Food Research 7 (3) : 105 - 110 (June 2023)
Journal homepage: https://www.myfoodresearch.com

FOOD RESEARCH

FULL PAPER

The effect of ajwa dates (*Phoenix dactylifera L*) consumption to anti-Mullerian hormone level of perimenopausal woman

[1,2]Mulyadi, F.E., [3]Natzir, R., [4,*]Mappaware N.A., [2]As'ad, S., [5]Sinrang, A.W. and [6]Kurniawan, L.B.

[1]*Master of Biomedical Sciences, Graduate School Hasanuddin University, Makassar 90245, Indonesia*
[2]*Department of Physiology, Faculty of Medicine, Universitas Muslim Indonesia, Makassar 90231, Indonesia*
[3]*Department of Biochemistry, Faculty of Medicine, Hasanuddin University, Makassar 90245, Indonesia*
[4]*Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Muslim Indonesia, Makassar 90231, Indonesia*
[5]*Department of Nutritional Science, Faculty of Medicine, Hasanuddin University, Makassar 90245, Indonesia*
[6]*Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Makassar 90245, Indonesia*

Article history:
Received: 15 December 2021
Received in revised form: 26 January 2022
Accepted: 21 January 2022
Available Online: 4 June 2023

Keywords:
Ajwa dates,
Perimenopause,
Anti-Mullerian Hormone (AMH)

DOI:
https://doi.org/10.26656/fr.2017.7(3).1004

Abstract

Ageing in the female reproductive system is most clearly seen when entering the perimenopausal period, where there is a decrease in the number and function of oocytes and significant endocrine changes. Inflammation and accumulation of reactive oxygen species (ROS) are considered to be the most responsible factors for the reduction in ovarian reserve. Anti-Mullerian Hormone (AMH) is used as a biomarker of ovarian reserve and clinically as a predictive biomarker of menopause. Ajwa dates contain phytochemicals with antioxidant and anti-inflammatory activities. This study aimed to analyse the effect of consuming ajwa dates on AMH levels in perimenopausal women. This research was a quasi-experimental study with a pre-post control design which was conducted at Sitti Khadijah 1 Muhammadiyah Hospital, Makassar, Indonesia, from May until October 2021. It involved 44 perimenopausal subjects aged 42 - 48 years, which were divided into 2 groups randomly (28 subjects consumed ajwa dates as the intervention group, sixteen as the control group). AMH levels were assessed before and after the 8-week intervention period and analysed using the ELISA method. The result showed that AMH levels in the intervention and the control groups after 8 weeks of treatment decreased by 0.37±0.36 ng/mL and 0.55±0.19 ng/mL, respectively. The decrease in AMH levels between the two groups was significantly different (p<0.05) where AMH levels in the intervention group declined less than in the control group. In conclusion, AMH levels in perimenopausal women who consumed ajwa dates decreased less than perimenopausal women who did not consume ajwa dates. The reduction of ovarian reserve in perimenopausal women can be inhibited through the intervention of exogenous antioxidants from ajwa dates which AMH levels were the indicator.

1. Introduction

The number of oocytes in both ovaries of a woman reaches a peak of about 7-8 million during fetal life at 20 weeks of gestation. Since then, oocyte atresia occurs rapidly, until finally entering puberty the number of oocytes remaining in both ovaries is only about 500,000. Furthermore, every month, the oocytes in the follicles in both ovaries will be activated under the influence of gonadotropin hormone stimulation, either to further ovulate or most of them will become atretic. Therefore, the number of oocytes within the ovaries decreases with increasing age. Eventually, a woman will experience menopause when there are no more follicles containing oocytes in her ovaries. The total number of follicles containing oocytes in a woman's ovaries at any given time is called the ovarian reserve (Care, 2019).

The most significant characteristic of ovarian ageing is the reduction of ovarian reserve. Free radical theory, the classic theory of ageing, proposes that oxidative stress caused by increased intracellular levels of reactive

*Corresponding author.
Email: *ernase@yahoo.co.id*

eISSN: 2550-2166
Published by Rynnye Lyan Resources

oxygen species (ROS) is the most significant contributor to cellular senescence (Liochev, 2013). ROS actually have a physiological role in the development of follicles in the ovaries, but increased levels of ROS, which overpower cellular antioxidants can trigger oxidative stress in cells, directly cause oxidative damage to all biomolecules in cells (including proteins, lipids, and DNA), and therefore contribute to the development of ovarian ageing. Furthermore, numerous studies have documented that oxidative stress is a major driver of the ovarian ageing process and promotes the development of other ovarian ageing-related aetiologies, such as telomere shortening, mitochondrial dysfunction, apoptosis, and inflammation (Yang *et al*., 2021).

Unfortunately, the continuous ageing process of the ovaries will only be recognized at the late stage with the onset of changes in the regularity of the cycle until the permanent cessation of the menstrual cycle (menopause). In this last decade, AMH has recently emerged as an important marker of ovarian reserve and has been clinically used as a predictive biomarker of menopause (Depmann *et al*., 2018). AMH is produced by granulosa cells of small follicles in the ovary and is detected in the peripheral circulation. Serum AMH concentrations decreased over time in young normoovulatory women, whereas other markers associated with ovarian ageing were unchanged (De Vet *et al*., 2002). The decrease in serum AMH levels was shown to be more consistent and more strongly correlated with age than antral follicle count by USG, inhibin B, or FSH (Righini *et al*., 2003; Freeman *et al*., 2012). This hormone appears to modulate two regulatory steps of folliculogenesis, inhibiting primordial follicle activation and decreasing the sensitivity of small antral follicles to FSH (De Vet *et al*., 2002). However, the role of AMH as a biomarker of ovarian ageing remains to be combined with other tests to holistically evaluate perimenopausal women. Assessment of clinical signs and symptoms of perimenopause needs to be confirmed by biomarker examination and ultrasonography (Taylor *et al*., 2020). Measurement of AMH levels combined with an evaluation of the number of antral follicles with transvaginal ultrasound is one of the ovarian reserve tests with the highest predictive value (Righini *et al*., 2003; Jirge, 2011).

Ajwa dates are a special fruit and one of the fruits that are mentioned repeatedly in the Qur'an (Surah Al Baqara verse 266, Surah Ar-Rahman verse 11, Surah Abasa verse 27-29) (Muhammad Taq-iud-Din Al-Hilali, 1985; Ahmad *et al*., 2009). Ajwa dates are rich in phenolic (22.11 mg/100 g), flavonoids (2.78 mg/100 g), and other micronutrients, which have a role as natural antioxidants that can modulate oxidative stress in the ageing process of the ovaries (Hamad *et al*., 2015). Several previous studies have also confirmed the antioxidant and anti-inflammatory effects of ajwa dates (Saleh *et al*., 2011; Zhang *et al*., 2013; Rahmani *et al*., 2014; Royani *et al*., 2019; Younas *et al*., 2020;). Therefore, this study aimed to evaluate the effect of ajwa dates consumption on AMH levels, a biomarker of ovarian reserve, in perimenopausal women.

2. Materials and methods

2.1 Study design

This research was a quasi-experimental study with a pre-post control design conducted at Sitti Khadijah 1 Muhammadiyah Hospital Makassar, South Sulawesi, Indonesia, from May until October 2021. Laboratory examination was performed at the Hasanuddin University Medical Research Center (HUMRC) Laboratory Makassar. This study has obtained an Ethics Approval Letter No.330/UN4.6.4.5.31/PP36/2021 from the Ethics Committee of Health Research, Faculty of Medicine, Hasanuddin University. This work was carried out per the research code of ethics.

2.2 Inclusion and exclusion criteria

The inclusion criteria of this study included (1) women aged 42 - 48 years, (2) married, (3) not in menopause, (4) parity ≥ 1, (5) willing to be a subject and sign a statement of willingness to be a respondent (informed consent). The exclusion criteria were as follows (1) fasting plasma glucose level ≥ 126 mg/dL, (2) having a history of polycystic ovarian syndrome (PCOS) or ovarian surgery, (3) smoking, (4) using hormonal contraception, (5) having a previous history of chronic infectious diseases (e.g. tuberculosis, malaria), (6) suffering non-communicable degenerative diseases (e.g. cancer, chronic kidney failure, and diabetes mellitus).

2.3 Procedures

All participants were given a detailed explanation of the objectives, benefits, and procedures of the study and each subject was asked to sign the written consent. The screening included history taking, physical examination, measurement of body mass index (BMI), evaluation of fasting plasma glucose levels, and transvaginal ultrasound were performed to determine selected subjects based on inclusion and exclusion criteria, then randomly assigned to the intervention group (n = 28) and the control group (n = 16).

Subjects in the intervention group consumed seven pieces of ajwa dates (60-80 g/7 dates) every morning before breakfast for eight weeks. A total of forty-nine

https://doi.org/10.26656/fr.2017.7(3).1004

ajwa dates packed into seven labelled plastic packages (each pack contained seven ajwa dates) were given per week to each subject in the intervention group. They also received a diary sheet to record the daily intake of ajwa dates during the eight weeks of treatment. Meanwhile, subjects in the control group were not allowed to consume ajwa dates during the study. A 24-hour food recall was performed on all subjects, both in the intervention and the control groups.

2.3 Data collection technique

Blood samples (3 mL of venous blood) were taken twice for all subjects after 8 hrs of fasting. The first sampling was carried out at the beginning of the study (on the 3rd day of the menstrual cycle of each subject) and the second at 8 weeks after the first blood sampling. AMH levels were checked by the ELISA method using a kit from BT Lab (catalogue number E1052Hu) with a sensitivity of 0.01 ng/mL and a value range of 0.05-15 ng/mL.

2.4 Statistical analysis

All data were presented in mean±SD. The Mann-Whitney U test was used to compare the intervention and control groups in terms of age, blood pressure, BMI, and contraceptive use. The chi-square test was used to compare the employment status, and the fisher test to compare education and parity. AMH levels before and after treatment in each group were compared using paired sample t-test. A comparison of the mean differences in intervention and control groups was analysed using an independent sample t-test. All statistical analyses were performed using SPSS 26.0 software.

3. Results and discussion

3.1 Demographic characteristics

The demographic characteristics of subjects in the intervention and control groups are shown in Table 1. There were no significant differences between the two groups in terms of age, blood pressure, BMI, parity, education, employment status, and contraceptive use.

3.2 Outcomes

The mean levels of AMH in the intervention and the control groups before treatment were 1.52 ng/mL and 1.24 ng/mL, respectively. After 8 weeks of treatment, the mean AMH levels in the intervention and control groups dropped to 1.15 ng/mL and 0.69 ng/mL, respectively (Table 2). The decrease in AMH levels in the intervention group was 0.37±0.36 ng/mL while in the

Table 1. Sample characteristics

Variable	Intervention Group (n = 28)	Control Group (n = 16)	*p-value*
Age[a] (years)	44.79±2.28	44.69±2.24	0.719[c]
Blood Pressure[a] (mmHg)			
Systolic	118.57±10.79	121.25±13.60	0.849[c]
Diastolic	81.07±7.37	80.00±12.65	0.776[c]
BMI[b]			0.384[c]
Underweight	2 (7.1%)	0 (0.0%)	
Normal	5 (17.9%)	3 (18.8%)	
Overweight	4 (14.3%)	7 (43.8%)	
Class 1 Obesity	13 (46.4%)	5 (31.2%)	
Class 2 Obesity	4 (14.3%)	1 (6.2%)	
Parity [b]			0.310[d]
Primipara	4 (14.3%)	4 (25.0%)	
Multipara	24 (85.7%)	12 (75.0%)	
Education [b]			0.600[d]
≤ 9 years	1 (3.6%)	1 (6.3%)	
> 9 years	27 (96.4%)	15 (93.7%)	
Employment Status [b]			0.932[e]
Employed	14 (50.0%)	7 (43.7%)	
Unemployed	14 (50.0%)	9 (56.3%)	
Contraceptive Use [b]			0.553[c]
Non-users	19 (67.9%)	12 (75.0%)	
Intra Uterine Device	5 (17.9%)	3 (18.7%)	
Tubectomy	4 (14.2%)	1 (5.3%)	

[a]Mean±Standard Deviation, [b]Frequency (%), [c]Mann-Whitney U test, [d] Fisher test, [e] Chi-Square test

https://doi.org/10.26656/fr.2017.7(3).1004

Table 2. Comparison of serum AMH levels in intervention and control groups

Groups	AMH Levels (ng/mL)[a]		Mean Δ AMH Levels	*p-value* [b]
	Before	After		
Intervention	1.52±0.39	1.15±0.56	0.37±0.36	0.041
Control	1.24±0.22	0.69±0.25	0.55±0.19	

[a]Mean ± Standard deviation, [b] Independent sample t-test, p<0.05 statistically significant

control group was 0.55±0.19 ng/mL. The decrease in AMH levels between the two groups was significantly different (p<0.05). AMH levels in the intervention group declined less than in the control group. The graph of changes in the mean serum AMH levels in the intervention and control groups before and after treatment can be seen in Figure 1.

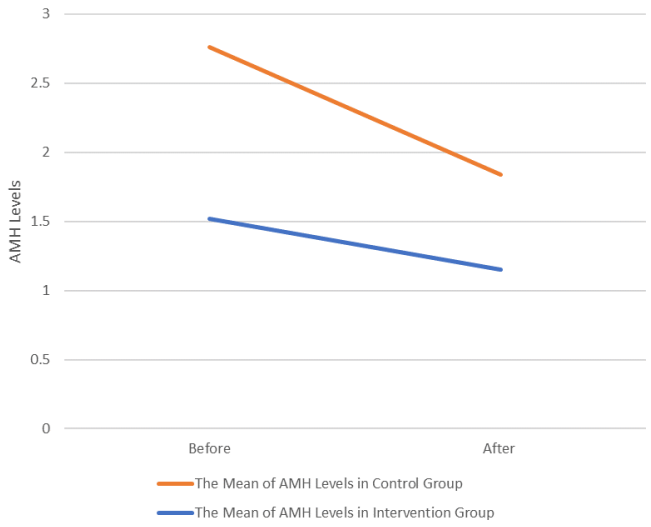

Figure 1. The changes of mean serum AMH levels in the intervention and control groups

The decrease in AMH levels that occurred in both groups at an interval of 8 weeks is following the theory that AMH, which describes the condition of the ovarian reserve will decrease with increasing age (time) (Freeman *et al*., 2012; Moslehi *et al*., 2019). However, the finding that the decrease in AMH levels in the intervention group was less than in the control group supports our hypothesis regarding the effect of ajwa dates to prevent damage to primordial ovarian follicles thereby inhibiting the reduction of ovarian reserves which AMH levels were the indicator.

Oxidative damage of the ovaries is caused by the multiplication of lipid peroxidation, which affects folliculogenesis, meiosis, ovulation, and induces granulosa cell (GC) apoptosis, which ultimately leads to ovarian ageing and decreased ovarian reserve. In addition, inflammation is associated with the pathogenesis of human ageing, and this also occurs in the ovaries. Recent studies have shown that inflammation is a major marker of ageing ovarian stroma and is considered a new mechanism of POI (premature ovarian insufficiency). Various studies have revealed that there is a strong link between inflammation and oxidative stress. ROS can serve as "firewood" to activate the inflammatory NLRP3, causing the secretion of pro-inflammatory cytokines (IL-1β and IL-18). ROS can also induce activation of nuclear factor kappa B ($NF_{ß}$-B), an important mediator of the inflammatory response, and is associated with the pathogenesis of many diseases. This makes the role of oxidative stress and inflammation in ovarian ageing inseparable (Yang *et al*., 2021).

The mechanism by which ajwa dates can inhibit the decrease in AMH levels is not known with certainty, but it is suspected through its role as a potent antioxidant and anti-inflammatory that can reduce free radical activity and production of proinflammatory cytokines that damage and decrease ovarian reserves. Other studies have also proven the benefits of exogenous antioxidant supplementation on female reproductive function, where it was found that AMA patients (advanced maternal aged, aged 39 years) who were given antioxidant supplementation had promising reproductive outcomes compared to the younger control group (Katz-Jaffe *et al*., 2020). Another study by Sadiyeh *et al*. (2021) reported an increase in AMH in a randomized controlled trial of the benefits of selenium and vitamin E supplementation on ovarian reserve in patients with premature ovarian insufficiency. This study documented that supplementation of 200 g of selenium and 400 units of vitamin E could increase ovarian reserve, as evidenced by a significant increase in the number of antral follicles and AMH levels in the intervention group. Analysis of the mineral content of dates has also revealed a selenium content of 0.24 – 0.4 mg/100 g dates (Al-Farsi and Lee, 2008). Selenium plays a role in forming the structure of the selenoprotein GPX1 enzyme which is one of the important cofactors in antioxidant enzymes. This enzyme in the ovary accumulates in the GC of healthy and large follicles but is absent in small and atretic follicles (Ceko *et al*., 2016).

The protective role of Ajwa dates on the ovaries can also be caused by the content of quercetin (1.219±0.071 mg/100 g) (Hamad *et al*., 2015). Quercetin is a bioactive form of flavonoid and has broad biological benefits including antioxidant, anti-inflammatory, anti-apoptotic effects, and stimulating mitochondrial biogenesis (Xu *et al*., 2019; Yang *et al*., 2021). In laboratory animals, quercetin has been shown to increase ovarian volume and prevent follicular cell degeneration, bleeding, vascular congestion, and oedema while decreasing

https://doi.org/10.26656/fr.2017.7(3).1004

follicular cell apoptosis. Besides that, in vitro studies using animal and human GC demonstrated that quercetin treatment increased GC viability, reduced apoptotic cells, inhibited oocyte quality decline, and enhanced subsequent embryonic development (Yang *et al*., 2021).

The benefits of ajwa dates as antioxidants were also reported through an in vivo study by Al-Yahya *et al*. (2016) which revealed the decrease in the activity of SOD (superoxide dismutase), and CAT (catalase) in isoproterenol-treated rats was significantly inhibited by the administration of ajwa date extract. Enzymes such as SOD and CAT are major defences against oxidative stress through the scavenging action of oxygen radicals, such as superoxide and hydrogen peroxide, and preventing the production of hydroxyl radicals. Another experimental study involving animals found that administering date palm extract to arthritis rats increased levels of vitamins A, C, and E, as well as plasma-carotene while plasma MDA levels were significantly reduced. These results indicate a reduction in oxidative stress and an increase in antioxidants with the administration of date palm extract (Mohamed and Al-okbi, 2004). Micronutrients such as vitamins and minerals in dates also contribute to the activation of endogenous antioxidant defence mechanisms. The minerals present in dates (magnesium, zinc, copper, potassium, and selenium) act as cofactors for various enzymes and increase their antioxidant activity (Younas *et al*., 2020). The above findings indicated that ajwa dates are rich sources of natural antioxidants and can be used as ovarian ageing protective agents. Even long before all scientific evidence went through a series of studies, the protective role of ajwa dates had also been conveyed by the Prophet Muhammad as in the hadith which reads, "Whoever consumes seven ajwa dates in the morning, then on that day he will not be exposed to poison or magic" (HR Al-Bukhari and Muslim).

4. Conclusion

AMH levels in perimenopausal women who consumed ajwa dates decreased less than perimenopausal women who did not consume ajwa dates. The reduction of ovarian reserve in perimenopausal women can be inhibited through the intervention of exogenous antioxidants from ajwa dates which AMH levels were the indicators.

Conflict of interest

The authors declare no conflict of interest associated with the manuscript or its funding.

Acknowledgements

The research work was funded by Research and Community Service Hasanuddin University Grants 2021. The authors wish to express their gratitude to all women who participated in this study.

References

Ahmad, M., Zafar, M. and Sultana, S. (2009). Fruit plant species mentioned in the Holy Qur'an and Ahadith and their ethnomedicinal importance. *Ethnomedical Study*, 5(2), 284–295.

Al-Farsi, M.A. and Lee, C.Y. (2008). Nutritional and functional properties of dates: a review. *Critical Reviews in Food Science and Nutrition*, 48(10), 877–887. https://doi.org/10.1080/10408390701724264

Al-Yahya, M., Raish, M., Alsaid, M.S., Ahmad, A., Parvez, M.K. and Rafatullah, S. (2016). Ajwa dates (*Phoenix dactylifera L*.) extract ameliorates isoproterenol-induced cardiomyopathy through downregulation of oxidative, inflammatory, and apoptotic molecules in the rodent model. *Phytomedicine*, 23(11), 1240-1248. https://doi.org/10.1016/j.phymed.2015.10.019

Care, S.F. (2019). ACOG Committee Opinion No. 773: The use of antimüllerian hormone in women not seeking fertility care. *Obstetrics and Gynecology*, 133(4), e274–e278. https://doi.org/10.1097/AOG.0000000000003162

Ceko, M.J., Harris, H.H., Hummitzsch, K. and Rodgers, R.J. (2016). Trace elements in ovaries: measurement and physiology. *Biology of Reproduction,* 94(4), 1-14. https://doi.org/10.1095/biolreprod.115.137240

De Vet, A., Laven, J.S.E., De Jong, F.H., Themmen, A.P.N. and Fauser, B.C.J.M. (2002). Antimullerian hormone serum levels: a putative marker for ovarian aging. *Fertility and Sterility*, 77(2), 357–362. https://doi.org/10.1016/S0015-0282(01)02993-4

Depmann, M., Eijkemans, M.J.C., Broer, S.L., Tehrani, F.R., Solaymani-dodaran, M., Azizi, F., Lambalk, C.B., Randolph, J.F., Harlow, S.D., Freeman, E.W., Sammel, M.D., Verschuren, W.M.M., van der Schouw, Y.T., Mol, B.W. and Broekmans, F.J.M. (2018). Does AMH relate to timing of menopause? Results of an individual patient data meta-analysis. *Journal of Clinical Endocrinology and Metabolism*, 103(10), 3593-3600. https://doi.org/10.1210/jc.2018-00724

Freeman, E.W., Sammel, M.D., Lin, H., Boorman, D.W. and Gracia, C.R. (2012). Contribution of the rate of change of antimullerian hormone in estimating time to menopause for late reproductive-age women. *Fertility and Sterility*, 98(5), 1254-1259. https://

doi.org/10.1016/j.fertnstert.2012.07.1139

Hamad, I., Abdelgawad, H., Jaouni, S.A., Zinta, G., Asard, H., Hassan, S., Hegab, M., Hagagy, N. and Selim, S. (2015). Metabolic analysis of various date palm Fruit (*Phoenix dactylifera L.*) cultivars from Saudi Arabia to assess their nutritional quality. *Molecules*, 20(8), 13620–13641. https://doi.org/10.3390/molecules200813620

Jirge, P.R. (2011). Ovarian reserve tests. *Journal of Human Reproductive Sciences*, 4(3), 108-113. https://doi.org/10.4103/0974-1208.92283

Katz-Jaffe, M.G., Lane, S.L., Parks, J.C., Mccallie, B.R., Makloski, R. and Schoolcraft, W.B. (2020). Antioxidant intervention attenuates aging-related changes in the murine ovary and oocyte. *Life*, 10 (11), 250. https://doi.org/10.3390/life10110250

Liochev, S.I. (2013). Reactive oxygen species and the free radical theory of aging. *Free Radical Biology and Medicine*, 60, 1–4. https://doi.org/10.1016/j.freeradbiomed.2013.02.011

Mohamed, D.A. and Al-okbi, S.Y. (2004). In vivo evaluation of the antioxidant and anti-inflammatory activity of different extracts of date fruit in adjuvant arthritis. *Polish Journal of Food and Nutrition Sciences*, 13(4), 397–402.

Moslehi, N., Mirmiran, P., Azizi, F. and Tehrani, F.R. (2019). Do dietary intakes influence the rate of decline in anti-Mullerian hormone among eumenorrheic women ? A population-based prospective investigation. *Nutrition Journal*, 18, 83. https://doi.org/10.1186/s12937-019-0508-5

Rahmani, A.H., Aly, S.M., Ali, H., Babiker, A.Y., Srikar, S. and Amjad, A. (2014). Therapeutic effects of date fruits (*Phoenix dactylifera*) in the prevention of diseases via modulation of anti-inflammatory, anti -oxidant and anti-tumor activity. *International Journal of Clinical and Experimental Medicine*, 7 (3), 483–491.

Righini, C., Guibourdenche, J., Fanchin, R., Schona, L.M. and Frydman, Â. (2003). Serum antimullerian hormone is more strongly related to ovarian follicular status than serum inhibin B, estradiol, FSH, and LH on day 3. *Human Reproduction*, 18(2), 323–327. https://doi.org/10.1093/humrep/deg042

Royani, I., As'ad, S., Mappaware, N.A., Hatta, M. and Rabia. (2019). Effect of ajwa dates consumption to inhibit the progression of preeclampsia threats on mean arterial pressure and roll-over test. *BioMed Research International*, 2019, 2917895. https://doi.org/10.1155/2019/2917895

Sadiyeh, F.D., Mojgan, M., Parviz, S., Sakineh, M.A. and Behnaz, S.O. (2021). The effect of selenium and vitamin E supplementation on anti-Mullerian hormone and antral follicle count in infertile women with occult premature ovarian insufficiency: a randomized controlled clinical trial. *Complementary Therapies in Medicine*, 56, 102533. https://doi.org/10.1016/j.ctim.2020.102533

Saleh, E.A., Tawfik, M.S. and Abu-Tarboush, H.M. (2011). Phenolic contents and antioxidant activity of various date palm (*Phoenix dactylifera L.*) fruits from Saudi Arabia. *Food and Nutrition Sciences*, 2 (10), 1134–1141. https://doi.org/10.4236/fns.2011.210152

Taylor, H.S., Pal, L. and Seli, E. (2020). Speroff's Clinical Gynecologic Endocrinology and Infertility. 9th ed. Philadelphia, USA: Wolters Kluwer.

Xu, D., Hu, M., Wang, Y. and Cui, Y. (2019). Antioxidant activities of quercetin and its complexes for medicinal application. *Molecules*, 24, 1123. https://doi.org/10.3390/molecules24061123

Yang, L., Chen, Y., Liu, Y., Xing, Y., Miao, C. and Zhao, Y. (2021). The role of oxidative stress and natural antioxidants in ovarian aging. *Frontiers in Pharmacology*, 11, 617843. https://doi.org/10.3389/fphar.2020.617843

Younas, A., Naqvi, S.A., Khan, M.R., Shabbir, M.A., Jatoi, M.A., Anwar, F., Inam-Ur-Raheem, M., Saari, N. and Aadil, R.M. (2020). Functional food and nutra-pharmaceutical perspectives of date (*Phoenix dactylifera L.*) fruit. *Journal of Food Biochemistry*, 44(9), e13332. https://doi.org/10.1111/jfbc.13332

Zhang, C.-R., Aldosari, S.A., Vidyasagar, P.S.P.V., Nair, K.M. and Nair, M.G. (2013). Antioxidant and anti-inflammatory assays confirm bioactive compounds in ajwa date fruit. *Journal of Agricultural and Food Chemistry*, 61(24), 5834-5840.

