Kirk-Othmer Encyclopedia of Chemical Technology.

HORMONES, SURVEY

The word hormone is derived from the Greek *hormaein,* meaning to set in motion or to excite. It was used initially to define the activity of secretin [1393-25-5] (1), a gastrointestinal polypeptide released into the blood by the duodenal mucosa to stimulate pancreatic acinar cells to release bicarbonate and water.

1. Vertebrate Hormones

The term hormone is used to denote a chemical substance, released from a cell into the extracellular fluid in low quantities, which acts on a target cell to produce a response. Hormones are classified on the basis of chemical structure; most hormones are polypeptides, steroids (qv), or derived from single amino acids (qv) (Table 1).

Polypeptide hormones are synthesized as part of a larger precursor molecule or prohormone. Cleavage of the prohormone by specific cellular enzymes, ie, peptidases, produces the secreted form of the hormone. In some cases, multiple bioactive hormones are produced from a single prohormone. In the anterior pituitary gland (see Hormones, anterior pituitary hormones), both adrenocorticotropic hormones (ACTH) and the endogenous opiate hormone, β-endorphin, are synthesized from a common prohormone (2) (see Opioids, endogenous). In the adrenal medulla, five to seven copies of another opiate hormone, methionine—enkephalin (Met-enkephalin), and one copy of leucine–enkephalin (Leu-enkephalin) are synthesized from each precursor molecule (3).

Steroids are synthetic products of cholesterol [57-88-5]. The chemical structure of a steroid hormone is determined by sequential enzymatic processing of the cholesterol molecule. Steroid products differ among steroid-secreting glands because of differences in enzyme processing, eg, the production of estrogen by the ovary requires enzymatic steps that do not occur in the adrenal cortex.

Amino acid-derived hormones include the catecholamines, epinephrine and norepinephrine (qv), and the thyroid hormones, thyroxine and triiodothyronine (see Thyroid and antithyroid preparations). Catecholamines are synthesized from the amino acid tyrosine by a series of enzymatic reactions that include hydroxylations, decarboxylations, and methylations. Thyroid hormones also are derived from tyrosine; iodination of the tyrosine residues on a large protein backbone results in the production of active hormone.

1.0.1. Mechanisms of Action

Biologically effective concentrations of hormones range between 10^{-7} to $10^{-12}M$. Although enzymes and vitamins (qv) are also effective in small amounts in producing cellular responses, a fundamental defining characteristic of a hormone is that it binds to a stereospecific cellular receptor to activate a response. Binding to a receptor protein activates an intracellular transduction process that mediates the hormone action. Hydrophilic molecules, eg, polypeptide hormones and catecholamines, bind to membrane receptors. Common intracellular transducers for these hormones include cyclic AMP, calcium, and phosphatidyl inositides. In contrast, lipophilic molecules, eg, steroid and thyroid hormones, readily diffuse through the cell membrane, enter the nucleus, and bind to receptors that activate or inactivate specific genes. Termination of the hormone action occurs after metabolism of the hormone or the hormone–receptor complex.

Table 1. Hormones in Vertebrates

Tissue of origin/hormone	CAS Registry Number	Chemical nature	Site of action	Effect
Adrenal				
adrenal cortex				
aldosterone	[52-39-1]	steroid	kidney	electrolyte and water metabolism
cortisol	[50-23-7]	steroid	multiple tissues	protein, lipid, and carbohydrate metabolism; cardiovascular stability; immune responses
corticosterone	[50-22-6]			
adrenal medulla				
epinephrine	[51-43-4]	catecholamine	cardiac muscle	increase heart rate
			skeletal muscle	vasodilation
			skin and kidney	vasoconstriction
			liver	vasodilation and glycogenolysis
			adipose tissue	lipolysis
			intestinal smooth muscle	relaxation
norepinephrine	[51-41-2]	catecholamine	cardiac muscle	increase heart rate
			skeletal muscle, skin, and kidney	vasoconstriction
			liver	vasoconstriction and glycogenolysis
			adipose tissue	lipolysis
			intestinal smooth muscle	relaxation
Leu-enkephalin, Met-enkephalin	[59141-40-1][a]	polypeptide	multiple tissues	endogenous opiates
Cardiovascular tissue				
endothelial cells				
endothelin	[116243-73-3]	polypeptide	vascular smooth muscle	vasoconstriction
heart				
atrial natriuretic hormone (ANH)	[9088-07-7]	protein	kidney	increased sodium excretion and decreased renin secretion
			vascular smooth muscle	vasodilation
			adrenal cortex	decreased aldosterone secretion
Gastrointestinal (GI) track				
gastrin	[53989-98-0, 60748-06-3, 60748-07-4]	polypeptide	stomach	increased acid secretion
secretin	[1393-25-5]	polypeptide	pancreas	increased water and biocarbonate secretion
cholecystokinin (CCK)	[9011-97-6]	polypeptide	gallbladder	contraction

Table 1. ***Continued***

Tissue of origin/hormone	CAS Registry Number	Chemical nature	Site of action	Effect
			pancreas	increased enzyme secretion
motilin	[52906-92-0]	polypeptide	gastrointestinal tract	smooth muscle contraction
neurotensin	[39379-15-2]	polypeptide	stomach	decreased acid secretion and emptying
			pancreas	increased bicarbonate secretion
			intestine	increased motor activity
peptide tyrosine tyrosine (PYY)	[106388-42-5]	polypeptide	stomach	decreased acid secretion and emptying
somatostatin	[38916-34-6]	polypeptide	GI tract	decreased GI hormone secretion; decreased adsorption of nutrients; decreased gastric emptying and gall bladder contraction
Gonadal tissue				
corpus luteum				
progesterone	[57-83-0]	steroid	uterus	proliferation and vascularization of the endometrium; preparation for ovum implantation and maintenance of pregnancy
			mammary glands	alveolar development
relaxin	[9002-69-1]	protein	uterus	cervical softening
ovary				
estrone	[53-16-7]	steroid	uterus	endometrial proliferation
estradiol	[5750-28-2]	steroid	ovary	increased cell division and follicle growth
			mammary glands	duct development; development of secondary sex characteristics
inhibin	[57285-09-3]	protein	pituitary	inhibits FSH
activin	[114949-22-3]	protein	pituitary	stimulates FSH
testis				
testosterone	[58-22-0]	steroid	accessory sex organs	maturation and normal function; development of secondary sex characteristics
inhibin	[57285-09-3]	protein	pituitary	inhibits FSH
activin	[114949-22-3]	protein	pituitary	stimulates FSH
Hypothalamic/brain hormones				
corticotropin-releasing hormone (CRH)	[9015-71-8]	polypeptide	pituitary	release of ACTH and β-endorphin
dopamine	[51-61-6]	catecholamine	pituitary	inhibition of prolactin

Table 1. ***Continued***

Tissue of origin/hormone	CAS Registry Number	Chemical nature	Site of action	Effect
gonadotropin-releasing hormone (GnRH)	[9034-40-6]	polypeptide	pituitary	release of LH and FSH
growth hormone-releasing hormone (GRH)	[9034-39-3]	polypeptide	pituitary	release of growth hormone
somatostatin	[38916-34-6]	polypeptide	pituitary	inhibition of growth hormone and TSH
thyrotropin-releasing hormone (TRH)	[9015-91-2]	tripeptide	pituitary	release of TSH and prolactin
vasopressin	[11000-17-2]	polypeptide	pituitary	release of ACTH and β-endorphin
Pituitary				
anterior pituitary (adenohypophysis)				
adrenocorticotropic hormone (ACTH)	[9002-07-2]	polypeptide	adrenal	secretion of adrenocortical steroids
β-endorphin	[60118-07-2]	polypeptide	multiple tissues	endogenous opiate
follicle-stimulating hormone (FSH)	[9002-68-0]	glycoprotein	gonads	steroid and peptide secretion
γ-melanocyte-stimulating hormone (γ-MSH)	[72711-43-4]	polypeptide	adrenal	potentiates response to ACTH
growth hormone	[9002-72-6]	protein	multiple tissues	growth of bone and muscle; metabolism of carbohydrate and lipid; anabolic effect on mineral metabolism
luteinizing hormone	[9002-67-9]	glycoprotein	gonads	steroid secretion
			ovary	ovulation
			testes	development of interstitial tissue
prolactin	[9002-62-4]	protein	mammary gland	proliferation; milk secretion
			corpus luteum	development and functional activity
thyroid-stimulating hormone (TSH)	[9002-71-5]	glycoprotein	thyroid	growth and secretion
intermediate pituitary (pars intermedia)				
β-endorphin	[60118-07-2]	polypeptide	multiple tissues	endogenous opiate
β-lipotropin	[37199-43-2]	polypeptide	adipose tissue	lipolysis
α-melanocyte-stimulating hormone (α-MSH)	[9002-79-3]	polypeptide	melanophores	skin pigmentation
γ-melanocyte-stimulating hormone (γ-MSH)	[72711-43-4]	polypeptide	adrenal	potentiates responses to ACTH
posterior pituitary (neurohypophysis)				

Table 1. ***Continued***

Tissue of origin/hormone	CAS Registry Number	Chemical nature	Site of action	Effect
oxytocin	[50-56-6]	polypeptide	uterus	contraction
			mammary gland	milk ejection
vasopressin	[11000-17-2]	polypeptide	kidney	water reabsorption
			vascular smooth muscle	vasoconstriction
			liver	glycogenolysis
Thyroid				
parathyroid				
parathyroid hormone	[52232-67-4]	polypeptide	kidney, bone, and GI tract	mobilization of calcium and phosphorus
pineal				
melatonin	[73-31-4]	indole	skin	inhibits pigmentation
			reproductive tissue	regulates function
thyroid				
thyroxine	[51-48-9]	amino acid derived	multiple tissues	increases metabolic rate and oxygen consumption
triiodothyronine	[6893-02-3]			
calcitonin	[9007-12-9]	polypeptide	bone and kidney	mobilization of calcium and phosphorus
Various Organs				
kidney				
erythropoeitin	[11096-26-7]	glycoprotein	bone marrow	erythrocyte production
renin	[9015-94-5]		adrenal	aldosterone secretion
angiotensin II (AII)	[11128-99-7]	polypeptide	vascular smooth muscle	vasoconstriction
			brain	drinking
pancreas				
glucagon	[9007-92-5]	polypeptide	liver	glycogenolysis and gluconeogenesis
insulin	[9004-10-8]	polypeptide	multiple tissues	carbohydrate utilization
			adipose tissue	lipogenesis
pancreatic peptide	[59763-91-6]	polypeptide		function unknown
somatostatin	[38916-34-6]	polypeptide		inhibition of all pancreatic hormones
placenta				
chorionic gonadotropin	[9002-61-3]	glycoprotein	corpus luteum	maintenance of function
placental lactogen	[9035-59-5]	polypeptide	material tissues	insulin-like effects
relaxin	[9002-69-1]	protein		cervical softening

[a] +++

1.0.2. Effects and Secretion

An endocrine gland is defined classically as a tissue consisting of hormone-secreting cells that synthesize products for release into the blood. The pattern of release is reflected by changes in plasma hormone concentration. Analysis of hormone concentration is performed using radioimmunoassay based on competition of a hormone for binding to a specific antibody, or bioassay based on measurement of a specific biological response (see Immunoassay). Most hormones are secreted episodically, showing minute-to-minute changes in the circulation. Also, rhythms of hormone secretion are common, having periodicities that vary from hours to days. For example, circadian rhythms, having a periodicity of approximately 24 h, have been described for many hormones, including adrenal corticosteroid hormones, pituitary thyrotropic hormone, and pineal melatonin. Both growth hormone and prolactin secreted from the anterior pituitary show daily maxima related to the sleep–wake cycle. Pituitary gonadotropins and gonadal steroids essential for reproductive functions demonstrate cycles ranging over periods of days.

The biological effect of a hormone traditionally has been defined both by the change in the physiology of an organism after endocrine gland ablation and by the reversal of the effect by replacement with glandular extracts. For example, removal of the pancreas, ie, pancreatectomy, results in hyperglycemia,orelevated plasma glucose, and injection of pancreatic extracts results inthe reestablishment ofeuglycemia, or elevated plasma glucose, and injection of pancreatic extracts results in the reestablishment of euglycemia, ie, normal plasma glucose. This experimental approach has led to the identification of pancreatic insulin as a hormone essential for the utilization of carbohydrates (see Insulin and other antidiabetic agents). Using a similar approach, the anterior pituitary gland has been characterized as the master gland. Its removal impairs the function of many other glands and is deleterious to the general well-being of the organism. The anterior pituitary secretes multiple hormones that are tropic, ie, maintains secretory function, and trophic, ie, maintains growth, for endocrine glands. Thus adrenocorticotropic hormone (ACTH) directly stimulates the growth and secretion of the adrenal cortex; thyrotropic hormone, ie, thyroid-stimulating hormone (TSH), stimulates the thyroid gland; and gonadotropic hormones, ie, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), stimulate the gonads. Maintenance of nonendocrine cell growth and metabolism is dependent on the anterior pituitary gland through its secretion of growth hormone (GH). Prolactin is required for proliferation and milk secretion by the mammary gland in mammals and for water and electrolyte metabolism in lower vertebrates.

The secretion of anterior pituitary hormones is controlled by stimulatory and inhibitory hormones secreted from nerve cells found in a region of the brain called the hypothalamus. The hypothalamic neurons secrete hormones into the blood that flows directly to the anterior pituitary gland. The brain hormones (see *H*ORMONES, BRAINOLIGOPEPTIDES) include corticotropin-releasing hormone (CRH), which stimulates the secretion of ACTH; thyrotropin-releasing hormone (TRH), which stimulates the secretion of TSH; gonadotropin-releasing hormone (GnRH), which stimulates FSH and LH; growth hormone-releasing hormone (GRH), which stimulates GH; somatostatin, which inhibits GH release; and the catecholamine dopamine, which inhibits the secretion of prolactin from the anterior pituitary.

Control of secretion of anterior pituitary hormones also includes inhibition by hormones produced by target organs. For example, CRH stimulates the anterior pituitary to secrete ACTH, which in turn stimulates the adrenal cortex to secrete corticosteroids. Corticosteroids then feed back to inhibit the secretion of ACTH. Feedback mechanisms are important for the control of most hormones. For example, insulin (qv) secretion from the pancreas increases in response to increased blood glucose resulting from ingestion of a meal. Insulin increases tissue uptake and metabolism of glucose, which lowers blood glucose and in turn reduces insulin secretion.

1.0.3. Endocrine Pathology

The health of an organism is dependent on the maintenance of hormone concentrations within a normal physiological range. Pathology occurs when hormone concentrations are higher or lower than normal for extended pe-

riods. Excess hormone concentrations can result from overproduction by endocrine cells, eg, hypercorticoidism owing to excess secretion of adrenal cortical hormones, or from reduced hormone metabolism. Endocrine cell tumors have been described that secrete excess amounts of polypeptide hormones, steroid hormones, or catecholamines. Hormone deficiency can result from reduced hormones production, eg, hypocorticoidism, or from increased metabolic clearance of a hormone from the circulation. Pathology also can result when adequate hormone concentrations are present, but the hormone receptor on target cells does not bind normally, eg, in certain forms of diabetes mellitus, insulin concentration are adequate, but insulin receptors on target cells are reduced. Thus target cells are unable to respond appropriately (4).

Endocrinologists use hormones or hormone analogues to treat endocrine disease. Potent analogues of some hormones have been synthesized that antagonize the action of the natural hormone. Their use is effective in treating endocrine problems related to excess or inappropriate hormone production, eg, hypertension, ie, elevated blood pressure, can result from excess constriction of vascular smooth muscle induced by high circulating concentrations of angiotensin II. Treatment with 1-sar-8-ala-angiotensin II (saralasin [34273-10-4]), an inactive angiotensin II analogue, lowers blood pressure (5) (see Cardiovascular agents). Saralasin binds to the angiotensin receptor and prevents angiotensin II activity. To offset endocrine gland removal or reduced function, replacement therapy is performed. In most cases, synthetic hormones are administered; steroid hormones and some peptide hormones can be obtained in pure form. The availability of protein hormones for therapeutic or experimental use has been increased greatly through the application of genetic engineering (qv) techniques. The deoxyribonucleic acid (DNA) sequence of the human gene coding for a specific protein hormone is cloned. When inserted into rapidly replicating bacteria, enormous quantities of mammalian hormones can be produced. This approach has generated highly purified recombinant human hormones, including insulin and growth hormone.

1.0.3.1. New Perspectives in Endocrinology. The field of endocrinology has as its primary focus the study of the structure and function of endocrine glands and their secretory products. However, findings (ca 1994) have fostered a broader scope for endocrinology. Hormone secretion from cells that exist outside the classic endocrine glands can occur. The ability to synthesize and secrete hormones has been demonstrated for nonglandular tissue, including neurons, ie, cells identified in the central and peripheral nervous systems, and leukocytes (see Neuroregulators). To identify cells that synthesize hormones, molecular biological approaches have been used to measure the messenger ribonucleic acid (mRNA) that encodes for a specific hormone or for an enzyme required for hormone synthesis.

Transport in the blood is no longer a requisite for a hormonal response. Responses can occur after release of hormones into the interstitial fluid with binding to receptors in nearby cells, called paracrine control, or binding to receptors on the cell that released the hormone, called autocrine control. A class of hormones shown to be synthesized by the tissue in which they act or to act in the local cellular environment are the prostaglandins (qv). These ubiquitous compounds are derived from arachidonic acid [506-32-1] which is stored in the cell membranes as part of phospholipids. Prostaglandins bind to specific cellular receptors and act as important modulators of cell activity in many tissues.

Cells synthesize and secrete multiple hormones. For example, some cells in the anterior pituitary have the capacity to secrete both polypeptide hormones, FSH and LH. Cells also can secrete different chemical classes of hormone, eg, cells in the adrenal medulla synthesize and secrete the amine-derived catecholamines, norepinephrine and epinephrine, as well as the polypeptide hormones, the enkephalins.

A hormone can have multiple biological effects that are conferred by binding to receptors on specific target cells. Angiotensin II stimulates the secretion of the steroid hormone aldosterone by binding to receptors in the adrenocortical cell and the constriction of blood vessels by binding to receptors on vascular smooth muscle cells; it also activates the drinking response by binding to neuronal receptors in the brain. A broader view of what constitutes a hormone is exemplified by the discovery that identical peptides are present as secretory products in neurons of the peripheral and central nervous system, as well as glandular cells in the gut, pancreas, and other tissues. For example, somatostatin, originally identified as a hypothalamic factor that affects anterior

Table 2. Brain–Gut Peptide Hormones in Vertebrates

		Effects[a]	
Hormone	CAS Registry Number	Brain	GI tract
bombesin	[74815-57-9]	motor activity (I); body temperature and feeding (D)	gastrin secretion (I)
calcitonin gene-related peptide (CGRP)	[83652-28-2]	motor activity and feeding (D)	acid secretion (D)
cholecystokinin (CCK)	[9011-97-6]	motor activity and feeding (D)	enzyme secretion (I)
leu- and met-enkephalin	[59141-40-1]	body temperature (D)	smooth muscle contraction (I); GI secretion (D)
motilin	[52906-92-0]	drinking (D)	smooth muscle contraction (I)
neuropeptide Y	[82785-45-3]	feeding and drinking (I)	gut motility (D)
neurotensin	[39379-15-2]	motor activity and body temperature (D)	acid secretion and emptying (D)
secretin	[1393-25-5]	motor activity (D)	H_2O and bicarbonate secretion (I)
somatostatin	[38916-34-6]	memory (I); aggressive behavior and body temperature (D)	hormone secretion, nutrient adsorption, gastric emptying, and gall bladder contraction (D)
substance P	[33507-63-0]	motor activity (I); aggressive behavior (D)	intestinal motility and exocrine pancreatic secretion (I)
vasoactive intestinal peptide (VIP)	[37221-79-7]	motor activity (D)	intestinal H_2O and Cl^- secretion and relaxation of esophageal sphincter (I)

[a](I), increases; (D), decreases.

pituitary secretion, is synthesized in the gut and pancreas and contributes to functional control in those tissues. Many peptides have been localized both in the gastrointestinal (GI) tract and in the brain. These are listed in Table 2 with some of their GI and brain effects. In addition to affecting local cell activity in the nervous system and in nonneural tissue, many of these peptides also have been shown to act after secretion into the circulation.

1.0.4. Nontraditional Hormones

Novel hormones identified in cardiovascular tissue have profound effects on maintenance of blood pressure and blood volume in mammals. Atrial natriuretic hormone (ANH) is a polypeptide hormone secreted from the atria of the heart. When the cardiac atrium is stretched by increased blood volume, secretion of ANH is stimulated; ANH in turn increases salt and water excretion and reduces blood pressure (6). Endothelin is a polypeptide hormone secreted by endothelial cells throughout the vasculature. Although endothelin is released into the circulation, it acts locally in a paracrine fashion to constrict adjacent vascular smooth muscle and increase blood pressure (7).

Two protein hormones, inhibin and activin, have been identified in gonadal tissue. Inhibin has been isolated from ovarian follicular fluid and found to inhibit pituitary secretion of FSH. Inhibin is a glyocoprotein heterodimer consisting of two disulfide-linked subunits, α and β; two types of β-subunit, β_A and β_B, exist in follicular fluid. Control of inhibin secretion involves a feedback relationship in which circulating FSH stimulates

inhibin secretion, which in turn reduces the secretion of FSH (8). Both the homo- and the heterodimers of the β-subunits of inhibin promote the secretion of FSH and thus have been termed activins. Activin is secreted by the ovary and the testes into the circulation. In addition, both inhibin and activin have intragonadal autocrine and paracrine effects that influence gonadal steroidogenesis (9).

Erythroid differentiation factor (EDF) is a protein isolated originally from the culture fluid of a human leukemia cell line; it induces the proliferation and differentiation of hematopoietic progenitor cells (10). Interestingly, the sequence of the EDF mRNA is identical to that of the β_A subunit of activin, and inhibin (11). Both activin and EDF are composed of two β_A subunits, and their biological activity is similar, eg, activin can augment the proliferation and differentiation of erythroid progenitor cells and EDF can stimulate secretion of FSH from anterior pituitary cells. These findings provide additional support for the concept that one hormone can have multiple biological effects. In this instance, the same hormone has been given two different names because it expressed specific biological activities in two different physiological systems.

2. Insect and Plant Hormones

2.0.5. Insect Hormones

Insects and crustaceans must shed their exoskeleton in order to grow. This molting process is called ecdysis and is initiated by a steroid hormone called ecdysone [3604-87-3], which is secreted by the Y-organ located at the base of the antennae. Secretion is under negative control by molt-inhibiting hormones secreted by a ganglion, the X-organ. To initiate release of ecdysone and molting, the nervous system inhibits the release of the peptide, molt-inhibiting hormone. In insects, a molt inhibitor is not involved. Instead, the corpus cardiaca of the brain produces prothoracotropic hormone [61583-57-1], which acts on the prothoracic gland to secrete ecdysone. Another hormone, juvenile hormone [23314-84-3], secreted by the corpora allata in insects, prevents development from the larval to the adult stage; when juvenile hormone concentrations decrease, metamorphosis is initiated. Multiple juvenile hormones have been isolated and all are derivatives of methyl-10,11-epoxytridecadienoate, a sesquiterpenoid compound (see Insect control technology).

2.0.6. Plant Hormones

Plant hormones are organic substances, active in small ($< \mu M$) amounts, which are formed in one part of a plant and usually translocated to other sites to induce specific biochemical or morphological responses. Auxins derived from the amino acid tryptophan induce elongation in shoot cells; the principal naive auxin in higher plants is indole-3-acetic acid [87-51-4]. Another class of hormones, the gibberellins, are four-ring structures that occur as 19-carbon or 20-carbon, mono-, di-, or tricarboxylic acids. Originally isolated from fungi, gibberellins are natural products of higher plants and an intact ring structure is essential for their activity in stimulating cell division and cell elongation. Cytokinins are isopentenyl adenine derivatives that promote cell division. Kinetin [523-79-1], the first cytokinin studied, has been isolated from autoclaved herring sperm DNA and identified as 6-furfurylaminepurine. The first natural plant cytokinin, zeatin [1637-39-4], has been isolated from immature corn kernels and identified as 6-(4-hydroxy-3-methyl-*trans*-2-butenylamino) purine. Growth-inhibiting hormones are important for inducing periods of plant dormancy; abscisic acid [21293-29-8] is a natural growth-inhibiting hormone. Plants also synthesize brassinosteroids that contain the steroid nucleus, are active in concentrations lower than those of other plant hormones, ie, p*M,* and act alone or synergise with other plant hormones to affect plant growth (see Growth regulators, plant).

3. Prerohormones

Pherohormones, or pheromones, are interorganismal hormones that transmit information between members of a species. Insect behavior is affected by different pheromones used as sex attractants or as chemical markers of food sources. The chemical structure of pheromones varies. These may be small molecules that rapidly disperse and serve to signal alarm, eg, 4-methyl-3-heptanone [6137-11-7] in ants, or larger, less volatile compounds that persist for longer periods and function as sex attractants, eg, 3,13-octadecadien-1-ol [66410-24-0], [66410-28-4]. There is evidence for olfactory communication in a variety of mammalian species, including humans. In male and female rodents, different volatile constituents in urine induce aggressive behavior, delay or accelerate puberty, or attract the opposite gender. Originally isolated from porcine testicles, 16-androstenes are C-19 steroids that are volatile, have a pronounced odor, and have been implicated as sex attractants in some mammals. It has not been established whether C-19 steroids are sex attractants in all mammals. However, these compounds, recently isolated from the axillae of human males, may be produced by bacterial metabolism of a native androgen to function as human pheromones.

BIBLIOGRAPHY

"Hormones, Survey" in *ECT* 1st ed., 7, 475–481, by O. Kamm, Parke Davis & Co.; in *ECT* 2nd ed., 11, 45–52, by J. Fried, University of Chicago; in *ECT* 3rd ed., 12, 538–545, by C. Rivier and J. Rivier, Salk Institute.

Cited Publications

1. W. M. Bayliss and E. H. Starling, *J. Physiol.* **28**, 325 (1902).
2. B. A. Eipper and R. E. Mains, *Endocrine Revs.* **1**, 1–27 (1980).
3. R. V. Lewis and co-workers, *Science* **208**, 1459 (1980).
4. C. R. Kahn and co-workers, *N. Engl. J. Med.* **294**, 739 (1976).
5. M. L. Horne and co-workers, *Kidney Int.* **15**, s115 (1979).
6. B. J. Ballermann and B. M. Brenner, *Circ. Res.* **58**, 619–630 (1986).
7. G. M. Rubanyi and L. H. Parker Botelho, *FASEB J.* **5**, 2713–2720 (1991).
8. F. H. De Jong, *Physiol. Revs.* **68**, 555–607 (1988).
9. S.-Y. Ying, in L. Martini and W. F. Ganong, eds., *Frontiers in Neuroendocrinology*, **10**, Raven Press Ltd., New York, Chapt. 8, pp. 167–184, 1988.
10. Y. Eto and co-workers, *Biochem. Biophys. Res. Commun.* **142**, 1095–1097 (1987).
11. M. Murata and co-workers, *Proc. Nat. Acad. Sci. U.S.A.* **85**, 2434–2436 (1988).

General References

12. K. L. Becker, *Principles and Practice of Endocrinology and Metabolism*, J. B. Lippincott Co., Philadelphia, Pa., 1990.
13. D. T. Krieger, *Endocrine Rhythms*, Raven Press, New York, 1979.

Related Articles

Adrenal cortical; Anterior pituituary; Anterior pituitary-like; Posterior pituitary; Human growth hormone, Brain oligopeptides; Sex hormones; Estrogens and antiestrogens; Opiods, endogenous; Growth regulators, plant; Neuroregulators; Thyroid and antithyroid preparations; Insulin