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The role of fenugreek (*Trigonella foenum-graecum*), sesame (*sesamum indicum*), and domperidone in detecting the mammary glands of lactating white rats

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ABSTRACT

This study was designed to impact the effect of fenugreek (*Trigonella foenum-graecum*), sesame (*sesamum indicum*), and domperidone on the mammary glands of pregnant white rats species *Rattus norvegicus* at different concentrations. Fenugreek was used in an oral dose of 0.5 ml / day as oil, while sesame was used with a dose of 1 g / day as powder and domperidone was used as liquid as an oral dose of 2 mg / day .

The results of the histological examination in the group that dosed the fenugreek showed an increase in the size of the lobules and alveoli, and the lumen was larger than the control group, as well as its branching. The cavities contain internal folds representing the branching of the vesicle wall and the increase of the secreted material in addition to containing an amount of fat in the form of fat droplet within the secretory materials in the lumen Alveoli.

In the group dosed with sesame observed an increase in the size of lobules and alveolitis and their branching and increased secretory material compared with the control group was also found, but that was less than the other two test groups.

In the domperidone group was found an increase in the size of lobules and alveoli and an increase in branching was observed. The secreted material inside the alveolar cavities also increased with an increase in lipid droplets within the secretory material compared with the control group and the other two experimental groups.

Introduction

Galactagogue is one of the substances or materials thought to help start, maintain, or increase breast milk production, and include chemotherapy and herbal supplements [1].

Other than drugs, there are reports that show that herbs are an essential diuretic such as fenugreek. Affects daily milk production, maternal serum prolactin levels, and weight gain in preterm infants [2].

Although there was no increase in prolactin levels, increasing daily milk production shows that there are alternative mechanisms affected by lactic diuretics. In a study by Liu et al. On mice, it was found that the herbal groups regulate the function and expression of receptors in the mammary glands, which increases the

secretion of milk. These herbs contain phytoestrogen that is similar to estrogen known for its cellular effects. The increase in blood estrogen causes an increase in cell activity, stimulating cell division, which leads to an increase in the secretory and ductal cells of the breast which It results in an increase in the breast size of the nursing infant [3].

Since 1980, preterm births have increased in the United States, so mothers of premature infants often worry that they are not able to produce enough milk for their babies, who are often immature to the point of breastfeeding. Several studies have been conducted to determine whether fenugreek increases the size of Breast milk and prolactin levels (PRL) in preterm

mothers. No harmful effects were also observed in mothers or infants [4].

Fenugreek contains phytoestrogen, which are chemical compounds similar to estrogen, and the consumed fenugreek may be used as a way to increase breast milk for breastfeeding. The extracts are related to the secretion of milk by affecting the growth and development of the mammary glands. Milk and ductal secretion in the mammary glands of lactating women, by giving it to lactating women regularly to increase milk flow [5].

The growth of the mammary glands is under the hormonal control of reproductive hormones, as progesterone combines with estrogen, prolactin and growth hormone to complete the alveolar lobular growth that becomes mature at the start of breastfeeding and one of the most important changes in pregnancy is the exposure of the secretory epithelial cells to a functional specialization to initiate the secretion of milk after childbirth and this specialization is stimulated. By synergistic action of insulin with prolactin [6].

Microscopic observations of the mammary glands in mice indicate that the cells suffer in the phase of specialization, an increase in size and changes in the shape of the cell, as are estrogen, progesterone, prolactin, and corticosteroids receptors in the mammary glands, and prolactin receptors increase in the secreted lactic tissues with an increase in milk supply under the influence of high levels of estrogen. Prolactin causes the formation of milk droplets. And secretion into the ducts after birth, and the effect of prolactin also includes an increase in mRNA in developing cells [7].

In addition to this, fenugreek seeds contain a very high level of lactogenic vitamins and may contain strong properties in improving blood circulation and blood flow to the mother's breast and thus increase the flow of milk to the infant [8].

Domperidone is used as a treatment that enhances breast milk production in most Western countries. The maximum approved limit in breastfeeding women is 20 mg, given 4 times daily, although most doctors recommend doses of 10 mg by mouth for 1-2 weeks. [9] Domperidone causes a significant increase in serum prolactin concentration (75%), and unlike metoclopramide, domperidone is less permeable to the blood-brain barrier and is transported in moderate quantities to breast milk due to its high molecular weight and 90% binding to plasma proteins. [10] In a study on dogs with low milk production, positive results were obtained and there were no side effects of domperidone, which makes it the best treatment for increasing milk production in lactating women, and it also led to an increase in the weights of young children. [11] In a study conducted by Osadehy and his group on lactating women who did not produce enough milk after childbirth, the results showed an increase in milk production after treatment with domperidone at a dose of 10 mg three times daily.

The results showed an increase in milk production by 74.72% as domperidone acts on dopamine receptors in the gastrointestinal tract and the part of the brain associated with vomiting, and unlike other dopamine antagonists, it travels weakly to the brain, so its side effects are few on the central nervous system such as depression and its association with plasma proteins is less. It binds to dopamine D2 and D3 receptors in the cells of the pituitary gland due to the chemical similarity, hindering the binding of dopamine known to its inhibitory effect on prolactin, and this leads to the secretion of increased amounts of prolactin, and its level in the blood increases, which enhances its function in stimulating the growth and differentiation of cells to the mammary glands, thus increasing the production of milk [12].

Materials and methods

The experiment was conducted in the laboratories of the College of Education and Veterinary Medicine and the Medical Rehabilitation Hospital in Tikrit, on the lactating females of laboratory white rats species *Rattus norvegicus* with age 5-6 months to demonstrate the effect of fenugreek, sesame and domperidone on the plants used in the experiment were obtained from the Department of Herbal Medicine of the Department of Technical Affairs of the Ministry of Health As the fenugreek was used as a natural oil prepared from ground fenugreek seeds. As for the sesame, it was used as a fenugreek by grinding it and mixing it with brown flour at a ratio of 10-1%. Domperidone was obtained from local pharmacies in the form of 2 mg hard tablets, and it is commercially called Motilium manufactured by the Portuguese company Janssen pharmaceutica NV, where it was ground and dissolved in hope of distilled water. The fenugreek was used at an oral dose of 0.5 ml / day as an oil [13]. As for sesame, it was used with a weight of 1 g / day [14] and domperidone was used as an oral dose of 2 mg / day [11]. 80 female rats were used in the experiment and it was divided into groups of 20 rats in each group and the lactating groups included as follows: -

- 1- The first group (control): - It included 20 breastfeeding females.
- 2- The second group: 20 lactating females dosed 0.5 ml of fenugreek oil.
- 3- The third group: included 20 lactating females who dosed 1 gm of sesame.
- 4- The fourth group: included 20 lactating females who dosed 2 mg domperidone.

Lactating females were numbed and dissected three weeks after birth, and the mammary glands were extracted for each of them, where glass slides were prepared for histopathology [15].

Results and discussion

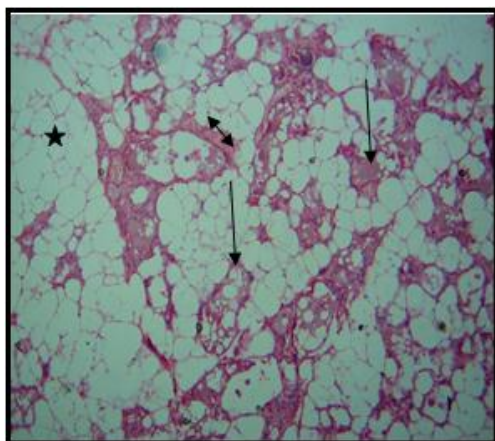
The histopathological results obtained from the current study showed, in general, an increase in the size and number of alveolar lobules compared with the control group, in addition to an increase in the size of the internal branches and secretory materials

with a decrease in the size of the surrounding adipose tissues and the dense connective tissue between the lobes.(pic.1,2)

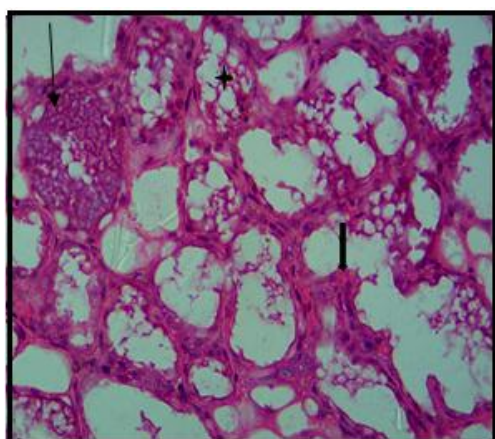
In the group that dosed the fenugreek, an increase in the size of the lobules and alveoli was observed, as the lumen was larger than the control group, as well as its branching. Hematoxylin and eosin.(pic.3,4,5)

In the group dosed with sesame, an increase in the size of lobules and alveolitis and their branching and increased secretory material compared with the control group was also observed, but less than the other two test groups.(pic.6,7)

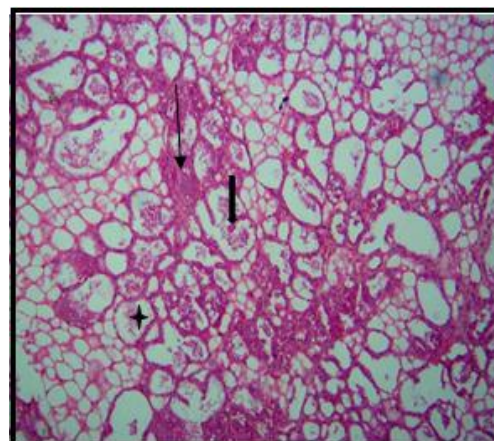
In the domperidone group, an increase in the size of lobules and alveoli and an increase in branching was observed. The secreted material inside alveolar cavities also increased with an increase in lipid droplets within the secretory material compared with the control group and the other two experimental groups. (pic.8,9,10).



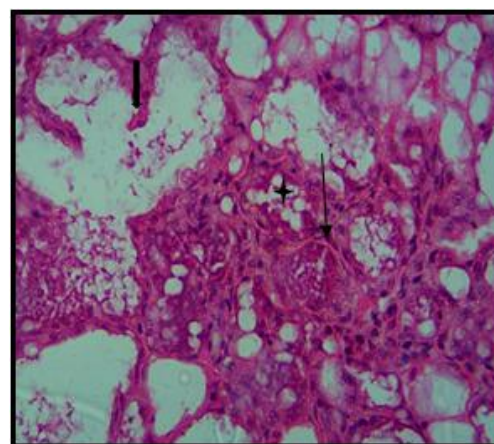
Picture 1: Histogram of the mammary gland of a female lactating rat (Control) notes the lobules and alveoli containing material secretor , connective and adipose tissue★ , 100X (hematoxylin-eosin).



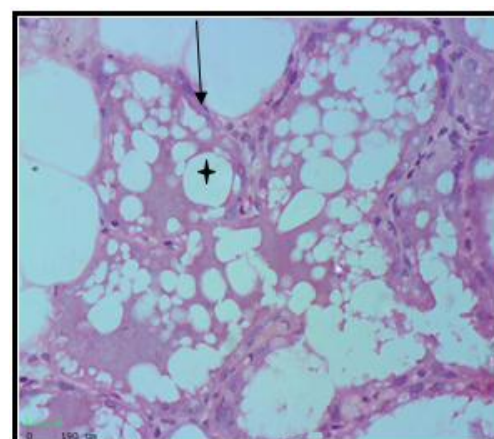
Picture 2: Histogram of the mammary gland of a female lactating rat (Control) notes the lobules and alveoli containing material secretor , and alveoli branches and fat droplets★ , 400X (hematoxylin-eosin).



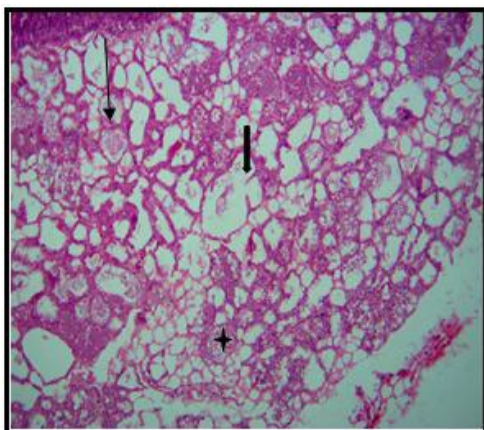
Picture 3: Histogram of the mammary gland of a female lactating rat (Fenugreek) notes the lobules and alveoli containing the material secretor , and alveoli branches and fat droplets★ , 100X (hematoxylin-eosin).



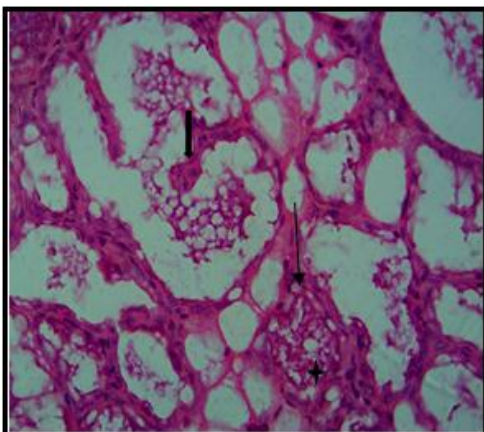
Picture 4: Histogram of the mammary gland of a female lactating rat (Fenugreek) notes the lobules and alveoli containing material secretor , and alveoli branches and fat droplets★ , 400X (hematoxylin-eosin).



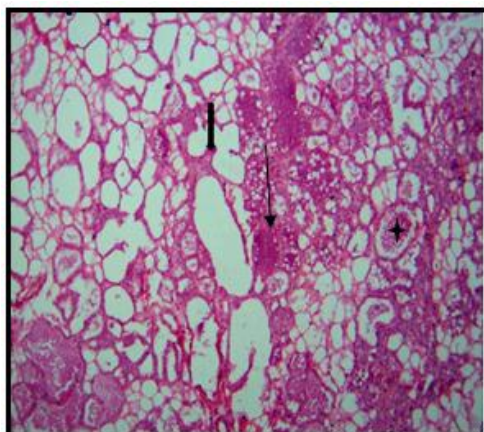
Picture 5: Histogram of the mammary gland of a female lactating rat (Fenugreek) notes the lobules and alveoli containing the material secretor , and large fat droplets★ , 400X (hematoxylin-eosin).



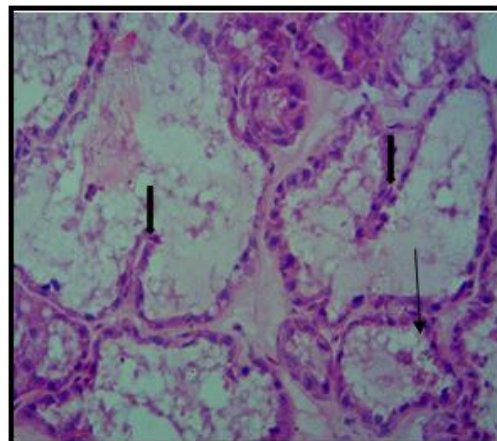
Picture 6: Histogram of the mammary gland of a female lactating rat (Sesame) notes the lobules and alveoli containing material secretor , and alveoli branches and fat droplets , 100X (hematoxylin-eosin).



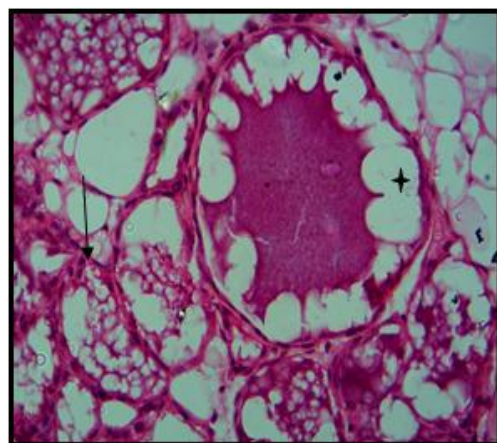
Picture 7: Histogram of the mammary gland of a female lactating rat (Sesame) notes the lobules and alveoli containing the material secretor , and alveoli branches and fat droplets , 400X (hematoxylin-eosin).



Picture 8: Histogram of the mammary gland of a female lactating rat (Domperidone) notes the lobules and alveoli containing material secretor , and alveoli branches and fat droplets , 100X (hematoxylin-eosin).



Picture 9: Histogram of the mammary gland of a female lactating rat (Domperidone) notes the lobules and alveoli containing the material secretor , Alveoli are large in size and their fork deep alveoli, 400X (hematoxylin-eosin).



Picture 10: Histogram of the mammary gland of a female lactating rat (Domperidone) notes the lobules and alveoli containing material secretory , the lipid is concentrated at the edge of the , 400X (hematoxylin-eosin).

These results are consistent with [5] who found that fenugreek is a good diuretic with its effect on the growth and secretion of the mammary glands. And she agrees with [16] who conducted his experiments on lactating rabbits to know the effect of fenugreek oil as a lactic acid, and the results were positive.

It also agrees with [17] who observed an increase in milk secretion in dogs and cats dosed with domperidone significantly, indicating an increase in the development of the mammary glands.

And it is consistent with [12] whose research results showed an increase in the secretion of milk for mothers who were dosed with domperidone, as it binds to dopamine D2 and D3 receptors in the cells of the pituitary gland due to the chemical similarity between them. This stimulates the growth and differentiation of cells in the mammary glands, increasing milk production.

Our results are consistent with [18], which showed an increase in the size and diameter of the mammary glands vesicles and their numbers, and the increase of secreted materials and branches in the alveoli or alveoli by studying the effect of mint extract on the mammary glands of female rats.

And in agreement with the results of [19] in her study of the effect of the sweet seed plant on the mammary glands, as she noticed an increase in the growth and development of the mammary glands in the lactating group, similar to the effect of estrogen and progesterone, as well as an increase in the amount of secreted substance and droplets of fat using the stain of hematoxylin and eosin.

These results also agree with [13] that studied the effect of fenugreek oil on the mammary glands and obtained results that show an increase in the development and growth of the mammary glands, an increase in the size of the follicles and their branching compared to the control and their containment of secretory materials in large quantities and a decrease in the height of the epithelial cells of the alveoli due to their filling with milk. Increasing the glandular tissue by increasing its divisions, which increases the secretory and manufacturing efficiency of the mammary gland. The increase in the hormone progesterone and prolactin at the beginning of the production and secretion of milk plays a role in increasing the metabolic activities of the cells of the mammary glands such as increasing the manufacture of proteins and the regulation of lipid metabolism in the liver and fatty tissues known for their role in supplying the mammary tissues with basic materials by activating enzymes For fat metabolism.

In a study conducted by [18] to find out the effect of sesame on the mammary glands of white mice, results were obtained similar to what was obtained from our current study, which included an increase in the number of lobules, accompanied by a decrease in

collagen fibers, and thus the stroma and an increase in the large vesicles and their branching with an increase in secretory material Due to the presence of active substances in sesame, such as sesamin, which is considered a plant estrogen stimulator for the role of prolactin in the growth and development of the mammary glands and their secretion, and sesame seeds lead to an increase in the expression of estrogen receptors in the womb [19].

Phytoestrogens are of two types (secoisolariciresinol and matariresinol) which are converted in mammals after ingestion to lignans (enterolactone and enterodiol) by coliform bacteria in the intestine. These substances have a chemical structure that is very similar to 17-estradiol present in the body and have the same estrogenic activity [20].

The substance quercetin present in sesame stimulates the expression in the prolactin receptors of the pituitary gland, which in turn stimulates the proliferation of epithelial cells of the mammary gland while sesamin has a stimulating effect to act on estrogen by binding to the estrogen receptors. Estrogen hormone works by binding to its ER α receptors in the mammary gland These receptors are necessary for reproduction The epithelial tissue of the lumen as well as the differentiation and survival process during pregnancy and lactation [21].

The estrogen receptor is the same as the progestogen hormone receptor and is necessary for the differentiation and formation of epithelial tissue and has a positive role in the development of the mammary gland. The mammary gland stem cells have the ability to produce the whole tissues of the mammary gland, as the primary stem cells of the mammary gland lead to the formation of a hierarchy of progenitor cells to produce the different cells of the epithelial tissue of the mammary gland. Mammary gland stem [22].

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دور الحلبة والسّمسم ودواء الدومبريدون في تكشف الغدد الثديية لاناث الجرذان البيض المرضعة

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الملخص

صممت هذه الدراسة لبحث تاثير كل من الحلبة والسّمسم والدومبريدون في الغدد الثديية للجرذان البيض الحوامل نوع *Rattus norvegicus* بتراكيز مختلفة حيث استخدمت الحلبة بجرعة فموية مقدارها 0,5 مل / يوم كزيت اما السّمسم استخدم بوزن 1 غم / يوم والدومبريدون استخدم كجرعة فموية 2 ملغم / يوم . أظهرت نتائج الفحص النسيجي في المجموعة التي جرعت الحلبة زيادة في حجم الفصيصات والاسناخ اذ كان التجويف اكبر من مجموعة السيطرة وكذلك تفرعها فالتجاويف تحوي طيات داخلية تمثل تفرع جدار الحويصلة وزيادة المواد المفرزة إضافة الى احتوائها على كمية من الدهن بهيئة قطيرات fat droplet ضمن المواد الافرازية في تجويف الاسناخ. اما في المجموعة التي جرعت السّمسم لوحظت أيضا زيادة في حجم الفصيصات والاسناخ وتفرعها وزيادة المواد الافرازية مقارنة مع مجموعة السيطرة لكنها اقل من مجموعتي الاختبار الأخرى. وفي المجموعة المجرعة دوميبريدون لوحظ زيادة حجم الفصيصات والاسناخ وزيادة التفرعات كما ازدادت المواد المفرزة داخل تجاويف الاسناخ مع زيادة قطيرات الدهن ضمن المواد الافرازية مقارنة مع مجموعة السيطرة ومجموعتي التجربة الأخرى. الكلمات المفتاحية: الاسناخ،الدومبريدون،الحلبة.