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BIOCHEMISTRY AND BIOPHYSICS

Role of the Plasma Membrane Lipid Matrix in Information Transfer by Regulatory Peptides

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Messages transmitted by biologically active substances, including regulatory peptides, to their target cells are materialized in altered rates and/or direction of intracellular biochemical processes. Such alterations are thought to result from stimulation or inhibition of secondary messenger systems (the adenylate cyclase, polyphosphoinositide, and other systems). The activity of these systems is regulated mainly by specific receptors found on the plasma membranes of effector cells. It is believed that the information contained in a regulatory peptide (RP) is transferred to the cell when the RP molecule binds to its specific receptor.

During the past decade, however, a large body of experimental evidence has been obtained demonstrating surface-active properties of RP and the ability of their molecules to modify lipid mono- and bilayers (as well as mono- and bilayers formed from isolated plasma membranes) by incorporating themselves between the lipids [1,3,5-8,12,14]. Such incorporation of an RP into the lipid matrix may precede its receptor binding and bring about alterations in the course of intracellular processes independently of the receptor. This indicates that the RP-lipid matrix interaction plays a role in information transfer to the cell's interior.

The purpose of the present study was to throw more light on the involvement of the plasma membrane's lipid phase in information transfer via RP.

MATERIALS AND METHODS

The amount of information contained in an RP molecule in solution was computed on the basis of the following considerations. The amount of information

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(H) in an RP molecule is given by Shannon's formula:

$$H = - K\Sigma p_i \ln p_i, \quad (1)$$

where K is a coefficient for determining H in bits ($K = 1/\ln 2$) and p_i is the probability of the ith conformation of the RP molecule, with $i = 1, 2, ..., N$ (N being the number of permissible low-energy conformations).

In solution, however, the probabilities of the RP molecule occurring in different conformational states are equal [2], so that

$$p_1 = p_2 = ... = p_i = 1/N.$$

In this case, H will be maximal and can be calculated by the formula:

$$H_{max} = K \ln N. \quad (2)$$

This formula was used to compute the amount of information carried by RP molecules in solution.

The redundancy of information was characterized by a redundancy coefficient calculated using the formula:

$$R = 1 - H_i/H_{max}, \quad (3)$$

where R is the redundancy coefficient and H_i is the amount of information carried by one conformer.

The ability of RP to modify artificial lipid membranes was determined by examining their interaction with monolayers formed from individual lipids, their mixtures, or isolated plasma membranes as described previously [5] and [8], and also with flat bilayer lipid membranes prepared by the method described else where [3].

RESULTS

At the molecular level, information is carried by the three-dimensional structure of RP molecules that is organized in a particular way [11]. In solution, however, peptide molecules do not have a fixed conformation. One can describe the structures of RP molecules in solution by a set of low-energy conformational states [2] and then use formula (2) to compute the amount of information carried by these molecules in solution.

The number of low-energy conformers of some RP molecules and the calculated amounts of information corresponding to them are shown in Table 1. It can be seen that the total information contained in an RP is directly proportional to the number of permissible structures of their molecules.

Yet the amount of information is not a crucial factor in the action of an RP on the effector cell. Here, a more important characteristic is the value of the information being transferred.

On the one hand, a valuable message is one that can lead to goal-directed alterations in the course of physiological processes occurring within the cells. Such alterations, as noted above, are mediated by the binding of RP molecules to their receptors. In this case, however, RP molecules would need to be present in only one stable conformation in which they would bind to the specific receptor and transfer information to the cell. The presence of a definite number of equally probably conformers presupposes the possibility of RP binding not just to one specific receptor for transmitting a message.

On the other hand, the "extra" conformers carry redundant information, i.e., information which, according to a widely accepted theory of hormone-receptor interaction, does not have to be materialized by the cell subsequently. Information redundancy is defined by the redundancy coefficient, whose calculated values for several RP are also shown in Table 1. As seen in this table, the coefficient is fairly high for virtually all of the peptides. Such "extravagance" on the part of nature seems unlikely. However, the possible acceptors of RP on the effector cell surface may also be the receptors of other ligands, mem-

Table 1. Quantity of Information Contained in Regulatory Peptide Molecules

Peptide	№ of conformers in solution	Quantity of information in solution (H), bits	Redundancy coefficient (R)	Lipid membrane modification	Reference(s)
Angiotensin II	5	2.322	0.800	+	[12]
Bradykinin	12	3.585	0.917	+	[8]
Vasopressin	11	3.459	0.909	+	[3]
Enkephalins	10	3.322	0.900	+	[1]
Luliberin	3	1.585	0.667	?	
α–Melanotropin	13	3.700	0.923	?	
Oxytocin	6	2.585	0.833	+	[5,6]
Substance P	13	3.700	0.923	+	[7]
Tuftsin	5	2.322	0.800	?	
Tetragastrin	22	4.459	0.955	?	
Thyroliberin	6	2.585	0.833	?	

brane-bound enzymes, and the membrane's lipid bilayer.

Indeed, increased value of the information being transferred is achievable owing to the presence of various receptor subtypes [9]. RP such as neurohypophyseal hormones, enkephalins, and substance P have been shown to be capable of acting on the cell by binding to receptors for other bioregulators [10,15]. Some RP can influence the activity of membrane-bound proteins in a direct fashion [4]. Furthermore, recent experimental evidence indicates that many peptides are able to interact directly with the plasma membrane lipid matrix of the effector cell [1,3,5-8,12,14].

The role of the peptide-lipid interactions mentioned above may be visualized as follows. By being adsorbed on the lipid bilayer, RP molecules can acquire the particular conformation required for their binding to the receptors, and this property probably enables the cell to receive information from various conformers of one peptide that are present in solution. Then, RP molecules residing in the lipid environment can influence various membrane-bound proteins and also can modify physicochemical characteristics of the plasma membrane lipid matrix itself. As a result, the quantity and, consequently, the value of the information carried by the RP and received by the cell can be considerably increased.

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Effect of Low-Dose Emoxypine and Pyridoxine Hydrochloride on Human Cataract and Glaucoma

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Synthetic antioxidants have been extensively used in ophthalmological practice as preparations protecting the retina from damage developing in the activation of free-radical oxidation reactions. The concept underlying their use implies that disturbances in the oxidative processes and antioxidation protection mechanisms affect the membrane structures of the

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