Caraway Seed Extract and Lactation: *in vivo* study

Tamadur Olaimat[1], Farah Al-Mamoori[1]*, Haneen Basheer[1], Feras El-hajji[2]

[1]Department of Pharmacy, Faculty of Pharmacy, Zarqa University, Zarqa, Jordan.
[2]Department of Clinical Pharmacy and Therapeutics, Faculty of Pharmacy, Applied Science Private University, Amman, Jordan

ABSTRACT

The aim of this study is to investigate the effect of caraway seed aqueous extract on milk production in female rats and elucidate its bioactive components. We used three groups of six virgin rats and three groups of six lactating rats. We kept each mother rat and her six pups apart. From the third to the seventeenth day of breastfeeding, these groups of animals received distilled water, metoclopramide (5 mg/kg), and aqueous extracts of caraway seed (200 mg/kg) daily by mouth. We used the indirect method, which established a link between the amount of milk nursing rats produced and the weight gain of pups who received no food. We also measure the prolactin levels of female rats who have never been pregnant on specific days. On Day 14, the groups that received caraway seed fluid extracts (200 mg/kg) or metoclopramide (5 mg/kg) showed significantly higher prolactin levels ($P > 0.01$ and $P > 0.001$, respectively). Studies have shown that caraway seed significantly increases prolactin levels ($P < 0.05$) as early as Day 7. Only with (5 mg/kg) of metoclopramide did milk production and pup weight gain go up significantly ($P > 0.05$). An extract of caraway seed affects prolactin levels in rats, but it does not affect milk production. Further research is necessary to explore the potential therapeutic benefits of caraway seed.

Keywords: Galagtagouge, *Carum carvi*, Metoclopramide, Milk production, Prolactin, Medicinal plants.

1. INTRODUCTION

Breastfeeding babies gives them the best diet, boosts their immune systems, and has many other health benefits that last a lifetime for both mother and child. One major issue that has dominated the lactation field for many years is hypogalactia (reduced milk production).[1] It is the most frequent cause of breastfeeding failure, leading to the cessation of breastfeeding. [2] According to reports, >20% of mothers who breastfed their infants experienced postpartum hypogalactia. The number of women with hypogalactia has gone up because the average age of mothers is getting older and the number of cesarean sections is going up all over the world.[3] 92% of children in Jordan experience breastfeeding at some point, making it a country with a high breastfeeding prevalence.[4] Nonetheless, prior research conducted in Jordan has indicated negative sentiments on breastfeeding practices. Furthermore, Jordanian population and family health surveys show that the percentage of six-month-old infants exclusively nursing is below optimal and has been falling, from 40% in 2007 to 26% in 2018.[4]

Medicinal plants are still used for medical purposes, especially in developing nations where access to contemporary therapeutic systems may be limited. [5]Asadbeigi et al. (2014) say that ethnomedicines are in high demand because they are a cheap, easy-to-find, and safe source of active compounds that can be used in pharmaceuticals.[6] Nowadays, medicinal plants continue to play an important role in the treatment of a variety of illnesses, particularly in rural areas due to budgetary constraints and inconvenience, as well as health concerns.[7] We can use herbal and pharmaceutical galactagogues to treat women who don't

****Corresponding author: Farah Al-Mamoori***
Fmamoori@zu.edu.jo
Received: 16/06/2024 Accepted: 31/10/2024.
DOI: https://doi.org/10.35516/jjps.v18i3.2799

make enough milk and don't respond to lactation counseling, as well as adoptive parents who want to start breastfeeding. Though the market for pharmaceutical and herbal galactagogues is growing, there is little information on how to use them.[1]

Caraway (*Carum carvi* L.), belongs to the family Umbelliferae. It is one of the first cultivated herbs in Asia, Africa, and Europe. Folk medicine particularly uses the plant's dried fruits and leaves to treat digestive disorders such as stomach aches, constipation, flatulence, and nausea. These oldest herbs are filled with a specific, pleasant aroma. Its aromatic properties make it a valuable flavoring agent. [8] Moreover, liqueurs, mouthwashes, toothpastes, perfumes, soaps, and cosmetics use it. [9] Traditional Persian medicine uses caraway, a galactogogue, to reduce excessive breast milk production. [10,11]

Up to our knowledge, there is not enough data about the exact galactogogue effect of caraway seed aqueous extract. The current study aimed to evaluate the effect of caraway aqueous extract on milk production in rats and identify the phytoconstituents in caraway seed aqueous extract.

MATERIAL AND METHODS

Plant materials

We conducted research on caraway seeds. In 2022, we procured caraway seeds from the traditional herbal market in Zarqa, Jordan. Associate Professor Mohammad M. Al-Gharaibeha from the Faculty of Agriculture, Jordan Department of Plant Production, University of Science and Technology assisted in taxonomically identifying the plant through direct comparison with authenticated samples. Zarqa University's College of Pharmacy (Pharmacognosy and Phytochemistry Lab) received the voucher specimen (No. CAR-2022).

Preparation of caraway extract

Experimental animals

Female Wistar laboratory rats (weight ranges of 170-200 g) were housed in cages with controlled temperatures (22-25°C) and relative humidity (50-60%). They provided unlimited access to normal pellet food and water. All animal care and use procedures followed established ethical criteria, and all experimental protocols were approved by the Research and Ethics Committee at the Faculty of Pharmacy-Applied Science University in Amman, Jordan (2022-PHA-23). Eighteen female Wistar rats weighing 170-200 g were mated with male rats a few days before parturition at a regulated temperature (22-25 °C) and relative humidity (50-60%). Each pregnant female Wistar rat was segregated from the other pregnant female Wistar rats. The rats were allowed to give birth to their offspring. Each mother was separated from her pups immediately after parturition. The number of pups per breastfeeding rat was six, and parturition occurred on Day 1 of lactation.[13]

Experiment design

Lactating rats were sorted into three groups (n= 6) using the procedure outlined.[13] Each group contains six lactating rats. From Day 3 to Day 17, we administered the following treatments to the lactating rats:

- **Group I**: Served as a negative control and was given unlimited access to water.
- **Group II**: Metoclopramide (5mg/kg) was used as the standard treatment.
- **Group III**: Caraway seed aqueous extract (200 mg/kg) was used.

Metoclopramide and plant extracts are dissolved in distilled water. The prepared solution was given to the rats through oral gavage. Based on prior research [14,15] the dose of metoclopramide (5 mg/kg) was chosen.

The puppies were not given any treatment, but their weights were taken at various times of the day from Day 3 to Day 17.

Milk production and body weight measurements

The weights of the puppies (P1) were measured at 8:00 AM subsequent to a period spent overnight with their maternal figures. They were subsequently segregated from the nursing rats for a duration of four hours. At 12:00 PM, a second weighing (P2) was conducted, after which they were reintegrated with the nursing rats for one hour of suckling. The third weight (P3) was ascertained at 1:00 PM to evaluate the quantity of milk ingested by the puppies. The determination of milk yield is predicated upon the disparity in weight between the puppies before and after the feeding sessions. This yield is computed through the utilization of a weight loss correlation coefficient. The absorbed milk by the puppies serves to furnish the requisite energy for their physiological activities such as locomotion and respiration. The formula employed to accurately predict milk yield is articulated as follows:[16]

Milk yield(g)=(P3-P2)+[(P2-P1)/4]

- (P3-P2) represents the growth in puppy weight subsequent to lactation,
- (P2-P1)/4 denotes the weight loss correlation coefficient.

Prolactin levels in blood measurements

Eighteen virgin rats weighing (170-200 g) were separated into three groups of six animals each for fourteen days.

- **Group I**: Served as a negative control and was given unlimited access to water.
- **Group II**: Metoclopramide (5 mg/kg) was used as the standard treatment.
- **Group III**: Caraway seed aqueous extract (200mg/kg) was used.

Virgin rats were given a single dose of caraway aqueous extract and metoclopramide every day. The serum prolactin level was tested on Days 0, 7, and 14. Blood samples were drawn from the animals' retro-orbital plexus and centrifuged at 1000 rpm for 20 minutes.[17] After collecting the supernatant, the serum prolactin level was determined using an immunoenzymatic technique (ELISA Kit).[18]

Caraway seed aqueous extract bioactive compound identification

UPLC equipped with Q-TOF/MS was used to characterize bioactive chemicals. The UPLC chromatographic conditions are shown in (Table 1).

Table 1: Summary of chromatographic conditions

UPLC conditions	**Injection volume**	**Autosampler temperature**	**Column oven temperature**	**Total run time**
	3µl	8ºC	40°C	35min.
Chromatography	**Mobile phase**	Solvents: (A) Water with 0.05% formic acid (B) Acetonitrile Gradient: 0 – 27 min linear gradient from 5% - 80% B; 27 – 29 min 95% B; 29.1 min 5% B		
	Column type	Bruker Daltonik C-18 column (100× 2.1mm× 1.8µm)(120 Aº)		

Ion Source's Apollo II ion funnel electrospray source was employed as a source in both positive and negative modes. The following were the mass spectrometry conditions:

- The capillary voltage was 2500 volts (VT).
- The nebulizer gas pressure was 2.0 bar.
- The flow rate of dry gas (nitrogen) was 8 L/min.
- The dry temperature was 200 degrees Celsius.

The mass resolution was 50000 FSR (Full Sensitivity Resolution), and the mass accuracy was 1 ppm. The TOF repetition rate was up to 20 kHz. Data analysis 4.2 software was used to analyze the MS data (Bruker Daltonics, Bremen, Germany).

Statistical analysis

Using IBM SPSS software, a one-way ANOVA followed by *Dunnett's post-hoc* test was performed on all examined parameters (Version 22.0). The information was reported as mean ± SD. P values of less than 0.05 were deemed statistically significant. P values less than 0.01 were deemed statistically significant. P values of less than 0.001 were considered statistically significant.

The effect of caraway seed aqueous extract on milk production

The female rats' milk production was monitored daily before and after the test drugs were administered. The data revealed that the milk yield of each experimental group's rats was not proportional to the number of days of lactation (Figure 1(A)).

When compared to the negative control group, caraway seed aqueous extract (200 mg/kg) in the treated groups did not substantially improve milk production ($P > 0.05$). Metoclopramide (5 mg/kg) significantly enhanced milk production in nursing rats ($P > 0.05$) (Figure 1(B)).

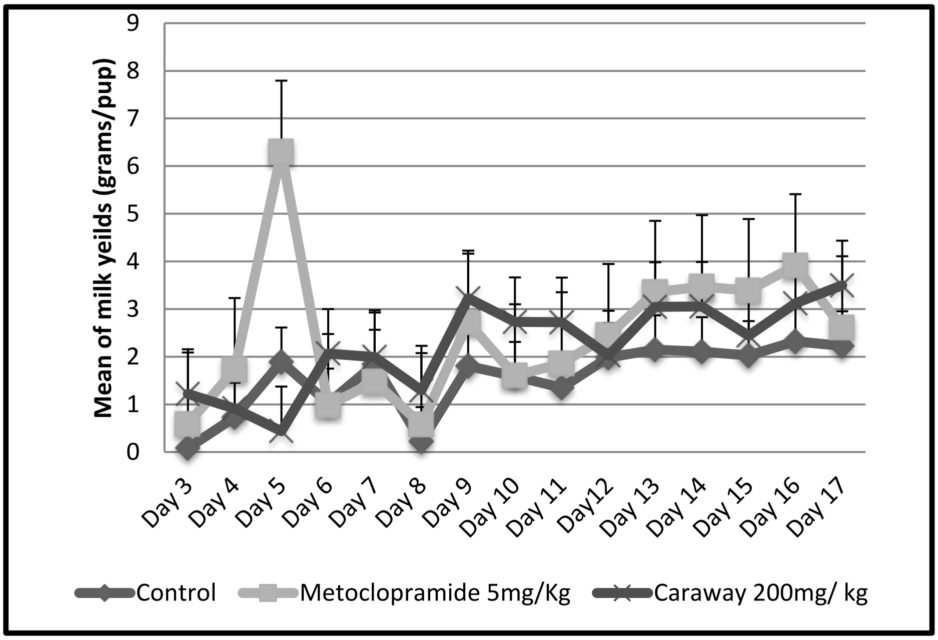

Figure 1 (A): Effect of the aqueous seed extract of caraway on the daily milk production in female Wistar rats from Day3 to Day17 of lactation. The values as expressed mean ± SD, with n=6.

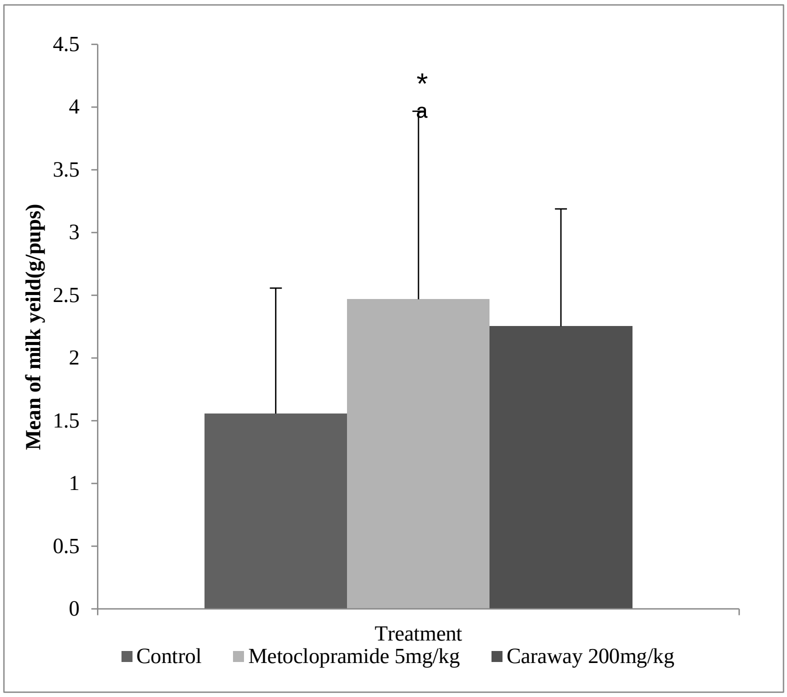

Figure 1(B): Effect of the aqueous seed extract of caraway on the average milk quantity in female Wistar rats from Day 3 to Day17 of lactation. Mean ± S.D (n = 6), *P<0.05, a: Compared with control.

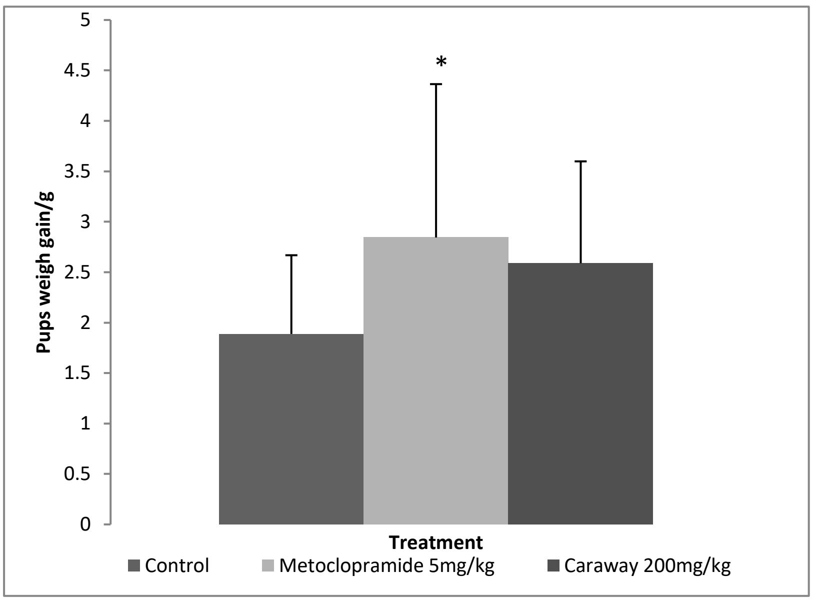

Figure 2: Effect of the aqueous seed extract of caraway on the average pups weigh gain from Day 3 to Day17 of lactation. Mean ± S.D (n = 6), *P<0.05, a: Compared with control.

Effect of the aqueous extract of caraway seed on pups' weight gain

Metoclopramide (5 mg/kg) showed significant increases (P< 0.05) in weight gain in lactating rats. In contrast, caraway seed aqueous extract (200 mg/kg) did not significantly increase the weight gain of pups (P > 0.05) (Figure 2).

Evaluation of serum prolactin levels

Metoclopramide (5 mg/kg) and caraway seed extract (200 mg/kg) were given to virgin female Wistar rats for 14 days. On Days 0, 7, and 14, prolactin levels were measured. No treatment resulted in prolactin levels higher than (0.9 ng/ml) on Day 0. On Day 7, caraway seed extract enhanced prolactin secretion considerably (P <0.05).

On Day 14, caraway (200 mg/kg) and metoclopramide (5 mg/kg) showed significantly increased prolactin levels (P< 0.01, P<0.001).

Identification of bioactive compounds in aqueous seed extract of caraway

The results showed the identification of many bioactive compounds in caraway seed aqueous extract, as well as a complete list of identified compounds together with their phytochemical class and chemical formula (Table 3).

Table 2: Effect of the aqueous seed extract of caraway on the serum prolactin level in virgin female rat.

Prolactin concentrations induced by treatments (ng/ml)			
Study period	**Control**	**Metoclopramide (5mg/kg)**	**Caraway aqueous extract (200mg/kg)**
Day 0	<0.9	<0.9	<0.9
Day 7	<0.9	0.98 ± 0.35[a]	1.56 ±0.68*[a]
Day 14	<0.9	6.9 ± 1.40***[a]	3.2 ± 0.96**[a]

**P<0.01, ***P<0.001. a: Compared with control group

Table 3: The identified phytoconstituents and their phytochemical class in the aqueous extract of caraway seed.

N	**RT (min)**	**Identified compound name**	**Phytochemical class**	**Chemical formula**	**Ion mode**
1.	0.59	Starch	Polysaccharide	$C_6H_{12}O_6$	[M-H]-
2.	0.59	Nicotinic acid	Pyridinecarboxylic acids.	$C_6H_5NO_2$	[MH]+
3.	0.64	Sugars	Carbohydrate	$C_{12}H_{22}O_{11}$	[MH]+
4.	1	Succinic acid	Dicarboxylic acid	$C_4H_6O_4$	[M-H]-
5.	1.45	Octadecanoic acid	Poly unsaturated fatty acid	$C_4H_6O_4$	[M-H]-
6.	5.64	Hyperoside	Flavanol glycoside	$C_{21}H_{20}O_{12}$	[MH]+
7.	6.75	Kaempferol	Tetrahydroxyflavone	$C_{15}H_{10}O_6$	[MH]+
8.	6.92	4 or 7 Hydroxy Coumarin	Coumarin derivative	$C_9H_6O_3$	[MH]+
9.	20.39	Caffeic acid	Phenolic acid (Cinnamic acid derivatives)	$C_9H_8O_4$	[MH]+
10.	24.05	18-Beta-glycyrrhetinic acid	Triterpenoid	$C_{30}H_{46}O_4$	[MH]+
11.	24.33	Tetradecanoic acid	Saturated fatty acid	$C_{14}H_{18}O_2$	[M-H]-

Compounds listed in order of retention time; RT= retention time (as min.)

DISCUSSION

The amount of milk each group of rats made was not related to the number of days they were lactating. This result is the same as what other studies have found about *Musa x paradisiaca* (Musaceae), *Euphorbia hirta* (Euphorbiaceae), *Pimpinella anisum* (Umbelliferae), and *Nigella sativa* (Ranunculaceae) as galactogogues.[19, 20, 21,17] The fact that mammary cells grow and die in the mammary glands at different times during lactation shows that milk production and days of lactation are not directly related. Because of this, the speed at which milk is made changes based on the phase of lactation. [22]

On Days 0, 7, and 14, rats that had never become pregnant before were given blood prolactin tests. To find out how galactagogues work, this was done.

The findings indicate that none of the treatment groups were successful in provoking a heightened prolactin response in virgin female rats at the onset of the experiment. This observation aligns with prior research findings. [17, 13]

Furthermore, it was observed that administration of aqueous extract of caraway seeds at a dosage of (200 mg/kg) led to a modest increase in lactation; however, this augmentation was not statistically significant. Hamed et al. (2015) have posited that the weight gain exhibited by offspring serves as an indicator of maternal lactation capability.[23]Contrary to expectations, supplementation of pups with caraway seed extract at the aforesaid dosage did not increase their weight gain ($P > 0.05$). This absence of accelerated weight gain suggests a potential correlation between insufficient milk production and the observed lack of weight gain in offspring.

Conversely, it was noted that the aqueous extract of caraway seeds, also administered at a dosage of (200 mg/kg), caused a notable increase in prolactin levels as early as Day 7, specifically in terms of serum prolactin release.

The effects of caraway seeds on milk production and prolactin release appear to be depending upon various factors such as parity, maternal nutrition, and hydration status. For instance, nutritional deprivation in offspring may result in increased milk consumption relative to satiated counterparts during lactation. [24]

During the lactation period of rat pups, significant developmental milestones occur. Primarily, a apparent modulation of sucking behavior emerges by Day 10 postpartum, indicative of a natural regulatory mechanism. Subsequently, by Day 14, observable alterations obvious in the maternal response to pup-initiated stimuli, notably in reaction to a nip or milk release. [25]

Moreover, the efficacy of nipple attachment necessitates sensitivity to a confluence of internal and external variables, including the pup's level of deprivation and the olfactory cues emanating from the lactating ventral surface. [26] Vorherr et al. (1967), Lincoln et al. (1973), and Drewett et al. (1974) have extensively explored facets of this phenomenon. Drewett et al. (1974), for instance, studied the constituent elements of rat pup behavior, delineating "treading" and "stretching" as salient components. [27,28,29]

Clearly, rat pups commonly disengage from the nipple following milk release, notwithstanding satiety, displaying a proclivity for locomotion to access alternative sources. The impetus driving this behavior remains speculative, although a plausible hypothesis implicates olfactory cues, potentially mediated by hormonal responses to oxytocin in the mammary gland region.[30]

Furthermore, it is noteworthy that each milk ejection event furnishes the pup with pertinent information regarding the occurrence and adequacy of milk uptake from the respective nipple. Consequently, in instances where milk is scant or absent despite a milk ejection event, the pup's instinctual response to seek an alternative nipple for sustenance appears rational and adaptive.

Also, the number of cells that make milk in the mammary glands has a big effect on milk production. Three-quarters of the increase in rats' daily milk production between birth and peak lactation can be explained by cell growth during early lactation. The other quarter can be explained by an increase in the activity of cells that were already there. [31]

Overall, both estrogen and sucking cause prolactin to be made by female rats. This is done by blocking the dopaminergic tone in the hypothalamus and stimulating it with a prolactin-releasing hormone, probably oxytocin. [32]

Now, let's talk about caraway seeds. A review of the studies shows that there is not much known about how caraway affects lactation. In this study, caraway seeds had the same effect on prolactin levels as an earlier study, which found that prolactin levels went up. [33]But it doesn't seem to match up with milk production, which might have something to do with the other things we've talked about. In another study, five nursing women were given no herb for 5 days and then 15 mL of a 10% infusion of caraway seeds three times a day for 10 days. Every day, the amount of milk was measured, and the amount of fat in the milk was tested on days 5, 10, 15, and 20. There was no change in the amount of milk or how much fat it had. [34]Ethanol or aqueous caraway extracts, on the other hand, had estrogenic effects at doses higher than (200 mg/kg). [35]

Additionally, LC-MS/MS analysis of caraway aqueous extracts showed the presence of polyphenolic compounds like hyperoside, kaempferol, vitexin, etc. These bioactive compounds act as antioxidants; [37]a study showed that the antioxidant compounds increase the prolactin hormone by affecting the hypothalamic-pituitary axis. [38] Thus, that might be interpreted as a significant effect of caraway seed aqueous extracts on prolactin levels in this study.

In the current study, metoclopramide served as a standard medication. Metoclopramide is considered a safe and effective stimulant of prolactin release. It achieves this by blocking dopamine receptors in the hypothalamus and reducing prolactin inhibitory factor. [39]Metoclopramide (5 mg/kg) significantly increased milk production and serum prolactin levels in this study.

CONCLUSION

An aqueous caraway seed extract was found to have a statistically significant impact on prolactin levels in the blood of nulliparous rats. This impact may be due to the bioactive chemicals included in the extract. Further work is needed to clarify the underlying process that causes a difference between prolactin levels and milk production. These findings add to the increasing evidence that medicinal plants have the potential to be used as new therapeutic agents in current medical practice.

Acknowledgments

The authors wish to thank Zarqa University for financial support. Thanks also to Applied Science Private University for permission to carry out preclinical research. Also, our immense appreciation goes to Dr. Mohammad M. Al-Gharaibeh for his assistance in plant authentication. Thanks to Mr. Salem Shawabka for his assistance with the *in vivo* study.

Ethical Approval

The study protocol was approved by approved by the Research and Ethics Committee at the Faculty of Pharmacy-Applied Science University in Amman, Jordan (2022-PHA-23).

Disclosure

The authors report no conflicts of interest in this work.

Abbreviations

ELISA, enzyme-linked immune-sorbent assay; FSR, full sensitivity resolution; Kg, kilogram; kHz, Kilohertz; L, Litter; LC-MS, Liquid-chromatography–mass spectrometry; Mg, Milligram; μg, Microgram; μL, Microlitre; ML, Millilitte Min, Minutes; Q-TOF,Quadrupole-Time-of-flight;.RT, Retention time; SD, Standard Deviation; SPSS, Statistical Package for the Social Sciences; UPLC, Ultra-Performance-Liquid Chromatography; VT, Voltage transformers.

REFERENCES

1. Bazzano AN, Hofer R, Thibeau S, Gillispie V, Jacobs M, Theall KP. A Review of Herbal and Pharmaceutical Galactagogues for Breast-Feeding. *Ochsner J*. 2016 Winter; 16(4): 511-524.
2. Penagos Tabares F, Bedoya Jaramillo JV, Ruiz-Cortés ZT. Pharmacological overview of galactogogues. *Vet. Med. Int*. 31; 2014.
3. Prentice AM. Breastfeeding in the modern world. *Ann. Nutr. Metab*. 2022; 78(Suppl. 2): 29-38.
4. Mea'ad MH, Mukattash TL, Al-Shatnawi S, Abu-Farha R, Abuhammad S, Jarab A, Taan W, D'Arcy D. Community Pharmacists' Perceptions of the most Important Interventions Implemented in Supporting Breastfeeding Women During Maternal Life: A Cross-Sectional Study in Jordan. *JJPS*. 2024 Mar 19; 17(1): 144-50.
5. Brahmi F, Khaled-Khodja N, Bezeghouche R, Bouharis S, Elsebai MF, Madani K, Boulekbache-Makhlouf L. Ethnobotanical study of the most Lamiaceae used as medicinal and culinary plants by the population of Bejaia Province, Algeria. *JJPS*. 2023 Jun 25: 268-81.
6. Asadbeigi M, Mohammadi T, Rafieian-Kopaei M, Saki K, Bahmani M, Delfan M. Traditional effects of medicinal plants in the treatment of respiratory diseases and disorders: an ethnobotanical study in the Urmia. *Asian Pac. J. Trop. Med*. 2014; 7: S364-8.
7. Boutlelis DA, Sabrina C, Mounia B, Salah B, Ibtissam L, Chaima B. Therapeutic potential of traditional medicinal plants from Algeria for treatment of liver diseases. *Jordan Journal of Pharmaceutical Sciences*. 2023 Sep 23; 16(3): 529-40.
8. Sachan AK, Das DR, Kumar M. *Carum carvi*-An important medicinal plant. *J. Chem. Pharm. Res*. 2016; 8(3): 529-33.
9. Agrahari P, Singh DK. A review on the pharmacological aspects of *Carum carvi*. *J. Biol*. *Earth Sci*. 2014; 4(1): 1-3.
10. Kabiri M, Kamalinejad M, Sohrabvand F, Bioos S, Babaeian M. Management of breast milk oversupply in traditional Persian medicine. *eCAM*. 2017; 22(4): 1044-50.
11. Yarnell E. Botanical medicine in pregnancy and lactation. *Altern Complement Ther*. 1997; 93–100.
12. Walli RR, Al-Musrati RA, Eshtewi HM, Sherif FM. Screening of antimicrobial activity of fenugreek seeds. *Int. J. Pharm*. 2015; 2(4): 1-4.
13. Sampson DA, Jansen GR. Measurement of milk yield in the lactating rat from pup weight and weight gain *J. Pediatr. Gastroenterol. Nutr*. 1984; 3(4): 613-7.
14. Koko BK, Konan AB, Kouacou FK, Djétouan JM, Amonkan AK. Galactagogue effect of *Euphorbia hirta* (Euphorbiaceae) aqueous leaf extract on milk production in female wistar rats. *Int. j. biosci. med.* 2019; 7(9): 51-65.
15. Simelane MB, Lawal OA, Djarova TG, Musabayane CT, Singh M, Opoku AR. Lactogenic activity of rats stimulated by *Gunnera perpensa* L.(Gunneraceae) from South Africa. *AJTCAM*. 2012; 9(4): 561-73.
16. Lompo-Ouedraogo Z, van der Heide D, van der Beek EM, Swarts HJ, Mattheij JA, Sawadogo L. Effect of aqueous extract of *Acacia nilotica* ssp adansonii on milk production and prolactin release in the rat. *J. Endocrinol.* 2004; 182(2): 257-66.
17. Bako IG, Mabrouk MA, Abubakar MS, Mohammed A. Lactogenic study of the ethyl-acetate fraction of *Hibiscus sabdariffa* linn seed on pituitary prolactin level of lactating albino rats. *Int. J. Appl. Res. Nat. Prod.* 2013; 6(2): 30-7.
18. Ogweje AE, Bako IG, Akor-Dewu MB. Evaluation of milk yield and some lactogenic hormones in lactating Wistar rats after treatment with ascorbic acid and α-tocopherol. *JAAPS*. 2019; 7(1): 38-
19. Mahmood A, Omar MN, Ngah N. Galactagogue effects of *Musa x paradisiaca* flower extract on lactating rats. *Asian Pac. J. Trop. Med*. 2012; 5(11): 882-6.

20. Hosseinzadeh H, Tafaghodi M, Abedzadeh S, Taghiabadi E. Effect of aqueous and ethanolic extracts of *Pimpinella anisum* L. seeds on milk production in rats. *JAMS*. 2014; 7(4): 211-6.
21. Hosseinzadeh H, Tafaghodi M, Mosavi MJ, Taghiabadi E. Effect of aqueous and ethanolic extracts of *Nigella sativa* seeds on milk production in rats. *JAMS*. 2013; 6(1): 18-23.
22. Wiart S, Boutinaud M. Le turnover des cellules dans la glande mammaire évalué par immunohistochimie, comme indicateur de la production de lait. In *XXVIème Congrès de l'Association Française d'Histotechnologie (AFH)*. 2013 Jun 13.
23. Hamed RS, Breakaa MA, Said HE. Effect of Acacia nilotica leaves extract and flaxseed oil supplementation on milk yield and reproductive performance of rabbit does. *EPSJ*. 2015; 35(2).
24. JAKUBOWSKI M, TERKEL J. Prolactin release and milk ejection in rats suckling underfed pups. *Endocr*. 1986; 118(1): 8-13.
25. Hall WG, Cramer CP, Blass EM. Developmental changes in suckling of rat pups. *Nature*. 1975; 258(5533): 318-20.
26. Dollinger MJ, Holloway WR, Denenberg VH. Nipple attachment in rats during the first 24 hours of life. *J. Comp. Physiol. Psychol.* 1978; 92(4): 619.
27. VORHERR H, KLEEMAN CR, Lehman E. Oxytocin-induced stretch reaction in suckling mice and rats: a semiquantitative bio-assay for oxytocin. *Endocr*. 1967; 81(4): 711-5.
28. 28.Lincoln DW, HILL A, Wakerley JB. The milk-ejection reflex of the rat: an intermittent function not abolished by surgical levels of anaesthesia. *J. Endocrinol.* 1973; 57(3): 459-76.
29. Drewett RF, Statham C, Wakerley JB. A quantitative analysis of the feeding behaviour of suckling rats. *Anim. Behav*. 1974; 22: 907-13.
30. Drewett RF, Trew AM. The milk ejection of the rat, as a stimulus and a response to the litter. *Anim. Behav.* 1978; 26: 982-7.
31. Knight CH, Wilde CJ. Mammary growth during lactation: implications for increasing milk yield. *JDS*. 1987; 70(9): 1991-2000.
32. Kennett JE, Poletini MO, Fitch CA, Freeman ME. Antagonism of oxytocin prevents suckling-and estradiol-induced, but not progesterone-induced, secretion of prolactin. *Endocr*. 2009; 150(5): 2292-9.
33. Sahoo, H. B., Bhaiji, A., Gupta, A., & Jain, A. P. The impact of *Carum carvi* on serum prolactin and cortisol in nursing rats: A preclinical evidence towards galactagogue claim. *Conference: 69th Indian Pharmaceutical Congress-2017*. At: Chitkara University, Chandigarh, Punjab, India.
34. Nikolov P, Avramov NR. Izv Meditsinskite Inst Bulg Akad Naukite Sofia Otd Biol Meditsinski Nauki. Investigations on the effect of *Foeniculum vulgare*, *Carum carvi*, *Anisum vulgare*, *Crataegus oxyacanthus*, and *Galga officinalis* on lactation. Izv Meditsinskite Inst Bulg Akad Naukite Sofia Otd Biol Meditsinski Nauki. 1951; 1: 169-82.
35. Thakur S, Bawara B, Dubey A, Nandini D, Chauhan NS, Saraf DK. Effect of *Carum carvi* and *Curcuma longa* on hormonal and reproductive parameter of female rats. *Int. J. Phytomedicine*. 2009; 1(1).
36. Tsao R. Chemistry and biochemistry of dietary polyphenols. Nutrients. 2010; 2(12): 1231-46.
37. McGuire TM. Drugs affecting milk supply during lactation. *Aust. Prescr*. 2018; 41(1): 7.
38. .Wirawati CU, Sudarwanto MB, Lukman DW, Wientarsih I. Local plants as feed supplementation to improve ruminant milk production and quality. *WARTAZOA. JITV*. 2018; 27(3): 145-57.
39. Judd SJ, Lazarus L, Smythe G. Prolactin secretion by metoclopramide in man. *J Clin Endocrinol Metab*. 1976; 43(2): 313-7.

مستخلص بذور الكراوية والإرضاع: دراسة في الجسم الحي

تماضر علايمات[1]، فرح المعموري[1]*، حنين بشير[1]، فراس الحجي[2]

[1] قسم الصيدلة، كلية الصيدلة، جامعة الزرقاء، الزرقاء، الأردن

[2] قسم الصيدلة السريرية والعلاجيات، كلية الصيدلة، جامعة العلوم التطبيقية الخاصة، عمّان، الأردن

ملخص

تهدف هذه الدراسة إلى التحقيق في تأثير مستخلص بذور الكراوية المائي على إنتاج الحليب لدى إناث الجرذان، وتحديد مكوناته الحيوية الفعالة. تم استخدام ثلاث مجموعات من الجرذان العذارى وثلاث مجموعات من الجرذان المرضعات، بحيث تحتوي كل مجموعة على ست جرذان. تم إبقاء كل أم مع صغارها الستة بشكل منفصل. وابتداءً من اليوم الثالث وحتى اليوم السابع عشر من الرضاعة، تلقت هذه المجموعات يوميًا عن طريق الفم الماء المقطر، أو دواء الميتوكلوبراميد (5 ملغم/كغم)، أو مستخلص بذور الكراوية المائي (200 ملغم/كغم). تم استخدام الطريقة غير المباشرة، التي تربط بين كمية الحليب التي تنتجها الأمهات المرضعات وزيادة وزن الصغار الذين لا يتلقون طعامًا آخر. كما تم قياس مستويات هرمون البرولاكتين لدى إناث الجرذان العذارى في أيام محددة. وفي اليوم الرابع عشر، أظهرت المجموعات التي تلقت مستخلص بذور الكراوية (200 ملغم/كغم) أو الميتوكلوبراميد (5 ملغم/كغم) زيادة ملحوظة في مستويات البرولاكتين (P < 0.01 و P < 0.001 على التوالي). وقد بينت الدراسات أن بذور الكراوية تؤدي إلى ارتفاع ملحوظ في البرولاكتين (P < 0.05) في وقت مبكر يصل إلى اليوم السابع. ولكن لوحظ أن الزيادة الملحوظة في إنتاج الحليب وزيادة وزن الصغار كانت فقط في مجموعة الميتوكلوبراميد (5 ملغم/كغم.(P > 0.05) (تشير النتائج إلى أن مستخلص بذور الكراوية يؤثر على مستويات البرولاكتين لدى الجرذان، لكنه لا يؤثر على إنتاج الحليب. وهناك حاجة إلى مزيد من الدراسات لاستكشاف الفوائد العلاجية المحتملة لبذور الكراوية.

الكلمات الدالة: محفز لإدرار الحليب، الكراوية ميتوكلوبراميد، إنتاج الحليب، البرولاكتين، النباتات الطبية.

* ***المؤلف المراسل: فرح فالح المعموري***

Fmamoori@zu.edu.jo

تاريخ استلام البحث 2024/06/16 وتاريخ قبوله للنشر 2024/10/31.