

The Preputial Gland and its Role in Pheromone Production in Relation to Some Endocrine Factors

Merza H Homady

Dean of Faculty of Science, Kufa University,
Kufa, Al-Najaf Al-Ashraf, Iraq

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Corresponding author: Merza H. Homady

✉ merzah.almurshidi@uokufa.edu.iq

Dean of Faculty of Science, Kufa University,
Kufa, Al-Najaf Al-Ashraf, Iraq.

Tel: + 964 (0) 780 183 5580

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The preputial glands are exocrine modified sebaceous glands that are located subcutaneously in the front of the genitals of many rodents such as mice and rats. The gland is surrounded by a capsule of connective tissue, from which trabeculae extend to the interior to divide the parenchymatous tissues into acini, the acini are at different stages of maturation with numerous normal cytoplasmic organelles and healthy oval shaped nuclei. The gland has a long excretory duct with a wide lumen lined by stratified squamous epithelium. The ducts empty into the preputial cavity. The preputial glands are the source of chemical signals (pheromones) that promotes reproduction and behavior of mice. In the house mouse, there are about 40 identified pheromonal compounds in preputial glands secretions, 31 were esters, 2 sesquiterpens, and 7 alcohols. Numerous studies have revealed that preputial glands and urine of male mice are main sources of pheromones. The preputial glands are androgen- dependent organ. Androgen, also called androgenic hormone or testoid, is the broad term for any natural or synthetic compound, usually a steroid hormone that stimulates or controls the development and maintenance of male characteristics in vertebrates by binding to androgen receptors. This includes the activity of the accessory male sex organs and development of male secondary sex characteristics. The primary and most well-known androgen is testosterone which is the product of Dihydrotestosterone (DHT). The activity of preputial glands depended on the Melanocortin 5- Receptor (MC5R), which is one of Melanocortin Receptors (MCRs) are a family of five G protein- coupled receptors (GPCRs; MC1R–MC5R) expressed in diverse tissues, which serve discrete physiological functions. The melanocortin 5- receptors (MCRs) that are activated by melanocortin ligands derived from the pro protein, proopi melanocortin POMC. Many Studies in mice have suggested that MC5R play a role in the generation of pheromones which in turn influences aspects of behavior. High levels of MC5R are found in multiple exocrine tissues where they are thought to regulate the synthesis and secretion of a diverse range of exocrine products.

Contraception may well be seen as the reverse side of the fertility coin, author will discuss the potential of some medicinal plants and especially the Ferula hormone is in affecting both the male and female reproductive tract.

The roles of medicinal plants and their crude extracts are widely utilized in the treatment of male and female infertility. The biological activities and the chemical constituents of many plants have attracted researchers for over a century. A large number of medicinal plants possess spermicidal and semen-coagulating properties in mice and rats where as others possess antioviulatory receptivity blocking and abortifacant activities in laboratory animals. We have shown impairments in the testicular germinal cell layers and the reduction in the seminiferous tubular diameters with a concomitant spermatogenic inhibition and germinal cellular disintegration in mice exposed to *Cinnamomum camphora*, *Mentha longifolia* and Ferula hormonis. Possibly, these effects may have been mediated through the testicular enzymatic alteration by administrated extract.

What is Ferula Hormonis?

Ferula hormonis in Arabic Shirsh Zallouh, is a plant with thin leaves and little white or yellowish flowers belonging to the Umbelliferae family. It grows at more than 8000 feet on Mount Hermon at the borders of Lebanon and Syria. Its roots are eaten by either being soaked in wine or as a liquid solution, or ground into powder and made into capsules or mixed with tea or honey. Commercially it is marketed as a natural product under the name of "sex roots" and is believed to be more powerful than Viagra, producing its effect within 30 minutes from the time of intake without any side effects. In the last five years, the root extracts of this plant has gained overwhelming popularity among Jordanian people and those from neighboring countries of the Middle East due to its potential as an anti-sterility treatment. However, the

benefits of this plant were highly exaggerated. For example, its extracts were used against frigidity and impotence; to increase sexual energy; to enhance circulation for sexual function; stimulate sexual desire; to increase sexual endurance; cure erectile dysfunction; a nervous system activator and tranquilizer. Furthermore, it used against neurasthenia and melancholia; to cauterize human wounds as well as to increase milk production of cows and give energy to goats in the mating season. *F. hormonis* contains a potent cocktail of alkaloids, coumarins, saponins and sterol/terpens. The cytotoxic effects upon the male reproductive tract.

Clues to the mechanism of action

Many researchers mentioned the use of medicinal plants to cure various diseases and the toxicity of their simultaneous use was in dilemma. The nature of the findings, listed below, deserves some speculations as to the potential mechanisms involved: The lower sperm counts, higher percentage of abnormalities and the reduction of activities suggest a direct action of the *F. hormonis* on the tissues within the damaged regions, perhaps at the level of the germinal cells of the testes. Another potential site of action may involve the disruption of a normal process within either the hypothalamic-pituitary axis or gonads, which secondarily produces the observed histological alterations. Treatment with *F. hormonis* exerts produced significant changes in total DNA contents in the testes and many biochemical, hematological parameters indicating that marked physiological disruption

caused by exposure might disturb mitosis in vivo as well as Sertoli cells proliferation. More experiments are necessary to confirm this idea. The administration of ethanolic extracts of *F. hormonis* by mice caused adenocarcinoma in the colon is probably due to multiple attributes, which are certainly dose dependant. Any alteration in estrogen/androgen balance can disturb the co-ordination between gonads and genital or alimentary tracts. According to these results, it is safely said that the pathological changes in the colonic structure are estrogenic motivated. By the virtue of estrogenic activity a large number of medicinal plants have been reported to alter the histological structures of both reproductive and digestive organs. The findings show that *F. hormonis* reduced male and female mice fertility, which indicates that this extract might have a heterogeneous nature, containing both estrogenic and anti-estrogenic components. It cannot be determined whether the reduction in fertility was due to a decrease in the fertilizing ability of the spermatozoa or to an increase in the incidence of preimplantation mortality of the fertilized ova.

In conclusion, the adverse health effects of *F. hormonis* concern mainly the occupational health and risk. It is clear that *F. hormonis* extract has shown the possibility of having an ingredient(s) which might be specific interms of its action as a carcinogenic agent and imposes toxic effects on fertility in male and female mice. These findings encourage further studies that focus on traditional medicinal plants that have the potential to cause sterility.