

## THE ROLE OF OMEGA-3 FATTY ACIDS IN OVARIAN FUNCTION AND HORMONAL BALANCE IN FEMALE RABBITS

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### Abstract

**Background:** Omega-3 fatty acids are now widely familiar for their physiological activity in reproductive processes, although their specific effects on ovarian function and hormonal balance remain less well known. The investigation was a mechanistic study on the action of omega-3 supplementation concerning folliculogenesis, ovarian morphology, and hormonal milieu in female rabbits through a controlled interventional study.

**Methods:** The experimental design used was controlled, meaning that the animals were divided into treatment and control groups. Each group consisted of 3 animals. Daily oral omega-3 administration was given using a syringe to the treated group for 30 days. Histological checks on ovarian morphological changes were assessed after 30 days of the experiment. Some of the things checked included follicular development and structural changes. Hormonal profiling for levels of estradiol, progesterone, FSH, and LH was done using ELISA, with statistical comparisons between the treated and control groups being presented.

**Results:** Results showed that there was marked improvement in follicular development and maturation in the omega-3-supplemented group, typified by increased density of healthy antral follicles, less atretic degeneration, and more preserved ovarian histoarchitecture. Analysis of hormonal assays revealed a significant increase in estradiol and FSH levels, which suggest stimulation of folliculogenesis, while progesterone and LH exhibited marginal changes suggesting feedback control.

**Conclusion:** These results emphasize the fact that omega-3 FAs have the potential to alter ovarian functions by interfering with steroidogenesis and follicular development pathways. This study undoubtedly confirms the therapeutic potential of omega-3 supplementation in reproductive health conditions, hence necessitating further research at molecular and mechanistic levels for its potential role in ovarian endocrinology.

### INTRODUCTION

Omega 3 fatty acids are a family of essential polyunsaturated FAs which are normally categorized as being important for health in general. They are referred in come to as 'essential' fatty acids because the human body can synthesize None of the Omega

fatty acids and therefore has to obtain them from the diet or supplements. Omega 3 FAs biosynthesis coupled to its metabolism is regulated by enzymatic reactions that are quite complex. ALA, the chief c Ω3FA consumed from dieting, gets elongated and

desaturated to be converted into EPA and DHA. That being said, this process is highly inefficient in humans converting only small amount of ALA into EPA and even less into DHA. This inefficiency underlines the necessity of EPA and DHA consumption in direct manner from marine or in the state of supplements.  $\Omega$ 3 fatty acids act together in integrating the composition of cell membranes, where they impact on structural integrity and provide substrates for eicosanoids, genuine signaling molecules. These molecules take part in many physiological systems including the cardiovascular, immune and even the nervous system.

The Omega-3 FAs have embedded in the gut and are being absorbed into TG from chylomicrons and from there, proceed to the liver. The liver makes VLDL from EPA and DHA and secretes them into the blood. free forms of omega-3s are seldom available (believed to be a small proportion of the total) almost all are associated with albumin, without this making them of lower quality. High cholesterol has always been considered a gateway to heart diseases but some newer evidence suggests that high triglycerides may also be as dangerous as or even more dangerous than cholesterol (Nordestgaard and Varbo, 2014).

However, fatty acids had an action on improving endothelial function as shown by flow-mediated dilation (FMD) and arterial stiffness measured by carotid-femoral pulse wave velocity (PWV) and had a direct anti-inflammatory effect in patients with the metabolic syndrome. In the same vein, Merino et al. established that Omega-3 fatty acids improved reactive capacity of small peripheral arteries within the intermediate to high CVD risk groups (Chan et al., 2016). Supplementation of  $\Omega$ -3 fatty acids improved arterial elasticity as indicated from pulse contour analysis measured with radial artery, specifically in patients under statin therapy for familial hypercholesterolemia (Tagetti et al., 2015). The response with heart rate is apparently not so linear as that with blood pressure against doses of omega-3 FAs compared with blood pressure, which shows a clear response even for low doses (Hisamatsu et al., 2014). Fish and other types of seafood have an abundance of  $\Omega$ -3 FAs with the richest sources being fatty fish such as salmon, mackerel, sardines and trout. It should be noted that these types of fish have high contents of

the two types of omega 3 fatty oils namely (EPA) and (DHA) (Mozaffarian et al., 2018)

Alpha-linolenic acid, which is primarily found in marine oils, can also be obtained from some plant-based oils including soybean, canola and flaxseed oils. It is important to note that ALA can only be converted in small proportions of EPA and DHA, hence it is advisable to supplement plant-based omega 3s with fish or fish oils. Regularly used plant food sources of omega 3 had lower levels of inflammatory markers (Nettleton et al., 2013). Some nuts and seeds contain omega 3 FAs primarily in the form of ALA, some of the best sources are walnuts, chia seeds, and flaxseeds. These can be consumed as a stand-alone snack or as a component of baked goods, salads, or yogurt. They are richer in omega 3 FAs than nuts and seeds significantly, however, nuts and seeds omega 3 content is not too far behind in comparison.

The reproductive functionality is regulated by the endocrine glands, where hormones produced act in different stages to bring about reproduction. In females, the hormones involved in reproduction are GnRH, FSH, LH, estrogen, and progesterone. Female animals go into estrus under the influence of estrogen. Low levels of estrogen may inhibit estrus symptoms, thereby preventing fertilization. Absence of fertilization implies lesser productivity (Ermayanti et al., 2019).

Differently from most species, rabbits show a special kind of ovarian cycle that is separate from the conventional estrous cycle. After the onset of puberty, FSH secreted by the anterior pituitary gland is responsible for the growth and development of follicles within the ovaries. The follicular development occurs in waves, with 5 to 10 follicles at any given instant in one ovary at a somewhat similar stage of development. That said, the development of these follicles is continuous, producing a constant stream of follicles undergoing different stages of maturity. With ovulation, LH is secreted from the anterior pituitary in response to stimulation of mating. This sudden rise in the level of LH hormone causes one or multiple dominant follicles to ovulate in one or both ovaries, usually approximately 10 hours post-mating stimulation. After the release of oocytes from the ovaries, LH further causes changes in the remaining follicular cells to develop quickly into the corpus luteum. The corpus luteum starts secrete

actively progestins within 3 days after ovulation (Kumcu et al., 2024).

### General Objectives:

- To collect blood samples after the supplementation period and determine changes in the levels of estradiol, progesterone, FSH, and LH using appropriate assays.
- To perform correlation analysis between levels of reproductive hormones (FSH, LH, estrogen, and progesterone) to understand the hormonal regulation of ovarian function under omega-3 supplementation.
- To compare hormonal levels within the same subjects and conduct statistical comparisons between treated and control groups to assess the effects of omega-3 supplementation on hormonal balance.
- To examine histological signs of inflammation, degeneration, or tissue preservation in ovarian samples, thereby assessing any protective or anti-inflammatory role of omega-3.

### METHODOLOGY:

This study was performed to investigate the impact of Omega-3 fatty acids on the serum level of reproductive hormones in female New Zealand White rabbits. Methodology includes experimental design, selection of animals, conditions of housing and feeding regime, supplementation procedure, health monitoring, blood sampling, and hormonal analysis.

#### Experimental Design:

The experiment used six female New Zealand White rabbits, divided equally between two groups:

**Control Group:** It received the standard basal diet without supplementation.

**Treated Group:** received Omega-3 fatty acid supplementation along with the same basal diet.

Each group had three rabbits, considering the ethical use of animals while yielding enough data to observe physiological changes. The animals were 3 months old at the start of the experiment—an age at which they were approaching sexual maturity and their reproductive hormones could be monitored with ease. Their weights ranged between 1.0-1.5 kg, and effort was made to ensure both groups had as close average weights as possible to rule out confounding factors.

The supplementation lasted for 30 days, wherein the treated group was orally administered with Omega-3 fatty acids extracted from fish oil every day. This length of time was determined based on previous literature, suggesting that a minimum period of 3-4 weeks can be adopted in order to get measurable changes in circulating reproductive hormones. The control group was normally fed to compare it with supplemented animals.

#### Housing conditions:

All rabbits were acclimatized to the standardized environmental conditions within the animal research facility. Individual rabbits were separately housed in stainless-steel cages, the dimensions of which were 65 cm × 45 cm × 45 cm. Stainless steel cages were used for their durability, easy sanitizing, and rust-resistant properties. The cage cleaning was carried out on a daily basis, and the bedding was changed every week. The environmental parameters were carefully controlled. The room temperature was maintained between 18-22°C, which is optimal for rabbits, preventing heat stress. Ventilation was sufficient to achieve at least 12 air changes per hour to decrease ammonia accumulation from urine and maintain air quality. Natural lighting maintained the circadian rhythms, which are closely related to hormonal regulation.

#### Feeding and Water Management:

All rabbits were given a nutritionally balanced commercial pellet diet, plus fresh, clean water ad libitum. Feeders and water bottles were washed daily to prevent bacterial contamination. Diets were kept the same for both groups to ensure that Omega-3 fatty acids were the only variable influencing hormonal changes.

Omega-3 fatty acids were administered orally using a syringe without a needle to the treated group. Dosages were estimated according to body weight in order to keep supplementation uniform. The time of day when the supplement was given was controlled to be the same each day.

#### Animal Care:

##### Daily monitoring:

The rabbits were examined daily for any alteration in activity, appetite, posture, coat condition, and behavior in general. Any signs of illness, stress, or discomfort were noted immediately. Body weight was

measured once a week since weight changes can indicate metabolic stress or diet-related effects.

**Veterinary care and management:**

The study was overseen by a qualified veterinarian who performed weekly physical examinations. The animals were handled humanely in feeding, cage cleaning, and collection of blood to minimize the level of stress; stress changes the levels of reproductive hormones. There was also enrichment of the environment, like cardboard rolls and chew toys, to reduce boredom and stress-related behaviors.

**Blood Sampling and Analysis:**

At the end of the experiment, blood samples were taken to determine serum hormone levels. About 3 mL of blood was sampled from the marginal ear vein by using sterile syringes. The site was always disinfected before sampling to avoid contamination. The collected blood was transferred into plain gel tubes and allowed to clot at room temperature. Consequently, the samples were centrifuged at 3000 rpm for 10 minutes to separate the serum. Serum was transferred to labeled Eppendorf tubes and stored at -20°C until hormonal analysis.

**Hormone Determination:**

The levels of estradiol, progesterone, FSH, and LH were determined by the use of respective ELISA kits



for rabbits. This analysis option was selected due to its high level of sensitivity, specificity, and reproducibility. All assays were performed according to the manufacturer's protocols, thus ensuring standardized and reliable results.

**Statistical Analysis:**

The statistical software was used for data analysis obtained from hormonal assays. The mean level of hormones in the treated group was compared with that of controls. Results were expressed as Mean ± SD and p < 0.05 were considered to be statistically significant.

**RESULTS**

The results of the ELISA test for follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and progesterone indicate that Ω3 FAs have an important role in ovarian activity and hormonal status in female rabbits. The analysis of hormonal parameters showed changes due to treatment between the groups, indicating the beneficial effect of Ω3 FAs supplementation on the reproductive hormonal parameters. These were the results obtained from ELISA test using kit AccuBind® FSH ELISA.

**Follicle-Stimulating Hormone (FSH) Concentration:**

**Table 1:** Showing FSH level in individual rabbits from the control and omega-3- treated groups after 30 days of supplementation

Group	Sample	FSH Level (mIU/mL)
Control	1	9.80
	2	9.20
	3	8.48
Treated Group	1	11.00
	2	11.48
	3	11.96

**Estradiol Concentration:**

**Table 2:** Showing estradiol level in individual rabbits from the control and omega-3- treated groups

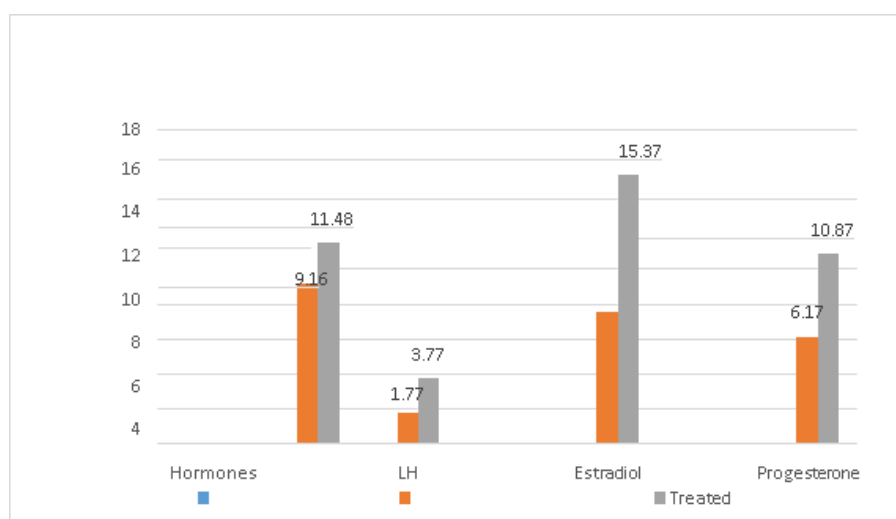
after 30 days of supplementation

Group	Sample	Estradiol (pg/mL)
Control	1	8.8
	2	7.0
	3	6.8
Treated Group	1	15.5
	2	17.2
	3	13.4

**Progesterone Changes in Response to Omega-3 Supplementation**

**Table 3:** Showing Progesterone level in individual rabbits from the control and omega-3- treated groups after 30 days of supplementation

Group	Sample	Progesterone (pg/mL)
Control	1	5.52
	2	6.17
	3	6.82
Treated Group	1	10.42
	2	10.87
	3	11.32



**Figure 1:** Presenting the average hormone levels with standard deviations. The treated group showed marked increases in estradiol and FSH levels, suggesting enhanced ovarian activity following omega-3 supplementation

Higher levels of FSH were noted within the treated group with Mean±SD (11.48 ± 0.48) compared to the control (9.16 ± 0.52,  $p < 0.05$ ), suggesting that omega-3 might stimulate the hypothalamic-pituitary-ovarian axis. Its anti-inflammatory effect may be in support of follicle growth, follicular development, ovarian function, and receptivity for reproduction. The FSH increase may assist with follicular maturation and thus hasten the beginning of puberty, preparing the rabbit for reproductive activity. This is an essential part of a healthy reproductive cycle. Even without mating, the body is preparing itself for potential ovulation, demonstrating that the reproductive system is functioning effectively.

LH is responsible for triggering ovulation, and the very little raised levels of this hormone could help in establishing regular ovulatory cycles where reproductive maturity becomes evident during puberty. Higher levels of LH may help, through omega-3 fatty acids, in causing timely ovulation, thus aiding in establishing regular reproductive cycles during puberty. If follicles are developing well, it suggests hormonal efficiency has improved due to omega-3's effects.

The treated group showed significantly higher estradiol levels (7.53 ± 1.10) than the control group (15.37 ± 1.90,  $p < 0.05$ ). Estradiol, a key estrogen in regulating the female reproductive system and folliculogenesis, is secreted by growing follicles in response to FSH. was likely elevated due to omega-3

enhancing steroidogenic enzyme activity. This increase may improve uterine receptivity and reproductive potential. Additionally, estrogen plays a regulatory role through feedback mechanisms on the hypothalamus and pituitary gland, ensuring that hormone secretion remains balanced. This feedback loop is crucial for maintaining regular hormonal rhythms and reproductive readiness. Together, the increased levels of FSH and estrogen signify a more stable and responsive hypothalamic-pituitary-ovarian (HPO) axis.

The progesterone level was significantly higher in the treated group (10.87 ± 0.45) than in the control (6.17 ± 0.65,  $p < 0.05$ ). Progesterone, mainly produced post-ovulation by the corpus luteum, was elevated despite the rabbits just reaching maturity. This suggests omega-3 fatty acids may have accelerated ovulation by upregulating steroidogenic pathways. Enhanced LH sensitivity could have led to early formation of functional corpora lutea. Alternatively, omega-3s may have induced partial luteinization of maturing follicles. These mechanisms could explain increased progesterone even without full ovulation. Overall, omega-3 supplementation supports both follicular and luteal development during sexual maturation.

## Effects on Haematological Parameters of Both Groups:

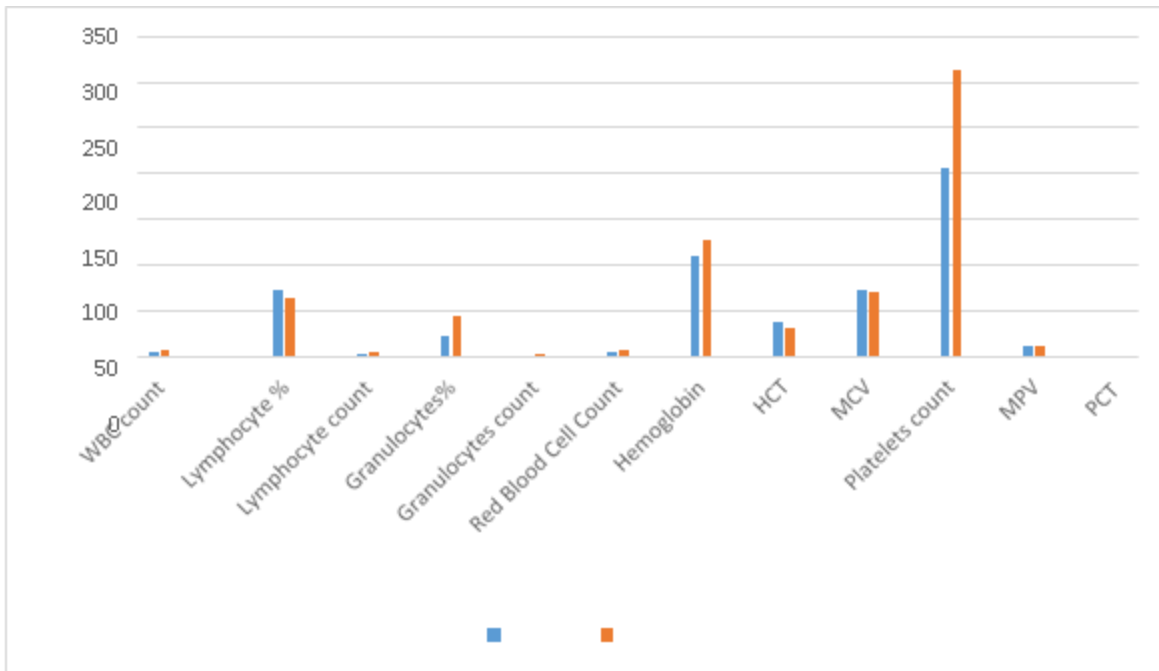


Figure 2: Presenting the average Haematological parameters with standard deviations. The treated group showed marked effect on haematological parameters

Supplementation with omega-3 fatty acids significantly ameliorated the haematological parameters amongst rabbits in the study. The treated group exhibited increased WBC counts compared with the untreated group, featuring granulocytes and lymphocytes, implying an enhanced immune response ( $p < 0.01$ ). Significant increases were noted in the RBC count, hemoglobin concentration implying better oxygen-carrying capacity. Platelet count and plateletcrit increased without any effect on the mean platelet volume, indicating balanced thrombopoiesis. These changes indicate that omega-3 might be beneficial in augmenting immunity and decreasing inflammation and vasculoprotective metabolic health. It warrants further studies for its effects with time in other species also.

**DISCUSSION:**

Omega-3 supplementation has been seen to have positive impacts on reproductive hormones in many studies. Studies in rabbits, rats, and other animal models showed an increased level of estradiol, progesterone, FSH, LH, and enhanced ovarian functions after Omega-3 supplementation. Studies by Ermayanti et al. (2019), Yan et al. (2013), Habeeb et al. (2021), and Abu-Heakal et al. (2016) confirm these

views. Komal et al. (2020), however, illustrated reduced LH in PCOS models, but most studies coincide with our findings of increased follicular development and hormonal regulation. Conclusion: Omega-3 enhances reproductive health by its anti-inflammatory and hormonal-modulating effects.

**CONCLUSION:**

This was a study to assess the influence of omega-3 fatty acid supplementation on ovarian functioning and hormonal balance in female rabbits. This study provides pertinent information on the possible role of omega-3 in the modulation of reproductive health. Much, very much, was made apparent in the histological observations concerning morphogenetic changes in the ovarian tissue especially in follicular development. Then, on hormonal analysis, the profile of changes in estradiol, progesterone, FSH, and LH is suggestive of the possible action of omega-3 in influencing endocrine regulation. That is how omega-3 fatty acids can empower the effects of dietary intervention on normal ovarian function and hormonal homeostasis. Changes in follicle development, coupled with appropriately altered hormone levels, could thus infer an area for the application of beneficial effects in reproductive health

management. In addition, further study is warranted on the long-term effects, optimum dosage, and mechanisms of action of omega-3 in different species. Future works can study the therapeutic potential of omega-3 regarding reproductive disorders. In conclusion, this study adds to the developing range of evidence about the advantages of omega-3 fatty acids on female reproductive physiology. The findings hold implications for both veterinary and human reproductive health, prompting further search for omega-3 as a nutritional strategy to promote fertility and hormonal balance.

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