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17/MHS01/287
Anatomy
BCH 308

Synthesis of Dopamine

Dopamine is synthesized in a restricted set of cell types, mainly neurons and cells in the medulla of the adrenal glands. The primary and minor metabolic pathways respectively are:

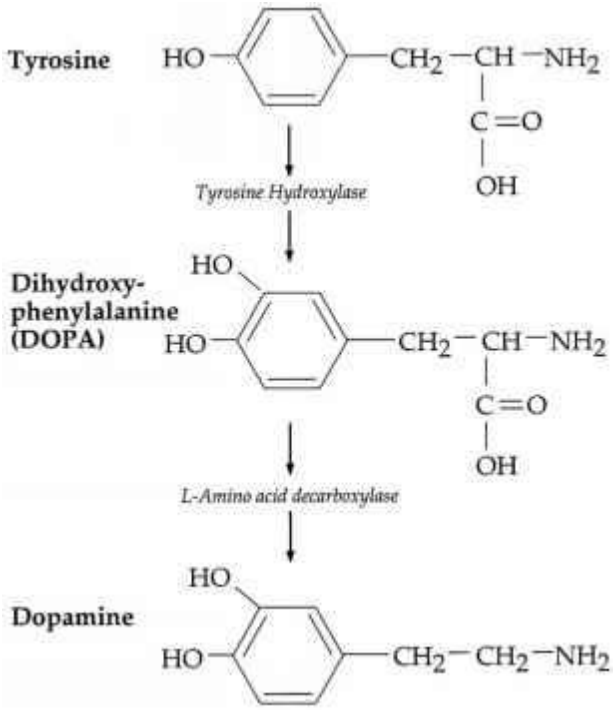
Primary: L-Phenylalanine → L-Tyrosine → L-DOPA → Dopamine
Minor: L-Phenylalanine → L-Tyrosine → p-Tyramine → Dopamine
Minor: L-Phenylalanine → m-Tyrosine → m-Tyramine → Dopamine

The direct precursor of dopamine, L-DOPA, can be synthesized indirectly from the essential amino acid phenylalanine or directly from the non-essential amino acid tyrosine. These amino acids are found in nearly every protein and so are readily available in food, with tyrosine being the most common. Although dopamine is also found in many types of food, it is incapable of crossing the blood–brain barrier that surrounds and protects the brain. It must therefore be synthesized inside the brain to perform its neuronal activity.

L-Phenylalanine is converted into L-tyrosine by the enzyme phenylalanine hydroxylase, with molecular oxygen (O_2) and tetrahydrobiopterin as cofactors. L-Tyrosine is converted into L-DOPA by the enzyme tyrosine hydroxylase, with tetrahydrobiopterin, O_2, and iron (Fe^{2+}) as cofactors. L-DOPA is converted into dopamine by the enzyme aromatic L-amino acid decarboxylase (also known as DOPA decarboxylase), with pyridoxal phosphate as the cofactor.

Dopamine itself is used as precursor in the synthesis of the neurotransmitters norepinephrine and epinephrine. Dopamine is converted into norepinephrine by the enzyme dopamine β-hydroxylase, with O_2 and L-ascorbic acid as cofactors. Norepinephrine is converted into epinephrine by the enzyme phenylethanolamine N-methyltransferase with S-adenosyl-L-methionine as the cofactor.

Some of the cofactors also require their own synthesis. Deficiency in any required amino acid or cofactor can impair the synthesis of dopamine, norepinephrine, and epinephrine.



Synthesis of Serotonin

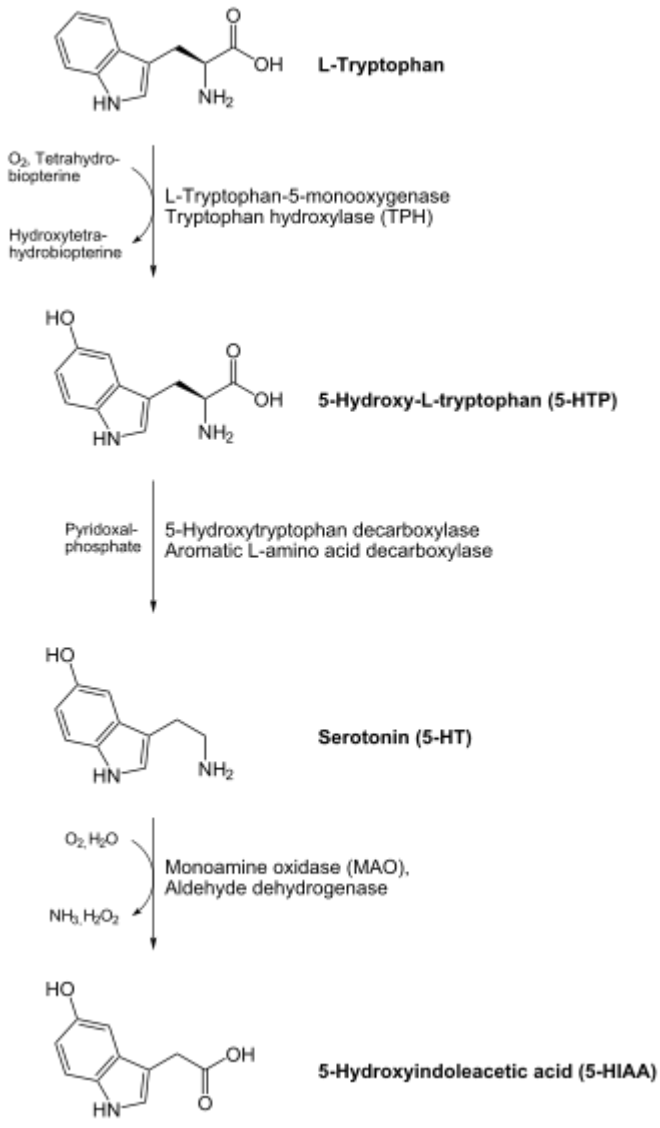
In animals including humans, serotonin is synthesized from the amino acid L-tryptophan by a short metabolic pathway consisting of two enzymes, tryptophan hydroxylase (TPH) and aromatic amino acid decarboxylase (DDC), and the coenzyme pyridoxal phosphate. The TPH-mediated reaction is the rate-limiting step in the pathway. TPH has been shown to exist in two forms: TPH1, found in several tissues, and TPH2, which is a neuron-specific isoform

Serotonin can be synthesized from tryptophan in the lab using Aspergillus niger and Psilocybe coprophila as catalysts. The first phase to 5-hydroxytryptophan would require letting tryptophan sit in ethanol and water for 7 days, then mixing in enough HCl (or other acid) to bring the pH to 3, and then adding NaOH to make a pH of 13 for 1 hour. Asperigillus niger would be the catalyst for this first phase. The second phase to synthesizing tryptophan itself from the 5-hydroxytryptophan intermediate would require adding ethanol and water, and letting sit for 30 days

this time. The next two steps would be the same as the first phase: adding HCl to make the pH = 3, and then adding NaOH to

make the pH very basic at 13 for 1 hour. This phase uses the Psilocybe coprophila as the catalyst for the reaction

Serotonin taken orally does not pass into the serotonergic pathways of the central nervous system, because it does not cross the blood–brain barrier. However, tryptophan and its metabolite 5-hydroxytryptophan (5-HTP), from which serotonin is synthesized, does cross the blood–brain barrier. These agents are available as dietary supplements, and may be effective serotonergic agents. One product of serotonin breakdown is 5-hydroxyindoleacetic acid (5-HIAA), which is excreted in the urine. Serotonin and 5-HIAA are sometimes produced in excess amounts by certain tumors or cancers, and levels of these substances may be measured in the urine to test for these tumors.


L-Tryptophan
O2, Tetrahydro-biopterine
L-Tryptophan-5-monooxygenase
Tryptophan hydroxylase (TPH)
Hydroxytetra-hydrobiopterine
5-Hydroxy-L-tryptophan (5-HTP)
Pyridoxal-phosphate
5-Hydroxytryptophan decarboxylase
Aromatic L-amino acid decarboxylase
Serotonin (5-HT)
O2, H2O
Monoamine oxidase (MAO),
Aldehyde dehydrogenase
NH3, H2O2
5-Hydroxyindoleacetic acid (5-HIAA)