The Term alkaloid was coined in 1819 by the German Scientist Carl F. W. Meissner [1] and is derived from Arabic al qualja "means ashes of plants". Alkaloids are groups of natural occurring simple or complex, low molecular weight nitrogen containing compounds which are basic in nature. They are secondary metabolites abundantly found in plants, but also to a lesser extent in microorganisms (bacteria and fungi) and animals [2]. Alkaloids perform various physiological functions in living organisms.

Alkaloid may be classified according to the structural relationship between the nitrogen-containing structure such as pyrrolidine, piperidine, quinoline, isolquinoline and indole and the alkaloid skeleton [3]. Generally, amino acids such as ornithine, lysine, phenylalanine, tyrosine, tryptophan and histidine are precursor for most of the alkaloids (figure 1).

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Decarboxylation of amino acid

Amino acids are the most common precursors in the biosynthesis of alkaloids. Decarboxylation of amino acids [4] is first step towards alkaloid biosynthesis. It is performed by an enzyme often using the cofactor pyridoxal phosphate. The reaction is initiated with the nucleophilic attack of the amino function of amino acid to the aldehyde function of pyridoxal...
phosphate. The resulting imine intermediate undergoes decarboxylation giving a carbanion in which the negative charge can be delocalized. Protonation of the carbanion followed by hydrolysis of imine gives an amine and pyridoxal phosphate which is available for further use in the next reaction (Figure 2).
Alkaloids derived from Ornithine

L-Ornithine is a natural amino acid not found in proteins. In animals, it is produced from arginine during urea cycle, a reaction catalyzed by the enzyme arginase. In plants, it is produced from L-glutamic acid. Ornithine contains two amino functions: α and δ- amino group, δ- amino group is a part of alkaloid structure along with the carbon chain excluding carboxyl group. Thus, pyrrolidine ring system (C4N) in alkaloid derived from ornithine. It is also present in tropane alkaloids (figure. 3).

Ornithine gives mainly two class of alkaloids: pyrrolidine and tropane alkaloids. Some of the common examples [4] of this series are shown below.
Biosynthesis of Polyamines

The simple polyamines such as putrescine, spermidine, and spermine play critical biological roles in eukaryotic cells and are synthesized from L-Ornithine and L-Methionine. Further, in animals, putrescine is synthesized from the ornithine through PLP dependent decarboxylation reaction. In plants and microorganisms, putrescine is also synthesized simultaneously from arginine [5]. In this route, L-ornithine is converted to L-arginine which undergoes decarboxylated via PLP to form agmatine. The hydrolysis of imine function in guanidino in agmatine yields N-carbamoyl putrescine, which on further hydrolysis gives putrescine. At this point, alkylation of putrescine gives spermidine and spermine respectively. It is noted here that aminopropyl group comes from a decarboxylated SAM (dcSAM) to putrescine. These reactions are catalyzed by enzyme spermidine synthase and spermine synthase respectively as shown in figure 4.
Biosynthesis of Cocaine

Cocaine is an example of tropane alkaloid which is generally found in plants of Solanaceae family [6]. This family also contains other alkaloids such as hyoscyamine, hygrine, cusohygrine etc. The biosynthesis of cocaine is very complex, involving many steps. First, putrescine is synthesized from amino acid glutamic acid as shown in figure 4. Next, putrescine is methylated to N-methylputrescine by enzyme, putrescine N-methyltransferase. N-methylputrescine undergoes oxidative deamination to yield the aldehyde which finally gives N-methyl-∆1-pyrrolinium cation as a result of Schiff base formation (Figure 5).

In the next step, the additional carbon atoms required for cocaine synthesis are provided by acetyl-CoA which in turn obtained from addition of two acetyl-CoA units. The first step is a Mannich-like reaction in which the enolate anion from acetyl-CoA acts as a nucleophile towards the pyrrolinium cation and give two products with S and R configuration. The second step is Claisen condensation that produces 2-substituted pyrimidine with the retention of the thioester group of the second acetyl-CoA. In the cocaine biosynthesis, tropane rings is only obtained by the cyclization of only (S)-enantiomer. This involves series of Mannich-line reaction. The oxidation of 2-substituted pyrrolidine yields the pyrrolinium cation and formation of an enolate anion in the side chain that undergoes intramolecular Mannich reaction to give tropane skelton. The tropane ring system undergoes hydrolysis, SAM-dependent methylation and reduction via NADPH to yield methylecgonine. Here, reduction of the carbonyl group of tropinone occurs from the opposite face. Thus, in ecgonine, hydroxyl group is on 3β configuration. Cocaine is a benzoyl ester of methylecgonine. At this stage, phenylalanine is converted into benzoyl-CoA via cinnamic acid that provide benzoyl group for esterification of methylecgonine to yield cocaine. The overall reactions [7] are schematically shown in figure 6.
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