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**QUESTION**

Describe, in details, the synthesis of two named neurotransmitters.

**ANSWER**

1. DOPAMINE

Dopamine is monoamine neurotransmitter. Dopamine is produced in the dopaminergic neurons in the ventral tegmental area of the substantia nigra, midbrain and the arcuate nucleus of the hypothalamus. Due to extensive localization of dopamine receptor to brain areas and its role in wide range of functions, dopaminergic dysfunction has been implicated in the pathophysiology of schizophrenia, mood disorders, obsessive compulsive disorder (OCD), autism spectrum disorder, attention deficit–hyperactivity disorder (ADHD), Tourette’s syndrome, substance dependency, Parkinson's disease and other disorders.

Synthesis;

Dopamine is synthesized from the amino acid, tyrosine, which is taken up into the brain via an active transport mechanism. Tyrosine is produced in the liver from phenylalanine through the action of phenylalanine hydroxylase. Tyrosine is then transported to dopamine containing neurons where a series of reactions convert it to dopamine. Within catecholaminergic neurons, tyrosine hydroxylase catalyzes the addition of a hydroxyl group to the Meta position of tyrosine, yielding L-dopa. This rate-limiting step in catecholamine synthesis is subject to inhibition by high levels of catecholamines (end-product inhibition). Because *tyrosine hydroxylase* is normally saturated with substrate, manipulation of tyrosine levels does not readily impact the rate of catecholamine synthesis. Once formed, L-dopa is rapidly converted to dopamine by *dopa* *decarboxylase*, which is located in the cytoplasm. It is now recognized that this enzyme acts not only on L-dopa, but also on all naturally occurring aromatic L-amino acids, including tryptophan, and thus it is more properly termed *aromatic amino acid decarboxylase*.

1. SEROTONIN

Serotonin (5-hydroxytryptamine), synthesized from the amino acid, *tryptophan*, is an important monoamine neurotransmitter in the brain and in the periphery. It is a small molecule that functions both as a neurotransmitter in the central nervous system and as a hormone in the periphery.

Synthesis;

Serotonin is a synthesized through a multistep pathway in which L-tryptophan is converted to L-5OH-tryptophan by an enzyme called *tryptophan hydroxylase* (*Tph*). L-5OH-tryptophan is then converted to serotonin by an enzyme called *tryptophan amino* *acid decarboxylase*. There are two Tph genes; Tph1 and Tph2. Tph1 are mostly expressed in enterochrommafin cells in the gut and are responsible for most of the serotonin present in the blood. The gene Tph2 is expressed exclusively in the serotoginic neurons of the brainstem and is responsible for the production of serotonin in the brain. These two pools of serotonin; one in the brain and one in the blood never cross paths; and so should be seen functionally, as two distinct molecules. Brain-derived serotonin (BDS) is used as a neurotransmitter while gut-derived serotonin is used as a hormone for many processes in the gut.

The importance of serotonin in the regulation of bone mass is underscored by two clinical observations; first, depressed patients who allegedly have low serotoginic tone, and second, serotonin reuptake inhibitors (SSRIs) when taken for a long time, often decreased bone mass.