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Histological Effect of Mint extract and Metoclopramide on Mammary Gland Tissues

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I. Abstract

Plants are considered a rich source of phytochemicals with significant medicinal value. Among these, spearmint (Mentha spicata L.) stands out as an important natural source of polyphenols known for their diverse biological activities. This study aimed to investigate the effects of both metoclopramide and spearmint extract on the histological structure of the mammary gland, using hematoxylin blue staining. The study was conducted from October 27, 2025, to November 27, 2025, in the Department of Veterinary Medicine at Tikrit University, in collaboration with the laboratories of the College of Science .The study included twenty-eight female mice, which were divided into four equal groups and maintained under normal conditions. Group A1 served as the control group and included lactating females that received no treatment, with free access to food and water. Group A2 was treated with a 10% spearmint solution, while Group A3 received a dose of 2 mg of metoclopramide. Group A4 was subjected to a combined treatment consisting of 2 mg of metoclopramide along with 10% spearmint extract .The histological results revealed clear changes in the mammary glands of the treated groups, including an increase in the size of lobules and alveoli, as well as dilation of their lumens compared to the control group. The combined treatment group showed a more pronounced increase in the number of these structures, along with elevated secretory activity, as indicated by the accumulation of secretory materials within the alveoli. This was accompanied by a noticeable reduction in adipose tissue.

In conclusion, both spearmint and metoclopramide, whether used individually or in combination, induce significant histological changes in the mammary gland that reflect enhanced secretory activity compared to the control group, with the greatest effect observed in the combined treatment group.

Keywords: Mint extract, Metoclopramide , Mammary histology

II. Introduction

Breastmilk is an exceptional source of nutrition for infants. Breastfeeding confers benefits for the health of both baby mice and mother. These benefits include not just advancements in health functioning by antagonising dopamine receptors in the hypothalamus and nutrition but also advancements in development, as well as psychological, immunological, and economic advantages. Fatigue, anxiety, stress, and many diseases can lead to diminished breast milk production and malnutrition in newborns(1, 2). The function and expression of receptors in the mammary glands can be modulated by herbal groups, which results in an increase in milk supply during pregnancy.These herbs possess phytoestrogens analogous to estrogen, recognized for their cellular effects. The elevation of blood oestrogen levels enhances cellular activity, promoting cell division, which results in an augmentation of the secretory and ductal cells in the breast, ultimately leading to an increase (3) . Since 1980, the incidence of preterm deliveries has risen in the United States, leading mothers of premature newborns to frequently concern themselves with their ability to make sufficient milk for their kids, who are often too young to nurse. Numerous research have been undertaken to ascertain whether fenugreek enhances breast milk volume

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and prolactin levels in preterm moms. No adverse effects were detected in mothers or infants (4). Histologically, the mammary gland is classified as a composite tubulo-alveolar gland featuring lactiferous ducts. The smaller ducts are lined with columnar epithelium, whereas the bigger ducts have two or three layers of these cells. Next to the openings of these ducts on the nipple, the lining changes to stratified squamous columnar epithelium. The architecture of the mammary gland's glandular components varies dramatically across different life stages in relation to milk production and secretion(5, 6). The therapy, particularly when applied topically, poses no adverse consequences for the mother and newborn. Metoclopramide, a dopamine antagonist, is believed to function as a galactagogue by elevating blood prolactin levels. This centrally-acting drug can enhance milk production by 66-100% within 2-5 days when administered at a dosage of 30-45 mg per day. No adverse effects on infants have been reported. The medication has demonstrated efficacy in alleviating post-operative nausea and vomiting, mitigating radiation sickness, and enhancing the management of specific forms of drug-induced emesis. Nonetheless, further controlled trials are required to confirm the efficacy of metoclopramide in these proposed applications (7). Metoclopramide is a pharmacological agent, and clinical evidence substantiates its efficacy in promoting lactation in women. It is a dopamine antagonist that increases prolactin levels, hence initiating or augmenting lactation. Metoclopramide is a potent stimulant of prolactin secretion, . The current investigation illustrated the impact of metoclopramide and mint on the mammary glands utilising haematoxylin blue stain. in breast size during lactation.

III. Materials and methods

Experimental Design

At the period beginning on October 27, 2025 and ending on November 27, 2025, the research was carried out at Tikrit University, specifically at the Veterinary Medicine Department as well as the laboratories of the College of Science. During the course of the experiment, there were a total of twenty-eight female mice that were each assigned to one of four groups, which were as follows:

1. Control Group A1: 7 lactating females given normal food and water.
2. Mint Group A2: 7 lactating females given 10% mint.
3. Metoclopramide A3 Group: 7 lactating females given 2 mg of metoclopramide.
4. Metoclopramide and mint Group A4: 7 lactating females given 2 mg of metoclopramide with 10% mint.

Females were anaesthetised with chloroform and dissected 21 days post-weaning. The abdomen was incised, and the mammary glands were excised. Microscopic slides were made as per reference (8), utilising eosin and haematoxylin staining.

Result

The result of the histological findings from the present investigation indicated an augmentation in both the size and quantity of lobules relative to the control group, alongside an enlargement of internal branches and secretory substances. This was accompanied by a reduction in the volume of adipose tissue surrounding the connective tissues between lobules, as illustrated in Figures 1. In the group administered mint, an augmentation in the dimensions of lobes and lobules of diverse sizes was noted, accompanied by an increase in the size of the alveoli. The lumen was larger than in the control group, as were its branches. The lumen contained internal folds representing the branching of the alveolar wall. An increase in secretory materials was also observed, including a large quantity of fat droplets within the secretory material. As shown in Figure 2.

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Compared to the control group, metoclopramide increased lobule size, epithelial cell size and shape, secreted material, and lipid droplets in the secreted material. It also decreased adipose tissue, increased alveolar branching, and thickened the alveolar septa. As shown in Figure 3.

In the group treated with mint and metoclopramide, an increase in lobules and alveoli was observed, along with a reduction in adipose tissue. The number and size of alveoli and secreted material increased, and a sharp decrease in the amount of adipose tissue was noted. An increase in secreted material and lipid droplets, and fullness of the alveoli with secreted material, were also observed. As shown in Figure 4.

40X

Control(A)

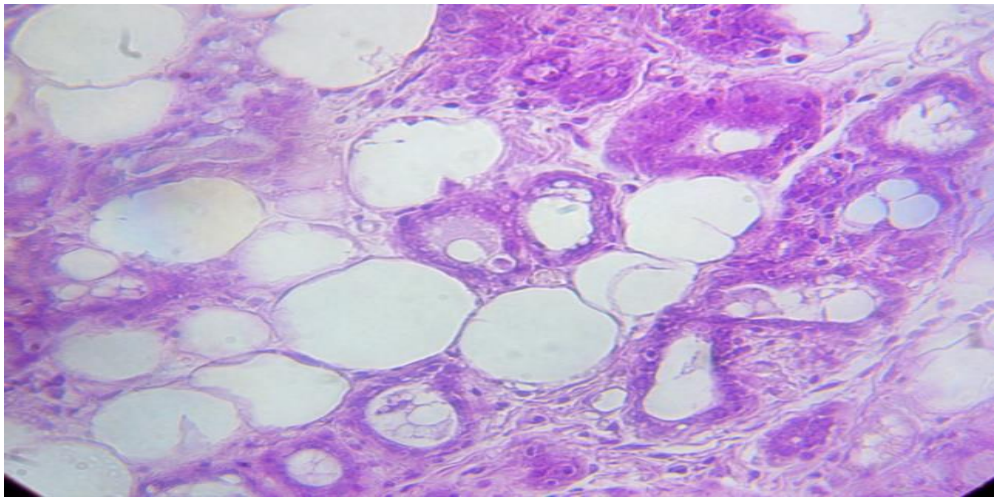

Figure (1) Histological Section of the Mammary gland of a Lactating female mouse (control) showing alveoli A and fat cells B, X 40 H&E).

A2

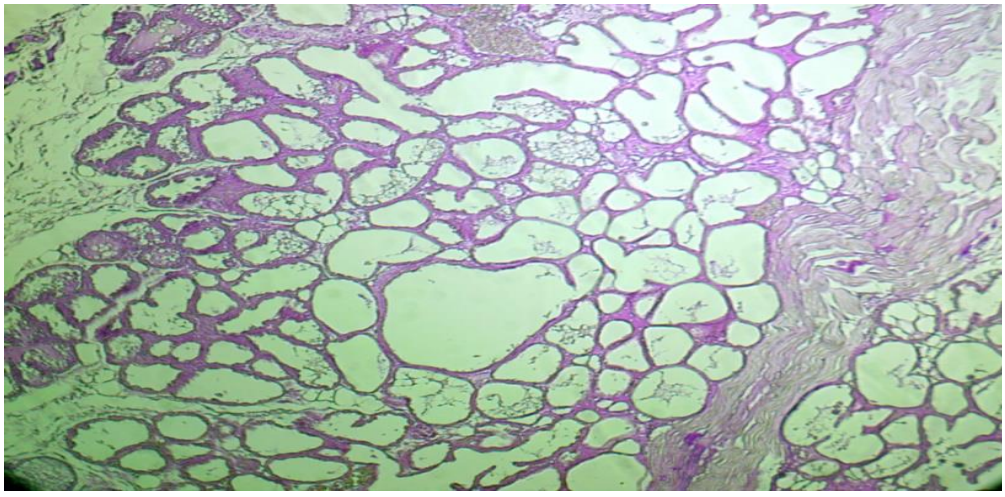

Figure (2) Histological Section of the Mammary gland of a Lactating female mouse (mint) showing lobules and alveoli containing secreted material of different sizes A and septa between lobules C,40X (H&E).

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A3

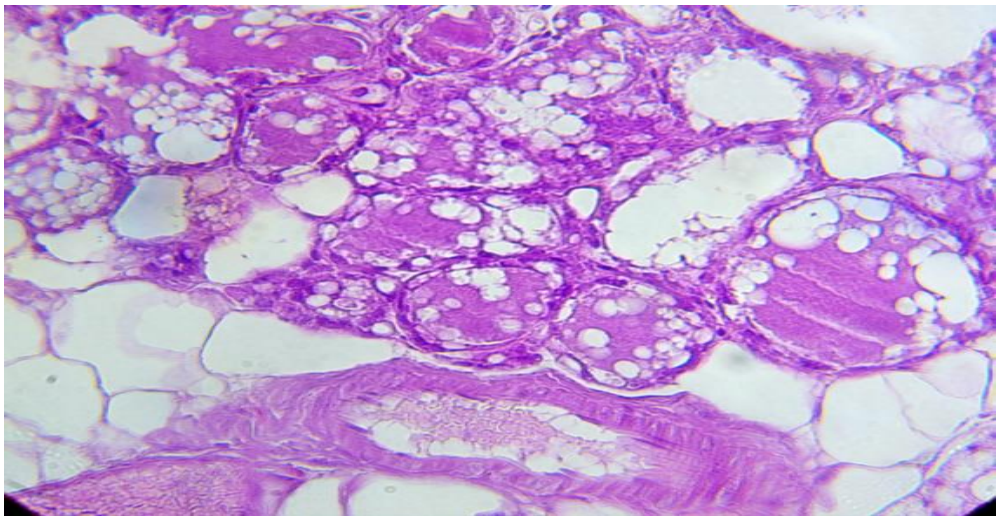

Figure (3) Image (4-9) Histological Section of the Mammary gland of a Lactating female mouse (metaclopramide). The alveoli contain secretory substances D and are thickened by the wall of some of them Z,40X (H&E)..

A4

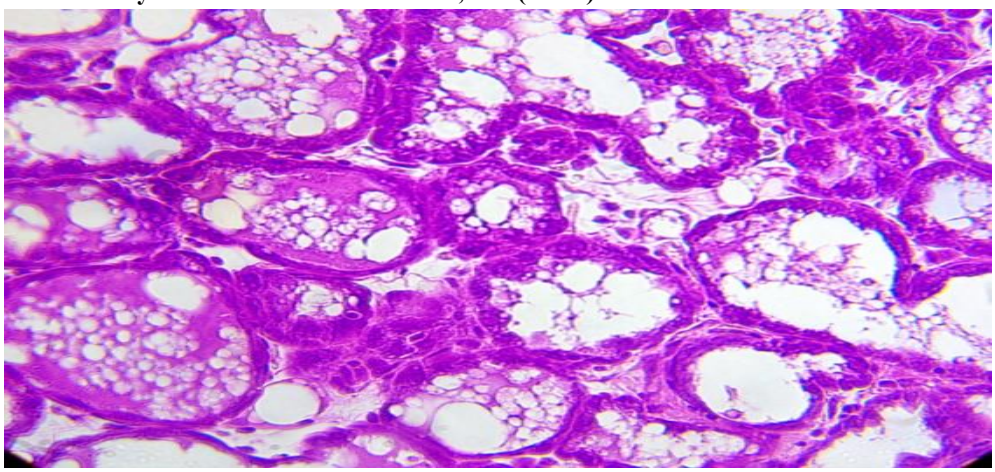

Figure (4) Histological Section of the Mammary gland of a Lactating female mouse (metaclopramide and mint). Alveoli containing secretory material D with fatty droplets E,40X (H&E).

IV. Discussion

The histological findings from the present investigation indicated a general increase in the size and quantity of alveolar lobules compared to the control group, along with an enlargement of the internal branches and secretory substances. The results reveal that the group treated with Mentha had enhanced growth and development of the mammary glands, together with an increase in the volume of produced material and fat droplets, as corroborated by haematoxylin and eosin staining. The current work concurs with (9), which demonstrated that hot aqueous extracts of spearmint (Mentha spicata) leaves exert a mammogenic impact on the mammary glands during the lactation period in rabbits.

Mentha spicata comprises menthol, menthone, and menthyl acetate as principal constituents. Minor constituents

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comprise 1,8-cineole (eucalyptol), pulegone, caffeic acid, flavonoids, tannins, and bitter compounds. Topical peppermint gel and solutions have been investigated for their efficacy in preventing pain and fissures in the nipples and areolas of lactating women. The formulations of Mentha spicata shown greater efficacy than both placebo and expressed breastmilk, and were comparably efficacious to lanolin in the majority of investigations(10-15), but not in (16). A meta-analysis of controlled trials found that Mentha spicata considerably reduced nipple damage in nursing moms(17).. Certain mothers in Türkiye allegedly utilise mint to enhance their milk production and improve the flavour and quality of their milk(18, 19). Mentha spicata is utilised to inhibit lactation, as evidenced by in vitro and animal studies involving high doses (21 ,20). Menthol and 1,8-cineol are present in breast milk in minimal amounts; however, the excretion of other constituents remains unexamined. In lactating mothers, the use of menthol results in the presence of menthol in breast milk (22). Furthermore, the topical application of menthol is absorbed into the body, indicating that MECs are subjected to menthol following oral or dermal administration of menthol(23).

Numerous investigations have indicated that herbal galactagogues promote secretory mammary cell proliferation (24, 25). A study by (24)found that Sesamum indicum seeds boost mammary glandular tissue growth in female white rats. Launaea taraxacifolia and resveratrol alone caused hyperprolactinaemia, but their combination increased milk production by increasing serum oxytocin activity, according to Sani and colleagues.

Histological findings indicated that metoclopramide augmented secretory granules, resulting in enhanced milk output. The impact on the structural makeup of the secretory vesicles was noted, leading to thicker walls and a marked increase in branching. This results in an augmented surface area for secretion, so elevating the quantity of secreted material per vesicle and amplifying overall breast activity. The findings of our present investigation align with those of (26), which indicated that metoclopramide elevated serum prolactin levels in mothers relative to the control group following three weeks of treatment. Metoclopramide induces hyperprolactinaemia by elevating prolactin levels through itsantagonistic impact on dopamine release in the central nervous system.Seven Moreover, metoclopramide is often favoured as a prokinetic agent (27).

Conclusion

The mint plant and metoclopramide demonstrated advantageous effects on the mammary glands, augmenting their secretion. The medicine's efficacy exceeded that of the extract, with best results observed in the group receiving both the extract and the treatment. The substances employed in the study affected the morphology of the mammary glands, as indicated by an enlargement of the secretory vesicles and a thickening of their walls, along with a significant increase in the branching of these vesicle walls, as illustrated in the histological sections of the research.

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