**The Mechanism of Perceiving Human Pheromones Through a Non-functional Vomeronasal Organ**

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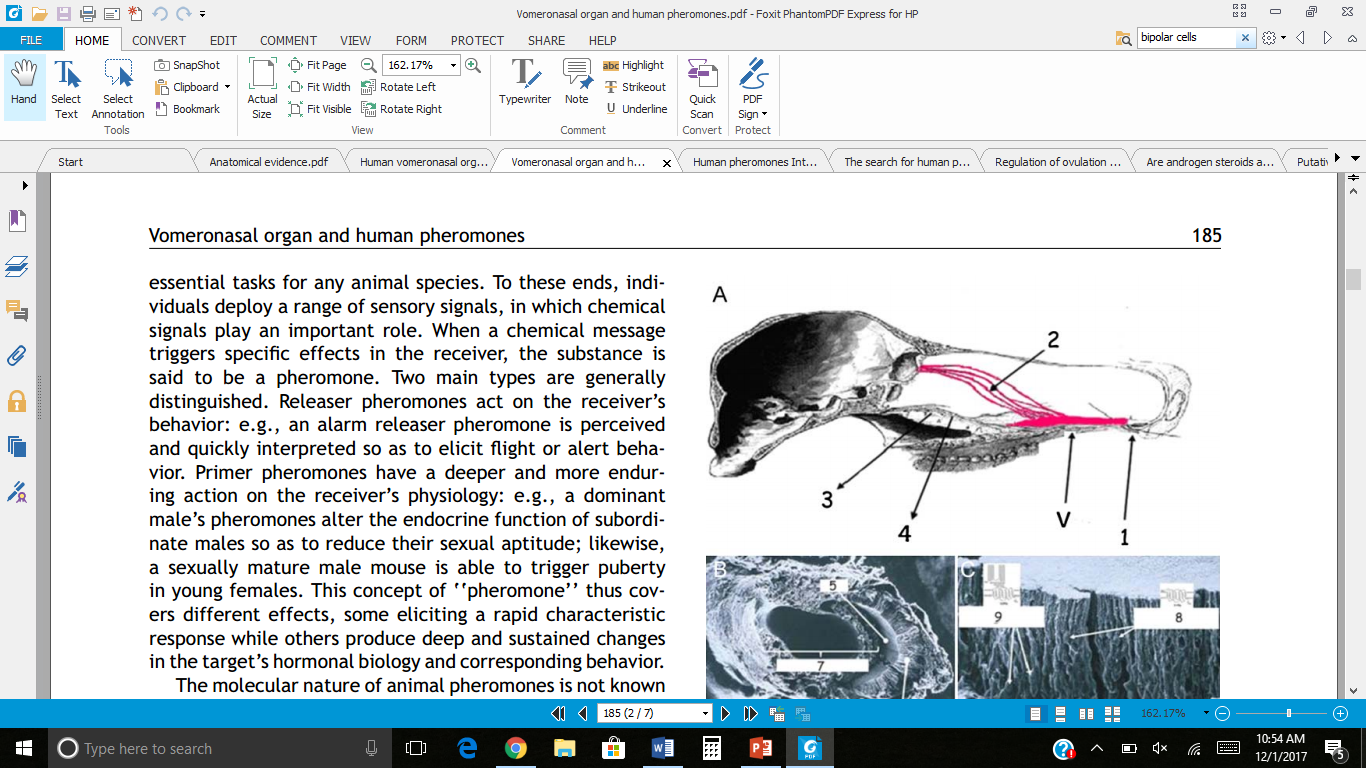
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**Abstract**

Scientists have an ongoing debate arguing that humans do/do not have a vomeronasal organ and that humans do/do not use pheromones to communicate with each other. The vomeronasal organ has been identified functional in fetuses and non-functional in adults. After 14-28 weeks of development, the nerve that connects the vomeronasal organ to the accessory olfactory bulb diminishes. It is unclear how humans can still respond to sex steroids, the equivalent of a human pheromone, when they have a nonchemosensory vomeronasal organ. Androstadienone and estratetraenol have been proven to improve men’s attractiveness to women and women’s attractiveness to men, respectively. Further research must be performed to determine how humans are perceiving these sex steroids and if we need to redefine “pheromone” for this phenomenon observed in humans.

**Introduction**

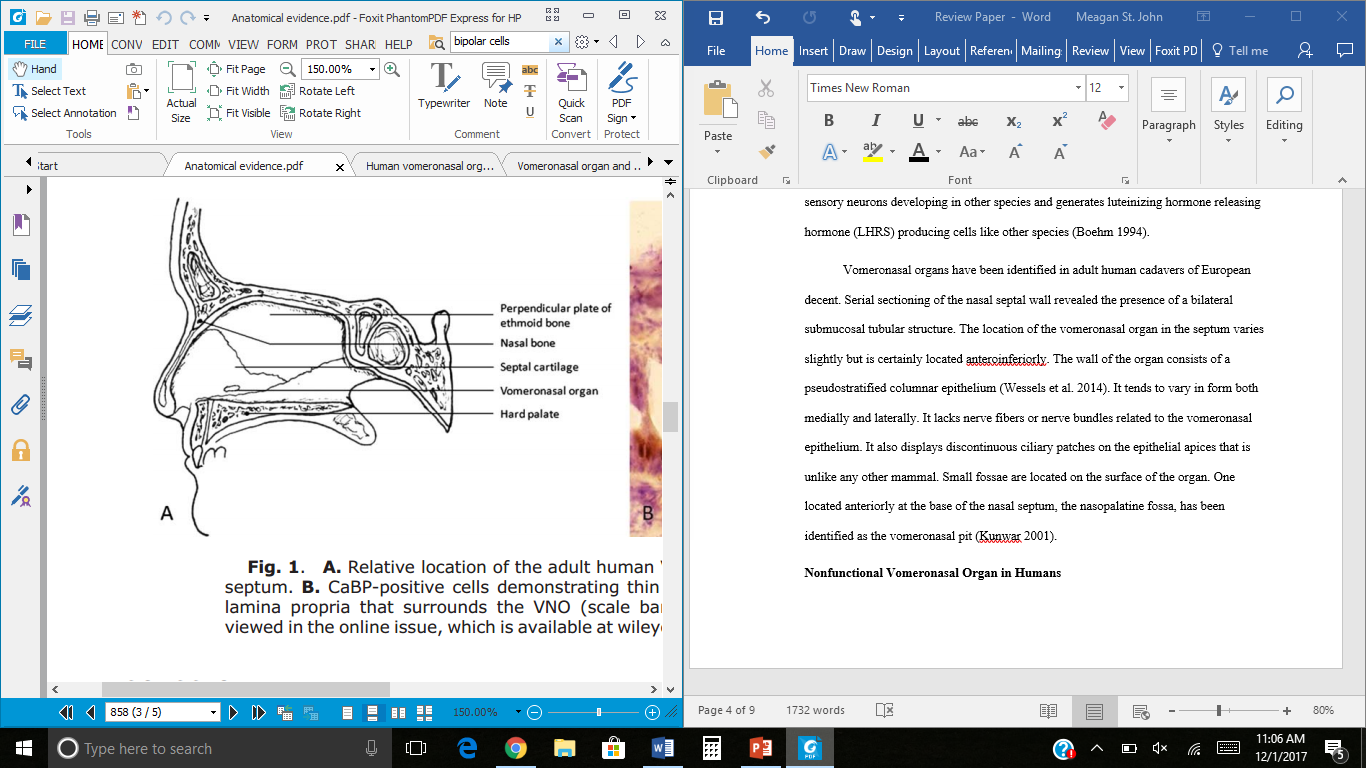
Scent is detected through the olfactory bulb. Air enters the nasal cavity and takes a hairpin turn to stimulate olfactory receptors, then sends the signals to the central nervous system. Humans have a sophisticated sense of smell that often only require a few molecules for activation of the olfactory neurons. The olfactory bulb works alongside the vomeronasal organ in many vertebrates. The vomeronasal organ is in the roof of the mouth of most amphibians, reptiles, and mammals. It is responsible for chemical communication as well as many behavior and physiological responses. In snakes, the vomeronasal organ is essential for tracking prey (Halpern 1987). This communication is possible through chemoreception of pheromones.

 Pheromones are chemical signals that are released by an individual that is said to affect other individuals of the same species’ behavior or physiology. The two main types are releaser pheromones, which act on the receiver’s behavior, and primer pheromones, which have a deeper and more enduring action on the receiver’s physiology (Trotier 2011). In most mammals, pheromones are sensed in the vomeronasal organ, which is situated in the nasal cavity (Figure 1). These sensory signals are sent via the accessory olfactory bulb to the medial amygdala, followed by the stria terminalis, to reach the anterior hypothalamus. However, in ferrets and pigs, an alternative pathway via the main olfactory bulb has been suggested. It is uncertain whether and how possible pheromone signals may be mediated in humans, because the accessory olfactory bulb diminishes after the fetal period. (Savic et. al 2001). The presence of a functional vomeronasal organ in humans has also been a widely controversial topic. When it was first identified by Ludvig Jacobson in the 1810s, he determined that the organ appeared to be vestigial in humans, although functional in mammals (Trotier 2011). Recent research has started the conversation if there is a presence or absence of the organ, and if it is functional if present.

**Figure 1. Location of a vomeronasal organ (V) in the nasal cavity of a deer, after the original drawing by Ludvig Jacobson.** The opening of the organ is near the nasopalatine duct (1). The vomeronasal neuron axons (2) transmit information to the accessory olfactory bulbs behind the main olfactory bulbs. The organ is vascularized (3) and innervated by sympathetic/parasympathetic fibers (4) (Trotier 2011).

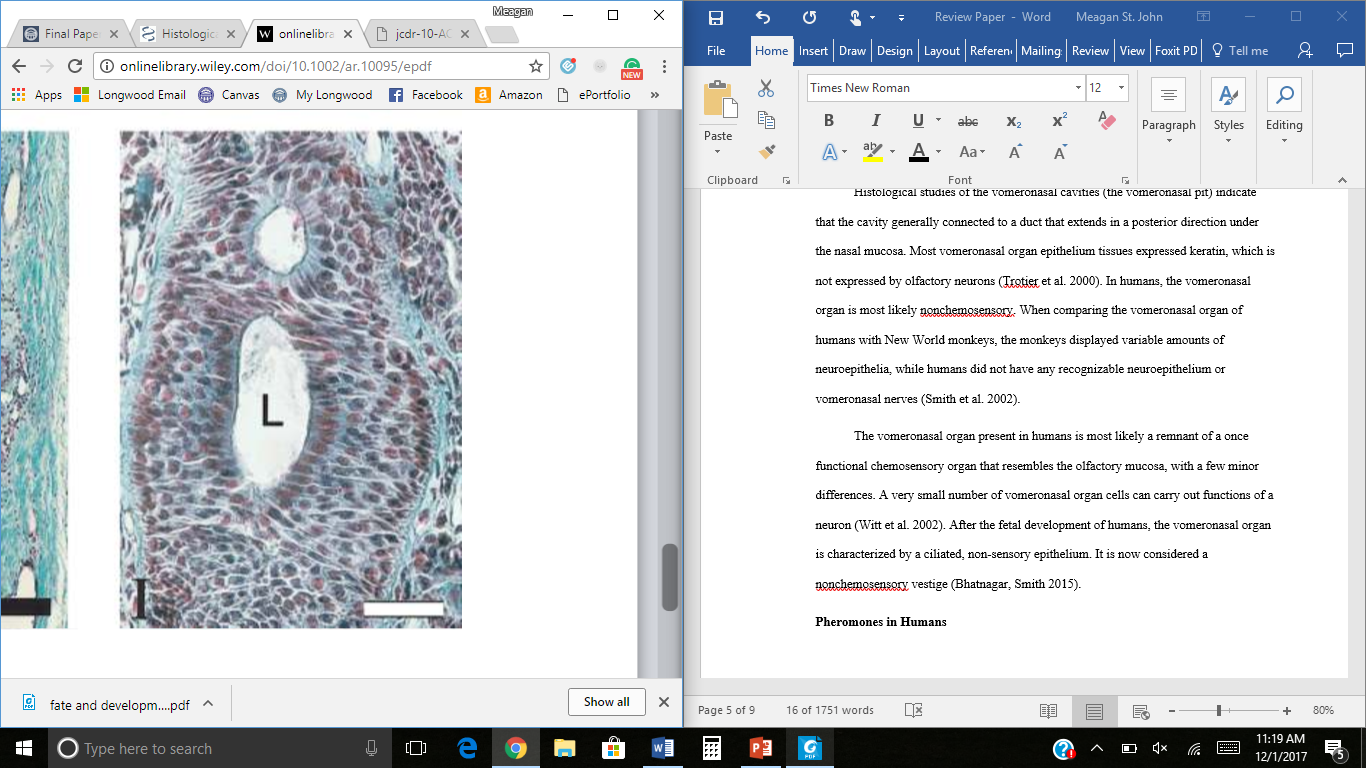
**Presence of the Vomeronasal Organ in Humans**

In humans, the vomeronasal organ develops in utero (Trotier 2011). Forty-five spontaneously aborted fetuses were observed by removing the nasal septum to identify the presence of the vomeronasal organ. Three stages of vomeronasal development were identified. Formation of a tubular structure was found in 33 days to 10 weeks of development. Ciliated cells were replaced with receptor populations between 10 to 15 weeks. Growth of the vomeronasal epithelium and expansion of lumen was observed from 14 weeks until birth. (Vasuki et al. 2016). The nerve that connects the vomeronasal duct with the accessory olfactory bulb degenerates between week 14 and 28 of development in utero. Thus, the pathway of chemo signals is unclear (Witt et al. 2002). The tissues of the vomeronasal organ in utero contain bipolar cells like vomeronasal sensory neurons developing in other species and generates luteinizing hormone releasing hormone (LHRS) producing cells like other species (Boehm 1994).

Vomeronasal organs have been identified in adult human cadavers of European decent. Serial sectioning of the nasal septal wall revealed the presence of a bilateral submucosal tubular structure. The location of the vomeronasal organ in the septum varies slightly but is certainly located antero-inferiorly. The wall of the organ consists of a pseudostratified columnar epithelium (Wessels et al. 2014). It tends to vary in form both medially and laterally. It lacks nerve fibers or nerve bundles related to the vomeronasal epithelium. It also displays discontinuous ciliary patches on the epithelial apices that is unlike any other mammal. Small fossae are located on the surface of the organ. One located anteriorly at the base of the nasal septum, the nasopalatine fossa, has been identified as the vomeronasal pit (Kunwar 2001).

**Figure 2. Relative location of the adult human vomeronasal organ antero-inferiorly in the nasal septum.** (Wessels et al. 2014).

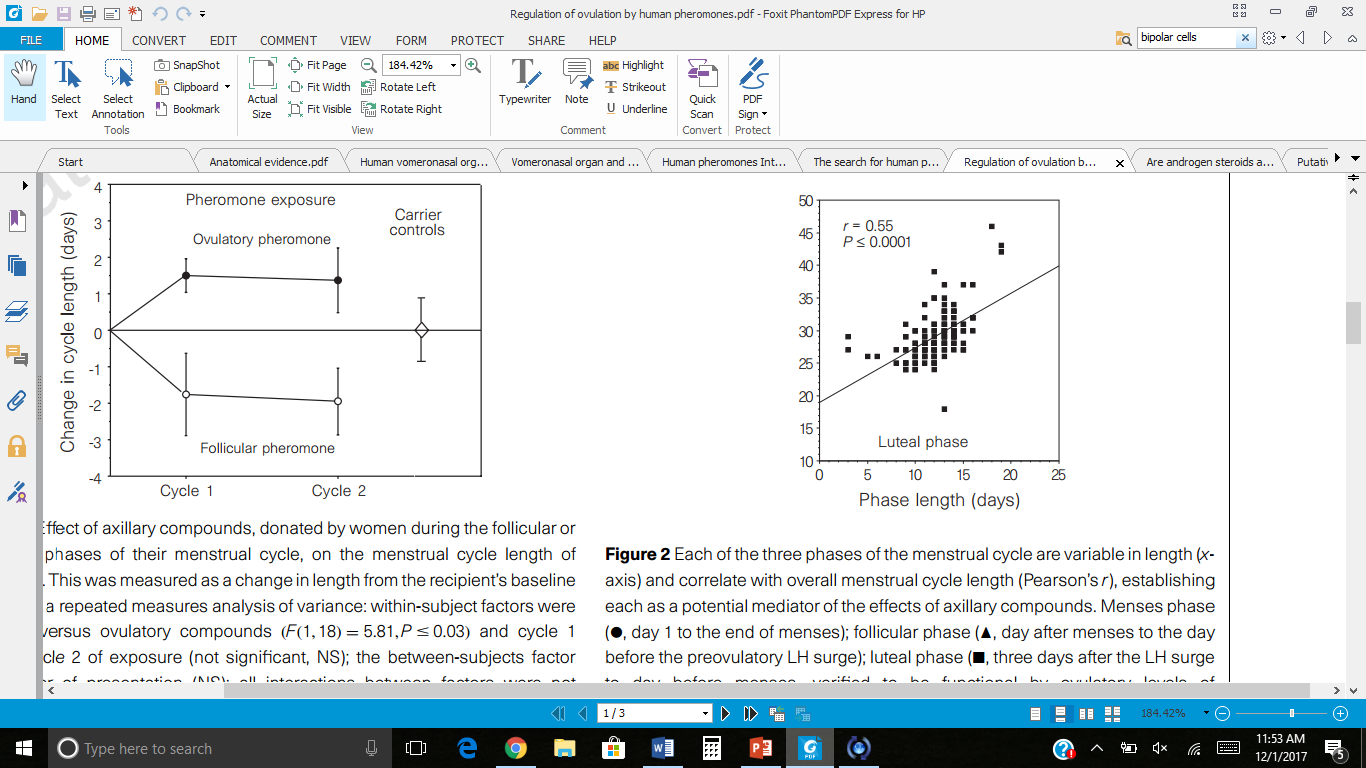
**Nonfunctional Vomeronasal Organ in Humans**

 Histological studies of the vomeronasal cavities (the vomeronasal pit) indicate that the cavity generally connected to a duct that extends in a posterior direction under the nasal mucosa. Most vomeronasal organ epithelium tissues expressed keratin, which is not expressed by olfactory neurons (Trotier et al. 2000). In humans, the vomeronasal organ is most likely nonchemosensory. When comparing the vomeronasal organ of humans with New World monkeys, the monkeys displayed variable amounts of neuroepithelia, while humans did not have any recognizable neuroepithelium or vomeronasal nerves (Figure 3) (Smith et al. 2002).

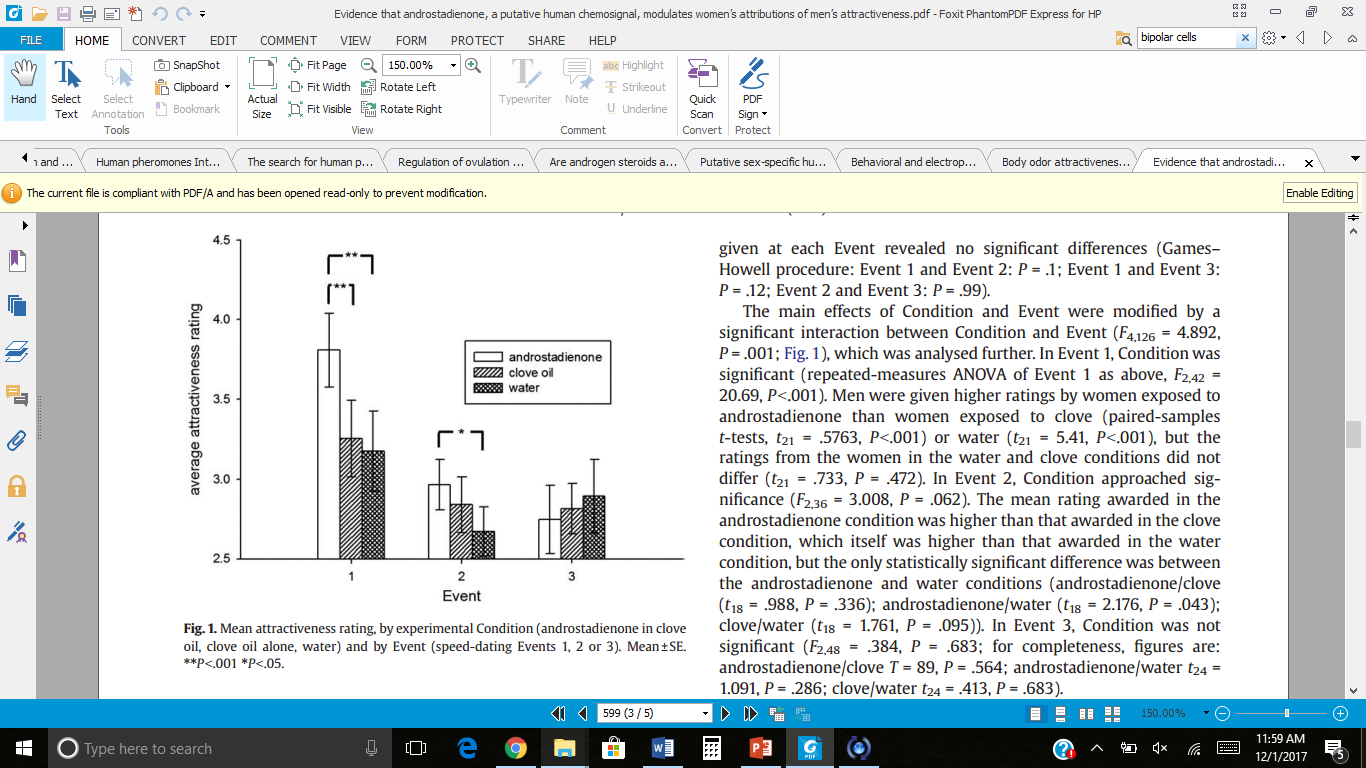
**Figure 3. Nonciliated cells of the human vomeronasal organ.** L shows the lumen of the vomeronasal organ. (Smith et al. 2002).

The vomeronasal organ present in humans is most likely a remnant of a once functional chemosensory organ that resembles the olfactory mucosa, with a few minor differences. A very small number of vomeronasal organ cells can carry out functions of a neuron (Witt et al. 2002). After the fetal development of humans, the vomeronasal organ is characterized by a ciliated, non-sensory epithelium. It is now considered a nonchemosensory vestige (Bhatnagar, Smith 2015).

**Pheromones in Humans**

 The first evidence that humans communicate chemically was from the observation of the phenomenon that when women live together, their menstrual cycles synchronize. Axillary compounds that were taken from the armpits of women during different times in their cycles presented that ovulation can be manipulated. The sample collected before ovulation (follicular pheromone) shortens the cycle of another woman exposed to the compound. The sample collected during ovulation (ovulatory pheromone) lengthens the cycle of another woman exposed to the compound (Figure 4) (Stern & McClintock 1998).

**Figure 4. Effect of axillary compounds, donated by women during the follicular or ovulatory phase of their menstrual cycle, on the menstrual cycle length of recipients** (Stern & McClintock 1998).

Androstadienone is the main component found in male axillary hair and sweat. When the vomeronasal organ was directly stimulated with this sex steroid in picogram quantities, women display reduction of nervousness, tension, and several other negative emotions (Grosser et al. 1999). Heterosexual women and homosexual men also present to choose a seat in a waiting room that has been sprayed with androstadienone over ones that have not been (Pause 2004). Women that are exposed to the sex steroid before going on a date also tend to rate men more attractive than women not exposed to androstadienone (Figure 5) (Saxton et al. 2008). This implies that androstadienone may be able to act as a pheromone by altering behavior and autonomic function.

**Figure 5. Mean attractiveness rating, by administration of androstadienone in clove oil, clove oil alone, and water on 3 different speed-dating rounds.** \* represents statistical significance. (Saxton et al. 2008).

Women also have androstadienone, found in urine, in smaller quantities than men. When women are in the third trimester of pregnancy, their bodies convert androstadienone to estratetraenol. When men are exposed to estratetraenol, they perceive women with high fertility body scents as more attractive than women with low fertility body scents (Gildersleeve et al. 2012).

**Conclusion**

Although there has been substantial evidence provided for sex steroids, androstadienone and estratetraenol, to act as pheromones, humans do not have a functional vomeronasal organ that is typically observed in mammals. Humans anatomically have remnants from a vomeronasal organ but do not display functional neurons. The pathway from the vomeronasal organ and the olfactory bulb has also been diminished, so that if the vomeronasal organ did accept a pheromonal signal, there would not be a pathway for the signal to reach the brain. The organ does not function as a sensory organ in adult humans. It may only be needed in the neonatal stage of life.

Further research should be conducted to determine how androstadienone and estratetraenol are affecting the mood and behavior of women and men. There is also the possibility that they are not acting as pheromones; they must be differently defined. It is also possible that there are other compounds that are acting as pheromones that have not been identified yet.

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