



Human Sex-Attractant Pheromones: Discovery, Research, Development, and Application in Sex Therapy

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THE SCIENCE OF ATTRACTION

Physical attraction is the fundamental precondition for the sexual dance between a man and a woman. Although appearance, self-confidence, and social behavior all contribute to sexual attractiveness, the reproductive endocrine system appears to play an independent role. Recent discoveries of invisible, odorless, sex attractants, called pheromones, offer biologic ways to use cosmetics for improving the romantic lives of men and women. As an adjunct to existing therapies, human pheromones may serve to catalyze the therapeutic process.

HISTORICAL OVERVIEW

Forty years ago, the term pheromone was first proposed to explain the puzzling findings of the previous few decades.¹ Active substances that resembled, yet did not fit, the definition of hormones increasingly were being observed in a variety of animals. A new biologic term, pheromone, was proposed as follows¹:

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A substance secreted by an animal to the outside of the individual, which is then received by another individual, classically of the same species, which then elicits some behavior or developmental response in the latter.

The scientific literature has now refined and confirmed the use of this term. If the chemical product of a body that manufactures it acts on another body some distance from the originating organism and serves the reproductive life of the species, the chemical is termed a pheromone.²

Several classes of pheromones have now been identified in a variety of species: the opposite-sex attractants, the same-sex repellents (territorial markers), and mother-infant bonding attractants.³

In nature, sex-attractant pheromones trigger a cease-fire in the war between the sexes in order to facilitate the propagation and perpetuation of the species. The research that led to the discovery of human pheromones, their synthesis, and their subsequent use as cosmetic fragrance additives began with studies on pigs.

In 1961, boar odor was shown to be sufficient to elicit the mating stance in the female pig; experiments showed that rubbing either the male's urine or the male's seminal fluid on the female's snout was similarly effective.⁴ These studies suggested to researchers the significant role of these musky-smelling substances in the sexual dynamic of porcine reproductive behavior.

Contemporaneously, psychiatrist Richard Michael, working at Emory University, searched for genitally secreted sex-attractant pheromones in rhesus monkeys, because of the mating rituals he observed. The female rhesus monkey "presents" her bright-red rear end to the face of males to obtain their sexual interest. A focus on these behavioral displays revealed that ovariectomy abolished both the typical cyclic variation in female receptivity and the invitation to the male. The complex repertoire returned when the ovarian hormones were appropriately replaced.⁵ A rhesus male would work continuously for access to an ovariectomized female that had been treated with estrogen, but would not work for access to untreated females.⁶ The mechanism appeared to involve substances the investigators termed "copulins" (previously identified as aliphatic acids), which are vaginally secreted and have sex-attractant (ie, pheromonal) properties. The production of these vaginal pheromones is dependent on circulating ovarian hormones.⁷ Their discovery suggested a treatment option for ovariectomy-induced loss of sexual attractiveness in monkeys: these copulins smeared on the posterior of an ovariectomized female rhesus monkey would restore the female's sexual attractiveness to males.³

ANIMAL PHEROMONES: RESEARCH TESTS ON HUMANS

Subsequently, monkey sex-attractant pheromones were tested on humans; aliphatic acid smears, formulated to mimic effective concentrations in Michael's studies of monkeys, were placed on the chests of 62 married women on 8 randomly preassigned nights through 3 menstrual cycles.⁸ No increased incidence of sexual intercourse on the test nights could be demonstrated.⁸

The sex-attractant pheromones of pigs were also considered in human tests. In 1950, the same 16-unsaturated C-19 steroid, androstenol, found in the pig was isolated in human urine by Brooksbank and Haslewood.³ Cross-sectional data showed that men and women produced a characteristic pubertal rise and climacteric-age fall in urinary concentrations. Although some individuals did not demonstrate the precipitous age-related loss of androstenol, the pattern was clear: during the reproductively fertile years, the levels of androstenol are high. However, as in the monkey pheromones, the pig sex-attractant pheromone (androstenol) does not act as a human sex attractant.

Experiments with androstenol reveal significant negative effects on perceptions of human attractiveness. For example, several experiments with college students tested whether the perceptions of attractiveness of seat mates (people sitting next to them) or photographs of strangers could be affected by sniffing androstenol.³ Those experiments comparing androstenol with other olfactants have shown statistically significant, negative, results. When sprayed on restroom stall doors, androstenol

appeared to have an aversive affect on the men (but not the women), resulting in the men's avoiding the treated stall.⁹

Androstenol also appears to affect the self-image of participants. Perceptions of the self as less attractive were significantly more common in individuals when judging (and simultaneously smelling) an androstenol-impregnated photograph of a man than when judging a photograph that was not impregnated with androstenol. In colloquial terms, one might say that exposure to the odor of androstenol lowered self-esteem. Thus, this sex-attractant pig pheromone would appear to work in humans as a territorial marker (ie, a repellent).

ANOSMIAS IN HUMANS AND EXPERIMENTAL ANIMALS

It has not been determined whether olfactory acuity and perception of odor affect the putative pheromonal action as translated in human behavior. According to Gower et al., women have great olfactory acuity; 70% find androstenone (one of a series of musky-smelling compounds isolated in pig testes and human urine³) repellent and a further 20% find it unpleasant and reminiscent of stale urine.^{10,11} However, humans who are anosmic do not appear to have sexual behavior deficits.³ Furthermore, sexually experienced animals that are experimentally altered do not show serious deficits in their sexual functioning when they are rendered anosmic; however, sexual novices are affected by anosmia. These animals never have normal reproductive behavior. Thus, sex-attractant pheromones are not necessary for a sexually experienced animal; rather, the appropriate (species-specific) forms seem to enhance the existing sexual repertoire.

SEXUAL BEHAVIOR OF WOMEN: HORMONES, PHEROMONES, AND REPRODUCTIVE HEALTH

From 1975 through 1986, in a series of studies at the University of Pennsylvania, my colleagues and I investigated relationships between the timing of women's sexual behavior and aspects of their reproductive endocrinology. At Stanford University with different colleagues, I investigated similar relationships among perimenopausal women. Each of the studies demonstrated health benefits from intimate connections with another person, provided the timing was appropriate.

Regular exposure to either sexual intercourse or genital stimulation in the presence of a man (but not masturbation) was associated with fertile-type menstrual cycles. Orgasm was not relevant; the presence of a partner was. Compared with sporadically active or abstaining women, the length of the cycle for *weekly* women (those who engaged in sexual contact at least once during each non-menstruating week) was less aberrant—rarely exceeding 29.5 ± 3 days.^{12,13} *Sporadic* and *celibate* women (those who engaged in sexual contact less than once during each non-menstruating week) showed a significantly higher incidence of aberrantly long

and short menstrual cycles.^{14,15} In 1991, this research was replicated by investigators in Arizona and New Mexico who confirmed these findings.¹⁶ Aberrant-length menstrual cycles are more likely to be anovulatory or have luteal phase deficiencies and be subfertile. Although some subfertile cycles are anovulatory, more often ovulation does occur followed by a "short luteal phase." Both of these abnormalities result in insufficient progesterone secretion for implantation of a conceptus. These hormonal changes lead to deficiencies in bone metabolism and beta-endorphin secretion, while increasing the incidence of atherosclerotic uterine arteries.²

Luteal phase estrogen levels were shown to be twice as high in weekly women as compared with sporadic or celibate women.¹⁷ Perimenopausal women who engaged in a regular, weekly sexual relationship entered menopause later than less sexually active women.¹⁸ In contrast, women with sporadic sexual behavior patterns—in both their younger reproductive and later perimenopausal years—showed half the level of estrogen as those with regular weekly patterns.^{18,19} Furthermore, half of the sporadically active young women had lower estrogen levels than are characteristic of women *after menopause*.¹⁷

Age at first coitus is associated with subsequent health. The onset of sexual contact within 7 years of menarche may enhance the likelihood of subsequent fertility.²⁰ Those who had their first coitus more than 7 years after menarche were significantly more likely to be infertile in their 30s.²⁰

In summary, studies of the timing of sexual behavior have revealed that both timing of first coitus (at puberty) and regular sexual exposure thereafter are associated with the reproductive endocrinology of women. Moreover, the predictive power of this association leads in one direction only. If the heterosexual behavior is regular, one can predict that the cycles will show a fertile pattern (circa 29.5 ± 3 -day cycle lengths, estrogen levels greater than 100 pg/ml, and basal body temperature [BBT] patterns that are ovulatory with luteal phase elevations longer than 12 days) and aging will be delayed. But the reverse does not occur (eg, physiology does not predict behavior). More (or less) fertile-type cycles do not predict the sexual behavior pattern of the woman.²¹ The studies also reveal that regular self-stimulation does not produce these associations.^{12,16}

This suggests the possibility that other persons or their pheromones influence the reproductive endocrine effects associated with increased fertility as well as delayed onset of menopause. Regular sex or appropriate pheromonal exposure appears to enhance the cardiovascular and bone health as well as producing the more easily recognized fertility benefits. My colleagues and I at the University of Pennsylvania began the search for a pheromon-

al source. An intriguing study by Russell et al. led us to focus on the axillae.

HUMAN PHEROMONES FROM THE HUMAN AXILLAE: THE EXPERIMENTAL EFFECT ON MENSTRUAL CYCLES

In 1980, Russell demonstrated one woman's olfactory influences on another's menstrual cycle. The donor soaked a pad with her underarm sweat and this was rubbed on the upper lip of a colleague (3 times per week for 4 months).²² The recipient showed a significant shift in the timing of onset of her menses to conform to the donor's cycle. The conclusion was that the menstrual synchrony effect (where college coeds begin to cycle together as they maintain regular social contact²³) could be accounted for by an underarm secretion. The study was not double blind or placebo controlled and, therefore, was more intriguing than confirming. Nonetheless, it was the first of its type.

In 1986 at the University of Pennsylvania, my colleagues and I reported our double-blind, placebo-controlled studies of pooled human axillary extracts from donors who were sexually active men and of sequentially pooled extracts from fertile, regularly cycling women. The underarm secretions were collected, extracted to remove the bacteria, and frozen for 1 year. Then the thawed extracts were dissolved in ethanol and applied above the upper lip of naive subjects 3 times a week for 14 weeks. The applications tested whether, in contrast to placebo, they would produce pheromonal effects that explained why regular exposure to a sex partner, and regular exposure to other women, shifted menstrual cycle timing toward a more fertile and more synchronous pattern.²⁴⁻²⁶ The results were positive. Pheromonal action of these thawed secretions was demonstrated.

For the female extract (ie, pheromone), our double-blind, placebo-controlled studies revealed a finding similar to that of Russell's report. Test subjects' menses onsets were synchronized with the sequentially timed female extracts, shifting their cycle onset toward coinciding with the donor samples.²⁴ For the male extract, obtained from a single pooling from a group of sexually active men, women with aberrant-length cycles at baseline experienced a shift toward normal, 29.5-day cycles.²⁵ In both cases, women receiving the placebo did not change cycles in any consistent pattern, whereas those who received the presumed pheromones did.^{24,25}

In 1998, a variation of this woman-to-woman experiment provided a replication. Psychologists at the University of Chicago published a letter to the editor in the journal *Nature* revealing that female pooled essences of preovulatory underarm secretion shortened the follicular phase. Postovulatory pheromones lengthened the follicular phase.²⁷ Citing the earlier work described above, they concluded that pheromonal communication in humans was now confirmed. Taken together, these experiments proved that human pheromones could explain

the influence of regular, stable, ongoing exposure to other persons on women's menstrual cycle patterns. The next inquiries addressed the role of human pheromones in human sexual life.

HUMAN PHEROMONE AS SEX ATTRACTANT: THE EXPERIMENTAL REPORTS

With colleagues, I have conducted two double-blind, placebo-controlled experiments of sexual responses to pheromones that have been reported to the scientific community. Our first study of women used the data collected in 1986 in the Cutler and Preti experiments cited above; these data were analyzed according to sexual behavior patterns.^{28,29} The first study of men, in 1994, added a man's proprietary pheromone formula to each man's usual aftershave fragrances and tested for changes in sexual behavior.³⁰ Both studies found that human pheromones, but not placebo, produced significant increases over baseline in sexual behavior involving a partner.

In women, non-odorous pooled axillary excretions collected across the menstrual cycle of normally cycling female donors were thawed, dissolved in ethanol, and applied above the upper lip 3 times per week for 14 weeks. These applications increased the incidence of weekly sexual behavior in the experimental group compared with the group that received placebo. This significant increase in behavior suggested that this "female essence" could be either increasing the desire for sexual contact, making recipients more receptive to the advances of male partners, making them more sexually attractive to their male partners, or all three.^{28,29}

A proprietary, patent-pending, cosmetic fragrance additive for women was brought to market in 1993 as a putative sex attractant with positive results among healthy women. Positive results were also reported in one medical sample of post-hysterectomy women taking hormone replacement therapy (HRT) and complaining of loss of sexual attractiveness³¹; the study was terminated by the medical group when its leader concluded that 70% of the women using the pheromone cosmetic were helped.

Published in 1998, our 1994 double-blind, placebo-controlled experiment of 38 heterosexual men tested a proprietary, patent-pending formula that contained a laboratory-synthesized version of human pheromones.³⁰ The study showed that compared with the placebo group, the men using the pheromone for 6 weeks recorded a statistically significant increase over their own 2-week baseline behavior in sexual intercourse and sleeping with a woman and borderline significance ($P < .08$) for affectionate behavior (hugging/kissing/petting) and informal dating. This increase in romantic attention from women was not accompanied by an increase in frequency of masturbation (Table).

Thus, in this prospective, double-blind, placebo-controlled study, human pheromones caused a statistically significant and distinct increase in those romantic behaviors in which a

**Table
Number of Subjects With an Increase Over Baseline for Each of Six Sociosexual Behaviors by Treatment Group**

Sociosexual Behavior	Treatment				P
	Pheromone (n = 17)		Placebo (n = 21)		
	n	%	n	%	
Sexual intercourse	8	47.0	2	9.5	.01
Sleeping next to a romantic partner	6	35.3	1	4.8	.02
Petting/affection/kissing	7	41.2	3	14.3	.07
Informal dates	6	35.3	2	9.5	.06
Formal dates	7	41.2	7	33.3	.62*
Self-stimulation to ejaculation	4	23.5	2	9.5	.23

* $\chi^2(1, N = 38) = 0.25$.
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woman plays a major role, but not in masturbation. These findings suggest an increased sexual attractiveness of the men without an influence on the men's sexual motivation, further supporting the hypothesis of the pheromonal nature of apocrine secretions in humans.

Practitioners should use skepticism and discrimination in recommending pheromone products to their sexual therapy patients. Any products claiming that they are an "aphrodisiac" should be avoided because this is a drug claim that is regarded by the Food and Drug Administration as illegal and no such studies have been reported. Many commercial products claiming they contain pheromone ingredients may actually contain the previously discussed boar pheromone and may act as a repellent. To date, the only product tested under double-blind, placebo-controlled conditions with a study published in a peer-reviewed journal³⁰ is Athena Institute's synthesized human male pheromone cosmetic fragrance additive. In this study, discussed above, 74% of the heterosexual men using the pheromone for 6 weeks recorded increased romantic attention from women compared with their own 2-week baseline. Not an aphrodisiac, these products are cosmetics that apparently work to increase romantic attention from others.

THE VOMERONASAL ORGAN (VNO)—POTENTIAL SITE OF ACTION

The role of the VNO within the olfactory system has been the subject of intense research in recent years as the interest in the mechanisms underlying pheromonal communication

has expanded. In 1993, the VNO was identified as a duct-like opening within the nose. Clearly visible macroscopically, approximately 400 μm in diameter, the VNO is lined with squamous respiratory epithelium close to the surface. The duct terminates in an ovoid-shaped cul-de-sac lined with pseudo stratified columnar epithelium. Monti-Bloch et al.³² identified the human VNO as an olfactory structure that is anatomically and physiologically distinct from the main nasal nerve system. Electrical recordings at the VNO, the respiratory epithelium, and the olfactory epithelium (OE) showed the VNO to be particularly sensitive to substances that did not trigger similar electrical firing at the OE.

The established role of the VNO for pheromonal reception in animal studies led inevitably to the search for the potential function of this organ in humans. Reports now suggest that the VNO is ubiquitous in humans unless there is a nasal pathology.³³ Although this olfactory organ is present in healthy men and women, it remains to be learned whether it plays a pheromonal role in humans. Research described earlier suggests a VNO role in receptivity to repellent (territorial-type) substances. But it may be that, in humans, the VNO is vestigial. Because experimental sniffing of androsthenol produced negative effects in humans, the pig sex-attractant pheromone androsthenol appears to be a territorial-type marker in humans.

CONCLUSION: USES FOR TOPICAL PHEROMONE COSMETIC IN SEXUAL THERAPY

Because an increase in sexual attractiveness from the use of a cosmetic pheromone was demonstrated by the recently published study,³⁰ it is logical to address possible uses and benefits. In nature, pheromone output appears to crest during the peak years of fertility and declines with passage into the post-fertile years. The frontier of therapeutic applications involving cosmetic pheromone additives has exciting potential. Some of the possible paths to pursue for topical pheromones in sexual therapy include:

- A patient adds pheromone to his or her own fragrance to increase his or her partner's sexual interest. In conjunction with psychotherapy, this change in the partner's response is incorporated into the healthy emotional functioning of the patient.

- A patient's sexual interest in his or her partner has declined; the patient adds sex-attractant-type pheromone to his or her partner's fragrance. If the problem was due to aging and diminished pheromonal output, a speedy conclusion to therapy is anticipated. Age-related declines in pheromones can occur disproportionately in one partner, generating imbalances in the physical attraction between them. The balance might be corrected with pheromone cosmetics. In this case, a patient uses the pheromones in his or her own fragrance or adds

them to his or her partner's fragrance.

- Both partners use pheromone additive to restore or experiment with their intimate activities. In conjunction with psychotherapy, new positive aspects of the relationship could develop.

- Within the dating and social environment, a single man or woman would wear fragrance mixed with pheromone additive as part of his or her daily routine. It is important for those who are not currently involved with a partner to seek out situations in which they are likely to meet others who are available.

- Patients with self-image deficiencies may benefit from a general increase in social attention, and romantic attention, from the opposite sex.

- Patients with infertility problems—with or without known pathology—need a romantic life. Studies reviewed above have shown that couples trying to conceive a viable pregnancy benefit from regular, weekly sexual intercourse, because the behavior increases the likelihood of a fertile-type cycle in the woman. Intrusive infertility treatments usually compromise some of the romance between the couple. Those involved in expensive and painful assisted reproductive technologies show twice the success rate when they have sexual intercourse than when they abstain, despite conditions prohibiting pregnancy (eg, blocked fallopian tubes).³⁴ Because cosmetic pheromones can promote or restore romance, they may serve as a useful adjunct to both the psychologic and the reproductive endocrine treatments.

- Hysterectomy, with or without ovariectomy, accelerates the endocrine changes characteristic of aging.³⁵ Despite adequate estrogen replacement therapy to overcome vaginal dryness, patients often complain of a loss of sexual attractiveness. Although this complaint had previously been considered psychological in origin, the rhesus monkey evidence reviewed here suggests that pelvic surgery does abolish or severely reduce pheromonal excretion in women. Sex-attractant pheromones added to the patient's usual fragrance may restore this loss. Unless HRT regimens replace the complex array of relevant pheromone-generating sex hormones, they may not be adequate in restoring a patient's own production of pheromones. One should note that even when ovaries are retained at hysterectomy, the surgery accelerates the ovarian senescence by approximately 5 years.³⁵ Thus, although aging can be expected to diminish the natural production of human sex attractants, pelvic surgeries are likely to accelerate this process.

Sex-attractant-type pheromone cosmetics can be incorporated into the user's daily routines to increase the chances for therapeutic benefits. Studies have revealed the importance of consistent, regular exposure—at least 3 and preferably 5 times per week—rather than recreational "weekend" applications. User feedback is

consistent with the scientific findings of a cumulative positive effect.

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