Overview

1. Biosynthesis of terpenes
2. Biosynthesis of phenols
3. Metabolism of fatty acids
4. Metabolism of glucose (glycolysis)
5. Anabolic pathways of fatty acids and carbohydrates
Biosynthesis of acyclic terpenoids

From the metabolic pathways of carbohydrates and fats

\[ \text{CH}_3\text{CO}\text{SCoA} \rightarrow \text{CH}_3\text{COCH}_2\text{CO}\text{SCoA} \]

\[ 2 \text{NADPH} \rightarrow 2 \text{NADP} \]

\[ 3 \text{ATP} \rightarrow 3 \text{ADP} \]

\[ \text{CO}_2, \text{Pi} \rightarrow \text{Terpenes} \]

Isoprene units
Condensation of isoprene units. Formation of acyclic terpenes
Formation of monoterpenes (examples)

- Geraniol
- Myrcene
- Limonene
- Fenchone
- Camphene
- 3-carene
- α- and β-pinene

α-terpinyl cation
Formation of sesquiterpenes (examples)

- bisabolene
- cadinene
- carotol
Formation of diterpenes (examples)

- Geranylgeranyl-OPP
- Labdadienol
- Kaurene
- Pimaradiene
Biosynthesis of squalene

\[ \text{farnesyl-OPP} \xrightarrow{\text{Enz-Nu}} \text{squalene} \]
Biogenesis of steroids and triterpene alcohols (examples)

1. Squalene

2. 2,3-epoxysqualene

3. Lanosterol

4. Cholesterol
Biogenesis of phenols through polyketides

\[ \text{CH}_3\text{COSCoA} \xrightarrow{\text{Claisen-type condensation}} \text{CH}_3\text{COCH}_2\text{COSEnz} \xrightarrow{\text{iteration}} \]

polyketide

\[ \text{Aldol C6-C1} \rightarrow \]

floroacetophenone

\[ \text{Aldol C2-C7} \rightarrow \]

orserilic acid

\[ \text{hydrolysis} \rightarrow \]

\[ -\text{H}_2\text{O} \rightarrow \]
Biogenesis of phenols: other examples

\[
\text{HOOCCH}_2\text{COSEnz} \xrightarrow{\text{-CO}_2} \text{HOOCCH}_2\text{COSEnz} \xrightarrow{\text{HOOCCH}_2\text{COSEnz}} \text{HOOCCH}_2\text{COSEnz}
\]

\[
\text{Aldol} \quad \rightarrow \quad \text{Me}_2\text{COSEnz} \quad \rightarrow \quad \text{Me}_2\text{COSEnz}
\]

\[
\text{salicylic acid} \quad \rightarrow \quad \text{Me}_2\text{COSEnz} \quad \rightarrow \quad \text{Me}_2\text{COSEnz}
\]

\[
\text{methylation} \quad \rightarrow \quad \text{Me}_2\text{COSEnz} \quad \rightarrow \quad \text{Me}_2\text{COSEnz}
\]

\[
\text{eugenone} \quad \rightarrow \quad \text{Me}_2\text{COSEnz} \quad \rightarrow \quad \text{Me}_2\text{COSEnz}
\]
Biogenesis of phenols through shikimic acid. Biosynthesis of shikimic acid
Biosynthesis of aromatic amino acids through shikimic acid

- **Shikimic acid**
  - Reaction with another molecule
  - Resulting in chorismic acid

- **Chorismic acid**
  - Undergone [3,3]-Claisen condensation
  - Resulting in prephenic acid

- **Prephenic acid**
  - Oxidation
  - Resulting in phenylalanine

- **Phenylalanine**
  - Conversion to tyrosine

- **Tyrosine**

- **Formulas:**
  - Shikimic acid: \(\text{COO}^\text{-} + \text{PO}^\text{-}\text{COO}^\text{-} \xrightarrow{\text{H}^\text{+}} \text{COO}^\text{-}\text{PO}^\text{-}\text{COOH}\)
  - Chorismic acid: \(\text{OOC}^\text{-}\text{OH} \xrightarrow{[3,3]-\text{Claisen}} \text{COOH}\)
  - Prephenic acid: \(\text{COOH} \xrightarrow{\text{OP}^\text{+}} \text{NH}_2\text{COOH}\)
  - Phenylalanine: \(\text{NH}_2\text{COOH}\)
  - Tyrosine: \(\text{NH}_2\text{OH}\)
An overview of catabolic pathways
Metabolism of fatty acids

Step 1
A double bond is introduced by enzyme-catalyzed removal of hydrogens from C2 and C3.

\[ \text{RCH}_2\text{CH}_2\text{CH}_2\text{CSCoA} \rightarrow \text{RCH}_2\text{CH}_2\text{CH} = \text{CHCSCoA} \]

\[ \text{RCH}_2\text{CH}_2\text{CH} = \text{CHCSCoA} + \text{H}_2\text{O} \]

\[ \text{OH} \]

Step 2
Water adds to the double bond in a conjugate addition reaction to yield an alcohol.

\[ \text{RCH}_2\text{CH}_2\text{CH}_2\text{CSCoA} \rightarrow \text{RCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CSCoA} \]

\[ \text{NAD}^+\]

Step 3
The alcohol is oxidized by NAD$^+$ to give a $\beta$-keto thiol ester.

\[ \text{RCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CSCoA} \rightarrow \text{RCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CSCoA} \]

\[ \text{NADH/}\text{H}^+ \]

Step 4
The bond between C2 and C3 is broken by nucleophilic attack of coenzyme A on the C3 carbonyl group in a retro-Claisen reaction to yield acetyl CoA and a chain-shortened fatty acid.

\[ \text{RCH}_2\text{CH}_2\text{CSCoA} + \text{CH}_2\text{CSCoA} \]
Metabolism of glucose (glycolysis)

Step 1
Glucose is phosphorylated by reaction with ATP to yield glucose 6-phosphate.

Step 2
Glucose 6-phosphate is isomerized to fructose 6-phosphate.

Step 3
Fructose 6-phosphate is phosphorylated by reaction with ATP to yield fructose 1,6-bisphosphate.

Step 4
Fructose 1,6-bisphosphate is cleaved into two three-carbon pieces by the enzyme aldolase.

Step 5
Dihydroxyacetone phosphate, one of the products of step 4, is isomerized to glyceraldehyde 3-phosphate, the other product of step 4.

Step 6
Glyceraldehyde 3-phosphate is oxidized and phosphorylated to yield 3-phosphoglyceroyl phosphate.

Step 7
A phosphate is transferred from the carboxyl group to ADP, resulting in synthesis of an ATP and yielding 3-phosphoglycerate.

Step 8
A phosphate group is transferred from the C3 hydroxyl to the C2 hydroxyl, giving 2-phosphoglycerate.

Step 9
Dehydration occurs to yield phosphoenolpyruvate (PEP).

Step 10
A phosphate is transferred from PEP to ADP, yielding pyruvate and ATP.
Conversion of pyruvate to acetyl coenzyme A

**Step 1**
Nucleophilic addition of thiamine pyrophosphate to the ketone carbonyl group of pyruvate yields an intermediate addition product.

**Step 2**
Decarboxylation occurs, analogous to the loss of CO₂ from a β-keto acid, yielding an enamine intermediate.

**Step 3**
The nucleophilic enamine double bond attacks a sulfur atom of lipoamide and does an S₂2-like displacement of the second sulfur atom.

**Step 4**
Elimination of thiamine pyrophosphate from the tetrahedral intermediate then yields acetyl dihydrolipoamide.

**Step 5**
Reaction with coenzyme A exchanges one thiol ester for another, giving acetyl CoA and dihydrolipoamide.
Anabolism of fatty acids from CH₃COSCoA
Anabolism of glucose (gluconeogenesis)

**Step 1**
Pyrurate undergoes biotin-dependent carboxylation to give oxaloacetate.

**Step 2**
Phosphorylation and decarboxylation then produce phosphoenolpyruvate.

**Step 3**
Conjugate addition of water to the double bond of phosphoenolpyruvate gives 2-phosphoglycerate.

**Step 4**
Isomerization by transfer of a phosphate group yields 3-phosphoglycerate.

**Step 5**
Phosphorylation with ATP gives 3-phosphoglycerol phosphate.

**Step 6-7**
Reduction yields the aldehyde 3-phosphoglyceraldehyde, which undergoes keto-enol tautomerization to give dihydroxyacetone phosphate.

**Step 8**
Two three-carbon units join in an aldol reaction to yield fructose 1,6-bisphosphate.

**Step 9**
Hydrolysis of the phosphate group at C1 occurs, giving fructose 6-phosphate.

**Step 10**
Keto-enol tautomerization shifts the carbonyl group from C2 to C1, yielding glucose 6-phosphate.