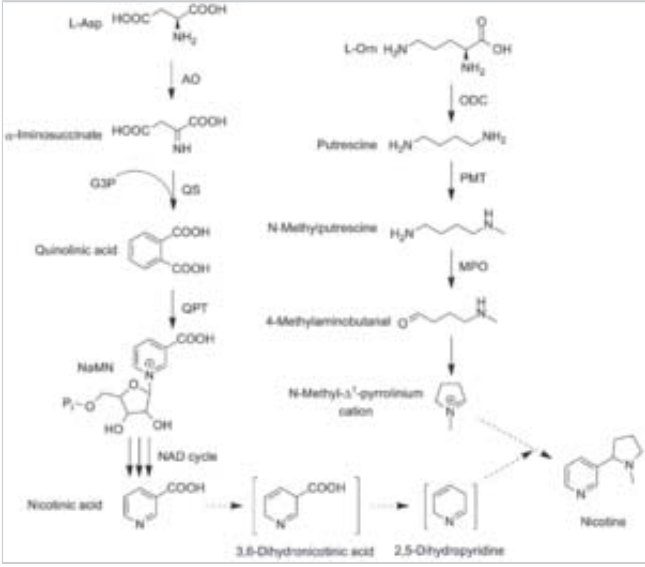
Occurrence and biosynthesis

Nicotine is a natural product of tobacco, occurring in the leaves in a range of 0.5 to 7.5% depending on variety.[84] Nicotine also naturally occurs in smaller amounts in plants from the family Solanaceae (such as potatoes, tomatoes, and eggplant).[85]



Nicotine biosynthesis

The biosynthetic pathway of nicotine involves a coupling reaction between the two cyclic structures that compose nicotine. Metabolic studies show that the pyridine ring of nicotine is derived from niacin (nicotinic acid) while the pyrrolidone is derived from N-methyl-Δ^1-pyrrollidium cation.[86][87] Biosynthesis of the two component structures proceeds via two independent syntheses, the NAD pathway for niacin and the tropane pathway for N-methyl-Δ^1-pyrrollidium cation.

The NAD pathway in the genus *nicotiana* begins with the oxidation of aspartic acid into α-imino succinate by aspartate oxidase (AO). This is followed by a condensation with glyceraldehyde-3-phosphate and a cyclization catalyzed by quinolinate synthase (QS) to give quinolinic acid. Quinolinic acid then reacts with phosphoriboxyl pyrophosphate catalyzed by quinolinic acid phosphoribosyl transferase (QPT) to form niacin mononucleotide (NaMN). The reaction now proceeds via the NAD salvage cycle to produce niacin via the conversion of nicotinamide by the enzyme nicotinamidase.

The N-methyl-Δ^1-pyrrollidium cation used in the synthesis of nicotine is an intermediate in the synthesis of tropane-derived alkaloids. Biosynthesis begins with decarboxylation of ornithine by ornithine decarboxylase (ODC) to produce putrescine. Putrescine is then converted into N-methyl putrescine via methylation by SAM catalyzed by putrescine N-methyltransferase (PMT). N-methylputrescine then undergoes deamination into 4-methylaminobutanal by the N-methylputrescine oxidase (MPO) enzyme, 4-methylaminobutanal then spontaneously cyclize into N-methyl-Δ^1-pyrrollidium cation.

The final step in the synthesis of nicotine is the coupling between N-methyl-Δ^1-pyrrollidium cation and niacin. Although studies conclude some form of coupling between the two component structures, the definite process and mechanism remains undetermined. The current agreed theory involves the conversion of niacin into 2,5-dihydropyridine through 3,6-dihydronicotinic acid. The 2,5-dihydropyridine intermediate would then react with N-methyl-Δ^1-pyrrollidium cation to form enantiomerically pure (–)-nicotine.[88]

Measurement in body fluids

Nicotine can be quantified in blood, plasma, or urine to confirm a diagnosis of poisoning or to facilitate a medicolegal death investigation. Urinary or salivary cotinine concentrations are frequently measured for the purposes of pre-employment and health insurance medical screening programs. Careful interpretation of