



Contents lists available at ScienceDirect

Journal of Acute Disease

journal homepage: www.jadweb.org



Document heading doi: 10.1016/S2221-6189(13)60140-7

Pheromones and their role as aphrodisiacs: A review

Alok Semwal^{1*}, Ratendra Kumar², Udai Vir Singh Teotia¹, Ramandeep Singh³

¹Department of Pharmacy, Shri Venkateshwara University, Gajraula, U.P (India)

²Meerut Institute of Engineering & Technology, Meerut-250005, UP (India)

³Department of Pharmacy, Himachal Institute of Pharmacy, Paonta Sahib-173025, H.P (India)

ARTICLE INFO

Article history:

Received 28 June 2013

Received in revised form 28 July 2013

Accepted 26 August 2013

Available online 20 December 2013

Keywords:

Pheromone

Aphrodisiacs

Reproduction

Steroids

ABSTRACT

Since the beginning of the human existence on the earth reproductive biology remained a main concern of research because of its importance. It is widely recognized and demonstrated that odors play an important role in mammalian reproduction. A large number of studies have been carried out in humans, in order to investigate possible pheromones, their properties, mechanism of action, and possible receptors for their action. Till now scientific studies indicated that humans use olfactory communication and are even able to produce and perceive certain pheromones. This review article aims to highlight the role of human pheromones as aphrodisiacs

1. Introduction

The term aphrodisiac originated from the Greek word Aphrodite, the Greek god of love, Sex and romance. Aztec and Incan cultures used aphrodisiacs for reproductive purposes they used plant and animal substances like, figs, bananas, chocolate, and cocoa bean. Ancient Asia used insects and animal parts for the same purpose. Aphrodisiacs are the substances which stimulate sexual desire, for e.g., basil, cinnamon, pine nuts, garlic, chilli-pepper, cardamom etc. Sexual desire is controlled by central nervous system which integrates tactile, olfactory, auditory and mental stimuli; Sexual performance which is not always dependant on sexual desire is also called sexual performance or sexual capacity^[1].

First aphrodisiac was human body odor later on it was found that it is caused by pheromones. Humans have

glands at the base of the hair follicles, especially in the armpits and in the genital region, which produce chemicals (pheromones), the odor of which might affect members of the opposite sex. The chemicals are spread over the hair surface and then very efficiently dissipated. Volatile aliphatic acids occur in the normal vaginal secretions of many primates, including humans. Their strong odors (e.g., butyric acid with its smell of rancid butter) have been shown to stimulate male monkeys to increased sexual activity. Many steroidal hormones and related chemicals have a noticeable odor, including chemicals called androsthenones^[2].

Pheromones in animals and insects have been known for a long time. These are the primary communication system for animals used to sense danger, food and mating. In fact animals rely on pheromones for their survival. Human pheromones may be defined as natural chemicals produced by an individual and transferred by air that affects the sexual physiology of another individual. They are believed to send out subconscious scent signals to the opposite sex that trigger very powerful responses. The word pheromone is derived from the Greek word "pherein"– to carry, and "hormon"– to excite. Karlson and Luscher^[3](1959) coined

*Corresponding author: Alok Semwal, Research Scholar, Department of Pharmacy, Shri Venkateshwara University, Gajraula, U.P (India).

Tel: +91-9736295124

E-mail: alokm.pharm01@gmail.com

the term pheromone for the first time. Pheromones are also called ectohormones, meaning chemical messengers that are transported outside the body and have the capability to trigger responses like physiological and behavior changes. Human pheromone detection has also been proposed to be the reason of instant attraction or dislike when first meeting someone. Currently, human pheromones remained ambiguous bioactive compounds, as only a few have been identified. Standard bioassays have suggested that they are nonvolatile, activate vomeronasal sensory neurons and regulate innate social behavior and neuroendocrine release, but unfortunately there is lack of scientific data to proof the following action.

Recent discoveries of potential pheromones reveal that they may be more structurally and functionally diverse than previously defined^[4]. With the progress in recent scientific research it was found that not only the natural scents such as pheromones but also the synthetic smells originated from jasmine, vanilla, pumpkin and cranberry are aphrodisiac in nature and arouses sexual desire. Scientists from worldwide continue to study the effects of foods, herbs and other substances on the body in order to find powerful aphrodisiac agents.

2. Pheromones

Small, volatile organic molecules are of extreme importance among many animals for the transmission of information on sexual availability to members of the opposite sex. Such molecules are called pheromones, after a Greek word meaning "to transfer excitement". The human body also secretes several compounds with strong scent, as well as compounds which can be transformed by bacteria into chemicals with a strong and lingering odor. Pheromones are chemical messengers that are emitted into the environment from the body where they can then activate specific physiological or behavioural responses in other individuals of the same species. According to their nature and mechanism pheromones are of various types, these include primers, releasers, signalers and modulators.

- Primer pheromones typically affect endocrine or neuroendocrine responses such as the onset of puberty, estrus/menstrual cycle timing and onset and pregnancy disruption.
- Releaser pheromones typically elicit a behavioral response. Sexual attractants are the most common examples of releasers.
- Modulator pheromones have been, thus far, uniquely described for humans: These are chemosensory cues that modulate affect or context of other people.
- Signaler pheromones have been discussed as chemical signals that provide a variety of information to the smeller: sex of the sender, reproductive status, age and dominance status of the sender.

In particular, it is assumed that primer pheromones trigger the secretion of GnRH from the hypothalamus, which in turn triggers the release of gonadotropins (LH, FSH) from the pituitary gland. These gonadotropins influence gonadal hormone secretion, e.g. follicle maturation in the ovaries in females, testosterone and sperm production in males^[5].

3. Occurrence of pheromones

One of the first discoveries of pheromones was in the 1930s. Entomologists noticed that female moths have the extraordinary ability to excite male moths even when the males cannot see or hear them. This was the first case when existence of certain type of chemical or fragrance was noticed by the scientists, which was responsible for the sexual activity in moths. They discovered that the males actually smell the fragrance of the females in the air with very sensitive antennae. Eventually the scientists were able to isolate the fragrance and they found out it can stimulate millions of moths with just three hundred millionths of an ounce^[6]. Later on it was determined that pheromones are very potent in nature and even a single molecule of this pheromone was enough to stimulate the receptor cells of the moths. Scientists later discovered that the pheromone was secreted from the abdomen of the moth and was a chemical named bombykol (named after the moth, *Bombyx mori*) and its chemical structure was trans-10-cis-12-hexadecadienol (Figure 1)^[7].

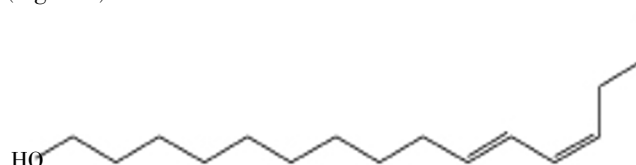


Figure 1. trans-10-cis-12-hexadecadienol.

Some of the most well known and studied pheromones exist in social insects, including honeybees, ants, and termites. The most popular uses of pheromones for these species include the caste system, or individual and class recognition, alarm, and assembly and recruitment^[8].

There are a minimum of 32 compounds just in the head of honeybee queens. Two of the most popular contrasting pheromones in honeybees are 9-keto-2-decenoic acid and 9-hydroxy-2-decenoic acid (Figure 2 and 3).

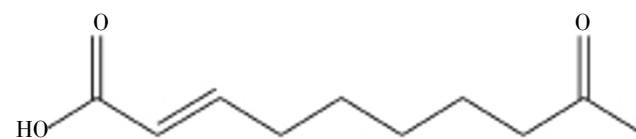


Figure 2. 9-keto-2-decenoic acid.

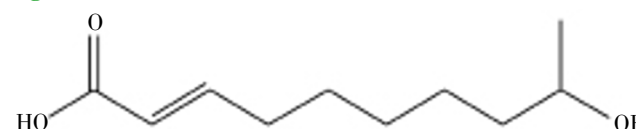


Figure 3. 9-hydroxy-2-decenoic acid.

9-keto-2-decenoic acid

The first one is an inhibitor that operates in conjunction with other body scents and it reduces the tendency of the other worker bees to construct royal cells and to rear new queens, which would be rivals of the mother queen. It also inhibits ovarian development in the workers, which prevents them from becoming rivals to the queen. Every spring the production of this pheromone is slightly lowered to allow the production of a few new queens.

9-hydroxy-2-decenoic acid-

The second pheromone causes clustering and stabilization of worker swarms and it helps to guide the swarms from one nest site to another[9].

Studies have also shown that the 9-ketodecenoic acid is initially transmitted by grooming between bees. This fact of the study is still not well developed, but it leads scientist to believe that other colony odors and pheromones are transferred by grooming[10].

A paper that was published by a psychologist named Martha McClintock claimed the existence of pheromones in human beings. This was a unique type of study may be influenced by the presence of pheromones in insects like moths, honeybees etc. McClintock was actually able to control the speed of the monthly menstrual cycle of women by exposing them to a whiff of sweat from other women. McClintock believes that it is pheromones that control the ovulatory command and that this insight can lead to new insights in human communication and medical application. This study concluded the use of pheromones as fertility enhancers[11].

Later on in the mid 90's various studies and researches was carried out to prove the existence of pheromones in humans, and it was found that apocrine (sweat) glands of human secrete pheromones. They carry characteristic odor. Freshly produced apocrine secretion has no odor while after the exposure to the environment they produces specific odor. Now the question arose that what is the exact cause behind this.

A study by Zeng et al. 1992[12]proved that the microbial conversion causes the odor. Pheromones are chemically similar to hormone dehydroepiandrosterone and are secreted by endocrine glands, apocrine glands occur in the armpits, face, nipples, and anal and genital regions of both sexes. The apocrine glands become functional after reaching puberty, which some believe, could contribute to people developing a sexual attraction for others at that time[13].

The underarms are the ideal location for the dispersion of odours because they are among the warmest parts of the body. This part of the body is embedded with apocrine and sweat glands, and also have strong growth of hair. These well distributed hairs helps to disperse odours and are

protected from excessive evaporation[14]. In a study Zeng et al[15]detected that the major contributors to the male sweaty axillary odour are C6–C11 unsaturated acids, with the most abundant being (E)-3-methyl-2-hexonic acid (3M2H). They could further demonstrate that 3M2H is carried to the skin surface in a non-volatile fashion, bound to a water-soluble precursor (Apocrine Secretion Odour-Binding Protein), where it is liberated by the action of coryneform bacterial[16].

4. Chemosensory systems detecting pheromones

It has been believed for a long time that two chemosensory systems, the main olfactory and the vomeronasal system, were responsible for different functions. The main olfactory system was considered to be responsible for recognizing the conventional volatile odorant molecules, whereas the vomeronasal system was thought to be tuned for sensing pheromones. Recent studies have demonstrated that both chemosensory systems, together with additional olfactory organs, are involved in pheromone detection. In these systems, peripheral chemosensory neurons located in the nasal cavity express distinct families of receptors that are believed to bind pheromones and trigger a cascade of molecular and electrical events that, ultimately, influence some aspects of the social behavior of the individual.

Although the main olfactory and vomeronasal systems share a similar histological organization, they also display relevant differences with regard to the receptor repertoire that they express and to the connections to specific central areas. Each system possesses primary sensory neurons that send axons to second-order neurons (mitral cells) in specific regions of the main olfactory bulb (main olfactory system) or of the accessory olfactory bulb (vomeronasal system). The mitral cells of the main olfactory bulb project to several higher centers including the piriform cortex and the cortical amygdala. Instead, projections from the accessory olfactory bulb only reach the medial amygdala and the posterior-medial part of the cortical amygdala. From here fibers terminate in the hypothalamus either directly or via the bed nucleus of the stria terminalis[16]. Figure 4 is demonstrating schematic diagram showing the anatomical pathways of the rodent vomeronasal and main olfactory systems.



Figure 4. Anatomical pathways of the rodent vomeronasal and main olfactory systems[16].

However, the adult human VNO, in different studies, has been reviewed as non-functional as it contains few neurons and has no sensory function where no cells were shown to express olfactory marker protein, have synaptic contacts or have evidence for a nerve connecting to/from the VNO. In addition, *Trpc2*, essential for vomeronasal signal transduction in some animals, is a pseudogene in human. Perhaps based on the false assumption that mammalian pheromones must work via the vomeronasal organ, some have formulated the following logic: because humans exhibit pheromonal responses they must therefore have a functional VNO, which is a non sequitur. But this does not mean that humans cannot respond to pheromones. As is true for some pheromonal responses in other mammals, the olfactory system can be the route of information input to the brain^[17].

5. Functions of pheromones

Four specific functions of pheromones have been determined: opposite-sex attractants, same-sex repellents, mother-infant bonding attractants and menstrual cycle modulators^[18].

6. Most commonly known human pheromones

A number of human pheromones have been isolated and studied. Some of them have been found effective for attracting members of the opposite sex and some were found aphrodisiac in nature. Most important human pheromones include. 5α -androstenone, androstadienone ($\delta 4, 16$ -androstadien-3-one), androstenol (5α -16-androsten-3 α -ol), androsterone, copulins and Estratetraenol ($estra-1, 3, 5(10), 16$ -tetraen-3-ol)^[20].

6.1. 5α -Androstenone

IUPAC name

($5S, 8R, 9S, 10S, 13R, 14S$)-10,13-dimethyl-1,2,4,5,6,7,8,9,11,12,14,15 dodecahydrocyclopenta[a]phenanthren-3-one (Figure 5).

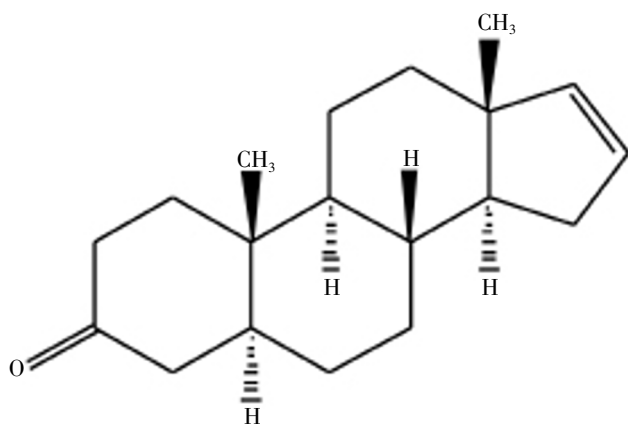


Figure 5. 5α -Androstenone.

Androstenone (5α -androst-16-en-3-one) is a steroid found in both male and female sweat and urine. It is also found in boar's saliva, and in celery cytoplasm. Androstenone was the first mammalian pheromone to be identified. Depending upon the subject, it is reported to be an unpleasant, sweaty, urinous smell, a woody smell, or even a pleasant floral smell^[21-23]. In humans, androstenone also has been suggested to be a pheromone; however, scientific data to support these claims are scant^[24].

Androstenone is a human pheromone that can be also found in pigs. In humans it is present in their sweat and urine and it is being considered as unpleasant smell. However, in small concentrations it is hardly detectable by the average person. In a study conducted by Van Toller and colleagues it was found that people exposed to androstenone undergo physiological changes in skin conductance^[25]. Furthermore, androstenone has also been found to be perceived as more pleasant to men at a woman's time of ovulation. It is hypothesized that this may be a way for a male to detect an ovulating female who would be more willingly to be involved in sexual interaction^[19]. Females are also most sensitive to this pheromone while ovulating. This pheromone is said to be only secreted by males as an attractant for women and is also thought to be a positive effect or for their mood. Depending on where a female is in her menstrual cycle, the pheromones seem to have different effects on women^[14].

So it can be concluded that Androstenone is much more common in males than females and its role is to signal dominance and project aggressive alpha male impression and, therefore, it is often being referred to as "alpha male pheromone". It is supposed to amplify mood^[26,27].

6.2. 3β -Androstenol

IUPAC name

($3R, 5S, 8S, 9S, 10R, 13R, 14S$)-5,10,13-trimethyl-2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradeca hydro-1H-cyclopenta[α]phenanthren-3-ol (Figure 6)

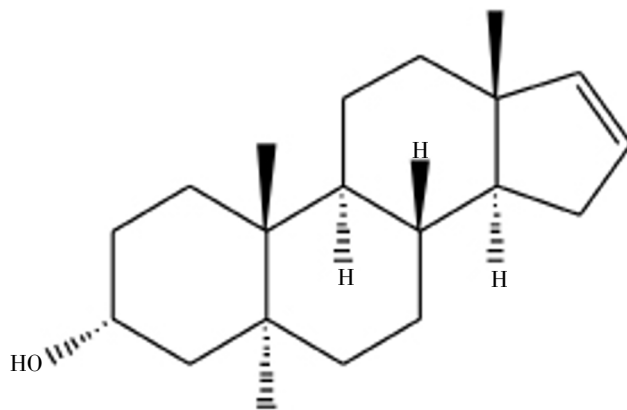


Figure 6. 3β -Androstenol.

Androstenol (5α -Androst-16-en-3 α -ol) is a sex pheromone having musk-like odor and found in smaller quantities in human sweat glands but the molecular targets of its pheromonal activity are still unknown. It is analogous to sex hormones yet has minimal or no androgenic

activity. Androstenol is secreted by the adrenal gland into systemic circulation in humans. A study conducted by Rafal M. Kaminski *et al.* 2006^[28] showed that androstenol has neurosteroid-like activity as a GABA_A receptor modulator. In whole-cell recordings from cerebellar granule cells, androstenol (but not its 3 β -epimer) caused a concentration-dependent enhancement of GABA-activated currents (EC₅₀, 0.4 μ M in cultures; 1.4 μ M in slices) and prolonged the duration of spontaneous and miniature inhibitory postsynaptic currents. The various actions of androstenol in the whole-animal models are consistent with its activity as a GABA_A receptor modulator. GABA_A receptors could represent a target for androstenol as a pheromone.

Androstenol is the putative female pheromone^[29]. In a study by Kirk-Smith, people wearing surgical masks treated with androstenol or untreated were shown pictures of people, animals and buildings and asked to rate the pictures on attractiveness. Individuals with their masked treated with androstenol rated their photographs as being “warmer” and “more friendly”^[30].

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 McClintock, of the University of Chicago)^[31]. 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^[31].

6.3. Androsterone

IUPAC name

(3R,5S,8R,9S,10S,13S,14S)-3-hydroxy-10,13-dimethyl-1,2,3,4,5,6,7,8,9,11,12,14,15,16-tetradecahydrocyclopenta[a]phenanthren-17-one (Figure 7)

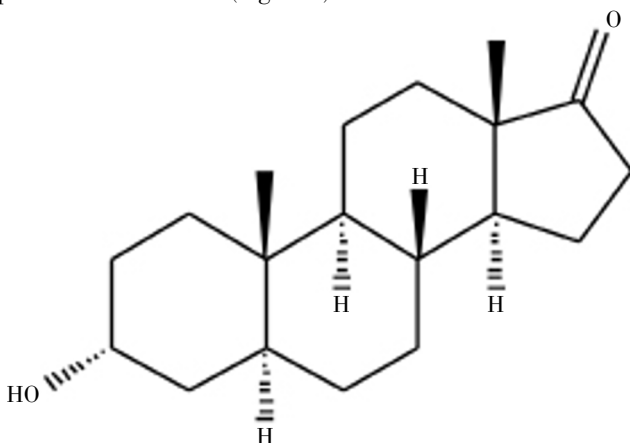


Figure 7. Androsterone.

Androsterone (3 α -hydroxy-5 α -androstan-17-one) is an endogenous steroid hormone and weak androgen with a potency that is approximately 1/7th that of testosterone^[35]. It was first isolated in 1931, by Adolf Friedrich Johann Butenandt and Kurt Tscherning. They distilled over 17 000 litres (3 700 imp gal; 4 500 US gal) of male urine, from which they got 50 milligrams (0.77 g) of crystalline androsterone, which was sufficient to find that the chemical formula was very similar to estrone.

6.4. Androstadienone

IUPAC name

(8S,9S,10R,13R,14S)-10,13-dimethyl-1,2,6,7,8,9,11,12,14,15-decahydrocyclopenta[a]phenanthren-3-one (Figure 8).

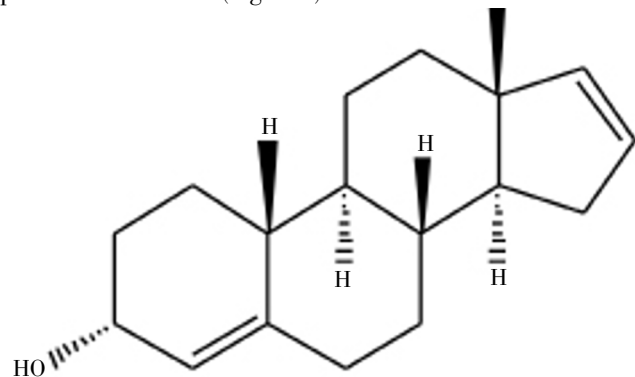


Figure 8. Androstadienone.

Another putative pheromone is androstadienone. Androstadienone (androsta-4,16,-dien-3-one) often referred to as A1 or vomeropherin, is a human pheromone, acting on the chemicals in the brain that are thought to affect mood and attention in women and homosexual men. It is not as smelly as androstenone but still detectable when present in higher concentrations. Like androsterone it is a metabolite of the male sex hormone testosterone which is also common in women. In addition to affecting mood and attention, androstadienone was shown to increase women's heart rate, decrease breathing frequency and help manage premenstrual stress syndrome. Hence, this “love pheromone” is often used to increase feelings of affection, intimacy and comfort in women^[36].

This steroid seems to affect the limbic system and causes a positive reaction in women, often improving their moods^[37]. Responses to androstadienone are dependent on the individual and the environment they are in^[29]. Androstadienone negatively influences the perception of pain in women^[38]. Women tend to react positively after androstadienone presentation while men are more negative. In an experiment by Hummer and McClintock, androstadienone or a control odor was put on the upper lips of fifty males and females and they were tested for four different effects of the pheromone: 1) automatic

attention towards positive and negative facial expressions, 2) the strength of cognitive and emotional information as distracters in a simple reaction time task, 3) relative attention to social and nonsocial stimuli (i.e. neutral faces), and 4) mood and attentiveness in the absence of social interaction. The androstadienone was found to draw attention towards emotional facial expressions. Those treated with androstadienone drew more attention to emotional words while it did not increase attention to neutral faces. These data suggest that androstadienone increases attention to emotional information resulting a feeling of being more focused. It is thought that androstadienone is a modulator on how the mind attends and processes information instead of being a mood-alerter^[38].

6.5. Copulins^[39]

IUPAC name

(5S,8R,9S,10S,13R,14S)-10,13-dimethyl-1,5,6,7,8,9,10,11,12,13,14,15-dodecahydro-2H-cyclopenta[a]phenanthren-3(4H)-one (Figure 9)

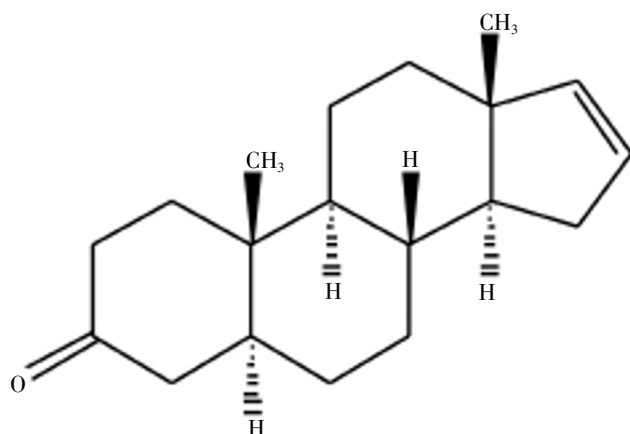


Figure 9. Copulins.

Copulins are chemicals secreted by a female's vagina. Chemically copulins are volatile C₂-C₅ aliphatic acids ^[40]. Huggins and Preti *et al.* 1976^[41] studied the chemical composition of copulins in 12 patients for 44 ovulatory cycles by means of gas chromatography tandem with mass spectroscopy to identify organic volatile components. These vaginal secretions contain mixture of aliphatic acids, alcohol, hydroxy ketones and aromatic compounds.

Research since the mid to late 90 s has proven that copulins can affect and even control a male's brain. They have been shown to increase testosterone levels in men by 150% (Astrid Jutte study). This increase in testosterone may cause feelings of arousal in men if a woman is present. It is said that once a man smells copulins on a woman she is deemed to be more attractive.

Whether or not human vaginal secretions contain a kind of sex pheromone (copulin) influencing male perception of females and inducing hormonal changes in males, is still

debated. Human vaginal secretions contain various short chain (C₂-C₆) fatty acids, with predominated acetic acid suggesting a possible correlation with the rise and fall of hormone levels during the menstrual cycle. To verify this, Waltman *et al.* 1973^[42] collected vaginal samples by tampon from 50 healthy young women, demonstrating that volatile aliphatic acids were increased during the late follicular phase of the cycle and declined progressively during the luteal phase, where women on oral contraceptives had lower amounts of volatile acids and did not show rhythmic changes in acid content during their menses.

In addition, Keith *et al.* 1975^[43] determined the odour composition of vaginal secretions before and after coitus using a condom to prevent male secretions or seminal fluid from entering vaginal secretions. They estimated 13 odourous compounds occurred regularly where components with acidic odour appeared at lower retention rates in post-coital samples concluding that differences exist in the odours of preand post-coital vaginal secretions.

6.6. Estratetraenol

(8S,9S,13R,14S)-13-methyl-7,8,9,11,12,13,14,15-octahydro-6H-cyclopenta[a]phenanthren-3-ol (Figure 10)

Estratetraenol, also known as estra-1,3,5(10),16-tetraen-3-ol, is a chemical compound produced by women that has been described as having pheromone-like activities in primates^[44, 45], including humans^[46-49]. It is derivative of the sex hormone estradiol, an estrogen, yet has no known estrogenic effects.

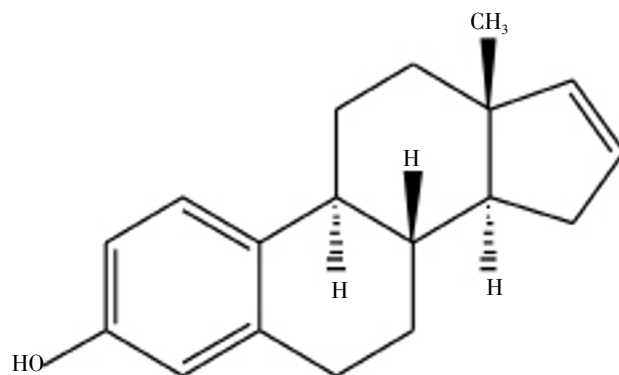


Figure 10. Estratetraenol.

7. Pheromone effects on human reproductive behaviour

From the past several years scientists of worldwide are busy in studying the effects of pheromones on human reproductive behaviour. In order to prove their effect several experiments and studies have been carried out. The following Table 1 consists of some of the studies and their observations which will defiantly help to understand the effect of pheromones.

Table 1.
Pheromones and their effects.

S. no	Study	Observation	References
1.	A group of women were exposed to a whiff of perspiration from armpits of other women.	Synchronization of the menstrual cycles among women based on unconscious odour cues (McClintock effect). This caused their menstrual cycles to speed up or slow down depending on the timing of when the sweat was collected; before, during, or after ovulation.	[31]
2.	Men secrete musk-like substances that women are maximally sensitive to during ovulation coupled with a noticeable increase in coitus during this period.	This phenomenon might be responsible for women's reputed tendency for unusual foods during pregnancy and menses.	[50]
3.	In a study the ability of sleeping babies to differentiate between pads worn by their own or by strange mothers was tested to find the reason that if the baby imprints on its mother's odour, or that the mother unconsciously marks her baby with a distinctive scent.	This is supported by the common observation that a child rejects his favourite blanket or stuffed toy after it has been washed, presumably because it has lost a specific odour acquired in previous contacts.	[50]
4.	Extracted underarm secretions from pads worn by men was placed under the noses of women volunteers while monitoring serum LH and emotion/mood.	The putative male pheromone(s) was demonstrated to advance the onset of the next peak of LH after its application, with reduced tension and increased relaxation, suggesting that male axillary secretions had constituent(s) that might act as modulator pheromones.	[51]
5.	Application of male axillary secretions to the upper lips of female.	Volunteers had a regulatory effect on their menses.	[52]
6.	The girls in stepfather-present homes experienced faster puberty than girls in single-mother homes.	The results showed that the smell of androstadienone of male sweat maintains higher levels of cortisol in females and therefore The younger the daughter when the new male arrived on the scene, the earlier her pubertal maturation.	[53]
7.	Skin conductance in volunteers exposed to androstenone was higher than that of non-exposed volunteers.	The study Provided evidence of the physiological effects of pheromone exposure.	[54]
8.	Males and females were asked to rate vignettes of a fictional target male and female using semantic differentials, and to provide a self-assessment of mood. The test materials, sealed into plastic bags, were either impregnated with androstenol, androstenone, a synthetic musk control, or a no-odour control.	Females exposed to androstenone produced a lower sexual attractiveness rating of the target male, while males exposed to androstenol perceived the male targets to be More sexually attractive.	[55]
9.	In a study it was found that females rated androstenone differently at various phases of their menstrual cycle. Contraceptive pill use appeared to influence female perception of androstenone.	The results suggested that the use of contraceptive pills may affect smell sensitivity or gonadal hormone levels, disrupting pheromone detection.	[56]
10.	Relation between menstrual synchrony and the ability to smell putative pheromones, 3alpha-androstenol and 5alpha-androstenone, among 64 women living together in a college dormitory was studied and the results indicated that twenty four (38%) of them became synchronized with roommates within three months.	Indicating that women who showed menstrual synchrony had a higher sensitivity to 3alpha-androstenol but not necessarily to 5alphaandrostenone.	[57]
11.	Shinohara et al examined the effect of axillary compounds collected from women in the follicular phase (FP), ovulatory phase (OP) treated with isopropyl alcohol (IPA) on pulsatile secretion of serum LH. The recipients were not exposed to either axillary compounds or to IPA for the first 4 h and were exposed to FP or OP compounds, or to IPA, during the next 4 h.	The frequency of LH pulse was increased by FP compounds and was decreased by OP compounds, but was not changed by IPA.	[58]
12.	Watanabe et al investigated changes of olfactory perception during the menstrual cycle using cyclopentadecanolide vapour.	The results obtained from 18 trials showed that olfactory contrast was significantly enhanced at the ovulatory and/or menstrual phases.	[59]
13.	One of the most cited studies on signalling effects of putative pheromones indicates that, in a dentist waiting room, females seem to use seats sprayed with androstenone more frequently than expected by chance.	The results of the study indicated that the choice, was directly related to individual androstenone sensitivity, and may thus be a simple matter of olfactory attraction.	[60]
14.	A study by Saxton <i>et al</i> [43] suggested that women exposed to androstadienone judged men who were physically present to be more attractive		[61]
15.	Women engage in sexual intercourse about six times more frequently and are much more likely to have an orgasm at the time of ovulation. During and in the 2–3 d after menses, they were several times less likely to have sexual intercourse or have an orgasm.	Coupled with women's odour sensitivity, these results could indicate a possible pheromonal trigger for sexual behaviour. More frequent sexual activity during the ovulation period	[62]
16.	In a study it was found that positive mood of females in response to androstadienone improved in combination with a male tester, but not with a female tester.		[63]
17.	Doty <i>et al.</i> 1975 reported the difference in vaginal odour between the ovulation time and other times. They observed the smell emitted at the time of ovulation was more acceptable to men.	Attraction to such smell may be responsible for coitus.	[64]
18.	Keith <i>et al.</i> 1975 observed a difference in odor of pre and post coital vaginal secretion.	They believed pheromone exuded from women on the day of ovulation, attracted men.	[65]

8. Conclusion

Synchronization of the menstrual cycles among women when a group of women were exposed to a whiff of perspiration from armpits of other women, more frequent sexual activity during the ovulation period, special sensitivity of woman's for the seats sprayed with androstenone, increased skin conductance in volunteers exposed to androstenone in comparison to that of non-

exposed volunteers and application of male axillary secretions to the upper lips of female and the regulatory effect on their menses and several other evidences like these indicate the presence of pheromones in human as well as animals. By these studies and their responses it is evident that the pheromones have the potential to influence human behaviour and physiology. Chemosensory systems, together with additional olfactory organs, are involved in pheromone detection. Studies also indicate that in these systems,

peripheral chemosensory neurons located in the nasal cavity express distinct families of receptors that are believed to bind pheromones and trigger the sexual response in humans. It is said that Aphrodisiacs are the agents which arouses the sexual desire so it can be concluded that pheromones acts as aphrodisiacs the presence of which in both male and females is responsible for the human physiological behavior and sexual activity.

Conflict of interest statement

We declare that we have no conflict of interest. The authors alone are responsible for the content and writing of the paper.

Acknowledgment

The authors are thankful to the authorities of Department of Pharmacy, Shri Venkateshwara University, Gajraula, U.P for providing support to the study and other necessary facility like internet surfing, library and other technical support to write this review article.

References

- [1] Zamble A, Sahpaz S, Brunet C, Bailleul F. Effects of *Microdesmis keayana* roots on sexual behavior of male rats. *Phytomedicine* 2008; **15**(8): 625–629.
- [2] Rodrigues RJ. Aphrodisiacs through the ages: The Discrepancy Between Lovers' Aspirations and Their Desires: Three Millenia of Search and Experimentation. A Historical Review Especially Researched for the Enlightenment and Entertainment of the Participants of the Amazon 2000; Boat Cruise, Organized by Dr. Heinz Gruber.
- [3] Karlson P, Luscher M. Pheromones: a new term for a class of biologically active substances. *Nature* 1959; **183**(4653): 55–56.
- [4] Stowers L, Marton TF. What is a pheromone? Mammalian pheromones reconsidered. *Neuron* 2005; **46**: 699–702.
- [5] Grammer K, Fink B, Neave N. Human pheromones and sexual attraction. *Eur J Obstet Gynecol Reprod Biol* 2005; **118**(2): 135–142.
- [6] Following our noses. *Time Magazine* 1998; **151**: 73–72.
- [7] Wilson, Edward O. *Sociobiology: The Abridged Edition*. Harvard University: Belknap Press of Harvard University Press; 1980, p. 93.
- [8] Wilson, Edward O. *Sociobiology: The Abridged Edition*. Harvard University: Belknap Press of Harvard University Press; 1980, p. 105.
- [9] Wilson, Edward O. *Sociobiology: The Abridged Edition*. Harvard University: Belknap Press of Harvard University Press; 1980, p. 97–107.
- [10] Wilson, Edward O. *Sociobiology: The Abridged Edition*. Harvard University: Belknap Press of Harvard University Press; 1980, p. 104.
- [11] Kathleen S, Martha K. McClintock. Regulation of ovulation by human pheromones. *Nature* 1998; **392**: 177–179.
- [12] Zeng, X–N, Leyden JJ, Brand JG, Spielman AI, McGinley K, Preti GJ chem. An investigation of human apocrine gland secretion for axillary odor precursors. *Ecol* 1992; **18**: 1039.
- [13] Cohn BA. In search of human skin pheromones. *Arch Dermatol* 1994; **130**: 1048.
- [14] Taymour Mostafa, Ghada E Khouly, Ashraf Hassan. Pheromones in sex and reproduction: Do they have a role in humans. *J Adv Res* 2012; **3**: 1–9.
- [15] Zeng X–N, Leyden JJ, Lawley HJ, Sawano K, Nohara I, Preti G. Analysis of characteristic odors from human male axillae. *J Chem Ecol* 1991; **17**: 1469–1492.
- [16] Spielman AI, Zeng X–N, Leyden JJ, Preti G. Proteinaceous precursors of human axillary odor: isolation of two novel odor–binding proteins. *Experientia* 1995; **51**: 40–47.
- [17] Roberto Tirindelli, Michele Dibattista, Simone Pifferi, Anna Menini. From pheromones to behavior. *Physiol Rev* 2009; **89**(3): 921–956.
- [18] Baxi KN, Dorries KM, Eisthen HL. Is the vomeronasal system really specialized for detecting pheromones? *Trends Neurosci* 2006; **29**: 1–7.
- [19] Cutler WB. Human sex–attractant pheromones: discovery, research, development, and application in sex therapy. *Psychiat Ann* 1999; **29**: 54–59.
- [20] Karl Grammer, Bernhard Finka, Nick Neaveb. Human pheromones and sexual attraction. *Eur J Obstet Gynecol Reprod Biol* 2005; **118**: 135–142.
- [21] Bettina M. Pause. Are androgen steroids acting as pheromones in humans? *Physiol Behav* 2004; **83**: 21–29.
- [22] Wysocki CJ, Dorries KM, Beauchamp GK. Ability to perceive androstenone can be acquired by ostensibly anosmic people. *Proc Natl Acad Sci U S A* 1989; **86**(20): 7976–7978.
- [23] Steenhuysen J. Sniffers' genes dictate if sweat smells sweet. *New Scientist* 2007.
- [24] Steenhuysen J. Stinky? It's not his sweat, it's your nose". *Sci Am* 2007.
- [25] Kirk–Smith MD, Booth DA. Effect of androstenone on choice of location in others' presence. In: H. van der Starre (Ed.). *Olfaction and Taste VII*. London: Information Retrieval Ltd; 1980, p. 397–400.
- [26] C. Van Toller; Kirk–Smith M, Wood N, Lombard J, Dodd GH. Skin conductance and subjective assessments associated with the odour of 5– α –androstand–3–one. *Biol Psychol* 1983; **16**(1–2): 85–107.
- [27] Anonymous. Androstenone. [Online]. Available from: <http://www.pheromones4u.com/androstenone.html> [Accessed on 2012].
- [28] Bruce Boyd. Androstenone. [Online]. Available from: <http://pherolibary.com/androstenone/421> [Accessed on 2011].
- [29] Rafal M. Kaminski, Herbert Marini1, Pavel I. Ortinski, Stefano

- Vicini, Michael A. Rogawski. The pheromone androstenol (5 α -Androst-16-en-3 α -ol) is a neurosteroid positive modulator of GABAA receptors. *J Pharm Exp Ther* 2006; **317**: 2694-2703.
- [30] Mostafa T, Khouly GE, Hassan A. Pheromones in sex and reproduction: Do they have a role in humans? *J Adv Res* 2012; **3**: 1-9.
- [31] Michael KC. Human social attitudes affected by androstenol. *Res Commun Psychol Psychiatry Behav* 1978; **3**(4): 379-384.
- [32] McClintock MK. Menstrual synchrony and suppression. *Nature* 1971; **229**(5282): 244-245.
- [33] Stern K, McClintock MK. Regulation of ovulation by human pheromones. *Nature* 1998; **392**(6672): 177-179.
- [34] Yang Zhengwei, Jeffrey C. Schank. Women do not synchronize their menstrual cycles. *Hum Nat* 2006; **17**(4): 434-447.
- [35] Strassmann BI. Menstrual synchrony pheromones: cause for doubt. *Hum Reprod* 1999; **14**(3): 579-580.
- [36] Thomas Scott. Concise encyclopedia biology. Walter de Gruyter 1996; 49.
- [37] Anonymous. Androstadienone. [Online]. Available from: <http://www.pheromones4u.com/androstadienone.html> [Accessed on 2012].
- [38] Warren ST Hays. Human pheromones: have they been demonstrated? *Behav Ecol Sociobiol* 2003; **54**(2): 98-97.
- [39] Tom A. Hummer. Putative human pheromone androstadienone attunes the mind specifically to emotional information. *Horm Behav* 2009; **44**(4): 548-559.
- [40] Taymour Mostafa, Khouly Ghada El, Hassan Ashraf. Pheromones in sex and reproduction: Do they have a role in humans? *J Adv Res* 2012; **3**(1): 1-9.
- [41] Michael RP, Bonsall RW, Warner P. Human vaginal secretions: Volatile fatty acid content. *Science* 1974; **186**: 1217.
- [42] Huggins GR, Preti G. Volatile constituents of human vaginal secretions. *Am J Obstet Gynecol* 1976; **126**: 129.
- [43] Waltman R, Tricomi V, Wilson Jr GE, Lewin AH, Goldberg NL, Chang MM. Volatile fatty acids in vaginal secretions: human pheromones? *Lancet* 1973; **2**: 496.
- [44] Keith L, Draunieks A, Krotoszynski BK. Olfactory study: human pheromones. *Arch Gynacol* 1975; **218**: 203-204.
- [45] Thyssen B, Elliott WH, Katzman PA. Identification of estradiol, 1,3,5(10),16-tetraen-3-ol (estratetraenol) from the urine of pregnant women (1). *Steroids* 1968, **11**(1): 73-87.
- [46] Laska M, Wieser A, Salazar LT. Sex-specific differences in olfactory sensitivity for putative human pheromones in nonhuman primates. *J Comp Psychol* 2006; **120**(2): 106-102.
- [47] Jacob S, Hayreh DJ, McClintock MK. Context-dependent effects of steroid chemosignals on human physiology and mood. *Physiol behav* 2001; **74**(1-2): 15-27.
- [48] Savic I, Berglund H, Gulyas B, Roland P. Smelling of odorous sex hormone-like compounds causes sex-differentiated hypothalamic activations in humans. *Neuron* 2001; **31**(4): 661-668.
- [49] Berglund H, Lindström P, Savic I. Brain response to putative pheromones in lesbian women. *Proc Natl Acad Sci U S A* 2006; **103**(21): 8269-8274.
- [50] Berglund H, Lindström P, Dhejne-Helmy C, Savic I. Male-to-female transsexuals show sex-atypical hypothalamus activation when smelling odorous steroids. *Cereb Cortex* 2008; **18**(8): 1900-1908.
- [51] Russell MJ. Human olfactory communication. *Nature* 1976; **260**: 520-522.
- [52] Preti G, Cutler WB, Garcia CR, Huggins GR, Lawley HJ. Human axillary secretions influence women's menstrual cycles: the role of donor extract of females. *Horm Behav* 1986; **20**: 474-482.
- [53] Cutler WB, Preti G, Krieger A, Huggins GR, Garcia CR, Lawley HJ. Human axillary secretions influence women's menstrual cycles: the role of donor extract from men. *Horm Behav* 1986; **20**: 463-473.
- [54] Ellis BJ, Garber J. Psychosocial antecedents in variation in girls' pubertal timing: maternal depression, stepfather presence, and marital and family stress. *Child Dev* 2000; **71**: 485-501.
- [55] Van Toller C, Kirk-Smith M, Lombard J, Dodd GH. Skin conductance and subjective assessments associated with the odour of 5 α -androst-16-en-3 α -ol. *Biol Psychol* 1983; **16**: 85-107.
- [56] Filsinger EE, Braun JJ, Monte WC. An examination of the effects of putative pheromones on human judgements. *Ethol Sociobiol* 1985; **6**: 227-236.
- [57] Grammer K. 5 α -Androst-16-en-3 α -ol: a male pheromone? A brief report. *Ethol Sociobiol* 1993; **14**: 201-208.
- [58] Morofushi M, Shinohara K, Funabashi T, Kimura F. Positive relationship between menstrual synchrony and ability to smell 5 α -androst-16-en-3 α -ol. *Chem Senses* 2000; **25**: 407-411.
- [59] Shinohara K, Morofushi M, Funabashi T, Kimura F. Axillary pheromones modulate pulsatile LH secretion in humans. *Neuroreport* 2001; **12**: 893-895.
- [60] Watanabe K, Umezu K, Kurahashi T. Human olfactory contrast changes during the menstrual cycle. *Jpn J Physiol* 2002; **52**: 353-359.
- [61] Kirk-Smith MD, Booth DA. Effect of androst-16-en-3 α -ol on choice of location in others' presence. In: van der Starre H, editor. *Olfaction and Taste, vol. VII*. London: IRL Press; 1980, p. 389-392.
- [62] Saxton TK, Lyndon A, Little AC, Roberts SC. Evidence that androstadienone, a putative human chemosignal, modulates women's attributions of men's attractiveness. *Horm Behav* 2008; **54**: 597-601.
- [63] Jacob S, Hayreth DJS, McClintock MK. Context-dependent effects of steroid chemosignals on human physiology and mood. *Physiol Behav* 2001; **74**: 15-27.
- [64] Doty RL, Ford M, Preti G, Huggins GR. Changes in the intensity and pleasantness of human vaginal odours during menstrual cycle. *Science* 1975; **190**(4221): 1316-1318.
- [65] Keith L, Draunieks A, Krotoszynski BK. Olfactory study: Human pheromones. *Arch Gynecol Obstet* 1975; **18**: 203-204.