ANSF APPLIED AND NATURAL SCIENCE FOUNDATION

Journal of Applied and Natural Science
16(1), 51 - 57 (2024)
ISSN : 0974-9411 (Print), 2231-5209 (Online)
journals.ansfoundation.org

Research Article

Effectiveness of the *Mentha spicata* leaves in reducing testosterone levels and aggressive behaviour in female Wistar albino rats treated with testosterone propionate

Zahraa A. Taha*
Department of Biology, College of Science, University of Babylon, Iraq
Halla Abdul-Hadi Chabuk
Department of Biology, College of Science, University of Babylon, Iraq
Alaa Jawad Hassan
Department of Biology, College of Science, University of Babylon, Iraq

*Corresponding author: Email zoza71047@gmail.com

Article Info
https://doi.org/10.31018/jans.v16i1.5279
Received: November 11, 2023
Revised: January 9, 2024
Accepted: January 20, 2024

How to Cite

Taha, Z.A. *et al.* (2024). Effectiveness of the *Mentha spicata* leaves in reducing testosterone levels and aggressive behaviour in female Wistar albino rats treated with testosterone propionate. *Journal of Applied and Natural Science*, 16(1), 51 - 57. https://doi.org/10.31018/jans.v16i1.5279

Abstract

High testosterone hormone levels play an important role in exhibiting aggressive behaviour and several disorders in female rodents and women. The present study aimed to determine the protective role of the alcoholic extract of *Mentha spicata* leaves (MSL) in the reduction of the level of testosterone and aggressive behaviour of female rats that suffer from high levels of testosterone. A total of 30 female Wistar albino rats were divided into 6 Groups. Group 1: Control rats received sesame oil(0.5 ml). Group 2: Rats injected with testosterone propionate (TP) alone. Group 3: Rats received MSL alone (100 mg/kg) orally. Groups 4, 5, and 6: Rats received TP + MSL, 6mg/rat of TP followed by 200, 400, and 600 mg/rat, respectively) for 60 days. The testosterone, dopamine, and aggressive behaviour were measured using specialized ELISA test kits. The results showed that testosterone and dopamine levels in the serum had a significant decrease (P<0.05) (4.82 (ng/ml) in testosterone and 272.83 (pg/ml) in dopamine) in animals treated with MSL only compared to Group 2, which found a significant rise (p<0.05) (16.52 (ng/ml) in testosterone and 607.59 (pg/ml) in dopamine) in the levels of testosterone and dopamine. The results exhibited a significant rise (P<0.05) in the aggressive behaviour in Group 2 of rats compared to the control and other Groups. In comparison, aggressive behaviour was significantly decreased (P<0.05) (7.40 (ng/ml) in testosterone and 263.49 (ng/ml) in dopamine) in Groups 2, 4, 5, and 6. Thus, the study revealed the protective role of the alcoholic extract of MSL in reducing levels of testosterone and aggressive behaviour in female rats suffering from higher levels of testosterone.

Keywords: Aggressive behaviour, Dopamine, Female rats, *Mentha spicata*, Testosterone

INTRODUCTION

Testosterone is a sex hormone created by males and females. In males, it is created and released from the leyding cells in the testes, while in females produced by the placenta and ovaries. In both sexes, testosterone is secreted by the adrenal cortex about 25% (Banihani, 2019). The testosterone levels differ significantly in both sexes, with males having higher testosterone levels than females. However, the typical serum testosterone levels in females are generally 10 to 20 times lower. Testosterone has physiological impacts on reproductive tissues in women (Parish *et al*., 2021). A woman of reproductive age produces three to four times as much testosterone as estrogen every day from her ovaries (Yang *et al*., 2010). But these androgen levels decrease with age, about in the mid-30s onward, with no clear significant rise in the speed of decrease at menopause due to the ova continuing to produce hormones (Donovitz, 2021). Testosterone is present in blood either unbound (free) or bound with albumin proteins. Moreover, inactive testosterone hormones are bound to globulin sex hormones-binding globulin (SHBG), carrier proteins created in the liver that have a high affinity to the testosterone hormones. Free testosterone hormone is the active portion of the androgens Group and hence free testosterone could connect more to the risk of detection aggressiveness (Regis *et al*.,

2015).
High levels of testosterone have an impact on the brain areas and may be the cause of some behavioural disorders in both sexes. Numerous studies have been conducted on testosterone's effects, particularly in models of anxiety and aggression (Domonkos *et al*., 2018). The neurophysiological mechanism of aggression is the same in all vertebrates, and aggression is a social activity that occurs naturally in mammals to protect their area, preserve resources, and increase the likelihood of fertile mating. However, when levels of aggression become excessive, harmful, disturb social order, and have a cost that is significantly greater than its benefit, the behaviour is no longer adaptive and is referred to as maladaptive or pathologic aggressiveness (Ishola, 2020).

Aggressive behaviour is a complex social behaviour and is commonly involved with intellectual disability and psychiatric disorders; it has received huge research attention for more than five decades. Two types of aggression have been identified, the first sub-type with automatic control and the interactive-impulsive subtype. The second is considered impulsive, usually associated with anger, while the first is more objective and directed towards the goal. Neurotransmitters refer to particles in the nervous system that function as signaling particles on specific receptors for each neurotransmitter such as dopamine. These molecules are major cofactors in a wide variety of molecules (Trifu *et al*., 2020). Aluja *et al*. (2015) studies in healthy men and women confirm the hypothesis that high testosterone levels impact risk-taking or impulsive behaviour. In a later study, it was exhibited that early-onset users under testosterone rage are more impulsive and show deficits in behavioural disinhibiting, affective processing, and planning.

Spearmint leaves are medical plants that are widely used as anti-bronchitis, antispasmodic, stomach pain-relieving agents, and carminative. The major compounds isolated from mint leaves include terpenoids, flavonoids, and phenols, and rosmarinic acid in essential oils of spearmint was found to have hypoglycemic, antimicrobial, hypocholesterolemic, insecticidal, and antioxidant properties (Bayani *et al*., 2017). A study shows that menthol in mint lowers testosterone levels in men, which ultimately leads to a decrease in libido. In addition, mint may reduce sperm production if consumed in excess, which causes impotence. So, spearmint may be advantageous in reducing free testosterone levels and hirsutism in women with PCOS, and its adverse histopathological impacts on the liver, kidney, and uterine tissues in animals were noticed (Alaee *et al*., 2020). *Mentha spicata* has a lethal effect on the testis by causing a significant in experimental rats. Past reports showed structural changes in testicular tissue, morphological distortions and spermatogenesis inhibition of different mammals treated with spearmint (Mohammed *et al*., 2021). Another study displays that female students who received *M. spicata* in capsule shape show dysmenorrhea with lesser acuteness compared to placebo. The ethanolic extracts of *M. spicata* possess antidepressant-like features in the rat. These responses might be recognized as interactions with the serotonergic, noradrenergic, and dopaminergic receptors. Furthermore, the enhancing impact of the *M. spicata* extract with conventional antidepressants looks promising and its potential as a complementary agent for depression management (Abbasi-Maleki *et al*., 2017). In the present study, a female rat model with elevated testosterone levels was used to examine the significance of utilizing a mixture of spearmint alcoholic extracts and its impact on reduced testosterone levels and aggressive behaviour in female Wistar albino rats.

MATERIALS AND METHODS

Ethical approval

The University of Babylon, the College of Sciences, and the Department of Biology approved the experimental protocol. (1522/3-6-2022), and the National Committee for Research Ethics in Science and Technology (NETNT) reports that the studies were conducted as per approved procedures and ethical standards.

Preparation extract of *Mentha spicata* leaves (MSL)

The alcoholic extract of *M. spicata* leaves was prepared by washing them well and then drying them at room temperature. The leaves were ground until they became a powder, dissolved in 70% ethanol, and put in the shaker for an hour, then filtered with gauze. At a temperature of 45°C, put it in the oven until it hardens and the pieces are ground (González-Montelongo, *et al*., 2010).

Testosterone propionate (TP) preparation

Testosterone was purchased from China (FedEx) and was prepared by taking 6 mg/rat of testosterone propionate powder and dissolving it in 0.5 ml of sesame oil.

Study design

In this study, 30 female Wistar albino rats were divided into six Groups, 5 rats in each.

Group 1: Negative control- Animals received sesame oil (0.5 ml) orally.

Group 2: Positive control- Animals were injected subcutaneously with TP (6 mg/rat).

Group 3: Animals were orally treated with an alcoholic extract of MSL (100 mg/rat).

Group 4: Animals were injected subcutaneously with TP (6mg/rat)+ MSL (200 mg/rat) orally.

Group 5: Animals were also injected subcutaneously with TP (6mg/rat)+MSL (400 mg/rat) orally.

Group 6: Animals were injected subcutaneously with TP(6mg/rat) + MSL (600 mg/rat) orally.
All Groups were treated for 60 days.

Physiological assay
Serum testosterone and dopamine were measured according to the manual procedure of Elabscience, a company based in the USA that offered specialized ELISA test kit sets.

Aggressive behaviour (Resident-intruder test)
The Resident-intruder test model was used to understand aggressive behaviour in which one rat (intruder) was permitted to build a territory (resident) in its home cage, another rat was in the resident's home cage and two animals were permitted to interact with each other for a fixed period. The duration and frequency of resident rats were determined by the following behavioural parameters: Attack latency: (the time between the introduction of the intruders and the first clinch attacks) (Rammal *et al*., 2010). Before this test, drops of 40% zinc sulfate were put in the nose of the intruder male prior to encounters to disrupt the sense of smell.

Statistical analysis
Data for parameters represent a mean ± SE and data of all behaviour tests represent a mean ± SD. A one-way analysis of variance (ANOVA) and the Duncan test for Post Hoc multiple comparisons were used to analyze the variation between the values statistically. SPSS statistical software version (23). A value of p<0.05 was considered statistically significant for all tests. Analysis of the correlation between parameters of Groups was done by Pearson test.

RESULTS AND DISCUSSION

Physiological study
Effect extract of *Mentha Spicata* leaves on the testosterone and dopamine levels
Table 1 illustrates data on the testosterone and dopamine levels in the serum of female rats treated with alcoholic extract of mint leaves. Rats treated with TP showed a significant rise (p<0.05) in the levels of testosterone hormone and dopamine compared to the Control Group and the other Groups, whereas the animals in the 4, 5 and 6 Groups treated with TP (6mg/rat) + MSL (200, 400 and 600 mg/kg) respectively exhibited a significant decline (P<0.**0** (5in the levels of testosterone and dopamine as compared to the Group 2. While no significant differences appeared in the levels of these hormones (p>0.05) between Groups 1 and 5, 6 of the rats were treated with TP + AML. It may be because mint leaves contain terpenoid compounds, namely carvone and menthol, which cause low testosterone levels and triglyceride (Ashkar *et al*., 2020). Spearmint leaves have strong inhibitory impacts, which stimulate cytochromes P450 3A4 (CYP3A4) that cause an alteration in the levels of androgen and steroid hormones and decrease free testosterone concentrations due to increased Sex hormone-binding globulin (SHBG). Spearmint tea can raise estradiol, FSH, and LH levels due to physiological alters in the menstrual cycle. It can can replace antiandrogenic treatment for women's hirsutism (Ashkar *et al.*, 2020). This result is consistent with Alaee *et al*. (2020), who noted anti-androgenic effects of mint are advantageous in reducing free testosterone levels and hirsutism in women with polycystic ovarian syndromes (PCOS) and reinforcing the antioxidant defense systems. Mohammed *et al*. (2021), in a study, showed that menthol in mint lowers testosterone levels in men, ultimately decreasing libido. In addition, mint may reduce sperm production if consumed in excess, which causes impotence. The pheromones, as well as the *Spicata* odor, stimulated neuronal Fos proteins' immunoreactivity in the medial amygdaloid nucleus and limbic hypothalamus segments of the olfactory pathways and thus affected the pituitary gland and reproductive system, resulting in hypothalamic-pituitary-testicular axis insufficiency (Nozhat *et al*., 2014).

Correlation between physiological parameters and extract of mint leaves
Correlation between the testosterone and dopamine levels in the female rats that were treated with TP showed that there was a significant positive linear relationship between the levels of testosterone and dopamine hormones; the equation was linear between them y= 34.82× - 39.217 and the correlation coefficient r = 0.810, as noted in Fig. 1.

Table 1. Effect of alcoholic extract of *Mentha Spicata* leaves on the testosterone and dopamine levels in the serum of female rats treated with testosterone propionate for 60 days. (n =5).

Parameters Groups	Testosterone (ng/ml) Mean±S.E	Dopamine (pg/ml) Mean±S.E
Group 1	4.74± 0.58	125.73±13.70
Group 2	16.52±1.20^{a}	607.59±62.88^{a}
Group 3	4.82± 0.42^{b}	272.83±24.28^{ab}
Group 4	7.40±0.65^{ab}	263.49±20.49^{ab}
Group 5	6.02±1.40^{b}	135.43±13.92^{bcd}
Group 6	6.81±1.161^{b}	131.334±2.786^{bcd}

a:Mean significantly different at the P≤0.05 as compared to Group 1 (controls);
b:Mean significantly different at the P≤0.05 as compared to Group 2;
c:Mean significantly different at the P≤0.05 as compared to Group3 ;
d:Mean significantly different at the P≤0.05 as compared to Group4;

The study exhibited a significant negative linear correlation between the levels of testosterone and dopamine in the female rats and the concentration of the alcoholic extract of mint leaves (*Mentha Spicata*) (200,400 and 600 mg/rat). The correlation coefficient for testosterone was r = -0.720. For dopamine, it was r = -0.847, as shown in Fig. 2. There are positive correlation between testosterone and dopamine and testosterone injections cause a high dopamine response in rats. Based on these results, it is suggested that mint leaves led to lower testosterone levels, which led to lower dopamine levels. Research on the effects of testosterone hormones on midbrain dopamine circuitry in adult male rats varies. Some studies in rats suggest that neuron release of dopamine is inhibited by testosterone (Aubele and Kritzer, 2011). Other studies suggested the opposite, where testosterone can raise dopamine levels and dopamine turnover in animals (Owens *et al*., 2018).

Aggressive behaviour study

Effect of alcoholic extract of *Mentha spicata* on the aggressive behaviour of the rats

The effect of the alcoholic extract of *M. spicata* on the aggressive behaviour of the female rats is shown in Table 2. Injection of TP into rats in Group 2 led to a significant decrease (P<0.05) in aggressive behaviour

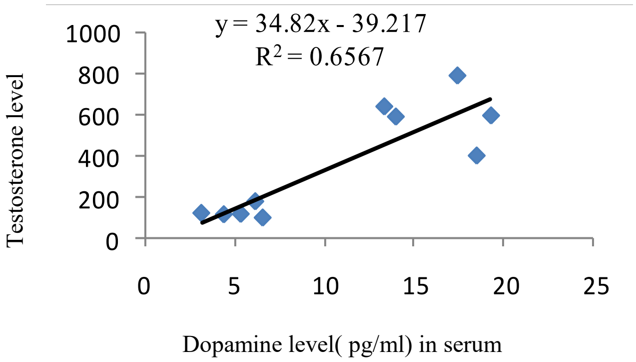

Fig. 1. *Correlation between testosterone and dopamine levels* .

parameters of all mean of latency to the first threat and thrust (second) and latency to the first attack (sec.), while the rats in Groups 3 4, 5 and 6 were treated with MSL (100, 200, 400, 600 mg/kg) showed a significant increase (p<0.05) in these parameters compared to Groups 1 and 2.

The result showed a significant increase (P<0.05) in all means the number of threats and thrusts, and the number of attacks and keep down in the Group 2 treated with TP compared to Group 1 as well as the rats in the Group 3 treated with MSL (100 mg/kg) that showed a significant decrease (P<0.05) in these parameters. The number of threats and thrusts in Group 6 significantly decreased in Group 1. No significant (*p*>0.05) difference was seen between control Group 1 and Groups 3, 4 and 5.

Aggressive behaviour is usually measured by the sum of the number of threats, thrusts, attacks and keep down. The pie chart demonstrates the effect of alcoholic extract of mint leaves (*Mentha Spicata*) on the female rats' decreased aggressive behaviour, as shown in Fig. 3. Injection of testosterone propionate (6 mg/kg) into rats in Group 2 for 60 days led to a significant rise (P<0.05) in aggressive behaviour. *Mentha* has an antifertility effect; therefore, it inhibits the levels of testosterone and will inhibit sexual and aggressive behaviour in men. Testosterone triggers dopamine liberat in the medial preoptic areas of the hypothalamus, which is the area controlling aggressive and sexual behaviour. Testosterone profoundly affects the brain circuits involved in threat and aggression, and this study agrees with (Geniole *et al*., 2020 and Njoroge *et al*., 2015) that a single dose of testosterone increased aggressive behaviour in female rats. This study agrees with Estumano *et al*. (2019), who showed that one injection of the hormone testosterone was sufficient to raise functional connectivity between and within the hemispheres, modify physiology, addiction and behaviour, and encourage hostility and aggression. The study showed that short-term oral testosterone administration to women shows a range of alterations, including traits

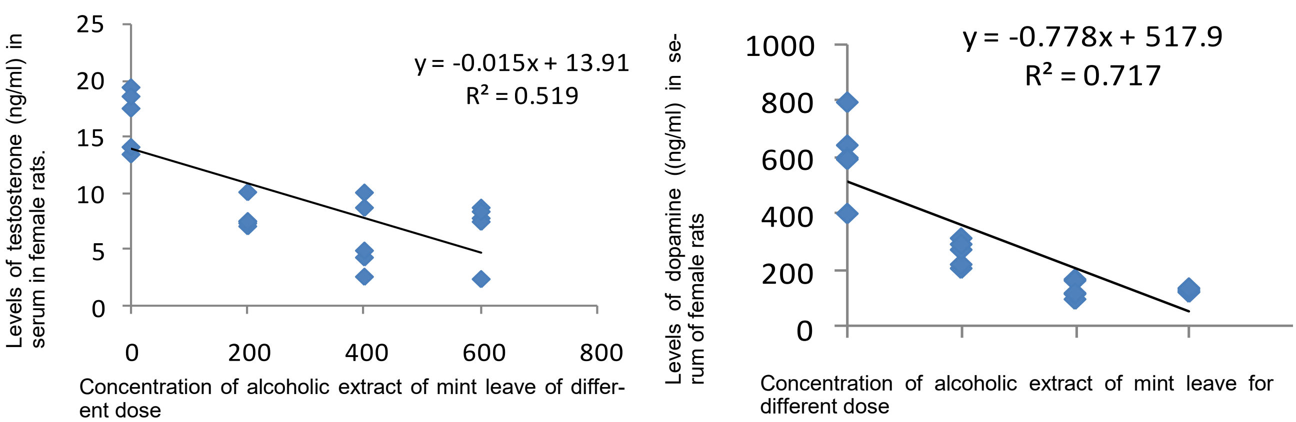

Fig. 2. *Correlation between testosterone, dopamine levels and alcoholic extract of mint leaves.*

Table 2. Effect of alcoholic extract of mint leaves (*Mentha spicata*) on the aggressive behaviour of the rats treated with testosterone propionate for 60 days (n =5)

Parameters/ Groups	Latency to the first threat and thrust (sec.)	Number of threat and thrust	Latency to the first attack (sec.)	Number of attack	Number of keep down
Group I	120.82±13.12 15.48±3.68a 306.18±16.69a 213.06±21.83a 238.21±14.76a 278.16±27.20a 15.48±3.68a 306.18±16.69a 213.06±21.83a 238.21±14.76a 278.16±27.20a	11.00±1.87	176.07±8.99	3.40±1.14	2.40±1.14
Group 2	15.48±3.68^{a}	45.00±7.97^{a}	31.69±5.59^{a}	17.60±2.07^{a}	22.40±3.65^{a}
Group 3	306.18±16.69^{ab}	8.40±1.52^{b}	359.79±60.45^{ab}	5.60±1.14^{bd}	1.20±0.45^{b}
Group 4	213.06±21.83^{ab}	14.00±3.39^{bc}	256.01±5.63^{abc}	9.40±1.82^{abc}	12.40±3.05^{abc}
Group 5	238.21±14.76^{ab}	7.00±1.87^{bd}	285.11±7.07^{abc}	8.00±1.58^{abc}	8.20±1.48^{abcd}
Group 6	278.16±27.20^{ab}	4.20±1.64^{abd}	350.98±11.97^{abd}	6.60±2.61^{abd}	4.40±1.14^{bcde}

a: Mean significantly different at the P≤0.05 as compared to Group 1 (control); b: Mean significantly different at the P≤0.05 as compared to Group 2; c: Mean significantly different at the P≤0.05 as compared to Group 3; d: Mean significantly different at the P≤0.05 as compared to Group 4e: Mean significantly different at the P≤0.05 as compared to Group 5;

associated with aggressive behaviour in female rats (Carré and Archer, 2018). The experiment on female rats' results support the effectiveness of the alcoholic extract of mint leaves in lowering the aggressive behaviour in female rats that suffer from a high testosterone level compared to the Control Groups and when comparing the Groups with each other. This is because of its soothing mint scent. This study agrees with Abbasi-Maleki et al. (2017) and Moss et al. (2023) that spearmint's ambient aroma may effectively decrease aggressive behaviour. It was hypothesized that spearmint aroma would decrease aggressive behaviour and negative feelings such as stress and aggression while raising calmness and alertness. Since the alcoholic extract of mint leaves reduced testosterone, we conclude from our study in this research that the alcoholic extract of mint leaves also reduced aggressive behaviour. Pheromone information processed by the accessory olfactory bulbs is necessary for appropriate social behaviour in rats, including sexual and aggressive behaviour. Disrupting the activation of either the olfactory or the vomeronasal organs causes males to evade aggressive behaviour and severely affects male sexual behaviour in many rodents (Quadros et al., 2020). Therefore, experiment animals treated with zinc sulfate (%4 Zinc sulfate) by putting one drop in the nose of the intruder rat for the destruction of the nasal epithelium to eliminate participant behaviour both in the experienced and inexperienced males (Angoa-Pérez and Kuhn, 2021).

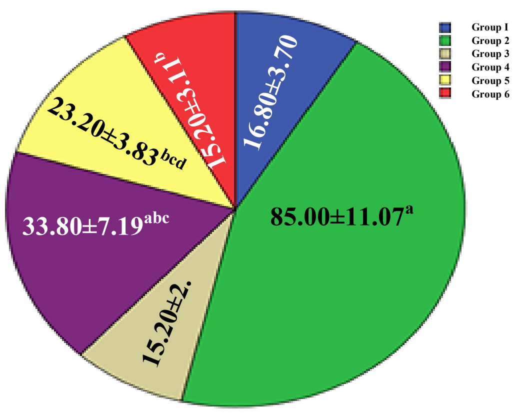

Fig. 3. *Aggressive behaviour in female rats treated with testosterone propionate*

Clinical signs

Animals in all Groups were carefully examined daily before and after the experimental period for likely clinical signs due to testosterone injections, and these signs are:

Hair loss and appearance of pimples in TP-injected animals compared to the Control Group and animals treated with TP+ ALMP are shown in Fig. 4 A and C.

Slight hair loss in the Group of animals that were given TP+ ALMP is shown in Fig. (4 B).

Female hair loss may be due to many factors like genetics and age but is most commonly due to hormonal alters and imbalances, some of the hormones associated with hair loss, such as the cortisol and thyroid hormones. Stressful cases and anxiety can cause an increase in cortisol levels, which can then influence hair growth. Females produce testosterone in small amounts. An imbalance of testosterone can cause females to lose hair on their scalp or grow rough body

Fig. 4. *Clinical signs noted in rats Groups:* ***A-*** *hair loss of rat in TP Group,* ***B-*** *Slight loss of hair rats in TP+ALMP Groups,* ***C****- appearance of blood pimples*

hair on the chest or face (Iamsumang *et al*., 2020).

Conclusion

The present study indicated the protective role of the alcoholic extracts of mint (*M. spicata)* leaves in reducing testosterone levels in the serum of Wistar female rats treated with testosterone propionate. The extract of mint leaves also improved aggressive behaviour in female rats suffering from high testosterone.

ACKNOWLEDGEMENTS

I am pleased to thank everyone who provided me with the necessary facilities and support to complete this study.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Abbasi-Maleki, S., Bakhtiarian, A. & Nikoui, V. (2017). Involvement of the monoaminergic system in the antidepressant-like effect of the crude extract of Mentha piperita (Lamiaceae) in the forced swimming test in mice. *Synergy*, *5*, 21-28. https://doi.org/10.1016/j.synres.2017.08.002
2. Alaee, S., Bagheri, M. J., Ataabadi, M. S. & Koohpeyma, F. (2020). Capacity of Mentha spicata (spearmint) Extract in Alleviating Hormonal and Folliculogenesis Disturbances in Polycystic Ovarian Syndrome Rat Model. *World*, *10*(3), 451-456. https://dx.doi.org/10.36380/scil.2020.wvj56
3. Aluja, A., García, L. F., Martí-Guiu, M., Blanco, E., García, O. Fibla, J. & Blanch, À. (2015). Interactions among impulsiveness, testosterone, sex hormone binding globulin and androgen receptor gene CAG repeat length. *Physiology & Behaviour*, 147, 91-96. https://doi.org/10.1016/j.physbeh.2015.04.022
4. Angoa-Pérez, M., & Kuhn, D. M. (2021). Evidence for modulation of substance use disorders by the gut microbiome: hidden in plain sight. *Pharmacological reviews*, *73*(2), 571-596. https://doi.org/10.1124/pharmrev.120.000 144
5. Ashkar, F., Rezaei, S., Salahshoornezhad, S., Vahid, F., Gholamalizadeh, M., Dahka, S. M., & Doaei, S. (2020). The Role of medicinal herbs in treatment of insulin resistance in patients with Polycystic Ovary Syndrome: A literature review. *Biomolecular concepts*, *11*(1), 57-75. https://doi.org/10.1515/bmc-2020-0005
6. Aubele, T., & Kritzer, M. F. (2011). Gonadectomy and hormone replacement affects in vivo basal extracellular dopamine levels in the prefrontal cortex but not motor cortex of adult male rats. *Cerebral Cortex*, *21*(1), 222-232. https://doi.org/10.1093/cercor/bhq083
7. Banihani, S. A. (2019). Mechanisms of honey on testosterone levels. *Heliyon*, *5*(7). https://doi.org/10.1016/j.heliyon.2019.e02029Bayani, M., Ahmadi-Hamedani, M., & Javan, A. J. (2017). Study of hypoglycemic, hypocholesterolemic and antioxidant activities of Iranian Mentha spicata leaves aqueous extract in diabetic rats. *Iranian J: IJPR,* 16(Suppl), 75.
8. Carré, J. M. & J. Archer (2018). Testosterone and human behaviour: the role of individual and contextual variables. *Current Opinion in Psychology* 19, 149-153. https://doi.org/10.1016/j.copsyc.2017.03.021
9. Domonkos, E., Hodosy, J., Ostatníková, D. & Celec, P. (2018). On the role of testosterone in anxiety-like behaviour across life in experimental rodents. *Frontiers in endocrinology*, 9, 441. https://doi.org/ 10.3389/fendo.2018.00441
10. Donovitz, G. S. (2021). Testosterone supplementation and the gender divide. *Neurourology and Urodynamics*, *40*(3), 938-940. https://doi.org/10.1002/nau.24622
11. Estumano, D. P., Ferreira, L. O., Bezerra, P. A. L., Da Silva, M. C. P., Jardim, G. C., Santos, G. F. S., ... & Hamoy, M. (2019). Alteration of testosterone levels changes brain wave activity patterns and induces aggressive behaviour in rats. *Frontiers in Endocrinology*, *10*, 654. https://doi.org/10.3389/fendo.2019.00654
12. Geniole, S. N., Bird, B. M., McVittie, J. S., Purcell, R. B., Archer, J. & Carré, J. M. (2020). Is testosterone linked to human aggression? A meta-analytic examination of the relationship between baseline, dynamic, and manipulated testosterone on human aggression. *Hormones and Behaviour*, *123*, 104644. https://doi.org/10.1016/j.yhbeh.2019.104644
13. González-Montelongo, R., Lobo, M. G. & González, M. (2010). Antioxidant activity in banana peel extracts: Testing extraction conditions and related bioactive com-

pounds. *Food Chemistry*, *119*(3), 1030-1039. https://doi.org/10.1016/j.foodchem.2009.08.012

14. Ishola, A. (2020). Exposure to aflatoxin and aggressive behaviour among wistar albino rats. *The Journal of Neurobehavioural Sciences*, *7*(2), 72-72.
15. Iamsumang, W., Leerunyakul, K. & Suchonwanit, P. (2020). Finasteride and its potential for the treatment of female pattern hair loss: evidence to date. *Drug Design, Development and Therapy*, 951-959. https://doi.org/10.2147/DDDT.S240615
16. Mohammed, H. E., Elrayess, R. A. & El-Hak, H. N. G. (2021). Combined effect of aqueous extracts of Artemisia monosperma and Mentha piperita on the reproductive integrity of male albino rats. *Pakistan J. Zool*, 53(4), 1329-1339. **:** https://dx.doi.org/10.17582/journal.pjz/ 20191029 001013
17. Moss, M., Ho, J., Swinburne, S., & Turner, A. (2023). Aroma of the essential oil of peppermint reduces aggressive driving behaviour in healthy adults. *Human Psychopharmacology: Clinical and Experimental*, *38*(2), e2865. https://doi.org/10.1002/hup.2865
18. Njoroge, R. W., Macharia, B. N., Sawe, D. J. & Maiyoh, G. K. (2015). Effects of crude kerosene on testosterone levels, aggression and toxicity in rat. *Toxicology Reports*, *2*, 175-183.https://doi.org/10.1016/j.toxrep.2014.11.017
19. Nozhat, F., Alaee, S., Behzadi, K. & Chegini, N. A. (2014). Evaluation of possible toxic effects of spearmint (Mentha spicata) on the reproductive system, fertility and number of offspring in adult male rats. *Avicenna J. of Phytomedicine*, *4*(6), 420.
20. Owens, S. J., Murphy, C. E., Purves□Tyson, T. D., Weickert, T. W., & Shannon Weickert, C. (2018). Considering the role of adolescent sex steroids in schizophrenia. *Journal of Neuroendocrinology*, *30*(2), e12538. https://doi.org/10.1111/jne.12538
21. Parish, S. J., Simon, J. A., Davis, S. R., Giraldi, A., Goldstein, I., Goldstein, S. W. & Vignozzi, L. (2021). International Society for the Study of Women's Sexual Health Clinical Practice Guideline for the use of systemic testosterone for hypoactive sexual desire disorder in women. *J. of Women's Health*, 30(4), 474-491. https://doi.org/10.1016/j.jsxm.2020.10.009
22. Rammal, H., Bouayed, J. & Soulimani, R. (2010). A direct relationship between aggressive behaviour in the resident/intruder test and cell oxidative status in adult male mice. *European J. of Pharmacology*, *627*(1-3), 173-176. https://doi.org/10.1016/j.ejphar.2009.11.001
23. Regis, L., Planas, J., Celma, A., de Torres, I. M., Ferrer, R. & Morote, J. (2015). Behaviour of total and free serum testosterone as a predictor for the risk of prostate cancer and its aggressiveness. *Actas Urológicas Españolas (English Edition)*, *39*(9), 573-581. https://doi.org/10.1016/j.acuroe.2015.09.001
24. Trifu, S. C., Tudor, A. & Radulescu, I. (2020). Aggressive behaviour in psychiatric patients in relation to hormonal imbalance. *Experimental and Therapeutic Medicine*, *20*(4), 3483-3487. https://doi.org/10.3892/etm.2020.8974
25. Quadros, I. M., Takahashi, A. & Miczek, K. A. (2020). Serotonin and aggression—an update. In *Handbook of Behavioural Neuroscience* (Vol. 31, pp. 635-663). Elsevier. https://doi.org/10.1016/B978-0-444-64125-0.00037-2
26. Yang, J. H., Weng, S. L., Lee, C. Y., Chou, S. Y., Hsu, C. S. & Hsu, M. I. (2010). A comparative study of cutaneous manifestations of hyperandrogenism in obese and non-obese Taiwanese women. *Archives of Gynecology and Obstetrics*, *282*, 327-333.