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Title:

PHARMACOLOGICAL AND CLINICAL PROFILE OF PHEROMONES:

AN OVERVIEW

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Abstract:

Pheromones are chemicals that are secreted in our sweat that release neurotransmitters that directly modify the behaviour of opposite sex, such as triggering sexual excitement or alternatively pheromones may be defined as chemicals released by an organism into its environment enabling it to communicate with other members of its own species. Scientists have long known that these pheromones are natural sex attractants that wield a powerful influence on their mating habits. Studies have shown that people who produce higher than average amounts of pheromones have greater success with members of the opposite sex. Pheromones in humans are postulated to be produced by the apocrine glands. The apocrine glands become functional after reaching puberty which, some believe, could contribute to people developing a sexual attraction for others at that time. Pheromone detection has also been proposed to be the reason why a person can sense "chemistry", or feel an instant attraction or dislike when first meeting someone. In the present article, we have concentrated on pharmacological and clinical profile of pheromones. The aim of present article is to provide in depth knowledge about pheromones, their different types as well as different uses of pheromones.

Keywords: pheromones; sex pheromones; ecto-hormones; chemical messengers

Introduction:

A pheromone is a secreted or excreted chemical factor that triggers a social response in members of the same species. Pheromones are chemicals capable of acting outside the body of the secreting individual to impact the behaviour of the receiving individual. There are alarm pheromones, food trail pheromones, sex pheromones, and many others that affect behaviour or physiology. Their use among insects has been particularly well documented. In addition, some vertebrates and plants communicate by using pheromones. The term "pheromone" was introduced by Peter Karlson and Martin Luscher in 1959, based on the Greek word *pherein* (to transport) and *hormone* (to stimulate).

They are also sometimes classified as ecto-hormones. These chemical messengers are transported outside of the body and result in a direct developmental effect on hormone levels or behavioural change. They proposed the term to describe chemical signals from conspecifics which elicit innate behaviours soon after the German Biochemist Adolf Butenandt characterized the first such chemical, Bombykol (a chemically well-characterized pheromone released by the female silkworm to attract mates). There are physical limits on the practical size of organisms employing pheromones, because at small sizes pheromone diffuses away from the source organism faster than it can be produced, and a sensible concentration accumulates too slowly to be useful. So, bacteria are too small to use pheromones as sex attractants but do use them to determine the local population density of similar organisms and control behaviours that take more time to execute (quorum sensing). Similarly, the simple animal's rotifers are apparently also too small for females to lay down a useful trail, but in the slightly-larger copepods the female leaves a trail that the male can



follow. Human body naturally produces pheromones every day. Individuals who give off higher than average amounts of pheromones usually have greater success with attracting members of the opposite sex, while individuals who don't produce a high level of pheromones attract fewer potential mates. Pheromones are odourless chemicals and they are detected through an organ inside the nose called the vomeronasal organ or VNO. When this organ detects the pheromone, it sends a signal to the hypothalamus part of the brain, which controls human sexual responses.

Some Important Aspects Related To Pheromones:

Pheromones are all completely different. Some products contain androstenol or androsterone, and others contain androstenone and copulins. Pheromone products are available in both unscented and scented versions. Every manufacturer has its own special pheromone mixes. The response to pheromones is a “survival of the species” concept that has been repeatedly detailed in examples of classical conditioning.

In more evolved species like mammals, classical conditioning of the response to pheromones involves at least one other sensory stimulus from the social environment (e.g., an environment that includes other members of the same species). In classical conditioning, one sensory stimulus is repeatedly paired with another sensory stimulus. This repeated pairing allows the second sensory stimulus to cause the same behavioural response that was initially caused by the first. In fact, after the response is conditioned to occur, the second sensory stimulus can then cause the same behavioural response even in the absence of the first stimulus. For example, after visual input is paired with the effect of pheromones on hormones and behaviour, what we see can cause us to respond as if the pheromones were causing changes in the hormones that affect our behaviour. One of the most interesting facts is that Pheromones are not consciously detected by the opposite sex. Pheromone molecules are detected inside the VNO ("vomeronasal organ") that is located in a small cavity inside the nose.

This information is transmitted to Hypothalamus, an almond size gland that is linked to other parts of limbic brain. These are the areas that control emotions and sexual activity. A woman exposed to human pheromones feels an instinctive, powerful attraction and she doesn't know why. This is what's called "chemistry". Even the tiniest amounts of pheromones can trigger these significant reactions;

- Relax Mood
- Happier Feelings
- Ovulation Cycle Change
- Readiness and Willingness to have Sex



Types of Pheromones:

1. Aggregation pheromones

Aggregation pheromones function in defence against predators, mate selection, and overcoming host resistance by mass attack. A group of individuals at one location are referred as aggregation, whether consisting of one sex or both sexes. Male-produced sex attractant have been called aggregation pheromones, because they usually result in the arrival of both sexes at a calling site and increase in density of conspecifics surrounding of the pheromone source. Most sex pheromones are produced by the females and small percentage of sex attractants are produced by males. In recent decades, the importance of applying aggregation pheromones in the management of the boll weevil (*Anthonomus grandis*), stored product weevils (*Sitophilus zeamais*), *Sitophilus granarius*, *Sitophilus oryzae* and pea and bean weevil (*Sitona lineatus*) has been demonstrated. Aggregation pheromones are among the most ecologically selective pest suppression methods. They are not toxic and they are effective at very low concentrations.

2. Alarm pheromones

Some species release a volatile substance when attacked by a predator that can trigger flight (in aphids) or aggression (in ants, bees, termites) in members of the same species. Pheromones also exist in plants: certain plants emit alarm pheromones when grazed upon, resulting in tannin production in neighbouring plants. These tannins make the plants less appetizing for the herbivore.

3. Epideictic pheromones

Epideictic pheromones are different from territory pheromones, when it comes to insects. Fabre observed and noted how "females who lay their eggs in these fruits deposit these mysterious substances in the vicinity of their clutch to signal to other females of the same species they should clutch elsewhere."

4. Releaser pheromones

Releaser pheromones are pheromones that cause an alteration in the behaviour of the recipient. For example, some organisms use powerful attractant molecules to attract mates from a distance of two miles or more. This type of pheromone generally elicits a rapid response but is quickly degraded. In contrast, a primer pheromone has a slower onset and a longer duration. Ex. Rabbit (mothers) release mammary pheromones that trigger immediate nursing behaviour by their babies.

5. Signal pheromones

Signal pheromones cause short term changes; such as, the neurotransmitter release which activates a response. For instance, GnRH molecule functions as a neurotransmitter in rats to elicit lordosis behaviour.



6. Primer pheromones

Primer pheromones trigger a change of developmental events (in which they differ from all the other pheromones, which trigger a change in behaviour).

7. Territorial pheromones

Laid down in the environment, territorial pheromones mark the boundaries of an organism's territory. In cats and dogs, these hormones are present in the urine, which they deposit on landmarks serving to mark the perimeter of the claimed territory. In social seabirds, the preen gland is used to mark nests, nuptial gifts, and territory boundaries with behaviour formerly described as 'displacement activity'.

8. Sex pheromones

In animals, sex pheromones indicate the availability of the female for breeding. Male animals may also emit pheromones that convey information about their species and genotype. At the microscopic level, male copepods can follow a three-dimensional pheromone trail left by a swimming female, and male gametes of many animals use a pheromone to help find a female gamete, for fertilization. Many insect species release sex pheromones to attract a mate, and many lepidopterans (moths and butterflies) can detect a potential mate from as far away as 10 kilometers (6.25 mi). Traps containing pheromones are used by farmers to detect and monitor insect populations in orchards. Pheromones are also used in the detection of oestrus in sows. Boar pheromones are sprayed into the sty, and those sows which exhibit sexual arousal are known to be currently available for breeding. Sea urchins release pheromones into the surrounding water, sending a chemical message that triggers other urchins in the colony to eject their sex cells simultaneously.

Other pheromones:

This classification, based on the effects on behaviour, remains artificial. Pheromones fill many additional functions.

- ❖ Nasonov pheromones (worker bees)
- ❖ Royal pheromones (bees)
- ❖ Calming (appeasement) pheromones (mammals)
- ❖ Necromones consisting of Oleic and Linoleic Acids helping animals identify the presence of dead conspecifics. (Crustaceans and Hexapods)

Uses of Pheromones:

Non-human animals

Pheromones of pest insect species, such as the Japanese beetle and the gypsy moth, can be used to induce much behaviour. As a result, a pheromone trap can be used to trap pests for monitoring purposes, to control the population by creating confusion, to



disrupt mating, as well as to prevent further egg laying. In mammals and reptiles, pheromones may be detected by the vomeronasal organ (VNO), or Jacobson's organ, which lies between the nose and mouth and is the first stage of the accessory. Some pheromones in these animals are detected by regular olfactory membranes.

Humans

Few well-controlled scientific studies have ever been published suggesting the possibility of pheromones in humans.

The best known case involves the synchronization of menstrual cycles among women based on unconscious odor cues (the *McClintock effect*, named after the primary investigator, Martha, of the University of Chicago). This study exposed a group of women to a whiff of perspiration from other women. It was found that it caused their menstrual cycles to speed up or slow down depending on the time in the month the sweat was collected; before, during, or after ovulation. Therefore, this study proposed that there are two types of pheromone involved: "One, produced prior to ovulation, shortens the ovarian cycle; and the second, produced just at ovulation, and lengthens the cycle". However, recent studies and reviews of the McClintock methodology have called into question the validity of her results.

Pheromone action in humans should not be confused with major histocompatibility complex interaction. Using a brain imaging technique, Swedish researchers have shown that homosexual and heterosexual males' brains respond differently to two odors that may be involved in sexual arousal, and that the homosexual men respond in the same way as heterosexual women, though it could not be determined whether this was cause or effect. The study was expanded to include homosexual women; the results were consistent with previous findings meaning that homosexual women were not as responsive to male identified odours, while their response to female cues were similar to that of heterosexual males. According to the researchers, this research suggests a possible role for human pheromones in the biological basis of sexual orientation. In 2008, it was found using functional magnetic resonance imaging that the right orbitofrontal cortex, right fusiform cortex, and right hypothalamus respond to airborne natural human sexual sweat.

Some body spray advertisers claim that their products contain human sexual pheromones which act as an aphrodisiac. In the 1970s, "copulins" were patented as products which release human pheromones, based on research on rhesus monkeys. Subsequently, androstenedione, axillary sweat, and "vomodorins" have been claimed to act as human pheromones. Despite these claims, no pheromonal substance has ever been demonstrated to directly influence human behaviour in a peer reviewed study.



Conclusion:

It may be concluded that pheromones are chemicals produced by a living organisms that transmits a message to other member of same species. There are alarm pheromones, sex pheromones, food trail pheromones and many others. Pheromone is a natural sexual attractant the body produces to subconsciously attract the opposite sex. This natural attractant can also contribute to intense love making during sexual foreplay and sexual intercourse. They may also contribute to the dating phrase, "chemical attraction" that couples experience. Pheromone is subconsciously detected by the (VNO) organ which is three inches inside the nose with nerve connections to the brain. In modern time's they are not as dominant because of personal hygiene and the masking of the scent caused by using deodorants. Although pheromone would probably become more dominant without personal hygiene, it would not be advisable since most people do follow a personal hygiene routine and would be attuned to bad hygiene. The pheromones are not detected consciously as odours, but presumably trigger the hormonal changes that mediate the menstrual cycle. The result of the study showed that uses of pheromones had:

- Increased frequency of dates
- Increased frequency of affectionate gestures
- Increased frequency of sleeping next to a romantic partner
- Increased frequency of foreplay
- Increased frequency of sexual intercourse

References:

1. Karlson P, Luscher M, Pheromones: a new term for a class of biologically active substances, *Nature*, Issue 183, 1959, Pages 55-56.
2. Sobotnik J, Hanus R, Kalinova B, Piskorski R, Cvacka J, Bourguignon T, Roisin Y, (E,E)-Farnesene, an Alarm Pheromone of the Termite *Prorhinotermes canalifrons*, *Journal of Chemical Ecology*, Volume 34, Issue 4, 2008, Pages 478–486.
3. Pantages E, Dulac C, A novel family of candidate pheromone receptors in mammals, *Neuron*, Volume 28, Issue 3, 2000, Pages 835–845.
4. Keverne EB, The vomeronasal organ, *Science*, Volume 286, Issue 5440, 1999, Pages 716–720.
5. McClintock MK, Menstrual synchrony and suppression, *Nature*, Volume 229, Issue 5282, 1971, Pages 244-245.



6. Stern K, McClintock MK, Regulation of ovulation by human pheromones, *Nature*, Volume 392, Issue 6672, 1998, Pages 177-179.
7. Yang Zhengwei, Jeffrey C. Schank, Women Do Not Synchronize Their Menstrual Cycles, *Human Nature*, Volume 17, Issue 4, 2006, Pages 434–447.
8. Wyart C, Webster WW, Chen JH, Wilson SR, McClary A, Khan RM, Sobel N, Smelling a single component of male sweat alters levels of cortisol in women, *The Journal of Neuroscience*, Volume 27, Issue 6, 2007, Pages 1261–1265.
9. Savic I, Heden-Blomqvist E, Berglund H, Pheromone signal transduction in humans: What can be learned from olfactory loss, *Hum Brain Mapp*, Volume 30, Issue 9, 2009, Pages 3057-3065.
10. Anders Winman, Do perfume additives termed human pheromones warrant being termed pheromones? *Physiology & Behaviour*, Volume 82, Issue 4, 2004, Pages 697–701.
11. Charles J. Wysocki, George Preti, Pheromonal Influences, *Archives of Sexual Behaviour*, Volume 27, Issue 6, 1998, Pages 627–641.
12. Berglund H, Lindstrom P, Savic I, Brain response to putative pheromones in lesbian women, *Proc. Natl. Acad. Sci*, Volume 103, Issue 21, 2006, Pages 8269–8274.
13. Zhou Wen, Denise Chen, Encoding human sexual chemosensory cues in the orbitofrontal and fusiform cortices, *J Neurosci*, Volume 25, Issue 53, 2008, Pages 14416–14421.
14. Liberles SD, Buck LB, A second class of chemosensory receptors in the olfactory epithelium, *Nature*, Volume 442, Issue 7103, 2006, Pages 645-650.
15. Pearson H, Mouse data hint at human pheromones, *Nature*, Volume 442, Issue 7102, 2006, Page 495.
16. Hays, Warren S. T, Human pheromones: have they been demonstrated? *Behavioural Ecology and Sociobiology*, Volume 54, 2003, Pages 89-97.