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Review

Tyrosine biosynthesis, metabolism, and catabolism in plants

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ABSTRACT

L-Tyrosine (Tyr) is an aromatic amino acid (AAA) required for protein synthesis in all organisms, but synthesized *de novo* only in plants and microorganisms. In plants, Tyr also serves as a precursor of numerous specialized metabolites that have diverse physiological roles as electron carriers, antioxidants, attractants, and defense compounds. Some of these Tyr-derived plant natural products are also used in human medicine and nutrition (e.g. morphine and vitamin E). While the Tyr biosynthesis and catabolic pathways have been extensively studied in microbes and animals, respectively, those of plants have received much less attention until recently. Accumulating evidence suggest that the Tyr biosynthetic pathways differ between microbes and plants and even within the plant kingdom, likely to support the production of lineage-specific plant specialized metabolites derived from Tyr. The interspecies variations of plant Tyr pathway enzymes can now be used to enhance the production of Tyr and Tyr-derived compounds in plants and other synthetic biology platforms.

Chemical compounds:
L-tyrosine (PubChem CID: 6057) (**1**)
L-phenylalanine (PubChem CID: 6140) (**2**)
L-arogenate (PubChem CID: 25244469) (**3**)
prephenate (PubChem CID: 1028) (**4**)
chorismate (PubChem CID: 12039) (**5**)
4-hydroxyphenylpyruvate (PubChem CID: 6971070) (**6**)
homogentisate (PubChem CID: 5460389) (**7**)
4-maleylacetoacetate (PubChem CID: 5280393) (**8**)
4-fumarylacetoacetate (PubChem CID: 5459934) (**9**)
fumarate (PubChem CID: 5460307) (**10**)
acetoacetate (PubChem CID: 6971017) (**11**)
vitamin E (PubChem CID: 2116) (**12**)
plastoquinone (PubChem CID: 11647660) (**13**)
(Z)-*p*-hydroxyphenyl-acetaldoxime (PubChem CID: 5459810) (**14**)
dhurrin (PubChem CID: 161355) (**15**)
L-3,4-dihydroxyphenylalanine (PubChem CID: 6047) (**16**)
betacyanin (PubChem CID: 6325284) (**17**)
betaxanthin (PubChem CID: 25245127) (**18**)
tyramine (PubChem CID: 5610) (**19**)
morphine (PubChem CID: 5288826) (**20**)
colchicine (PubChem CID: 6167) (**21**)
rosmarinic acid (PubChem CID: 5281792) (**22**)
p-coumarate (PubChem CID: 54708745) (**23**)
epinephrine (PubChem CID: 5816) (**24**)
feruloyltyramine (PubChem CID: 5280537) (**25**)
crinine (PubChem CID: 398937) (**26**)
hordenine (PubChem CID: 68313) (**27**)
salidroside (PubChem CID: 159278) (**28**)
4-hydroxyphenylacetaldehyde (PubChem

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CID: 440113) (**29**)
Beta-tyrosine (PubChem CID: 440311) (**30**)

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Primary metabolism
Specialized metabolism
Natural products
Shikimate pathway
Arogenate dehydrogenase
Prephenate dehydrogenase

1. Introduction

L-Tyrosine (Tyr) (**1**) is synthesized *de novo* in plants and microbes but required for protein synthesis in all organisms. In animals, Tyr needs to be obtained through their diet or via the hydroxylation of L-phenylalanine (Phe) (**2**) by Phe hydroxylase (PheH, Fitzpatrick, 1999; Pribat et al., 2010). In plants, Tyr and a Tyr pathway intermediate, 4-hydroxyphenylpyruvate (HPP) (**6**), also serve as the precursors to the formation of numerous specialized metabolites that have various functions in plants: such as defense (rosmarinic acid (**22**), dhurrin (**15**) and benzylisoquinoline alkaloids; BIAs), pollinator attraction (betalain pigments), electron transport (plastoquinone (**13**) and ubiquinone), and structural support (lignin). In humans, Tyr-derived compounds function as neurotransmitters (catecholamines), UV protectants (melanin), analgesics (morphine (**20**)), and antioxidants (vitamin E (**12**)). Considering the tremendous competition for Tyr imposed by many downstream pathways, it is particularly important to understand how carbon is allocated toward Tyr biosynthesis and downstream pathways and how Tyr homeostasis is maintained in plants.

Tyr is synthesized downstream of the shikimate pathway, which also provides the precursors to the other aromatic amino acids (AAA), Phe and L-tryptophan (Trp). In plants, upwards of 30% of deposited carbon passes through the shikimate pathway, the bulk of which is used to synthesize Phe-derived compounds such as lignin (Boerjan et al., 2003). Free Tyr levels can vary widely in different plant lineages, tissues, and during different developmental stages. Some plant tissues, like bamboo shoots and *Inga umbellifera* young leaves, accumulate free Tyr at up to 30% and 10% dry weight, respectively (Lokvam et al., 2006; Nomura and Yamada, 1974). On the other hand, some tomato fruits have low abundance of bound Tyr, representing 0.1% of the total protein amino acids (Pratta et al., 2011), as compared to the natural abundance of Tyr residues in proteins being ~3% (Ischiropoulos, 1998). Some Tyr-derived specialized metabolites, such as dhurrin (**15**), also accumulate up to 30% of dry weight (Halkier and Møller, 1989). These observations suggest that Tyr biosynthesis and metabolism are regulated differently depending on plant species.

AAA biosynthesis and the shikimate pathway in plants have been reviewed previously; however, less attention has been paid to Tyr biosynthesis (Herrmann, 1995; Maeda and Dudareva, 2012; Schmid and Amrhein, 1995; Siehl, 1999; Tzin and Galili, 2010). This article provides a comprehensive review on Tyr biosynthesis, catabolism, and metabolism to downstream plant specialized metabolites, highlighting the unique diversification of the Tyr pathway architecture and regulation among different plant lineages.

2. Physical and chemical properties of tyrosine

L-Tyr [Y, α-amino-β-(*p*-hydroxyphenyl)propionic acid, $C_9H_{11}NO_3$; Fig. 1] was first isolated from crude cheese proteins (casein), and named after the Greek word "*tyros*" meaning cheese in 1846 by Justus Von Liebig (Greenstein and Winitz, 1961; Vickery and Schmidt, 1931). The structure of Tyr was defined by De La Rue in 1848, and later confirmed through its chemical synthesis in 1883 by Erlenmeyer and Libb (Greenstein and Winitz, 1961; Vickery and Schmidt, 1931). Three ionizable groups are present in Tyr with pKa values of the hydroxyl, amino, and carboxyl groups being 10, 9.1, and 2.2, respectively. Under most physiological conditions, the amino and carboxyl groups are positively and negatively charged, respectively, while the hydroxyl group is uncharged. Tyr has a fluorescence property with an excitation and emission at 275 and 305 nm, respectively (Baker, 2002), which has been used to directly detect Tyr after chromatographic separation without derivatization and in studies of the folding states of various proteins (Bedouelle, 2016). Notably, Tyr has a much lower solubility (0.48 g L^{-1} water at 25 °C) than Phe (11.4 g L^{-1}) (Dalgliesh, 1955) due to the extra ring hydroxyl group of Tyr that can participate in hydrogen-bonding with the carboxylate and amino groups, making its crystal structure more energetically favorable than dissolution (Hitchcock, 1924).

Tyr residues are often found on the surface of proteins and can be post-translationally modified either through phosphorylation as a part of signaling cascades (Tarrant and Cole, 2009) or through nitrosylation to regulate enzymatic activity (Abello et al., 2009). Only about 15% of Tyr residues are buried within proteins (Kyte and Doolittle, 1982), some of which play crucial roles in acid/base chemistry (Gutteridge and Thornton, 2005). Tyr also plays a key function in oxygenic photosynthesis: A Tyr residue in the D1 protein of photosystem II serves as an essential electron carrier between the oxygen-evolving complex and the reaction center (Metz et al., 1989).

3. Biosynthesis of tyrosine in plants

3.1. Overall Tyr pathway architecture

Tyr is synthesized from chorismate (**5**), the final product of the shikimate pathway and the common precursor of all three AAAs, as well as various vitamins (K_1 and B_9), hormones (auxin and salicylic acid), and AAA-derived specialized metabolites (Herrmann, 1995; Maeda and Dudareva, 2012; Tzin and Galili, 2010). The essential roles of AAAs in plants and microbes and the absence of the AAA biosynthetic pathways in animals make the shikimate pathway a prime target for non-selective herbicides and antimicrobial compounds (Pereira et al., 2007; Powles and Yu, 2010). Since a significant amount of carbon flux passes through the shikimate pathway (Boerjan et al., 2003), it is crucial that plants properly regulate the shikimate pathway and allocate carbon towards biosynthesis of different AAAs and their downstream metabolic branches (Maeda and Dudareva, 2012; Tzin and Galili, 2010).

Chorismate (**5**) is first converted into prephenate (**4**) by