Kirk-Othmer Encyclopedia of Chemical Technology.

HORMONES, POSTERIOR PITUITARY HORMONES

The posterior lobe of the pituitary, ie, the neurohypophysis, is under direct nervous control (1), unlike most other endocrine organs. The hormones stored in this gland are formed in hypothalamic nerve cells but pass through nerve stalks into the posterior pituitary. As early as 1895 it was found that pituitrin [50-57-7], an extract of the posterior lobe, raises blood pressure when injected (2), and that Pitocin [50-56-6] (Parke-Davis) causes contractions of smooth muscle, especially in the uterus (3). Isolation of the active materials involved in these extracts is the result of work from several laboratories. Several highly active posterior pituitary extracts have been discovered (4), and it has been determined that their biological activities result from peptide hormones, ie, low molecular weight substances not covalently linked to proteins (qv) (5).

The principal hormones of the human posterior pituitary include the two nonapeptides, oxytocin [50-56-6] and arginine vasopressin [11000-17-2] (antidiuretic hormone, ADH). Many other hormones, including opioid peptides (see Opioids, endogenous), cholecystokinin [9011-97-6] (CCK) (see Hormones, brain oligopeptides), and gastrointestinal peptides, also have been located in mammalian neurohypophysis (6), but are usually found in much lower concentrations (7). Studies have demonstrated that oxytocin and vasopressin are synthesized in other human organs, both centrally and peripherally, and there is considerable evidence for their role as neurotransmitters (see Neuroregulators) (8).

Oxytocin, although found in large quantities in both males and females, primarily functions in contracting the uterus during childbirth and releasing milk from mammary tissue. The fowl-pressor effect, ie, elevation of chicken blood pressure following iv administration of peptide, is a third action. It is fundamentally pharmacological, but an assay based on the effect often has been useful for rapid screening of potential active analogues. Arginine vasopressin (AVP) promotes water readsorption by the kidney, ie, the antidiuretic effect, and contraction of the smooth muscle of vascular tissue, ie, the pressor effect. Additional biological activities based on the behavioral properties of both hormones represent areas of intense research interest (9–11).

The structure of oxytocin was the first of the peptide hormones to be elucidated and synthesized by conventional methods of solution synthesis and fragment condensation (5, 12); structure elucidation and synthesis of AVP followed (Fig. 1) (13). At least 12 related nonapeptides have been isolated from various vertebrate species (8, 14). An additional 3 analogues have been described among the invertebrates. Oxytocin seems ubiquitous among higher mammals, although lysine vasopressin [50-57-7] (lysipressin, [Lys-^{8}]VP, LVP), a generally less potent analogue, is found in place of arginine vasopressin, [Arg-^{8}]VP or AVP, in the pig and related species.

1. Structure of the Principal Neurohypophyseal Hormones

The primary structures of oxytocin, the vasopressins, and some of the other natural neurohypophyseal analogues are given in Table 1. Each compound contains nine amino acids and each has a disulfide bridge between cysteine residues at positions 1 and 6. All are amidated at their C-terminal glycine residue. Variations among naturally occurring nonapeptides are found primarily in positions 3, 4, and 8. The relative activities of these compounds, when contrasted with their phyletic distributions and structural variations, suggest an

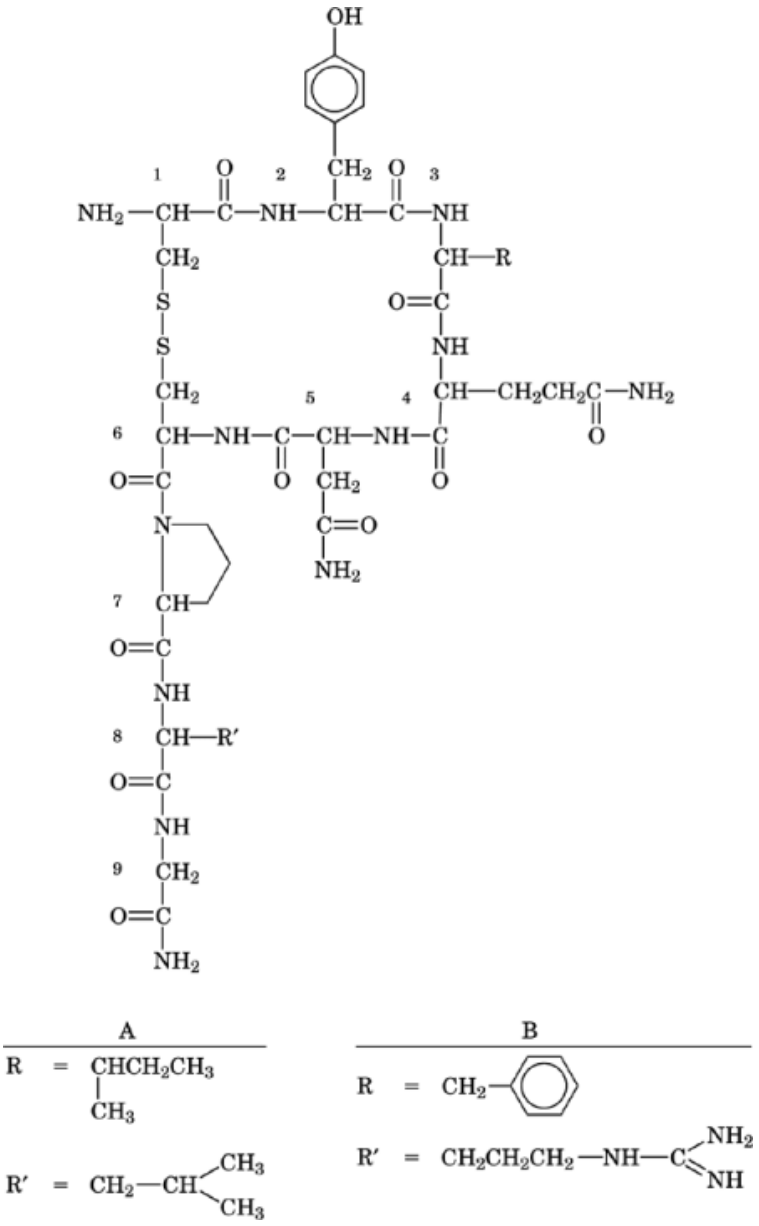
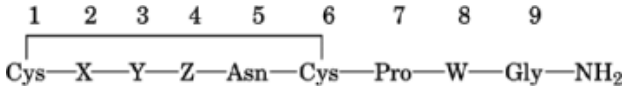


Fig. 1. Structure of oxytocin and arginine vasopressin. Numbers indicate approximate location of amino acids sequences found in Table 1. A, oxytocin; B, arginine vasopressin.

evolutionary relationship among the various peptides (14). A common link may be arginine vasotocin, which is found in lower vertebrates as well as in the most complex mammals.

The wide-ranging differences in biological activities among peptide congeners that have small structural variations, eg, oxytocin and aspartocin [4117-65-1], are remarkable; in determining their conformation—activity parameters (15, 16) and their evolutionary significance (17–19), such variations have made the

Table 1. Structures of the Neurohypophyseal Hormone-Like Peptides[a,b]



Species	Peptide	X,Y,Z	W
	Oxytocin-like peptides		
tetrapods	oxytocin	Tyr-Ile-Gln	Leu
	mesotocin	Tyr-Ile-Gln	Ile
bony fishes	isotocin	Tyr-Ile-Ser	Ile
cartilaginous fishes			
rays	glumitocin	Tyr-Ile-Ser	Gln
spiny dogfish	valitocin	Tyr-Ile-Ser	Val
	aspartocin	Tyr-Ile-Asn	Leu
spotted dogfish	asvatocin	Tyr-Ile-Asn	Val
	phasvatocin	Tyr-Phe-Asn	Val
octopus	cephalotocin	Tyr-Phe-Arg	Ile
	Vasopressin-like peptides		
mammals	arginine vasopressin	Tyr-Phe-Gln	Arg
pig, marsupials	lysine vasopressin[c]	Tyr-Phe-Gln	Lys
macropodids	phenypressin	Phe-Phe-Gln	Lys
nonmammalian vertebrates	arginine vasotocin	Phe-Phe-Gln	Arg
invertebrates	locust suboesophagial ganglia peptide	Leu-Ile-Thr	Arg
Conus striatus	arginine conopressin	Ile-Ile-Thr	Arg
Conus geographicus	lysine conopressin	Phe-Ile-Arg	Lys

[a]Ref. 14.
[b]Numbers represent the position of the amino acids relative to the N-terminus.
[c]Lysipressin.
(Courtesy of Elsevier Science.)

neurohypophyseal hormones very valuable. In general, oxytocin and analogues that bind well to oxytocic receptors all contain tyrosine at the 2 position and a hydrophobic residue, eg, Leu, Ile, Val, or Gln, at the 8 position. In contrast, vasopressin and other analogues that bind to the vasopressin receptor classes are characterized by a Phe at the 3 position and basic residues, ie, Arg or Lys, at the 8 position.

Other, more recently described, naturally occurring neurohypophyseal hormone analogues include phenypressin [30635-27-9] ([Phe-^{2}]-arginine vasopressin), found in kangaroos and other macropodidae (20), and conopressins found in *Conus* snails (21). *Conus* snails are representative of invertebrate classes that diverged from vertebrates over 700×10^6 years ago and also represent rich sources of many other biologically active peptides such as ion-channel blockers. In the opposum, an American marsupial, four hormones are found, ie, oxytocin, mesotocin [362-39-0], lysine vasopressin, and arginine vasopressin.

The structural similarities between oxytocin and vasopressin analogues can be contrasted to their distinct physiological roles and even their separate receptor second messengers. Oxytocin seems to have evolved from the more primitive isotocin [550-21-0], found in fish, to mesotocin, found in amphibians and reptiles, to oxytocin, found in higher mammals. In contrast, vasotocin is found in fish, amphibians, and reptiles, but evolved to

vasopressin in mammals. Because there are separate oxytocin receptors in mammals, the presence of vasotocin, which has significant oxytocic activity, could have proven problematic and led to this evolutionary change. Vasotocin is an antidiuretic in amphibians and reptiles but is a diuretic in freshwater fishes, including lungfish (14).

2. Conformation and Structure-Activity Relationships

Hundreds of analogues of both oxytocin and vasopressin have been synthesized, and the conformations of many of these have been studied (23, 23). Several large structural compilations are available. Conformational and topographic features of these analogues have been studied by nmr (24–26), raman spectroscopy (27), and circular dichroism (28). These methods, supplemented by conformational calculations, have provided a reasonably clear understanding of the structures of the neurohypophyseal hormones in various solutions (16). Newer techniques in nmr spectroscopy have improved the quality and quantity of structural information regarding peptide hormones (see Magnetic spin resonance). For example the presence of a minor amount of a *cis*-6-7-amide bond in oxytocin was revealed by one- and two-dimensional proton and carbon spectroscopies; as of this writing the physiological relevance of this finding is not apparent (29).

Disulfide bridging and hydrogen bonds greatly limit the number of possible structures. The Urry-Walter proposed conformation (30) is the representative and, for the most part, biologically relevant model (16). Highly active analogues of oxytocin have been synthesized, based partly on this structure. A similar and key feature in oxytocin and LVP is the presence of a β-turn, involving residues 2–5, which is stabilized by a hydrogen bond from the 2-tyrosine CO to the 5-asparagine NH (31). The 5-asparagine of oxytocin also may contribute to structural rigidity by a second hydrogen bond from its side chain to the oxytocin tail -(Pro-Leu-Gly-NH_2); in contrast to a more compact structure when dissolved in organic solvents, eg, dimethyl sulfoxide, the tail is free to move in aqueous media (32). An x-ray structure (Fig. 2) of the potent oxytocin analogue deaminooxytocin [113-78-0] provides additional support for this model (33) and has been used to guide both new agonist and antagonist design (34).

In water, the aromatic rings of vasopressin in residues 2 and 3 are believed to be in close proximity. However, the 2-tyrosine residue of oxytocin is folded over the 20-membered ring in the proposed biologically active conformer. The [2-D-tyrosine]AVP analogue, which can maintain a hydrophobic interaction with phenylalanine pointing away from the ring, retains significant antidiuretic activity, whereas the corresponding [2-D-tyrosine]oxytocin derivative is practically devoid of uterotonic potency (35). General findings support the concept that neurohypophyseal hormones are relatively flexible peptides which have various binding and active elements that can, in theory, be modified to form either superagonists or hormone inhibitors. A relevant example is a bicyclic oxytocin analogue formed by cyclizing a Glu^4 to a Lys^8. This lactam bridge converts a weak agonist, ie, the noncyclized form, to a more rigid and fairly potent oxytocin antagonist (36). Equally significant, however, is the report of linear analogues of vasopressin (37) that have been found to be surprisingly potent antagonists toward vasopressin receptor subclasses.

3. Synthesis of Posterior Pituitary Hormones and Their Analogues

3.0.1. Agonists

Both oxytocin and the vasopressins have been synthesized by numerous routes using both rapid-solution (38) and solid-phase methods (39). The latter route has facilitated the syntheses of hundreds of analogues which are extremely useful in establishing cogent structure—activity relationships (23, 34, 40, 41). In general, large structural variations, which alter overall geometries, prove destructive to activity. Subtle variations, however, have led to compounds with retained and even markedly enhanced hormonal activities; several of these

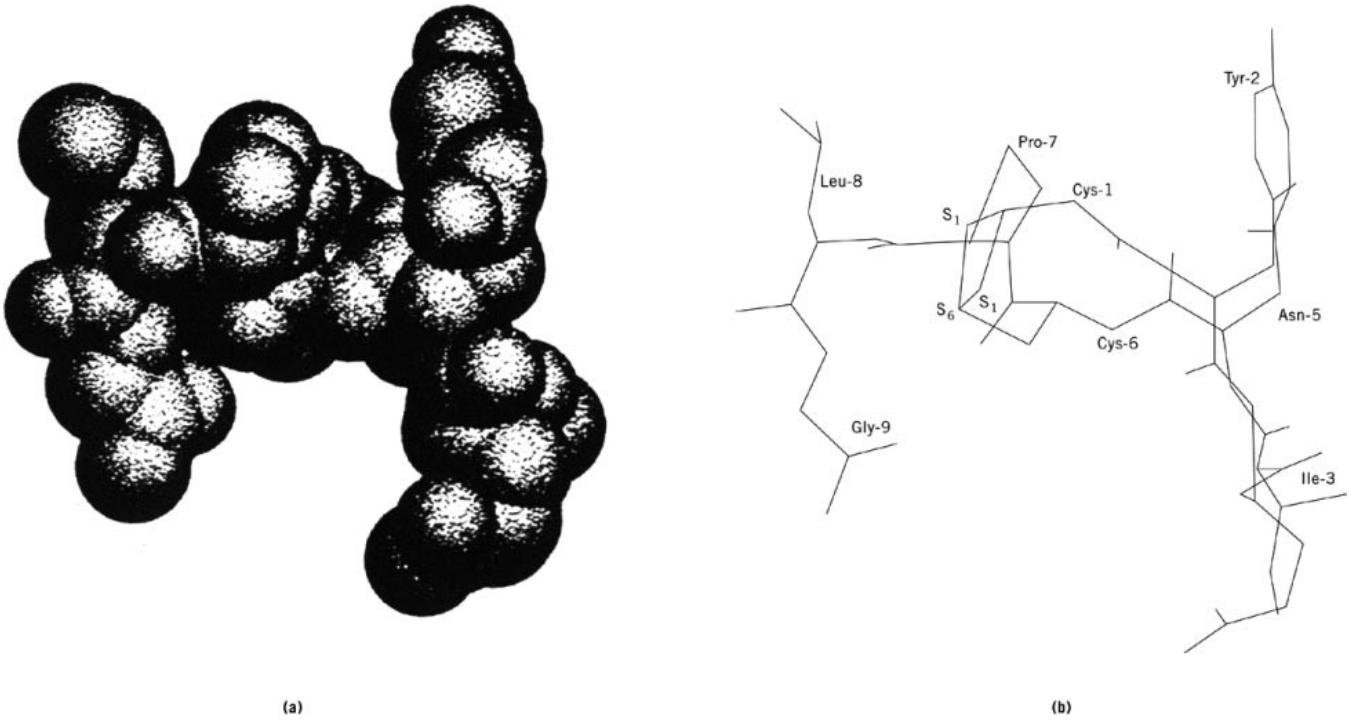


Fig. 2. X-ray structure of deaminooxytocin: (**a**) space-filling model; (**b**) equivalent stick model. Numbers and amino acids refer to positions indicated in Table 1. S_1–S_6 bond is indicated (Fig. 1) (33).

Table 2. Synthetic Analogues of Oxytocin with High Potency or Selectivity

	UBiological activities[a]				
Peptide	Oxytocic	Milk ejection	Antidiuretic	O/A ratio[b,c]	Reference
oxytocin	520	474	4	130	23
1-deamino-oxytocin	803	541	19	42	23
[Thr-4]-oxytocin	923	543	0.9	1026	41
[Thr-4,Gly-7]-oxytocin	166	802	0.002	83,000	41

[a] Biological activities are in USP units/mg.
[b] O/A ratio = oxytocic/antidiuretic ratio.
[c] In the absence of Mg^{2+}.

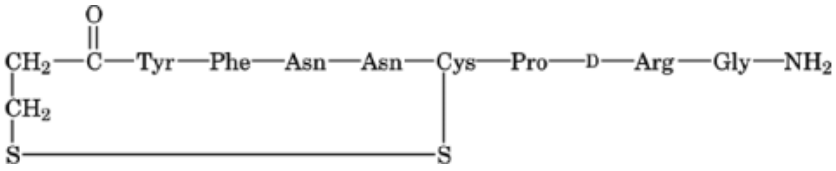
are summarized in Tables 2 and 3. In some cases, certain variations, eg, deaminooxytocin and carba analogues which substitute methylene groups for the disulfide bridge, apparently retard biodegradation, whereas others, eg, 7-thiaproline- [59095-56-6] and 7-dehydroproline-oxytocin, appear to increase the hormones' affinities to their respective receptors. A particularly potent synthetic analogue is the vasopressin derivative [1-deamino,2-phenylalanine,7-(3,4-dehydroproline)]arginine vasopressin [66185-31-3]; its antidiuretic potency is $13{,}000 \pm 1{,}250$ IU/mg as compared to 503 ± 53 IU/mg for authentic AVP (42). In addition, this analogue has negligible pressor activity and thus exhibits the dissociated biological activity which frequently is a goal of synthetic analogue studies.

Table 3. Synthetic Analogues of Vasopressin with High Potency or Selectivity

Peptide	Biological activities[a]		A/Pratio[b]	Reference
	Antidiuretic activity	Vasopressor activity		
arginine vasopressin	503	487	1	34
1-deamino[D-Arg]-8-vasopressin	1200	0.39	3000	41
1-deamino-Val-4, Arg-8	1230	antagonist	infinite	41

[a] Biological activities are in USP units/mg.
[b] A/P ratio = antidiuretic/pressor activity ratio.

Hormone analogues have been tested that have nonparallel dose—response curves and that yield analogues with unusually high activities at low doses. This characteristic was exploited in the synthesis of the AVP analogue, [1-deamino,4-asparagine,8-D-arginine]vasopressin [65919-02-0] and yielded a hybrid having almost pure antidiuretic activity of ca 11,000 IU/mg (43).



3.0.2. Antagonists

Another goal of structure—function studies of peptide hormones is the design of antagonists or hormone inhibitors that may have potential clinical usage (44). Modifications of the N-terminus of oxytocin and the vasopressins have yielded structures having significant *in vitro* inhibitory activities. As shown in Table 4, synthetic inhibitors of oxytocin contain variations in the 1 and 2 positions, eg, 1,1-dialkylmercaptopropionic acid and 2-*O*-alkyltyrosine. Conformationally restricted structures, especially near the N-terminus, yield some of the most potent inhibitory analogues (45, 46). Analogues of vasopressin have been synthesized that are either potent pressor antagonists, such as [Mcpr-1, Tyr(CH_3)-2]AVP, or that have potent antiantidiuretic activity, ie, [Mcpr-1,Phe-2,Ile-4,Ala-9]AVP. Similarly, oxytocin analogues have been found having impressive antioxytocic activity but limited antipressor activity, eg, [deamino-1,cyclo(Glu-4, Lys-8)]oxytocin (36).

Two fundamental questions have emerged from these studies, ie, to what extent are agonists and antagonists binding similarly or differently to the respective receptors, and can inhibitory compounds be developed that are active *in vivo* in humans as well as *in vitro*. An oxytocin antagonist that can block premature uterine contractions presents a promising example of the clinical utility of such structures (47). Both linear as well as bicyclic modifications of these hormones also have provided new antagonist structures.

Other potential oxytocin antagonists are being developed using leads from naturally occurring, nonpeptide structures, such as an extract from *Streptomyces* (48). A selective nonpeptide vasopressin V_1 receptor antagonist also has been found (49).

3.0.3. Degradation

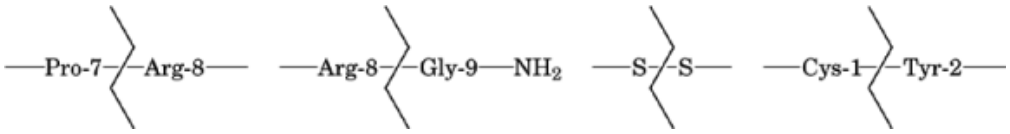
Both oxytocin and vasopressin have short plasma half-lives in humans; oxytocin has a half-life of several minutes (50, 51); and ^{125}I vasopressin has a half-life in humans of 24 min (52). A pattern of hormone metabolism in various species, including identification of sites vulnerable to enzymic cleavage, has been developed by using radioactively labeled oxytocin and vasopressin analogues and by detecting hormone fragments (see Radioactive tracers) (53). Cleavage sites of oxytocin include the 8–9 bond, yielding glycinamide, and the 7–8 bond by virtue

Table 4. Synthetic Analogues of Oxytocin and Vasopressin Having Antagonist Activities

Analogue[a]	Activity, pA_2[b]		Ref.
	Antioxytocic	Antipressor[c]	
Oxytocin			
[Mcpr-1]oxytocin	7.61	weak	34
[penicillamine-1]oxytocin	6.86	0	45
[deamino,cyclo(Glu-4, Lys-8)]-oxytocin	8.74	6.3	36
[Mcpr-1, Tyr(CH_3)-2,Orn-8]-oxytocin	8.52	7.96	34
Vasopressin			
[Mcpr-1,Tyr(CH_3)-2]AVP	8.13	8.62	44
[Mcpr-1,Tyr(CH_2CH_3)-2,Val-4]AVP	7.88	8.16	44
[Mcpr-1,Phe-2,Ile-4,Ala-9]AVP		7.71	44

[a] $\mathrm{Mcpr} = 3 - \mathrm{mercapto} - 3, 3 - \mathrm{cyclopentamethylene\ propionic\ acid}$.
[b] $p\mathrm{A}^2 = -\log\ \mathrm{A}_2$, where A_2 refers to concentration required to cause 50% inhibition of agonist response.
[c] Antiantidiuretic activity for [Mcpr-1,Tyr(CH_2CH_3)-2, Val-4]$\mathrm{AVP} = 7.57$; for [Mcpr-1,Phe-2, Ile-4,Ala-9]$\mathrm{AVP} = 8.38$.

of post-proline cleaving enzyme (50), yielding the dipeptide $\mathrm{Leu{-}{-}Gly{-}{-}NH^2}$ (54). In addition, oxytocin may be degraded in the testes by disulfide reduction (30%) and by cleavage of the 1–2 bond (70%) (55). A similar pattern of enzymic cleavage for vasopressin has been reported to have four main sites (56):



In the placenta, the aminopeptidase oxytocinase, ie, cysteine aminopeptidase, is a principal catalyst for oxytocin hydrolysis and prevents premature uterine contractions.

3.0.4. Neurophysins, Hypothalamic Hormones, and Hormone Processing

The neurophysins represent a group of medium-sized (9000–10,000 mol wt) proteins found in the posterior pituitary that act as carriers of oxytocin and the vasopressins (57, 58). Although the pattern is species-variant, the two principal forms found in higher mammals are neurophysin I (NP-I) and II (NP-II) (59); these appear to be associated with vasopressin and oxytocin, respectively. According to the concept of one neurophysin—one hormone, the carrier proteins and their respective hormones are synthesized as linear peptide chains on human chromosome 20 (60) and then cleaved and cyclized to yield NP-I and vasopressin and NP-II and oxytocin (61, 62). The posterior pituitary hormones and their carrier proteins are synthesized in the supraoptic and paraventricular neurons of the hypothalamus (63, 64) as part of larger preprohormone sequences, ie, prepro-oxytocin and prepro-vasopressin. These precursors have been verified from nucleotide sequence analysis of complementary deoxyribonucleic acid (cDNA) as well as by more traditional peptide sequencing studies (65). Following initial translation of the prepro sequences, the N-terminal signal peptide region is cleaved to yield pro-oxytocin or pro-vasopressin. These prohormones are then further processed in the neurosecretory vesicles to yield three components, ie, the peptide hormone, the neurophysin, and a C-terminal glycopeptide having an N-terminal glycosylation site (Asn-Ala-Thr) (66). As for the neurophysins, no clear biological role has been established for either of the glycopeptides. Figure 3 shows a representation of the processing steps for rat and bovine preprovasopressins (14).

In humans, the hypothalamic-derived protein and the hormone noncovalent complexes are packaged in neurosecretory granules, then migrate along axons at a rate of $1 - 4\ \mathrm{mm/h}$ until they reach the posterior

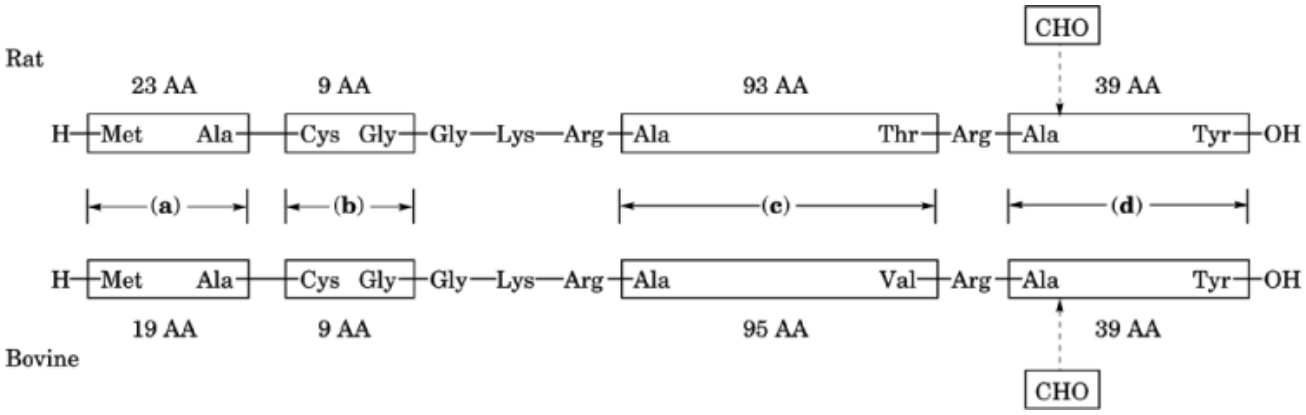


Fig. 3. Processing steps of rat and bovine prepro-vasopressin leading to the hormone vasopressin and its carrier protein, neurophysin (14). (**a**) Putative signal peptide; (**b**) vasopressin; (**c**) neurophysin; (**d**) glycopeptide. CHO=carbohydrate .(Courtesy of Elsevier Science.)

pituitary where they are stored prior to release into the bloodstream by exocytosis (67). Considerable evidence suggests that posterior pituitary hormones function as neurotransmitters (68); vasopressin acts on the anterior pituitary to release adrenocorticotropic hormone [9002-60-2] (ACTH) (69) as well as on traditional target tissues such as kidneys. Both hormones promote other important central nervous system (CNS) effects (9, 70).

The nature of the hormone—NP link is unclear. Although the binding is quite specific, it is sufficiently weak, ie, binding constant $10^{-5} - 10^{-6} M$ (71), as to cast doubt upon a protective role. However, no compelling evidence for a biological function for the neurophysins, other than as hormone carriers, has been elucidated (59, 72).

Sequences and partial sequences of several of the neurophysins, including those in rat, cod, and sheep, have been determined (73, 74). Most neurophysins contain 90–95 individual amino acid residues. Considerable sequence homology exists among the various neurophysin classes and between vertebrate species, especially in the region between 10 and 76. The molecules contain seven disulfide bridges, and 13 or 14 cysteine residues are found within the highly conserved 10–76 region. Some repetition within the peptide chain suggests a possible second binding site, but most evidence is supportive of a single strong binding site for oxytocin and vasopressin under physiological conditions. The principal site for attachment of oxytocin to neurophysin appears to be mainly via the N-terminal residues (59).

3.0.5. Oxytocin and Vasopressin Receptors

The actions of oxytocin and vasopressin are mediated through their interactions with receptors. Different receptor types as well as different second messenger responses help explain their diverse activities in spite of the hormones' structural similarities. Thus oxytocin has at least one separate receptor and vasopressin has been shown to have two principal receptor types, V_1 and V_2. Subclasses of these receptors have been demonstrated, and species differences further complicate experimental analysis. It is apparent that both oxytocin and V_1 receptors function through the GP/1 phospholipase C complex (75), while the V_2 receptors activate cyclic AMP (76).

The ultimate goal of structure—function studies is complete understanding of the hormone's interaction with its receptor(s). Evidence continues to support an oxytocin model in which residues 2 and 5, ie, Tyr and Asn, are vital for interaction with the uterine smooth muscle receptor (77–79). In this model, the residues at positions 3, 4, 7, and 8 are at the corners of two β-turns and, as binding elements, in principle can be modified to provide greater affinity with the receptor. Early studies examined the binding of oxytocin and vasopressin

analogues to porcine (78) and bovine (79) receptors. The correlation found between activation of adenylate cyclase from renal membrane preparations and the known relative activities or affinities of the preparations is good evidence for the suggested mechanisms and site of action for these hormones.

V_1 receptors, found in vascular smooth muscles (80) and in the liver (81), function by means of a calcium-dependent pathway. V_2 receptors, found in the kidney (82), modulate the antidiuretic response of vasopressin analogues through a cyclic adenosine monophosphate (AMP)-dependent pathway. With the development of potent and reasonably selective agonists and antagonists of vasopressin, the elucidation of additional physiological roles for VP has been shown (70). Similarly, through the use of oxytocin superagonists and inhibitors, a variety of behavioral properties affecting maternal, sexual, and social behavior have been discerned (83).

Several human receptors for the neurohypophyseal hormones have been cloned and the sequences elucidated. The human V_2 receptor for antidiuretic hormone presumably contains 371 amino acids and seven transmembrane segments and activates cyclic AMP (76). The oxytocin receptor is a classic G-protein-coupled type of receptor with a proposed membrane topography also involving seven transmembrane components (84). A schematic representation of the oxytocin receptor structure within the membrane is shown in Figure 4 (85).

4. Uses

Oxytocin has been used widely to induce labor, although its suitability has been questioned; prostaglandin E_2 may be a practical alternative (86) (see Prostaglandins). Among side effects cited with oxytocin use are water intoxication as a result of the natural natriuretic effect of oxytocin, venospasm, and increased incidence of neonatal jaundice. Oxytocin also is used clinically to facilitate milk ejection in nursing mothers. It is available for intravenous, oral, or nasal modes of administration, ie, it is supplied as Pitocin (Parke-Davis) for intravenous use and as its citrate for buccal administration, and is marketed as Syntocinon (Sandoz) for injection or as a nasal spray. Syntocinon is one of the first examples of a solid-phase-derived synthetic polypeptide licensed for clinical use. The nasal spray is administered 2–3 min before nursing to induce contraction of the breast myoepithelial elements, thereby making milk more readily available in the larger mammary ducts. A number of synthetic oxytocin analogues are also finding clinical use, especially in Europe under such trade names as Sandopart, carbetocin, and methyloxytocin, and in Japan as Cargutocin (Statocin) (87).

Hyposecretion by the hypothalamic supraoptic nuclei or injury to the posterior pituitary can give rise to diabetes insipidus; a gene deletion in the rat also has been shown to lead to diabetes insipidus (88). The symptoms of the disease can be controlled by chronic administration of antidiuretic hormone (ADH). Vasopressin infusion also has been used in the management of gastrointestinal hemorrhage (see Gastrointestinal agents). A vasopressin analogue, desamino-8-D-arginine vasopressin [16679-58-6] (desmopressin, DDAVP), has prolonged biological activity and a high antidiuretic:pressor ratio which has led to its use in clinical trials as a substitute for AVP (89, 90). In addition, it has proven useful in hemophilia as a hemostatic agent, reducing the need for blood and plasma products (91).

Vasopressin is supplied as Pitressin Tannate (Parke-Davis) for use as an antidiuretic agent administered intramuscularly (see Diuretic agents). Lysine vasopressin is marketed in nasal spray form as an antidiuretic under the trademark Diapid (Sandoz).

4.0.6. Vasopressin and Memory

Several hormones, eg, ACTH, vasopressin, and the catecholamines, may be involved in memory retention or consolidation (9, 11, 85) (see Antiaging agents; Memory-enhancing drugs). LVP and AVP and analogues significantly reduce the effect of puromycin-induced amnesia in mice (92), and vasopressin is present in several regions of the brain (93). The utility and long-lasting effect of vasopressin on retention of conditioned avoidance response has been demonstrated (94). These memory and learning effects are probably not related to the

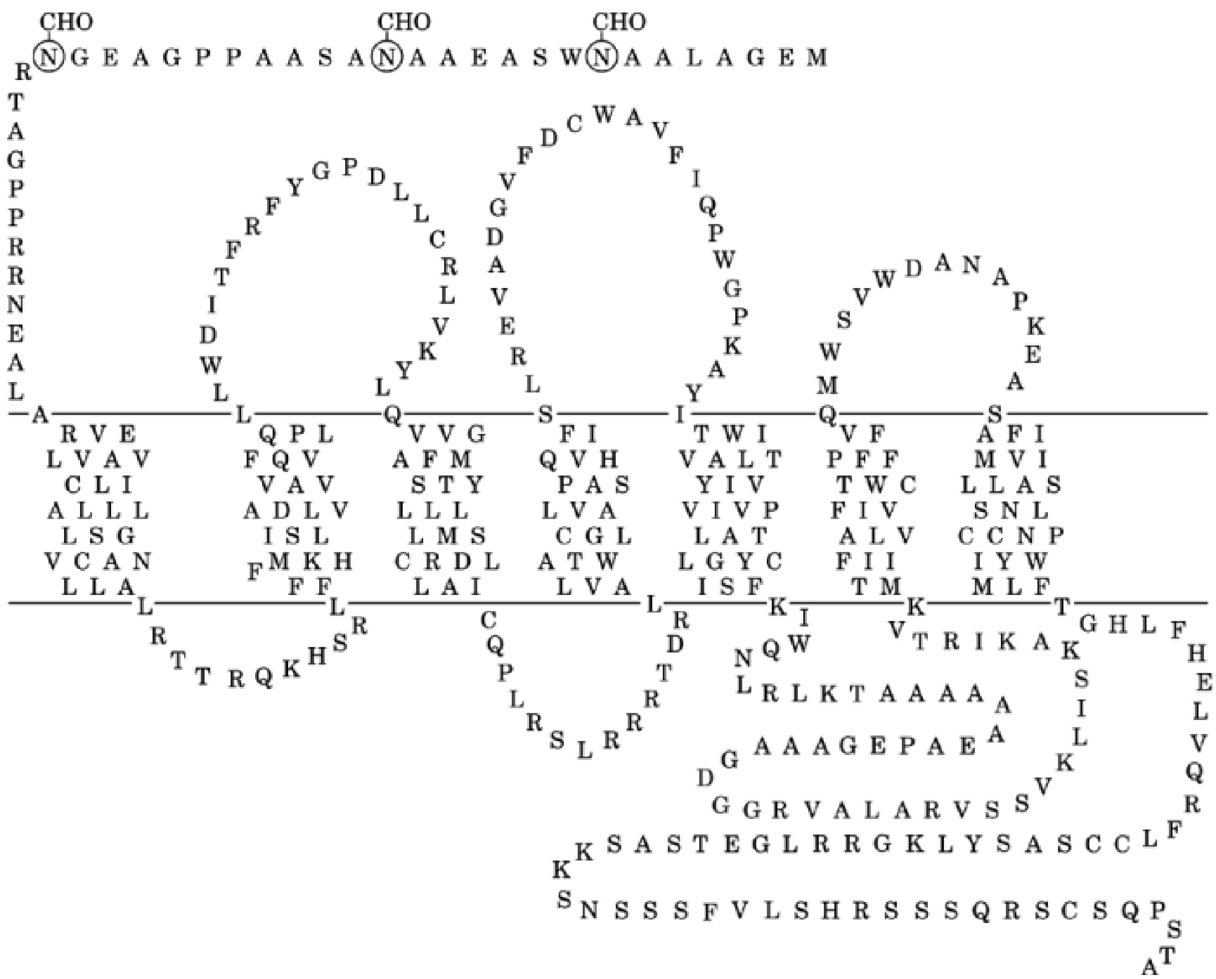


Fig. 4. Representation of proposed topography of human oxytocin receptor (85) where CHO represents carbohydrate.(Courtesy of Elsevier Science.)

primary action of the vasopressins, since similar activities are seen using an octapeptide fragment, ie, desglycinamide LVP [32472-43-8], isolated from porcine pituitary and inactive in pressor and antidiuretic assays (95). While there is not universal agreement regarding the role of vasopressin and memory (86), a variety of clinical studies, including ones designed to test the effects of vasopressin analogues on memory retention in both the young and the elderly, continue to be performed (87).

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