of the mixture Date extract: Fermented milk, 1:1)	–	Mean litter weight increased significantly in ewes given dates alone (85% more kg than control) Fermented milk or mixture with dates did not significantly increase the litter weight. Fermented milk alone did not show alteration in litter birth weight	[57]
Barley and date fruit (Anti hypercholesteremia Impact)	Female Wistar Albino Rats	Ovarian function and infertility	Eight Groups (n = 12) Control (C) Barley Group (B): Diet containing	Phytomicro nutrients polyphenols, Beta-glucan, and trace elements	Concomitant supplementation of barley and date fruit to the hypercholesterolemic group revealed	[58]

Date and Date Products	Subjects	Target	Material and Method	Active Component	Result	References
			10% barley grains Date Palm fruit group (D): A diet containing 10% fruit Barley and date group (BD) High cholesterol diet group (H) High cholesterol and barley grains (HB) High cholesterol and date palm fruit group (HD) High cholesterol and both barley and date palm fruit (HBD)		marked improvement of ovarian structure and function	

DPP, date palm pollen; mg, milligram; kg, kilogram; BW, body weight; ROT, Roll-over-Test; MAP, mean arterial pressure.

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