

NAME: EMELE UCHECHUKWU EMMANUEL

MAT.NO: 17/MHS01/112

LEVEL: 300

DEPT: ANATOMY

COURSE: BCH 308 (CELLULAR BIOCHEMISTRY)

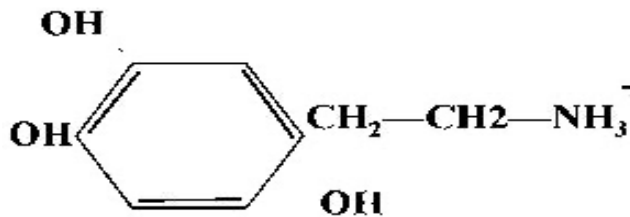
Question

1. Describe in details the synthesis of two named neurotransmitters

Answer

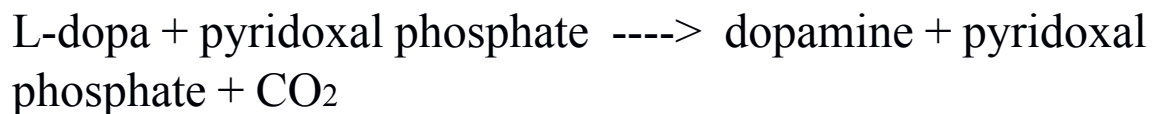
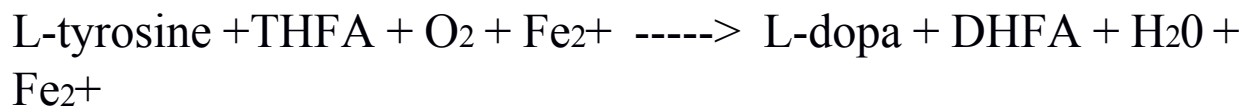
1. **Dopamine :**

Dopamine belongs to a class of neurotransmitters known as catecholamines, which are structurally defined by a catechol ring and an amine side chain.



Dopamine is synthesized from the amino acid tyrosine; the majority of circulating tyrosine originates from the dietary sources, but small amounts are derived from hydroxylation of phenylalanine by the liver enzyme phenylalanine hydroxylase. Blood-borne tyrosine is taken up into the brain by a low affinity amino acid transport system and subsequently from brain extracellular fluid into dopaminergic neurons by high and low affinity amino acid transporters. Tyrosine is converted to dopamine by the enzymes tyrosine hydroxylase (TH) and L-amino acid decarboxylase (AADC) also called dihydroxyphenylalanine (DOPA) decarboxylase (DDC). TH is

the rate-limiting step in their biosynthetic pathway; the TH gene is localized to chromosome 11p in humans and encodes a single form of TH that can be alternatively spliced. The mRNA expression of the TH is abundant throughout the human mesencephalon. The mature enzyme is a soluble cytosolic protein composed of four subunits of approximately 60kDa each. TH activity is the most critical factor that controls dopamine synthesis, and considerable efforts have been devoted to understanding activation and inactivation to this enzyme. Amino acid decarboxylase(AADC) is the second and terminal enzyme in dopamine synthesis. The enzyme uses pyridoxal phosphate as a cofactor and can convert dihydroxyphenylalanine(DOPA) to dopamine and 5-hydroxytryptophan to serotonin [5-hydroxytryptamine(5-HT)]. The complete reaction:

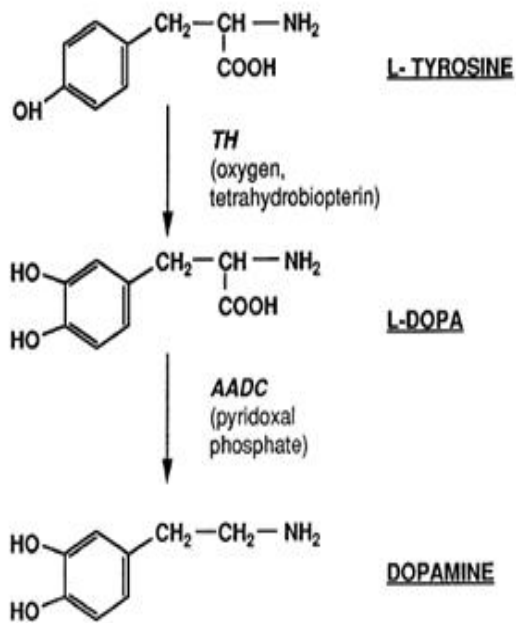


So for L-dopa formation, L-tyrosine, THFA (tetrahydrofolic acid), and ferrous iron are essential and for dopamine biosynthesis from L-dopa, pyridoxal phosphate is essential. The activity of the enzyme rises and falls according to how much pyridoxal phosphate there is. Besides two enzymes being required for the formation of dopamine from L-tyrosine, three coenzymes are also required. They are :

- THFA(for L-tyrosine to L-dopa)

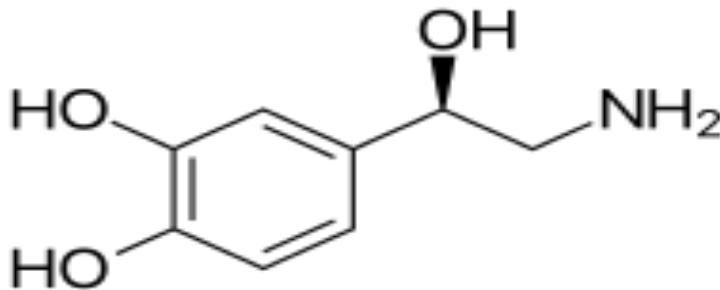
- Pyridoxal phosphate (for L-dopa to dopamine)
- NADH (for the formation of THFA and pyridoxal phosphate)

The cofactor tetrahydrobiopterin(BH4) donates the hydrogen atom needed for hydroxylation of tyrosine to DOPA. Because pterin also serves as a cofactor for other monooxygenases as well as nitric oxide synthase, its availability is a determinino factor in the control of TH activity.



2. Norepinephrine

Norepinephrine is also called noradrenaline (NA). It is an organic chemical in the catecholamine family that functions in the brain and body as a hormone and neurotransmitter. The general function of norepinephrine is to mobilize the brain and body for action.

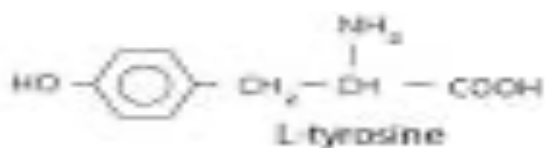


Norepinephrine is synthesized from the amino acid tyrosine by a series of enzymatic steps in the adrenal medulla and postganglionic neurons of the sympathetic nervous system. While the conversion of tyrosine to dopamine occurs predominantly in the cytoplasm, the conversion of dopamine to norepinephrine by dopamine β -monooxygenase occurs predominantly inside neurotransmitter vesicles. The metabolic pathway is:

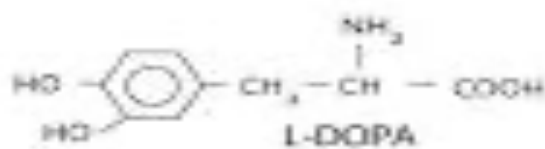
- Phenylalanine – tyrosine – L-DOPA – dopamine – norepinephrine

Thus the direct precursor of norepinephrine is dopamine, which is synthesized indirectly from the essential amino acid phenylalanine or the non-essential amino acid tyrosine. These amino acids are found in nearly every protein and, as such, are provided by ingestion of protein-containing food, with tyrosine being the most common.

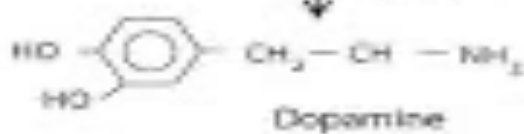
Phenylalanine is converted into tyrosine by the enzyme phenylalanine hydroxylase, with molecular oxygen (O_2) and tetrahydrobiopterin as cofactors. Tyrosine is converted into L-DOPA by the enzyme tyrosine hydroxylase with tetrahydrobiopterin, O_2 , and probably ferrous iron (Fe^{2+}) as cofactors. L-DOPA is converted into dopamine by the enzyme aromatic L-amino acid decarboxylase (DOPA decarboxylase), with pyridoxal phosphate as a cofactor. Dopamine is then converted into norepinephrine by the enzyme dopamine β -monooxygenase with O_2 and ascorbic acid as cofactors. Norepinephrine itself can further be converted into epinephrine by the enzyme phenylethanolamine N-methyltransferase with S-adenosyl-L-methionine as cofactor.



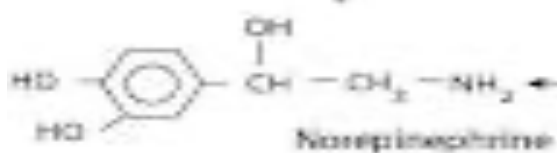
↓ TH



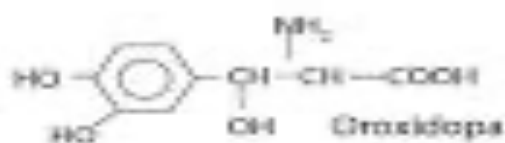
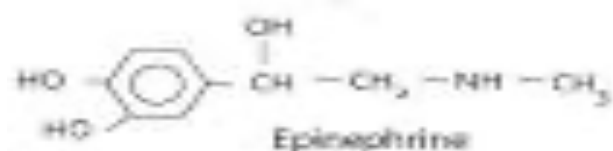
↓ AADC



↓ DBH



↓ PNMT



← DDC