A S S I G N M E N T

 **BCH 308: Cellular Biochemistry**

***Topic:* Describe in details the synthesis of two named neurotransmitters.**

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**300 Level.**

SYNTHESIS OF DOPAMINE

Dopamine is a neurotransmitter found in the amine group. It is a monoamine neurotransmitter. Dopamine is synthesized from the amino acid tyrosine, which is taken up into the brain via an active transport mechanism.

Tyrosine is initially produced in the liver from phenylalanine through the action of an enzyme (Phenylalanine hydroxylase). The tyrosine is then transported to dopamine containing neurons. Series of reactions within the neurons convert the tyrosine to dopamine.

Within catecholaminergic neurons i.e. aromatic neurons, a hydroxyl group is added to the meta-position of the tyrosine and is catalyzed by tyrosine hydroxylase to yield L-dopa. This is a rate limiting step and is subject to inhibition from high levels of catecholamine.

Once formed, the L-dopa is rapidly converted to dopamine by an enzyme known as dopa decarboxylase, located in the cytoplasm. This enzyme acts on other aromatic L-amino acids.

There are five subtypes of dopamine receptors: D1, D2, D3, D4, and D5, which are members of the large G-protein coupled receptor family. The dopamine receptor subtypes are divided into two major subclasses: types 1 and 5 are similar in structure and drug sensitivity, and these two receptors are referred to as the "D1-like" group or class of receptors. Dopamine receptor types 2, 3, and 4 are also similar in structure and are, therefore, grouped together as the "D2-like" group.

The ultimate effect of D1-like activation (D1 and D5) can be excitatory (via opening of sodium channels) or inhibitory (via opening of potassium channels); while that of D2-like activation (D2, D3, and D4) is usually inhibition of the target neuron. The effect of dopamine on a target neuron depends on which types of receptors are present on the membrane of that neuron and on the internal responses of that neuron to the second messenger cAMP (cyclic Adenosine Monophosphate).

D1 and D5 receptors are mostly involved in post synaptic inhibition. D2, D3, and D4 receptors are involved in both pre-and postsynaptic inhibition. D2 receptors regulates mood, emotional stability in the limbic system and movement control in the basal ganglia [3,4].

D1 receptors are the most numerous dopamine receptors in the human nervous system and D2 receptors are the second most abundant receptors. D3, D4, and D5 receptors are present at significantly lower levels.

Consequently, after other series of reactions, dopamine can be converted to norepinephrine and ultimately to epinephrine.



SYNTHESIS OF GABA (GAMMA AMINOBUTYRIC ACID)

GABA, found in the amino acid group is the chief inhibitory group in a developmentally mature mammalian central nervous system. It can be sold as a dietary supplement. GABA acts at inhibitory synapses in the brain by binding to specific receptors in the plasma membrane of both pre- and postsynaptic neuronal processes. This binding causes the opening of ion channels to allow the flow of either negatively charged chloride ions into the cell or positively charged potassium ions out of the cell, resulting in hyperpolarization.

 GABA is primarily synthesized from glutamate via the enzyme glutamate decarboxylase (GAD) with pyridoxal phosphate as a cofactor. This pyridoxal phosphate is the active form of vitamin B6. This process converts glutamate (the principal excitatory neurotransmitter) into GABA (the principal inhibitory neurotransmitter).

 GABA can also be synthesized from putrescine by diamine oxidase and aldehyde dehydrogenase.

 There are two general classes of GABA receptor:

* GABAA receptor: The GABAA receptor is an ionotropic receptor and ligand-gated ion channel. Its endogenous ligand is γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system. The GABAA receptor is selectively permeable to chloride ions (Cl−) and, to a lesser extent, to bicarbonate ions (HCO−), in which the receptor is part of a ligand-gated ion channel complex.
* GABAB receptor: They are metabotropic G protein-coupled receptors that open or close ion channels e.g. potassium channels via intermediaries (G proteins).