

## REVIEW ARTICLE

# Sunnah Foods for the treatment of Infertility in women with PCOS: A Literature Review

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## ABSTRACT

Infertility is a global health issue that is on the rise. The leading cause of female infertility, PCOS, is considered incurable and lifelong in conventional medicine. Challenging and delayed diagnosis, ineffective treatment modalities and long-term treatment has left both physicians and patients disgruntled. Islamically however, it is believed that every illness has a cure. This paper is therefore aimed at reviewing the effect of Sunnah foods in treating infertility among patients with PCOS. The study will also provide future recommendation for researchers and practitioners.

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## INTRODUCTION

Fertility has a key impact on the quality of a couple's relationship and their lives in general. However, World Health Organization (WHO) estimated that about 16% (48 million couples or 186 million individuals) of people of reproductive age suffer from infertility. Infertility is defined as the inability to achieve a pregnancy after 12 months of regular, unprotected sexual intercourse (1). Infertility may be due to male factor, female factor, both female and male factor or may be unexplained in which no cause can be identified. Female infertility can result from various causes but the commonest cause is anovulation from Polycystic Ovary Syndrome (PCOS), (2).

PCOS is a lifelong disorder affecting women of reproductive age that is associated with infertility, menstrual irregularity, hirsutism and obesity (3). However, conventional treatment is largely symptomatic and both clinicians and patients have expressed dissatisfaction with current management modalities. Internationally, women have reported delayed diagnosis, dissatisfaction

with information provided and treatment prescribed and have expressed that they would prefer a safe and

effective alternative (4-6).

PCOS diagnosis, therefore is associated with a lot of psychological distress to the patient as the condition is considered incurable and treatments are unsatisfactory (7). High conversion risk for depression over 1 – to 2- year period together with significant risk for mood disorders are usually found associated with PCOS diagnosis (8). However, the Prophet ﷺ mentioned "there is no disease that Allah has created, except that He has created its treatment" (9). Based on this Hadith, this paper aims to review the effects of Sunnah foods on infertility in PCOS patients. The study will also provide future recommendation for researchers and practitioners.

## PCOS

Polycystic ovarian syndrome (PCOS) is considered the most prevalent endocrine disorder among women of childbearing age with an estimated prevalence of 5-10%. It affects women of all races and ethnicities (10). The term was derived from the appearance of the ovaries which contain enlarged small underdeveloped follicles that appear as cysts (11). However, isolated polycystic ovarian morphology can be found in 16-25% of the population (12).

Other clinical features include irregular or absence of menstruation, excessive male pattern hair growth, thinning hair and hair loss on the head, oily or acne prone skin, weight gain, infertility and adverse

pregnancy outcomes (11). PCOS is a lifelong disorder associated with reproductive, endocrine, metabolic and cardiovascular complications manifesting as infertility, diabetes mellitus, metabolic syndrome, dyslipidemias and cerebrovascular diseases.

**PCOS and Infertility**

Infertility in women with PCOS can be attributed to various factors, primarily related to the hormonal imbalances, specifically elevated levels of androgens (male hormones), which can disrupt the normal menstrual cycle and impair ovulation (10). The unreleased follicles appear as cysts and gradually causes the thickening of the surface of the ovaries, preventing any developed follicle from being released (11).

PCOS can disrupt the normal ovulation process, leading to irregular or absent menstrual periods and difficulty in releasing a mature egg for fertilization. Additionally, the hormonal imbalances in PCOS can result in the formation of multiple cysts in the ovaries, further interfering with ovulation and fertility (10, 11).

Moreover, PCOS is often associated with insulin resistance, a condition in which the body’s cells do not respond effectively to insulin, leading to elevated insulin levels. Insulin resistance can contribute to hyperandrogenism and disrupt ovarian function, further exacerbating infertility in women with PCOS (13). Additionally, PCOS may also impact the quality of eggs and the lining of the uterus, affecting the implantation and maintenance of a pregnancy (14).

It is important to highlight that infertility in women with PCOS can be influenced by various other factors, including age, body weight, and coexisting medical conditions. Age-related decline in fertility, particularly after the age of 35, can further complicate the reproductive challenges faced by women with PCOS (15). Furthermore, certain lifestyle factors, such as obesity and lack of physical activity, can exacerbate the hormonal imbalances and metabolic disturbances associated with PCOS, further impacting fertility (16).

**Causes of PCOS.**

The exact cause of PCOS is still unclear but some of the postulated causes of PCOS include; hormonal imbalance, insulin resistance/hyperinsulinemia, use of contraceptive pills, genetic predisposition, chronic inflammation and stress (17).

**Signs and Symptoms of PCOS**

Table I shows the signs and symptoms of PCOS.

**Table I: Signs and Symptoms of PCOS (18, 19)**

Absent or irregular menstrual period
Excess body hair or male pattern of hair distribution.
Acne.
Infertility
weight gain.
Lower abdominal or pelvic pain.
Increase in Luteinizing hormone and reduction in Follicle stimulation hormone.
Signs and symptoms of insulin resistance e.g. acanthosis nigricans

**Histological features of PCOS**

The histological features of PCOS is presented in Table II.

**Table II: Histological features of PCOS (20, 21)**

Ovarian enlargement or hypertrophy.
Thickening of the ovarian capsule (>100 µm).
12 or more Sub capsular follicle cysts
Few corpora lutea or corpora albicans
Stromal fibrosis or hyperplasia.
Abnormal luteinization of theca cells.
Reduced follicles in the granulosa cell layer
Hypertrophic theca cell layer

**Complication of PCOS**

The various complication of PCOS is shown in Table III.

**Management of PCOS**

Management of this disorder is dependent on the presenting symptoms which can be generalized into: menstrual abnormalities and androgen-related disorders and infertility (23)

**Pharmaceutical management**

The Oral Contraceptive Pill (OCP) is the predominant drug used in the treatment of PCOS (3). This drug however, has potential adverse effects on insulin resistance, glucose tolerance, coagulability and vascular reactivity (3). Additionally, it is not ideal for PCOS patients that are battling infertility. Clomiphene citrate is used for ovarian stimulation in the treatment of infertility but is found to have a higher risk of ovarian hyper stimulation syndrome in women with PCOS (24). Metformin is used to treat insulin resistance and improve and metabolic functions (25) in PCOS patients but has a slew of side effects that can hinder compliance and effective treatment (26). The Aromatase inhibitor, Letrozole, used in ovulation induction is associated menopause like symptoms as it reduces the levels of estrogen in the body. (27). All these

**Table III: Complication of PCOS (19, 22)**

<b>Reproductive</b>
Irregular menstruation
Chronic anovulation
Infertility
Pregnancy complications
<b>Metabolic</b>
Insulin resistance
Impaired Glucose Tolerance
Type 2 Diabetes mellitus
Gestational diabetes
Non-alcoholic fatty liver disease
Metabolic syndrome
<b>Psychological</b>
Depression
Anxiety
Eating disorders
Psychosexual dysfunction
Negative body image
Reduced quality of life
<b>Dermatologic</b>
Hirsutism
Acne
Androgenic alopecia
Acanthosis nigricans
<b>others</b>
Endometrial cancer
Obstructive sleep apnea
Cardiovascular diseases.
Endometrial cancer.
Obesity

has led to both doctors and patients to express desire for safer and more effective alternatives (6).

### **Nutrition and PCOS**

PCOS is a disorder with a huge metabolic component. Insulin resistance, diabetes mellitus and metabolic syndrome are significant and very frequent associations of PCOS (3, 28). Nutritional and lifestyle modifications in patients with PCOS have benefits that does not only address its metabolic aspects but also improve reproductive, endocrine, cardiovascular profiles (29).

The Diet Approach to Stop Hypertension or DASH diet, designed primarily to reduce or prevent hypertension, is now universally modified and applied to different conditions (30, 31). It is based on high intake of fruits and vegetables, low intake of fat, dairy products and complex carbohydrates and reduce intake of meat and simple carbohydrates (32). In a study conducted by Azadi-Yazdi et al. in 2016, the effect of a hypocaloric DASH diet was compared with standard hypocaloric diet in 60 women with PCOS (32). The DASH diet contained reduced simple sugars and cholesterol, low

dairy, fat, and high fruit and vegetable. Both diets were similar in macronutrients (carbohydrates 50-55% of daily calories, protein 15-20% of daily calories). At the end of the study, women in the hypocaloric DASH diet were found to have improved androgen serum levels as well as reduction in fat mass, weight and Body Mass Index (BMI) (33).

The effect of the Sunnah diet was assessed together with Ramadan fasting in a study done by Dashti et al. (2019) on PCOS patients through an educational module. Findings from the study showed reduced triglycerides, low-density lipoprotein (LDL), total cholesterol and fasting plasma glucose (FPG) even though the difference between the cases and control is not very significant (34). More studies are needed to bring to light the effects of sunnah foods on the various aspects of PCOS.

### **SUNNAH**

Sunnah is defined as “the traditions and practices of the Islamic Prophet Muhammad ﷺ that constitute a model for Muslims to follow” (35). It is the normative way of life followed by Muslims from the teachings and practices of the Prophet Muhammad ﷺ based on the interpretation of the holy Quran. The Prophet Muhammad ﷺ is believed by Muslims to be the final messenger sent by God to guide humanity to the right way. Sunnah is therefore, believed by Muslims to be the concrete interpretation of divine will (36). The sunnah is documented through Hadith, which are “verbally transmitted record of teachings, sayings, silent permissions or disapprovals of Muhammad ﷺ” (37). As the Sunnah covers the complete life of the Muslims, there are a lot of Hadith regarding food and diet.

The Hadith, as a source of Sunnah foods and practices, was transmitted by the companions of the Prophet Muhammad (SAW) to subsequent generations and later collected, deeply authenticated, and compiled into Books of Hadith. Among the most renowned Hadith collections are those of Al-Bukhari, Muslim, and At-Tirmidhi, with Al-Bukhari’s book considered the most authentic by Muslims. These Hadiths underwent extensive authentication processes, including recording the chain of narrators and scrutinizing each narrator’s credibility. Each Hadith is assigned a degree of authentication based on this process. Dietary recommendations, health guidelines, first aid measures, and treatments for ailments are found within chapters dedicated to health matters in these Hadith collections. Some scholars further explored these Hadith collections, resulting in books of “Prophetic medicine”. Notable examples include “Zad al Ma’ad” and “Tibb-al Nabawi,” both authored by Muhammad ibn Abi Bakr ibn Ayyub, also known as Ibn Qayyim al Jawziyya, who was not only a theologian but also a practicing physician (38).

Sunnah foods are the food items present within the

teachings and traditions of the Prophet Muhammad ﷺ. They are a part of Prophetic medicine which is a term given to the medical knowledge gained from teachings, sayings (hadeeths), advices and deeds of prophet Muhammad ﷺ related to health and disease treatment (39). It also includes recommendations relevant to human health in all aspects of life including eating, drinking, housing and matrimony. It encompasses legislations pertaining to medication, medical practice and the protection of the patient in the viewpoint of Islamic law (39).

The famous theologian and scholar of 13th century, Ibn Al Qayyim, wrote in his book *Zad Al Ma'ad Fe Haday Khair Al Abad* "The medicine of the Messenger ﷺ is not similar to the conventional medicine. The medicine of the Prophet ﷺ is certain, categorical, and godly medicine; issued by the revelation, prophethood niche, and sagacity; while the medicine of others is inductive, assumptive, and experimental" (40).

The Prophet ﷺ used medicine himself and prescribed medicine for his family and his companions but the type of these medicines were unlike the synthetic drugs that are produced by pharmaceutical companies today. A medicine consisting of a single substance is preferred from the one containing a compound. An additional substance might be added to help with the taste. This was and is still the tradition of many cultures like the Turks, Arabs, nomads and Indians while the Greeks and Romans use a mixture of substances in their medicine (40).

Sunnah foods has been extensively researched in the treatment of diabetes, cancer and cardiovascular diseases. This has led to the unravelling of profound ethnopharmacological information, discovery of novel phytochemicals, potential molecular mechanisms and pharmacological actions of these foods. Furthermore, Sunnah foods are easily available, have less side effects and are more affordable. These properties made them even more ideal for the treatment of both acute and chronic diseases (41).

Loukas et al in 2010 studied the heart and cardiovascular system in the light of Quran and Hadith and concluded that both Quran and Hadith contain knowledge that is in astounding agreement with modern medical knowledge and both can be a source of beneficial knowledge to humanity (42).

It is with this background that this article endeavors to conduct a comprehensive review of the impact of sunnah foods on fertility. All food items presented in this review are taken from Hadith that are graded as Sahih, the highest grading for a hadith. A list of food items found in Sahih Hadiths was made. A search is then made on Pubmed and google scholar, using each of the sunnah foods as key words in addition to "PCOS",

"female fertility" and "female infertility". The articles were screened for duplication, relevance and access to full text to arrive at 7 articles that are presented below.

### **Nigella sativa**

Narrated Abu Huraira: I heard Allah's Apostle saying, "There is healing in black cumin for all diseases except death". (9) (hadith classified as Sahih). Also known as black seed, black cumin or Kalonji is a herb that is widely available and used as medicine in a variety of conditions. The seeds of *Nigella sativa* contain mainly proteins (26- 50%), essential oils (0.13-0.39%), phenolic compounds, sterols, alkaloids and saponins (43).

Most of the medicinal properties of *Nigella sativa* are attributed to its thymoquinone (TQ) component and it's been found to be anti-inflammatory, antioxidant, immunomodulatory, bronchodilator, anti-helminthic, analgesic, reno and hepatoprotective, antihypertensive, antidiabetic, anti-cancer, spasmolytic, antimicrobial, diuretic and gastroprotective (44).

A double-blinded placebo-controlled clinical trial consisting of 84 patients with PCOS and oligomenorrhea was conducted in Iran by Naeimi et al (39). The patients were randomly assigned to either intervention group which received 2 soft gel capsules of *Nigella sativa* oil (500mg) or control group which received placebo, for 16 weeks. Only 55 patients (32 in intervention group and 23 in placebo group) completed the study. The intervention group showed significantly lower menstrual interval (45 days, 95% CI) compared to control group (86 days).

Furthermore, the frequency of menstrual cycle in the intervention group (0.79) was significantly higher than in the control group (0.48) (45).

In another study done by Nafi'u et al in 2019, female Sprague-Dawley rats were divided into 4 groups of 10. One Control and three PCOS groups induced by the administration of letrozole. Only 2 PCOS groups were administered different doses of *Nigella sativa* oil from day 7 to day 56. At the end of the study, histomorphological features were assessed after dissection of the rats.

The results showed that the higher dose of the *Nigella sativa* oil significantly improved PCOS symptoms in the rats with regular cycles, appearance of corpus luteum, reduced number of cystic follicles. It also decreases body weight, normalize hormone levels and blood glucose (46). Javanshir et al. conducted another study in 2018 in which the researchers induced PCOS in Wistar rats by injecting them with estradiol valerate for 25 days. They then administered thymoquinone at a dose of 8mg/kg and 16mg/kg for 30 days. The rats were divided into 5 groups: control, PCOS or sham, experiment 1 (PCOS and 8mg/kg thymoquinone administration), experiment 2 (PCOS and metformin administration, 100mg/kg) groups and metformin (PCOS and metformin administration,

100 mg/kg) groups. Biochemical and histopathological examination of the ovaries were made and the results showed that PCOS was induced by estradiol valerate and reversed by thymoquinone administration which resulted in normalization of LH and FSH levels, improved ovarian morphology, ovulation and body weight. It also normalizes glucose and lipid parameters (47).

In 2016, Arif et al. conducted another study in which they evaluated the impact of thymoquinone in an in vivo system using super ovulated, polycystic ovary (PCO) and mifepristone (RU486) + TQ treated Wistar rats. The results showed that pretreatment with TQ in the PCOS rat model lead to significant improvement in ovarian function, including reduced cyst formation, increased ovulation rate, and normalization of key ovarian factors and enzymes involved in follicular maturation. Furthermore, TQ supplementation inhibited Nuclear factor kappa B (NF- $\kappa$ B) nuclear translocation, Cyclooxygenase 2 (COX2) expression and reactive oxygen species (ROS) production in Mifepriston treated mouse granulosa cells (48).

Oxidative stress resulting in chronic inflammation has been implicated in the pathogenesis of PCOS. Oxidative stress results from an imbalance between the antioxidant capacity of the body and the amount of reactive oxygen species within it (49). It has been shown that there is reduced levels of endogenous antioxidant activities in letrozole induced PCOS rats with increased level of malondialdehyde (MDA). Oxidative stress in the ovary resulting from inflammatory mediators such as Tumor Necrosis Factor- $\alpha$  (TNF $\alpha$ ) and Interleukin 6 leads to anovulation and premature atherosclerosis in the endothelial system of patients with PCOS (50). The therapeutic effect of *Nigella sativa* is largely accounted for by its monoterpene compound, thymoquinone, which is a molecular scavenger of reactive oxygen species. It reduces the damaging effects of free radicals on endocrine tissues thereby restoring normal functions (44). On the pancreas, thymoquinone restores and preserves pancreatic beta cells thereby increasing insulin production. It also improves insulin resistance manifested by weight loss and blood glucose control which is another mechanism through which it can regulate menstrual cycle. Thymoquinone has also been shown through both in vivo and in vitro studies, to up regulate the actions of antioxidant enzymes. It also prevents toluene-induced loss of the antioxidant glutathione within cells and hepatic tissues (51,52). *Nigella sativa* also possess some phytoestrogenic properties and act both as agonists and antagonists on the estrogen receptors to mediate the regulation of the menstrual cycle (53,54,55). This estrogenic effect of *Nigella sativa* is attributed to its linoleic and oleic acid contents (56). Thymoquinone's ability to reduce synthesis of cholesterol has been shown to be through its regulation of Apo-A1, Apo-B100, hydroxymethylglutaryl-coenzyme A reductase (HMG-CoA reductase) and

low-density lipoprotein-receptor (LDL-R) genes in the liver (57,58). The Nigellamin content of *Nigella sativa* also has clofibrate and antioxidant functions which boosts lipid metabolism and reduce lipid levels (59,60). Another study by Akash et al demonstrated that another way *Nigella sativa* exhibit antioxidant action is through the inhibition of eicosanoid generation and peroxidation of lipid membrane (61).

### Honey

Narrated Jabir bin Abdullah:

I heard the Prophet saying, "If there is any healing in your medicines, then it is in cupping, a gulp of honey or branding with fire (cauterization) that suits the ailment, but I don't like to be (cauterized) branded with fire." (9). (hadith classified as sahih).

Honey is an ageless remedy that has been used for centuries. Honey contains 80-85% carbohydrates, 15%-17% water, vitamins, phenols and amino acids in different quantities (62,63). It is anti-inflammatory, anti-cancer, anti-diabetic, anti-oxidative and an excellent estrogenic natural substance. It improves hormonal profile and oxidative stress. It increases antral follicle, decrease cystic follicles and normalize the estrous cycle (64).

Kamal et al did a study in 2022 in which the researchers induced PCOS in female Sprague- Dawley rats by administering 1mg/kg of letrozole for 21 days. The PCOS rats were then divided into 6 groups: untreated, metformin (500mg/kg/day), clomiphene (2mg/kg/day), Kelulut honey (KH) (1g/kg/day), combined KH (1g/kg/day) and metformin (500mg/kg/day) and combined KH (1g/kg/day) and Clomiphene (2mg/kg/day). All treatments were given orally for 35 days. The result showed KH alone or in combination with metformin or clomiphene, improved the estrous cycle, hormonal profile and oxidative stress in PCOS rats (65).

Another use of honey in fertility is in cryopreservation. Honey has been found to be an excellent cryoprotectant. It is highly effective, non-toxic, reduces ice formation because of its viscosity and improves post-thaw quality and viability (66).

The antioxidant effect of honey is executed through its ability to significantly increase the levels and actions of superoxide dismutase (SOD), catalase and glutathione peroxidase. These in turn brings about the changes seen in this study as one of the most important pathologies underlying PCOS is chronic inflammation brought about by oxidative stress (65). Honey has also been shown to be able to regulate the function of the pituitary gland by modulating its feedback level to alter sex steroid hormone levels (67). According to another study, Kelulut honey possesses both estrogenic and antiestrogenic properties depending on its concentration and these could be the pathways through which it regulates menstrual cycle

(68,69).

The properties that make honey an excellent cryopreservative include its thermal, rheological and antioxidant properties (66). Rheology is the study of the flow and deformation of a material under a given pressure (70). The main rheological property of honey is its viscosity which is mainly due to its low water and high sugar content (71,72). Decreasing the temperature and water content of honey increases its molecular friction and hydrodynamic forces which lead to higher viscosity (73,74). Scientifically, studies have shown some types of honey to be Newtonian fluids while others are not. Rheologically, Newtonian fluids are characterized by constant viscosity at a fixed temperature with a linear relationship between shear stress and shear rate (75,76). Anti-oxidants present in honey include the enzymes catalase and glucose oxidase, vitamin C in the form of galagin, chrisin, pinocembrin, pinobaxin and amino acids like threonine, glycine, glutamate, aspartic acid and glutamin. It also contains phenolic compounds such as tocopherol, quercetin, flavonoids and phenolic acids (77,78). The abundance of these antioxidants helps to prevent cellular damage and genetic structure disruption that can occur due to oxidative stress (79,80). The activities of cellular transcription factor are inhibited by quercetin and phenolic acid which protects cells against the cellular effect of free radicals (81).

Using honey as a cryopreservative decreases the levels of reactive oxygen species in the embryo and overall improve the success of the fertility assisting procedure.

### Dates

"There is a tree among the trees which is similar to a Muslim (in goodness). Its leaves do not fall. What is that tree? The Prophet (saw) himself said, "That is the date palm tree"(9).

Dates are the fruit of the date palm. It contains carbohydrates, protein, fat, dietary fiber, enzymes, minerals, vitamins, carotenoids and phenolic acids (82). Several studies have shown that dates have anti-oxidant, anti-inflammatory, anti-cancer, immunostimulant, gastroprotective, nephroprotective and hepatoprotective properties (83).

The efficacy of date palm pollen (DPP) on PCOS was studied using rats as models in which the rats were divided into groups. The control group received only distilled water at a dose of 0.2ml/kg body weight. The PCOS group was administered a daily oral dose of 1 mg/kg body weight (Letrozole) for 21 days to induce PCOS. The treatment 1 (T1) group received the same Letrozole treatment as the PCOS group for 21 days, followed by a suspension of DPP (100 mg/kg body weight) for an additional 30 days. The treatment 2 (T2) group received the Letrozole treatment for 21 days and was also given metformin (50 mg/kg body weight) for 30

days. The results showed that Letrozole administration in the PCOS group led to a significant decrease in serum estrogen levels and a significant increase in testosterone levels. However, treatment with DPP and metformin in the T1 and T2 groups resulted in a significant decrease in testosterone levels and an increase in estrogen and progesterone levels compared to the PCOS group. Histopathological analysis revealed that the PCOS group exhibited follicular cysts, the T1 group showed thin walled cysts, while the T2 group showed regressed cysts. Based on these findings, it can be concluded that the DPP component could be considered an effective treatment for PCOS syndrome in rats (84).

In a one-arm clinical trial conducted at Alzahraa University Hospital from 2018 to 2020, 50 women diagnosed with PCOS based on the Rotterdam criteria were enrolled. The study involved administering 3 gm of date palm pollen (DPP) daily for three months, followed by monitoring of sex hormones such as FSH, LH, estrogen, and progesterone. Additionally, the growth of follicles was monitored each month. The results showed significant improvements in sex hormone levels, including decreased estrogen and LH levels, and increased progesterone and FSH levels. Furthermore, there was a cumulative effect on ovulation. However, it's worth noting that only 6% of the participants became pregnant during the study period (85).

Another study also assessed the effects of palm pollen extract on PCOS induced rats. Forty-eight adult female Wistar rats were divided into six groups, including control and sham groups. The remaining groups received intramuscular injections of estradiol valerate to induce PCOS. Two experimental groups were orally administered different doses of palm pollen extract for 21 days. At the end of the experiment, blood samples were taken to evaluate hormone levels, and the ovaries were studied microscopically. The group receiving 400 mg/kg of palm pollen extract showed a significant decrease in LH and estrogen levels compared to the PCOS group, while FSH and progesterone levels significantly increased. Additionally, there was a reduction in cystic follicles and an increase in primary, antral, and graafian follicles, as well as corpus luteum in the PCOS group receiving 400 mg/kg of palm pollen extract. Overall, palm pollen extract demonstrated potential in improving tissue symptoms and regulating sex hormone levels in PCOS (86).

Date palm pollen contains estradiol, flavonoids and gonadotrophin like components through which it improves the action of LH, FSH and testosterone and also enhances the actions of estradiol. Methanolic Extract of Ajwa Date (MEAD) has been found to express its antioxidant activity through the repression of hormone dependent breast cancer cells in vitro by upregulation of gene expression of apoptosis leading to cell cycle arrest at S-phase (87). Dates also contains phenolic

compounds which are effective bioactive compounds and anti-oxidants (88). It also improves the levels of antioxidant enzymes within the body thereby restoring endocrine organs to normal functions (89).

### Olives

It was narrated from 'Umar that the Messenger of Allah (ﷺ) said: 'Season (your food) with olive oil and anoint yourselves with it, for it comes from a blessed tree (90). Its botanical name is *Olea europaea* L. It is a species of small tree or shrub belonging to the family Oleaceae. This fruit is native to the Mediterranean basin and is grown majorly for its oil. It contains 50% water, 1.6% protein, 22% oil, 19.1% carbohydrates, 5.8% cellulose, 1.5% inorganic substances and 1-3% phenolic compounds, pectin, organic acids and pigments (91). It also contains triglycerides, phenolic compounds like alpha tocopherol (vitamin E), hydrophilic phenolic compounds (e.g. hydroxytyrosol and sacroiridoid) and carotenoids. Majority of the triglycerides are monounsaturated fatty acids (MUFA) of which 70-85% is oleic acid. Other triglycerides include linoleic and palmitoleic acid. Olive oil has been shown to have anti-inflammatory, anti-oxidant, cardioprotective and anti-tumor properties. It also regulates intestinal microbiota (92).

Egba et al. in 2014 studied the hormonal effects of oral administration of soybean oil, olive oil, and margarine in female Wistar albino rats. The rats were given the three dietary lipids for 21 days, while a control group received only water. Various reproductive hormones were measured, including testosterone, progesterone, estradiol, follicle-stimulating hormone, luteinizing hormone, and prolactin. The results showed that soybean oil led to a significant decrease in serum testosterone levels, while olive oil and margarine showed a non-significant decrease compared to the control group. Progesterone levels were non-significantly decreased in the soybean oil and olive oil groups, but slightly increased in the margarine group. Estradiol levels showed non-significant differences between the groups. Luteinizing hormone and follicle-stimulating hormone levels were significantly increased in the olive oil and soybean oil groups, with a non-significant increase in the margarine group. Prolactin levels were significantly increased in the olive oil and margarine groups, with a nonsignificant increase in the soybean oil group. Overall, the results suggest that olive oil and soybean oil, in particular, have the potential to enhance hormonal functions and fertility in females, indicating that their consumption could reduce the risk of infertility (93).

Olive oil contains a substance called Oleuropein aglycone which enhances the pituitary gland to increase the plasma level of noradrenaline which in turn increases GnRH and subsequently luteinizing hormone. Olive oil contains Omega-3 and Omega-6 fatty acids which can greatly improve hormonal profile by stimulating Hypothalamo-pituitary-ovarian axis and subsequently

improve fertility (94).

## DISCUSSION AND CONCLUSION

Oxidative stress resulting in chronic inflammation is a pathological feature in the development of PCOS. It results in disturbance of the endocrine system leading to dysregulation of the Hypothalamo-pituitary-ovarian/adrenal axes. Both increased frequency of GnRH pulsatility and insulin resistance can increase the LH:FSH ratio in PCOS patients which results in increased androgens, failure of follicles to mature and disruption in ovulation and menstrual cycle (95).

Conventional treatment of this disorder has been challenging for both physicians and patients with majority reporting dissatisfaction with current treatment options and long-term treatment (96). Sunnah foods, as we have seen, are found to contain among others: antioxidants, vitamins, amino acids, phenolic compounds and fatty acids. Through these compounds they are able to act as antioxidants, anti-inflammatory, immunostimulants, anti-diabetic, anti-cancer, antimicrobial, anti-helminthic, bronchodilator, hepato/reno/nephro/gastro-protective and estrogenic compounds (43,44,62-64,82,83,91,92). Most of the fertility promoting benefits seen in sunnah foods comes from anti-oxidation and insulin regulating properties. As hormonal imbalance is one of the cardinal features of PCOS, reducing reactive oxygen species, increasing antioxidants helps to restore endocrine organs back to normal functions and improve the symptoms of PCOS (94).

Sunnah foods provide a safe and effective alternative to conventional treatment which is plagued with long treatment duration, side effects and less than satisfactory results in the treatment of infertility which affects 70-80% of patients with PCOS (14). These Sunnah foods also boost immunity and improve different aspects of a person's health in addition to balancing hormonal profile which is the hallmark of PCOS. It therefore treats it at its roots and not merely offer symptomatic relief. As reported in a famous Hadith, the Prophet SAW said "Indeed, Allah created disease and also its cure. Hence, seek medication" (9). Sahih hadith.

Exploring alternative treatment options, such as incorporating Sunnah foods, provides a diversified approach to fertility enhancement. This approach acknowledges that fertility is a multifaceted issue influenced by various factors, including diet and lifestyle choices. By expanding the range of treatment options, individuals and couples have the opportunity to explore different avenues and potentially enhance their chances of conception.

Emphasizing Sunnah foods for fertility improvement aligns with a holistic approach to health and well-being. Islam encourages a balanced lifestyle that considers

physical, mental, and spiritual aspects of well-being. By incorporating Sunnah foods, individuals can promote overall health while addressing specific fertility concerns. This approach recognizes the interconnectedness of various body systems and aims to optimize overall wellness, which can positively impact fertility outcomes.

The emphasis on Sunnah foods for fertility improvement also holds cultural and spiritual significance for many individuals and couples. It allows them to incorporate their faith and traditions into their fertility journey, fostering a sense of conviction and hope. For those who draw strength from their religious beliefs, the inclusion of Sunnah foods can provide an additional layer of support and a sense of purpose during the fertility treatment process.

However, it is still imperative to note that further clinical research is necessary to validate the efficacy of natural medicine, including Sunnah medicine. As can be noted, most of the research available are animal studies. More clinical studies and control trials are therefore needed to establish efficacy in humans and also superiority over existing treatment options.

## REFERENCES

- World Health Organization. Infertility (Internet). World Health Organization. Available from: [https://www.who.int/health-topics/infertility#tab=tab\\_1](https://www.who.int/health-topics/infertility#tab=tab_1) (Accessed 2022).
- Barbieri RL. Female infertility. In: Yen and Jaffe's reproductive endocrinology. Elsevier; 2019. p. 556-581. doi: 10.1016/B978-0-323-47912-7.00022-6
- Ehrman DA, Barnes RB, Rosenfield RL. Polycystic ovary syndrome as a form of functional ovarian hyperandrogenism due to dysregulation of androgen secretion. *Endocrine reviews*. 1995;16(3):322-353. doi: 10.1210/edrv-16-3-322
- Fraser IS, Kovacs G. Current recommendations for the diagnostic evaluation and follow-up of patients presenting with symptomatic polycystic ovary syndrome. *Best Practice & Research Clinical Obstetrics & Gynecology*. 2004;18(5):813-823. doi: 10.1016/j.bpobgyn.2004.06.009.
- Moran L, Gibson-Helm M, Teede H, Deeks A. Polycystic ovary syndrome: a biopsychosocial understanding in young women to improve knowledge and treatment options. *Journal of Psychosomatic Obstetrics & Gynecology*. 2010;31(1):24-31. doi: 10.3109/01674820903477593.
- Sills ES, Perloe M, Tucker MJ, Kaplan CR, Genton MG, Schattman GL. Diagnostic and treatment characteristics of polycystic ovary syndrome: descriptive measurements of patient perception and awareness from 657 confidential self-reports. *BMC women's health*. 2001;1(1):3. doi: 10.1186/1472-6874-1-3.
- Hoeger KM, Dokras A, Piltonen T. Update on PCOS: consequences, challenges, and guiding treatment. *J Clin Endocrinol Metab*. 2021;106(3):e1071-e1083. doi: 10.1210/clinem/dgaa839.
- Kerchner A, Lester W, Stuart SP, Dokras A. Risk of depression and other mental health disorders in women with polycystic ovary syndrome: a longitudinal study. *Fertil Steril*. 2009;91(1):207-212. doi: 10.1016/j.fertnstert.2007.11.022.
- Isma'il BM, Khan MM. The translation of the meanings of Sahih al-Bukhari: Arabic- English. Riyadh: Darussalam; 1997.
- Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical Prevalence of Polycystic Ovary Syndrome as Determined by Region and Race/Ethnicity. *Int J Environ Res Public Health*. 2018;15(11):2589. doi:10.3390/ijerph15112589.
- Zeng LH, Rana S, Hussain L, Asif M, Mehmood MH, Imran I, Younas A, Mahdy A, Al- Joufi FA, Abed SN. Polycystic ovary syndrome: a disorder of reproductive age, its pathogenesis, and a discussion on the emerging role of herbal remedies. *Front Pharmacol*. 2022 Jul 18;13:874914. doi: 10.3389/fphar.2022.874914.
- Carmina E, Lobo RA. Polycystic Ovary Syndrome (PCOS): Arguably the Most Common Endocrinopathy Is Associated with Significant Morbidity in Women. *J Clin Endocrinol Metab*. 1999;84(6):1897-1899. doi:10.1210/JCEM.84.6.5803.
- Palomba S, Daolio J, La Sala GB. Oocyte Competence in Women with Polycystic Ovary Syndrome. *Trends Endocrinol Metab*. 2017;28(3):186-198. doi:10.1016/j.tem.2016.11.008.
- Dewailly D, Gronier H, Poncelet E, Robin G, Leroy M, Pigny P, Duhamel A, Catteau- Jonard S. Diagnosis of polycystic ovary syndrome (PCOS): Revisiting the threshold values of follicle count on ultrasound and of the serum AMH level for the definition of polycystic ovaries. *Hum Reprod*. 2011;26(11):3123- 3129. doi:10.1093/humrep/der297.
- Kicińska AM, Maksym RB, Zabielska-Kaczorowska MA, Stachowska A, Babińska A. Immunological and Metabolic Causes of Infertility in Polycystic Ovary Syndrome. *Biomedicines*. 2023;11(6):1567. doi: 10.3390/biomedicines11061567.
- Ennab F, Atiomo W. Obesity and Female Infertility. *Best Pract Res Clin Obstet Gynaecol*. 2023;89:102336. doi: 10.1016/j.bpobgyn.2023.102336.
- Dunne N, Slater W. The Natural Diet Solution for PCOS and Infertility: How to Manage Polycystic Ovary Syndrome Naturally; Natural Solutions for PCOS. Health Solutions Plus: Seattle, WA, USA; 2006.
- Elsheikh M, Murphy C. Polycystic Ovary Syndrome. Oxford University Press; 2008.

19. Witchel SF, Teede HJ, Peca AS. Curtailing pcos. *Pediatric research*. 2020 Jan;87(2):353- 61. doi: 10.1038/s41390-019-0615-1.
20. Azziz R, Nestler JE, Dewailly D. Androgen excess disorders in women: polycystic ovary syndrome and other disorders. Humana Press; 2006. p. 184. doi: 10.1007/978-1-59745-179-6
21. Bevilacqua A, Dragotto J, Giuliani A, Bizzarri M. Myo-inositol and D-chiro-inositol (40: 1) reverse histological and functional features of polycystic ovary syndrome in a mouse model. *Journal of cellular physiology*. 2019 Jun;234(6):9387-98. doi: 10.1002/jcp.27623
22. Goswami PK, Khale A, Ogale S. Natural remedies for polycystic ovarian syndrome (PCOS): a review. *Int J Pharm Phytopharm Res*. 2012;1(6):396-402.
23. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clin Epidemiol*. 2013;6(1):1-13. doi: 10.2147/CLEP.S37559.
24. Kubota T. Update in polycystic ovary syndrome: New criteria of diagnosis and treatment in Japan. *Reprod Med Biol*. 2013;12(3):71-77. doi:10.1007/S12522-013-0145-1
25. Afefy NA, Ebrahium A, Elrehim A. Comparing the effectiveness of herbal remedies and lifestyle modification on minimizing polycystic ovarian syndrome symptoms. *J Indian Dent Res*. 2019;30(3):431-436.
26. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. *Diabetes Metab*. 2011;37(2):90-96. doi: 10.1016/j.diabet.2010.11.002.
27. Tshzmachyan R, Hambartsoumian E. The role of Letrozole (LE) in controlled ovarian stimulation (COS) in patients at high risk to develop ovarian hyperstimulation syndrome (OHSS). A prospective randomized controlled pilot study. *J Gynecol Obstet Hum Reprod*. 2020;49(2):101643. doi: 10.1016/j.jogoh.2019.101643.
28. Wild RA. Long-term health consequences of PCOS. *Hum Reprod Update*. 2002;8(3):231-241. doi: 10.1093/humupd/8.3.231.
29. Farshchi H, Rane A, Love A, Kennedy RL. Diet and nutrition in polycystic ovary syndrome (PCOS): pointers for nutritional management. *J Obstet Gynaecol*. 2007;27(8):762-773. doi: 10.1080/01443610701667338.
30. Whitt-Glover MC, Hunter JC, Foy CG, Quandt SA, Vitolins MZ, Leng I, Hornbuckle LM, Sanya KA, Bertoni AG. Translating the Dietary Approaches to Stop Hypertension (DASH) Diet for Use in Underresourced, Urban African American Communities, 2010. *Prev Chronic Dis*. 2013;10:130029. doi:10.5888/pcd10.130029.
31. Baker EA, Barnidge EK, Schootman M, Sawicki M, Motton-Kershaw FL. Adaptation of a Modified DASH Diet to a Rural African American Community Setting. *Am J Prev Med*. 2016;51(6):967-974. doi:10.1016/j.amepre.2016.07.018.
32. Tyson CC, Nwankwo C, Lin PH, Svetkey LP. The Dietary Approaches to Stop Hypertension (DASH) Eating Pattern in Special Populations. *Curr Hypertens Rep*. 2012;14(5):388-396. doi:10.1007/s11906-012-0284-8.
33. Azadi-Yazdi M, Karimi-Zarchi M, Salehi-Abargouei A, Fallahzadeh H, Nadjarzadeh A. Effects of Dietary Approach to Stop Hypertension Diet on Androgens, Antioxidant Status and Body Composition in Overweight and Obese Women with Polycystic ovarian syndrome: A Randomised Controlled Trial. *J Hum Nutr Diet*. 2016;30(3):275-283. doi: 10.1111/jhn.12433.
34. Dashti S, Abdul Hamid H, Mohamad Saini S, et al. A Randomised Controlled Trial on the Effects of a Structural Education Module Among Women with Polycystic Ovarian Syndrome on Nutrition and Physical Activity Changes. *BMC Womens Health*. 2022;22(1):1-11. doi:10.1186/s12905-022-01861-4.
35. Qazi MA, El-Dabbas MS. *A Concise Dictionary of Islamic Terms*. Lahore, Pakistan: Kazi Publications; 1979. p. 65
36. Yusuf SM. *The Sunnah: Its Place in Islam*. Islamic Studies. 1962;1(4):41-50. Available from: <https://www.jstor.org/stable/20832656>
37. Brown R. *Rethinking tradition in modern Islamic thought*. 1996:7.
38. Nagamia HF. *Prophetic Medicine: 'A Holistic Approach to Medicine'*. Journal of the Islamic Medical Association of North America. 2010 Apr 9;42(1). doi:10.5915/42-1-4736
39. Sheikh BY. The role of prophetic medicine in the management of diabetes mellitus: A review of literature. *Journal of Taibah University Medical Sciences*. 2016 Aug 1;11(4):339-52. doi: 10.1016/j.jtumed.2015.12.002
40. Ibn Qayyim al-Jawziyya. *Zaad al-Ma'ad*. Translated by Muhammad A. Hafeez. Riyadh: Dar-us-Salam Publishers; 2003
41. Sheikh BY, Sarker MM, Kamarudin MN, Ismail A. Prophetic medicine as potential functional food elements in the intervention of cancer: A review. *Biomedicine & Pharmacotherapy*. 2017 Nov 1;95:614-48. doi: 10.1016/j.biopha.2017.08.043
42. Loukas M, Saad Y, Tubbs RS, Shoja MM. The heart and cardiovascular system in the Qur'an and Hadeeth. *Int J Cardiol*. 2010; 140: 19-23. doi: 10.1016/j.ijcard.2009.05.011
43. Benazzouz-Smail L, Achat S, Brahmi F, Bachir-Bey M, Arab R, Lorenzo JM, Benbouriche A, Boudiab K, Hauchard D, Boulekbache L, Madani K. Biological Properties, Phenolic Profile, and Botanical Aspect of *Nigella sativa* L. and *Nigella damascena* L. Seeds: A Comparative Study. *Molecules*. 2023;28(2):571. doi: 10.3390/molecules28020571.
44. Wani JA, Tsagkaris C, Majid S, Ganie MA, Akhter R, Ahmad SB, Ovais S, Khan MS, Wani HA. Therapeutic Effects of *Nigella sativa* on Hormonal

- Dysfunctions. In: Black Seeds (*Nigella sativa*). Elsevier; 2022:217-238. doi: 10.1016/B978-0-12-824462-3.00001-9
45. Naeimi SA, Hajimehdipoor H, Saber S. Comparing the Effect of *Nigella sativa* Oil Soft Gel and Placebo on Oligomenorrhea, Amenorrhea and Laboratory Characteristics in Patients with Polycystic Ovarian Syndrome, a Randomized Clinical Trial. *Res J Pharmacogn*. 2020;7(1):49-59. doi: 10.22127/RJP.2019.206178.1530
  46. Nafiu AB, Alimi S, Babalola A, Ogunlade AT, Muhammad FD, Abioye AR, Oyewole LA, Akinola O, Olayemi JO, Amin A, Abdulmajeed WI. Anti-androgenic and Insulin- sensitizing Actions of *Nigella sativa* Oil Improve Polycystic Ovary and Associated Dyslipidemia and Redox Disturbances. *J Complement Med Res*. 2019;10(4):186-199. doi:10.5455/jcmr.20190613045154
  47. Javanshir ST, Yaghmaei P, Hajebrahimi Z. Thymoquinone ameliorates some endocrine parameters and histological alteration in a rat model of polycystic ovary syndrome. *Int J Reprod Biomed*. 2018;16(4):275.
  48. Arif M, Thakur SC, Datta K. Implication of thymoquinone as a remedy for polycystic ovary in rat. *Pharm Biol*. 2016;54(4):674-85. doi: 10.3109/13880209.2015.1072565.
  49. Shirsath A, Aundhakar N, Kamble P. Study of oxidative stress and antioxidant levels in polycystic ovarian. *Int J Healthcare Biomed Res*. 2015; 3(4): 16-24.
  50. Blagojevic IP, Ignjatovic S, Macut D, Kotur-Stevuljevic J, Bozic-Antic I, Vekic J, Bjekic-Macut J, Kastratovic-Kotlica B, Andric Z, Ilic D. Evaluation of a summary score for dyslipidemia, oxidative stress and inflammation (the doi score) in women with polycystic ovary syndrome and its relationship with obesity. *J Med Biochem*. 2018; 37(4): 1-11. doi: 10.2478/jomb-2018-0008.
  51. Heshmati J, Nemati N. Effects of black seed (*Nigella sativa*) on metabolic parameters in diabetes melitus: a systematic review. *Complement Ther Med*. 2015; 23(2): 275- 282. doi: 10.1016/j.ctim.2015.01.013.
  52. Ashraf SS, Rao MV, Kaneez FS, Qadri S, Al-Marzouqi AH, Chandranath IS, Adem A. *Nigella sativa* extract as a potent antioxidant for petrochemical-induced oxidative stress. *Journal of chromatographic science*. 2011 Apr 1;49(4):321-6. doi: 10.1093/chrsci/49.4.321.
  53. Latiff LA, Dollah MA, Hanachi P, Rahman SA. A randomized control trial on the effect of black seeds (*Nigella sativa*) on climacteric symptoms and quality of life of perimenopausal women in Rawang, Selangor, Malaysia. *Clin Biochem*. 2011; 44(13): 20- 21. doi: 10.1016/j.clinbiochem.2011.08.060
  54. Naftolin F, Stanburg MG. Phytoestrogens: are they really estrogen mimics. *Fertil Steril*.2002; 77(1): 15-17. doi: /10.1016/S0015-0282(01)02006-4.
  55. Parhizkar S, Latif LA, Sabariah AR, Dollah MA. Evaluation of estrogen-like activity of *Nigella sativa* in ovariectomized rats. *Afr J Pharm Pharmacol*. 2011; 5(8): 1006-1011. doi: 10.5897/AJPP10.257
  56. Suzuki KM, Isohama Y, Maruyama H, Yamada Y, Narita Y, Ohta S, Araki Y, Miyata T, Mishima S. Estrogenic activities of fatty acids and a sterol isolated from royal jelly. *Evid Base Complement Altern Med*. 2008; 5(3): 295-302. doi: 10.1093/ecam/nem036.
  57. Ibrahim RM, Hamdan NS, Mahmud R, Imam MU, Saini SM, Rashid SN, et al. A randomized controlled trial on hypolipidemic effects of *Nigella sativa* seeds powder in menopausal women. *J Translational Med* 2014; 12:82. doi: 10.1186/1479-5876-12-82.
  58. Al-Naqeep G, Ismail M, Allaudin Z. Regulation of low-density lipoprotein receptor and 3-hydroxy-3-methylglutaryl coenzyme a reductase gene expression by thymoquinone-rich fraction and thymoquinone in HepG2 cells. *J Nutrigenet Nutrigenomics* 2009; 2:163–72. doi: 10.1159/000227264.
  59. Burits M, Bucar F. Antioxidant activity of *Nigella sativa* essential oil. *Phytother Res* 2000; 14:323–8. doi: 10.1002/1099-1573(200008)14:5<323::AID-PTR621>3.0.CO;2-Q
  60. El-Dakhkhny M, Mady NI, Halim MA. *Nigella sativa* L. oil protects against induced hepatotoxicity and improves serum lipid profile in rats. *Arzneimittelforsch* 2000; 50:832– 6. doi: 10.1055/s-0031-1300297
  61. Akash MS, Rehman K, Rasool F, Sethi A, Abrar MA, Irshad A, Abid A, Murtaza G. Alternate therapy of type 2 diabetes mellitus (T2DM) with *Nigella* (Ranunculaceae). *J Med Plants Res*. 2011; 5(31):6885-9. doi: 10.5897/JMPR11.1425
  62. Bogdanov S, Jurendic T, Sieber R, Gallmann P. Honey for nutrition and health: a review. *J Am Coll Nutr*. 2008;27(6):677-689. doi: 10.1080/07315724.2008.10719745.
  63. Miguel M, Antunes M, Faleiro M. Honey as a complementary medicine. *Integr Med Insights*. 2017; 12:1178633717702869. doi: 10.1177/1178633717702869.
  64. Ullah A, Aldakheel FM, Anjum SI, Raza G, Khan SA, Gajger IT. Pharmacological properties and therapeutic potential of honey bee venom. *Saudi Pharm J*. 2022;30(11):1742-1754. doi: 10.1016/j.jsps.2022.11.008.
  65. Kamal DAM, Ibrahim SF, Uqusman A, Mokhtar MH. Kelulut Honey Ameliorates Oestrus Cycle, Hormonal Profiles, and Oxidative Stress in Letrozole-Induced Polycystic Ovary Syndrome Rats. *Antioxidants*. 2022;11(10):1879. doi: 10.3390/antiox11101879.
  66. Cheepa FF, Liu H, Zhao G. The natural cryoprotectant honey for fertility cryopreservation. *Bioengineering*. 2022;9(3):88. doi: 10.3390/bioengineering9030088.
  67. Nervey D, Igbigbi P, Avwioro G. The Influence of

- Excessive and Prolonged Ingestion of Honey on Sex Hormones and Prostate Specific Antigen in Adult Male Wistar Rats. *Med. Sci. Int. Med. J.* 2012; 1: 161–170. doi:10.5455/medscience.2012.01.8017
68. Erejuwa OO, Sulaiman SA, Wahab MS. Effects of honey and its mechanisms of action on the development and progression of cancer. *Molecules.* 2014;19(2):2497-522. doi: 10.3390/molecules19022497.
  69. Tsiapara, A.V.; Jaakkola, M.; Chinou, I.; Graikou, K.; Tolonen, T.; Virtanen, V.; Moutsatsou, P. Bioactivity of Greek honey extracts on breast cancer (MCF-7), prostate cancer (PC-3) and endometrial cancer (Ishikawa) cells: Profile analysis of extracts. *Food Chem.* 2009; 116:702–708. doi: 10.1016/j.foodchem.2009.03.024
  70. Bambang, N.; Ikhsan, M.; Sukri, N. Rheological Properties of Honey and its Application on Honey Flow Simulation through Vertical Tube. *IOP Conf. Ser. Earth Environ. Sci.* 2018; 334:012041. doi: 10.1088/1755-1315/334/1/012041
  71. Sopade, P.; Halley, P.; Bhandari, B.; D'arcy, B.; Doebler, C.; Caffin, N. Application of the Williams–Landel–Ferry model to the viscosity–temperature relationship of Australian honeys. *J. Food Eng.* 2003; 56:67–75. doi: 10.1016/S0260-8774(02)00149-8
  72. Ahmed, J.; Prabhu, S.; Raghavan, G.; Ngadi, M. Physico-chemical, rheological, calorimetric and dielectric behavior of selected Indian honey. *J. Food Eng.* 2007; 79:1207–1213. doi: 10.1016/j.jfoodeng.2006.04.048
  73. Juszcak, L.; Fortuna, T. Rheology of selected Polish honeys. *J. Food Eng.* 2006;75:43– 49. doi: 10.1016/j.jfoodeng.2005.03.049
  74. Bakier, S., Miastkowski, K. and Bakoniuk, J.R., Rheological properties of some honeys in liquefied and crystallised states. *Journal of Apicultural Science*, 2016;60(2):153-166. doi: 10.1515/JAS-2016-0026
  75. Bhandari, B.; D'Arcy, B.; Chow, S. Rheology of selected Australian honeys. *J. Food Eng.* 1999;41(1): 65–68. doi:10.1016/S0260-8774(99)00078-3
  76. Lazaridou, A.; Biliaderis, C.G.; Bacandritsos, N.; Sabatini, A.G. Composition, thermal and rheological behaviour of selected Greek honeys. *J. Food Eng.* 2004; 64:9–21. doi: 10.1016/j.jfoodeng.2003.09.007
  77. Gül, A. Pehlivan, T. Antioxidant activities of some monofloral honey types produced across Turkey. *Saudi J. Biol. Sci.* 2018; 25:1056–1065. doi: 10.1016/j.sjbs.2018.02.011
  78. Khalafi, R.; Goli, S.A.H.; Behjatian, M. Characterization and classification of several monofloral Iranian honeys based on physicochemical properties and antioxidant activity. *Int. J. Food Prop.* 2016; 19:1065–1079. doi: 10.1080/10942912.2015.1055360
  79. Pisoschi AM, Pop A. The role of antioxidants in the chemistry of oxidative stress: A review. *Eur. J. Med. Chem.* 2015; 97:55–74. doi: 10.1016/j.ejmech.2020.112891
  80. Grune, T. Free Radicals and Diseases: Gene Expression, Cellular Metabolism and Pathophysiology; IOS Press: Amsterdam, The Netherlands, 2005; Volume 367.
  81. Milner, J.A.; Romagnolo, D.F.; Connor, J.; Lee, S. Bioactive Compounds and Cancer; Springer, Humana Press: New York, NY, USA, 2010. doi: 10.1007/978-1-60761-627-6
  82. Vayalil PK. Date fruits (*Phoenix dactylifera* Linn): an emerging medicinal food. *Crit Rev Food Sci Nutr.* 2012;52(3):249-71. doi: 10.1080/10408398.2010.499824.
  83. Tang ZX, Shi LE, Aleid SM. Date fruit: chemical composition, nutritional and medicinal values, products. *J Sci Food Agric.* 2013 Aug 15;93(10):2351-61. doi: 10.1002/jsfa.6154.
  84. Koser HN, Mubarak R, Jaffar HM, Rizwan B, Mubashar H, Kousar S, Sultan H, Abbas R, Tasleem F, Islam Z. A Review on Nutritional Composition of *Phoenix Dactylifera* L. And Its Pharmacological Functions: Pharmacological Properties of *Phoenix dactylifera* L. *Pakistan BioMed J.* 2022;1:5-9. doi: 10.54393/pbmj.v5i1.121
  85. El-Wahed A, Mahfouz R, Nasr AAA. Effects of Date Palm Pollen on Women with the Polycystic Ovarian Syndrome. *Egypt J Hosp Med.* 2022;89(1):4622-4625. doi: 10.21608/ejhm.2022.259120
  86. Karimi Jashni H, Kargar Jahromi H, Bagheri Z. The effect of palm pollen extract on polycystic ovary syndrome (POS) in rats. *Int J Med Res Health Sci.* 2016;5(5):317-321
  87. Khan, F., Ahmed, F., Pushparaj, P. N., Abuzenadah, A., Kumosani, T., Barbour, E., . . . Gauthaman, K. Ajwa date (*Phoenix dactylifera* L.) extract inhibits human breast adenocarcinoma (MCF7) cells invitro by inducing apoptosis and cell cycle arrest. *PLoS One*, 11(7), e0158963. doi: 10.1371/journal.pone.0158963
  88. Mirza MB, Elkady AI, Al-Attar AM, Syed FQ, Mohammed FA, Hakeem KR. Induction of apoptosis and cell cycle arrest by ethyl acetate fraction of *Phoenix dactylifera* L. (Ajwa dates) in prostate cancer cells. *J Ethnopharmacol.* 2018 May 23;218:35-44. doi: 10.1016/j.jep.2018.02.030.
  89. Elhemeidy, R. M. M., Lyrawati, D., & Widjajanto, E. Date Fruit Extract (*Phoenix dactylifera*, Ajwa) Modulates NK Cells and TNF-Alpha in DMBA-Induced Mammary Cancer Sprague-Dawley Rats. *Journal of Tropical Life Science*, 2018;8(3):227-235. doi:10.36108/pajols/1202/50.0160
  90. Majah I. Sunan Ibn Majah. Beirut: Darul Kutub Al Ilmiyyah; 1952.
  91. Boskou D. History and characteristics of the olive tree. In: Boskou D, editor. *Olive Oil Chemistry and Technology*. Champaign, IL: Am. Oil Chem. Soc. Press; 1996. doi: 10.4324/9781003040217

92. Jimenez-Lopez C, Carpena M, Lourenço-Lopes C, Gallardo-Gomez M, Lorenzo JM, Barba FJ, Prieto MA, Simal-Gandara J. Bioactive Compounds and Quality of Extra Virgin Olive Oil. *Foods*. 2020;9(8):1014. doi: 10.3390/foods9081014.
93. Egba SI, Udom ID, Okonkwo CO. Comparative effect of oral administration of some dietary lipids on fertility hormones of female Wistar albino rats. *Global J Biotech Biochem*. 2014;9:24-9. doi: 10.5829/idosi.gjbb.2014.9.1.8399
94. Moghissi KS. Gonadotropin releasing hormones. Clinical applications in gynecology. *J Reprod Med*. 1990;35(12):1097-107.
95. Gopal M, Duntley S, Uhles M, Attarian H. The role of obesity in the increased prevalence of obstructive sleep apnea syndrome in patients with polycystic ovarian syndrome. *Sleep Med*. 2002 Sep;3(5):401-4. doi: 10.1016/s1389-9457(02)00033-3. .
96. Teede HJ, Joham AE, Paul E, Moran LJ, Loxton D, Jolley D, Lombard C. Longitudinal weight gain in women identified with polycystic ovary syndrome: Results of an observational study in young women. *Obesity*. 2013;21(8):1526-1532. doi:10.1002/oby.20213