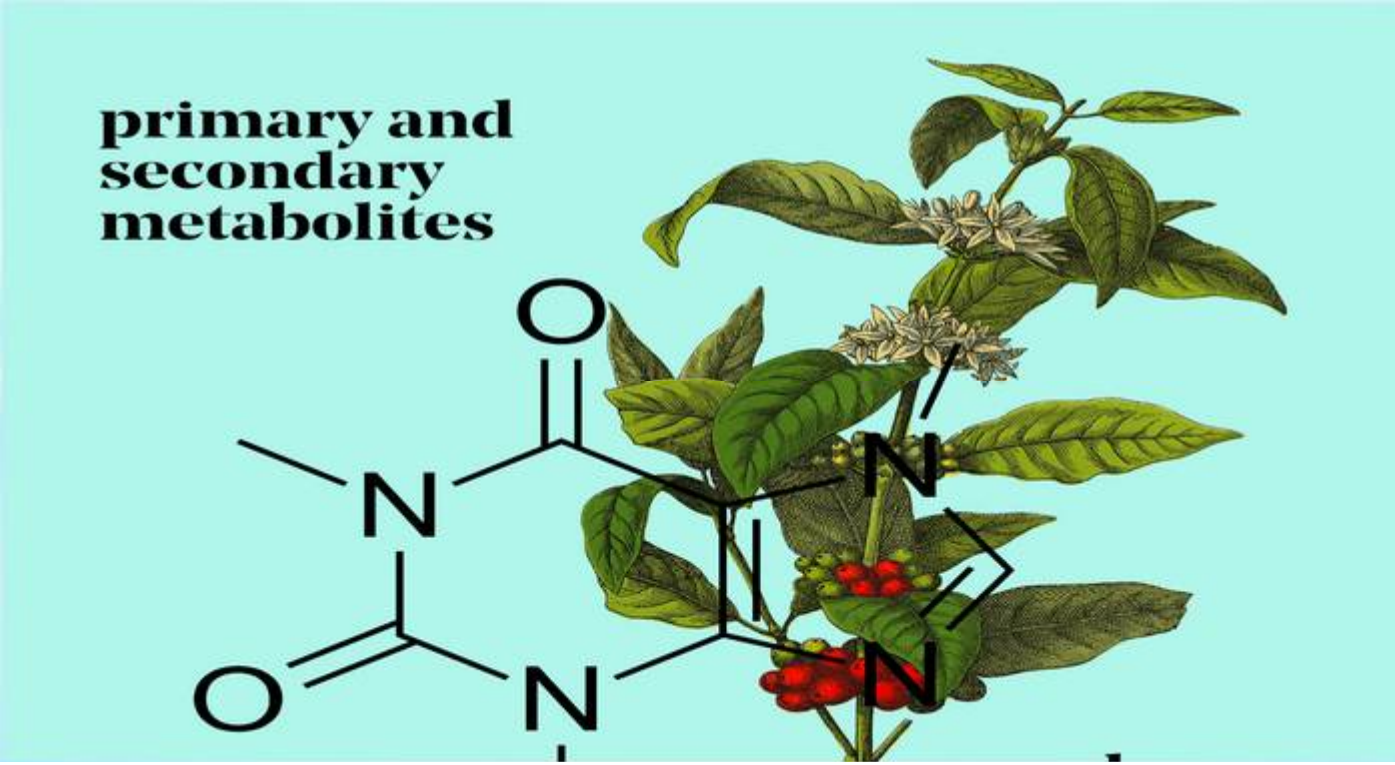
Introduction to Secondary Metabolism and the Biosynthesis of Natural Products

3rd stage /1st semester

Dr. Zahraa Shubber



secondary metabolites are classified according to their structure, function, and biosynthesis.

There are five main classes of secondary metabolites such as:

1.terpenoids and steroids,

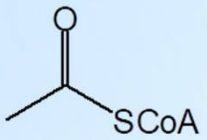
2. fatty acid-derived substances and polyketides,

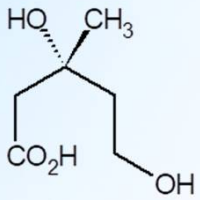
3. alkaloids,

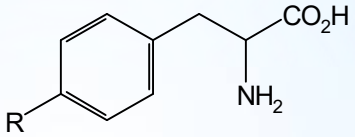
4.nonribosomal polypeptides, and

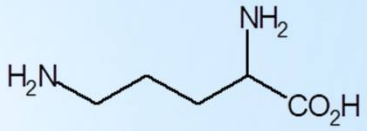
5.enzyme cofactors.

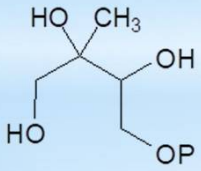
Biogenesis: overview of the origin of compounds starting from the set of intermediate building blocks: acetyl-CoA, MVA and MEP, shikimic acid, and the amino acids phenylalanine and tyrosine, tryptophan, ornithine and lysine.

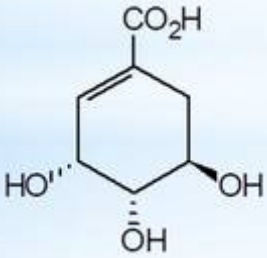


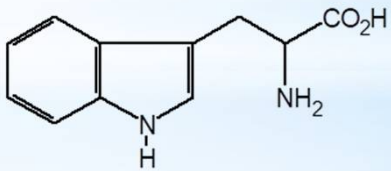


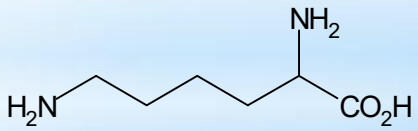




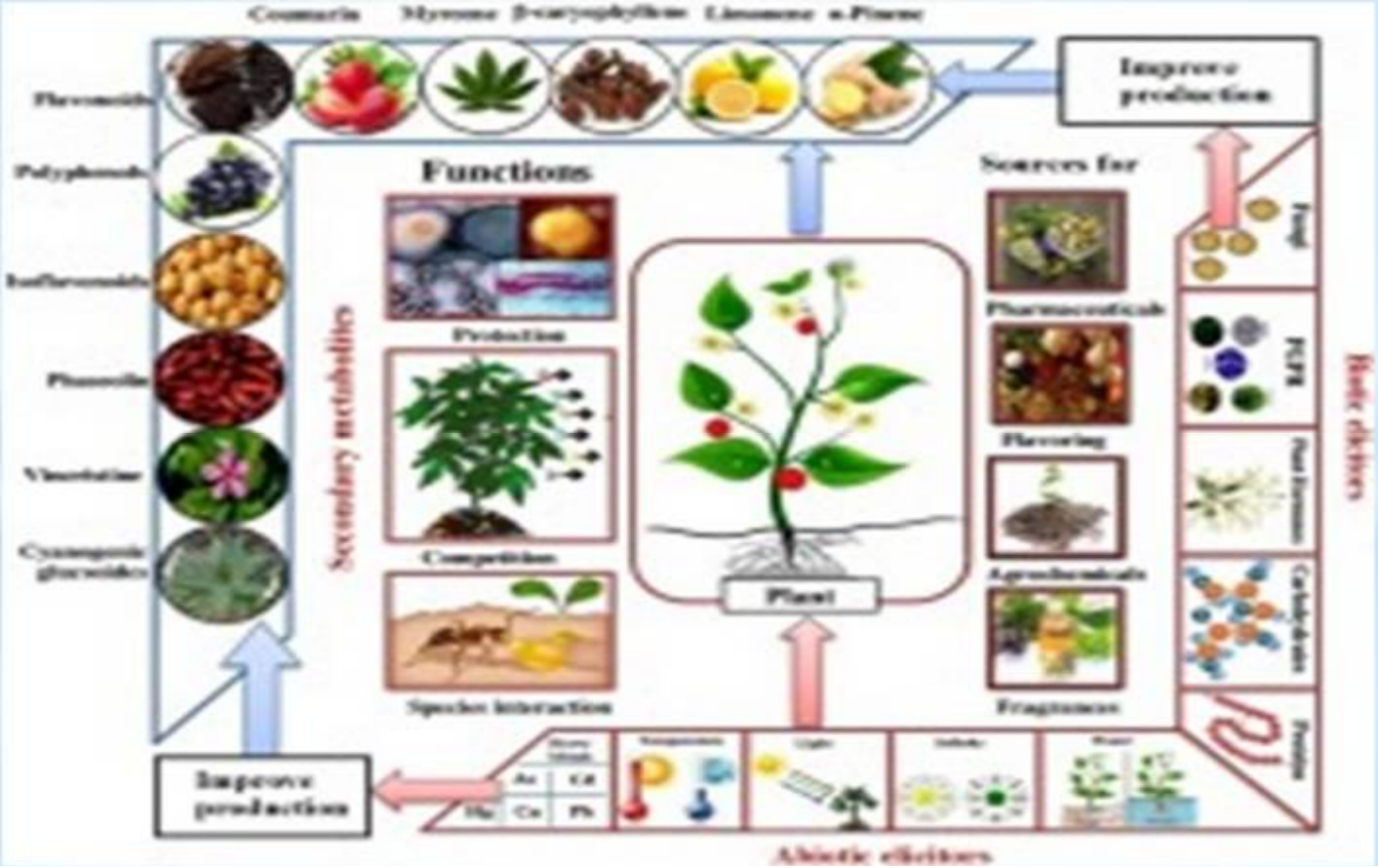


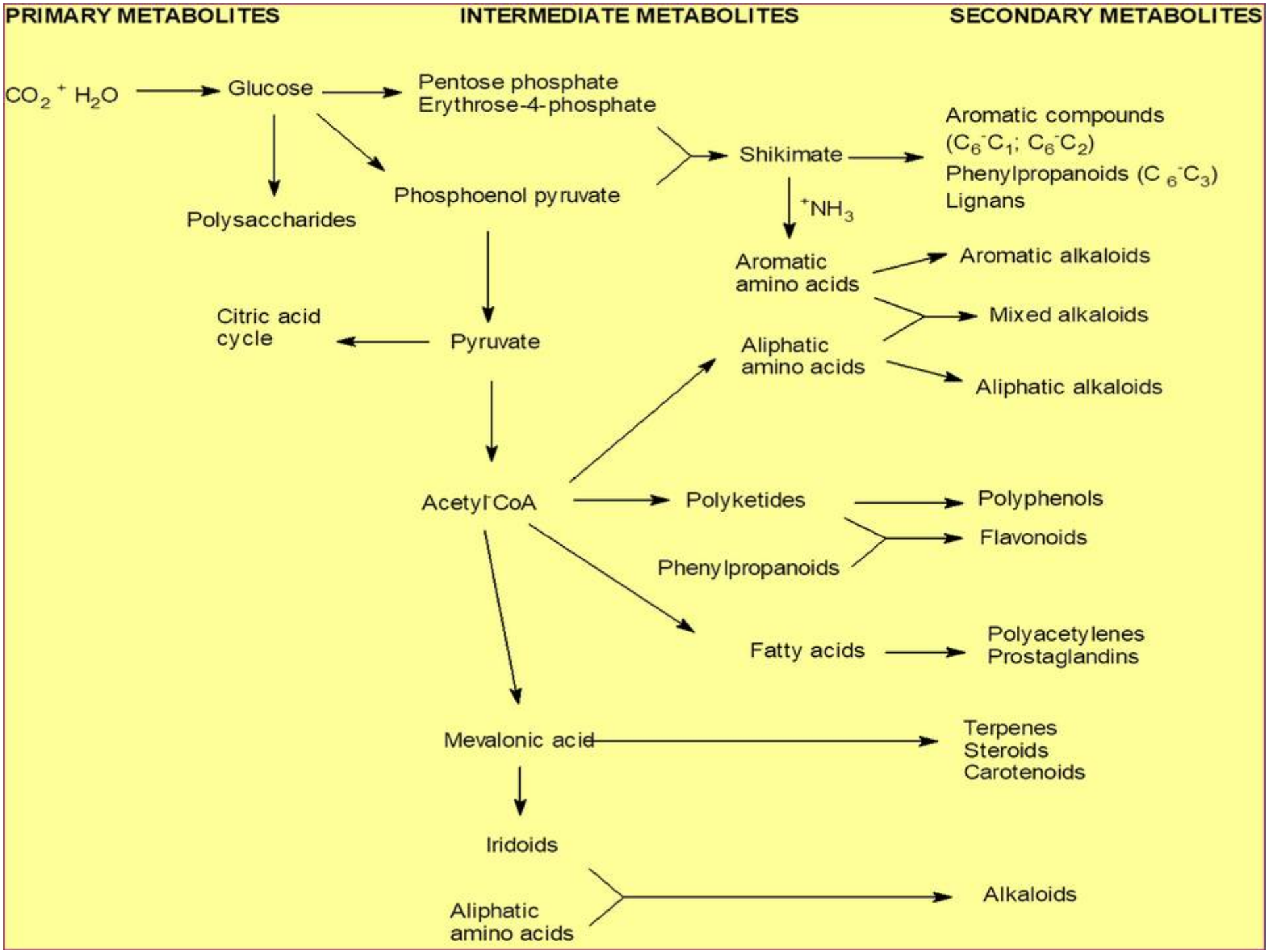






Biosynthesis: detailed study of the step-wise formation of secondary metabolites. At more detailed levels, the specific enzymes, genes and signals are also identified.

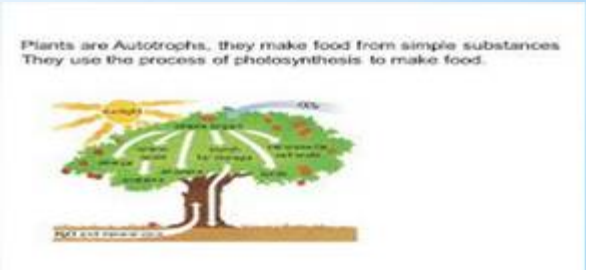



PRIMARY METABOLITES
INTERMEDIATE METABOLITES
SECONDARY METABOLITES
CO_2 + H_2O
Glucose
Pentose phosphate
Erythrose-4-phosphate
Shikimate
Aromatic compounds
(C_6-C_1; C_6-C_2)
Phenylpropanoids (C_6-C_3)
Lignans
Polysaccharides
Phosphoenol pyruvate
$^+NH_3$
Aromatic amino acids
Aromatic alkaloids
Mixed alkaloids
Citric acid cycle
Pyruvate
Aliphatic amino acids
Aliphatic alkaloids
Acetyl-CoA
Polyketides
Polyphenols
Flavonoids
Phenylpropanoids
Fatty acids
Polyacetylenes
Prostaglandins
Mevalonic acid
Terpenes
Steroids
Carotenoids
Iridoids
Aliphatic amino acids
Alkaloids

Importance of photosynthesis in formation of primary metabolites :

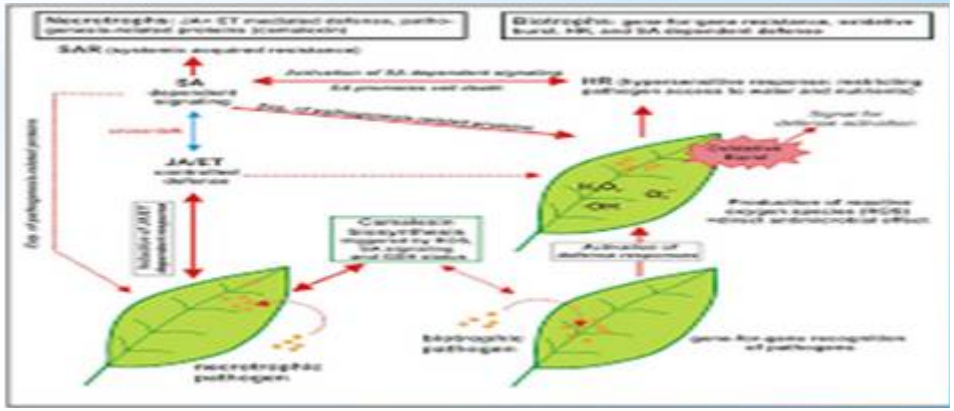
- **Photosynthesis** is the process where plants convert sunlight into energy, then store it as carbohydrates, sugars, such as glucose.
- ***Photosynthesis has three basic steps:***

1. Energy is captured from the sunlight.
2. **Light** energy is converted into **chemical** energy in the form of ATP and NADPH.
3. Chemical energy is used to power the synthesis of organic molecules (e.g. **carbohydrates**) from carbon dioxide (CO_2).



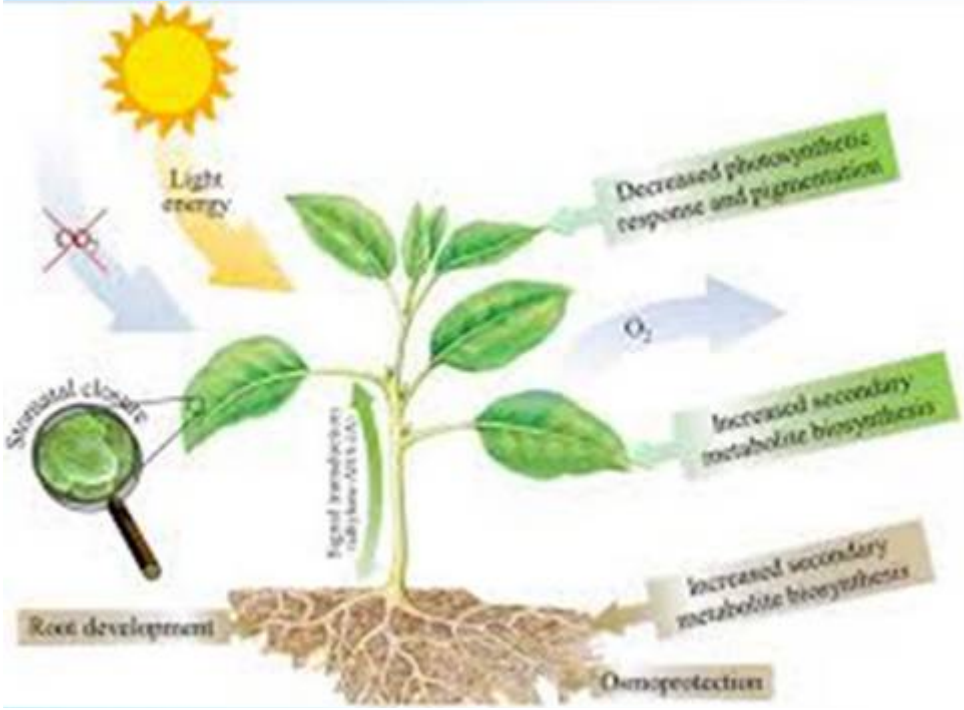
Organic natural

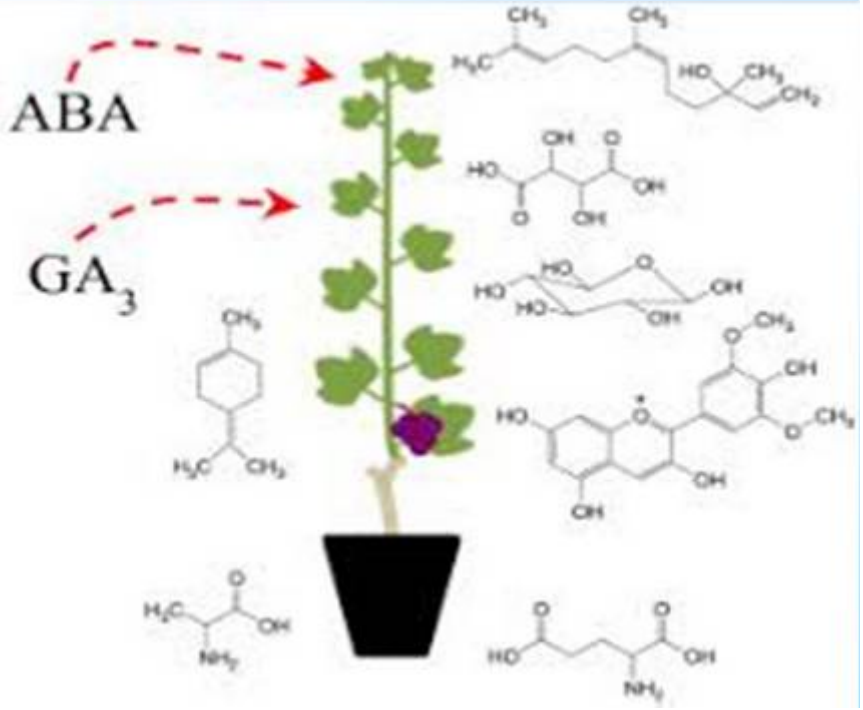
- products are constructed of **carbon**, **hydrogen**, and **oxygen** atoms; frequently **nitrogen** atoms are also involved, and less frequently **sulphur, phosphorus, chlorine**, **bromine**, and **iodine** atoms.
- **Organometallic** compounds, especially metal complexes, also occur. The ultimate sources of these elements are the soil, sea, and the air.



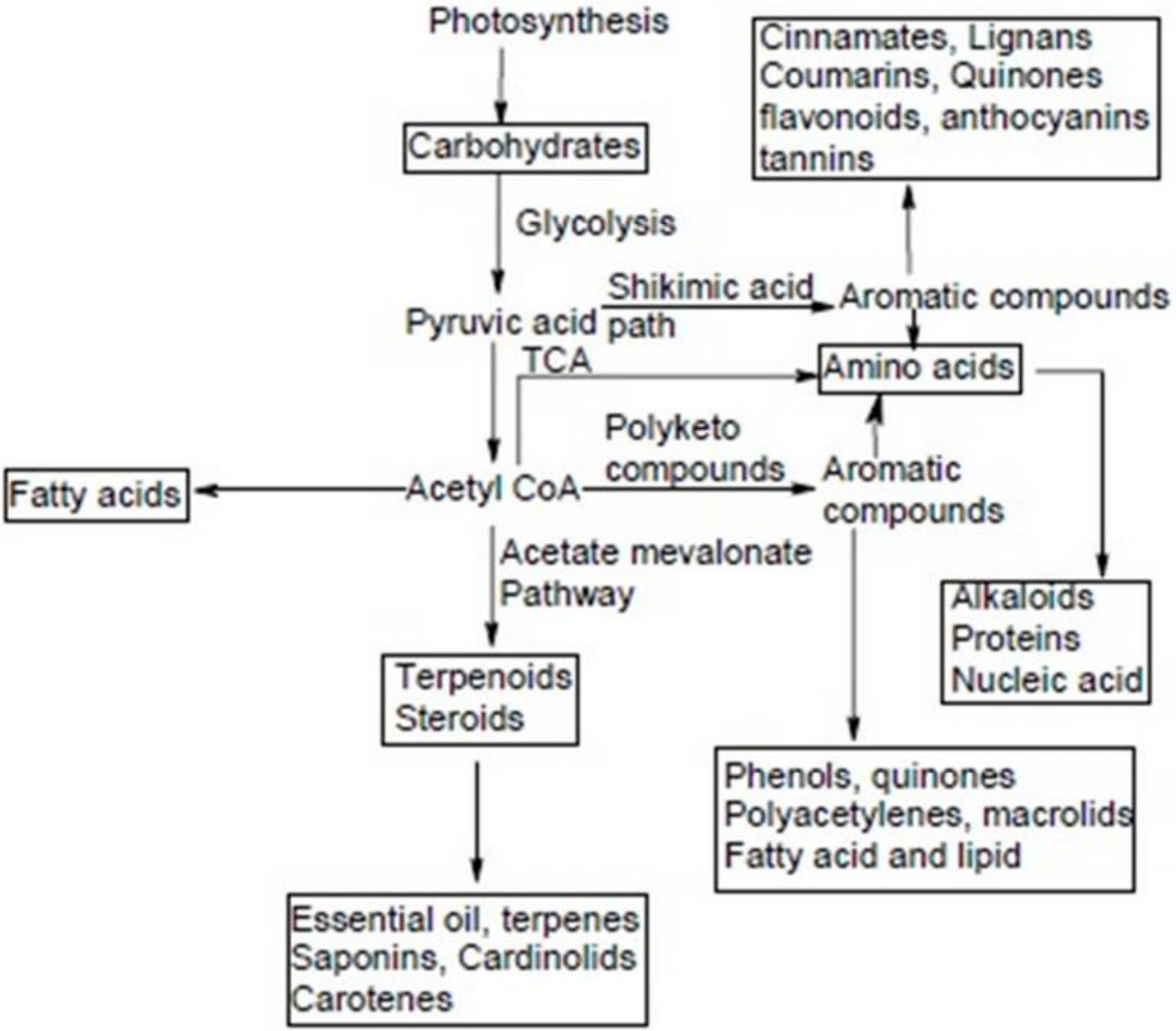
Biosynthesis begins with photosynthesis.

- Green plants and other photosynthetic organisms use the energy of absorbed **visible light** to make **organic compounds**.
- These organic compounds are the **starting point** for all other biosynthetic pathway





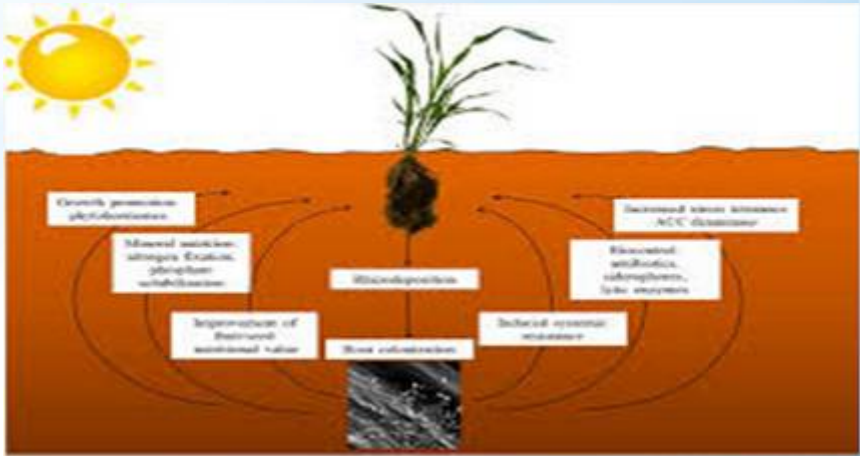
- The **products** of photosynthesis provide not only the **substrate** material but also **chemical energy** for all subsequent biosynthesis.
- The **light** of appropriate wavelengths is absorbed by **chloroplast.**
- **carbon dioxide** is reduced to the level of **sugar**, and **gaseous oxygen**, equal in volume to the CO_2 reduced is liberated.
- The direction of these changes is exactly the reverse of those accomplished during the **oxidation of food**-stuffs in the process of respiration, and indeed, plants are important in the balance of nature because they restore to air the O_2 needed for respiration.

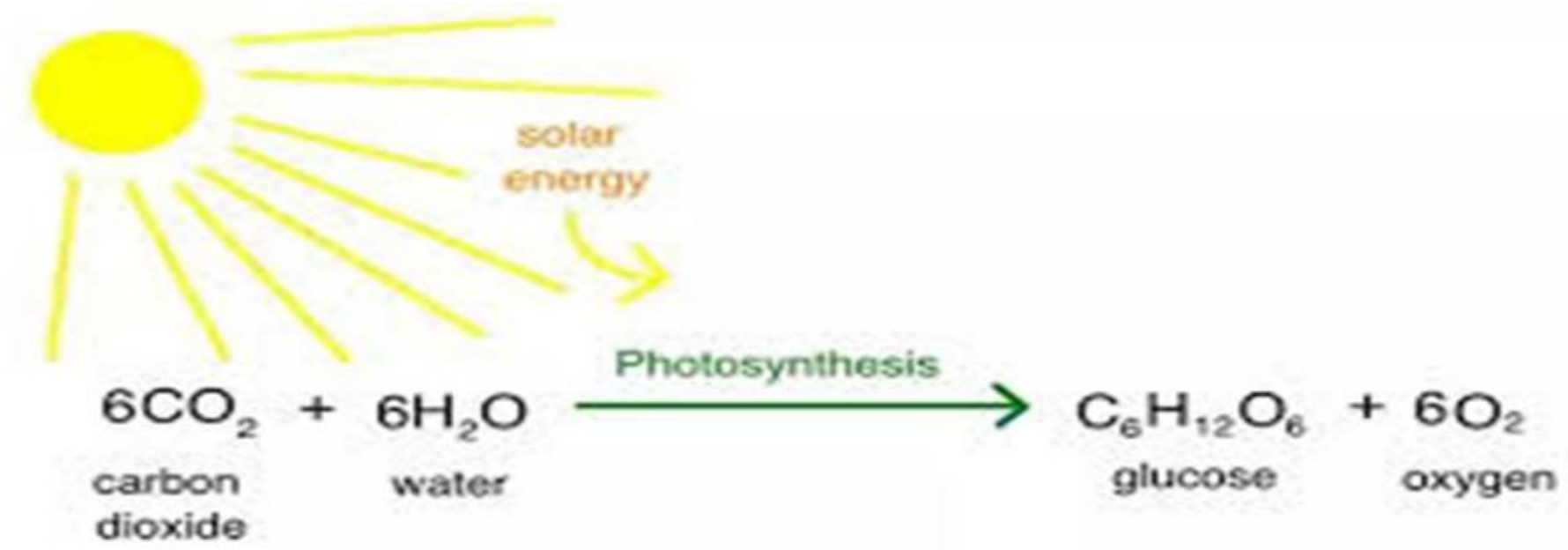

Photosynthesis
Carbohydrates
Glycolysis
Pyruvic acid
Shikimic acid path
Aromatic compounds
Cinnamates, Lignans
Coumarins, Quinones
flavonoids, anthocyanins
tannins
TCA
Amino acids
Polyketo compounds
Aromatic compounds
Fatty acids
Acetyl CoA
Acetate mevalonate Pathway
Alkaloids
Proteins
Nucleic acid
Terpenoids
Steroids
Phenols, quinones
Polyacetylenes, macrolids
Fatty acid and lipid
Essential oil, terpenes
Saponins, Cardinolids
Carotenes

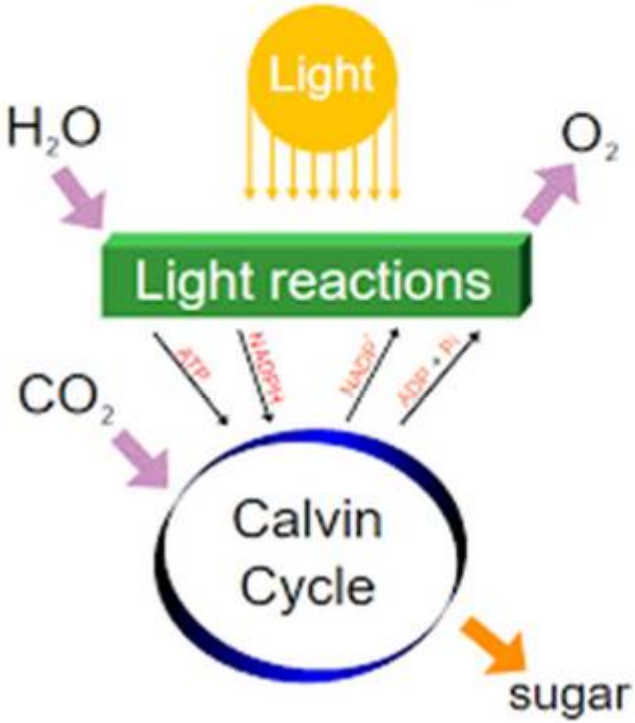
Calvin Cycle: The Calvin cycle is the last step in photosynthesis.

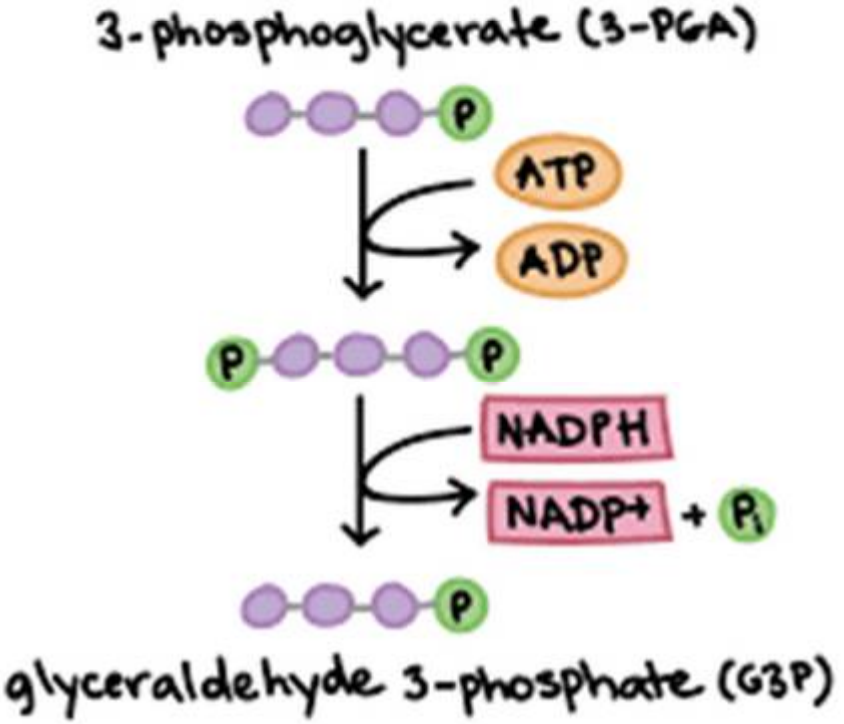
- The purpose of the Calvin Cycle is to **take the energy** from photosystem I and fix carbon.
- Carbon fixation means building organic molecules by adding carbon onto a chain.
- The following formula summarizes the Calvin cycle.

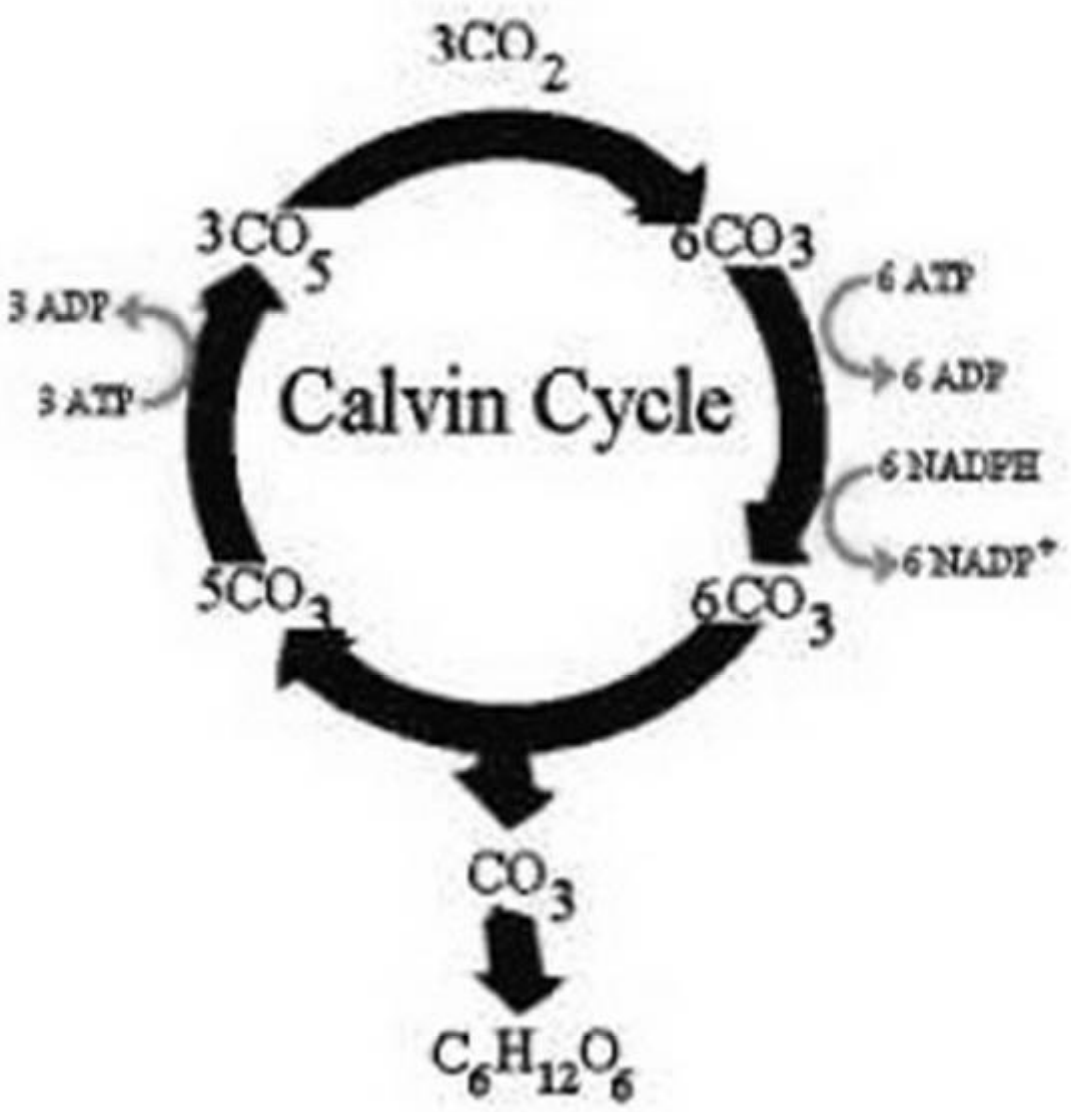
$C5 + CO2 + ATP + NADPH \rightarrow C6H12O6$




solar
energy
Photosynthesis
6CO2 + 6H2O
carbon dioxide
water
C6H12O6 + 6O2
glucose
oxygen


Light
H2O
O2
Light reactions
CO2
ATP
NADPH
NADP+
ADP + Pi
Calvin Cycle
sugar

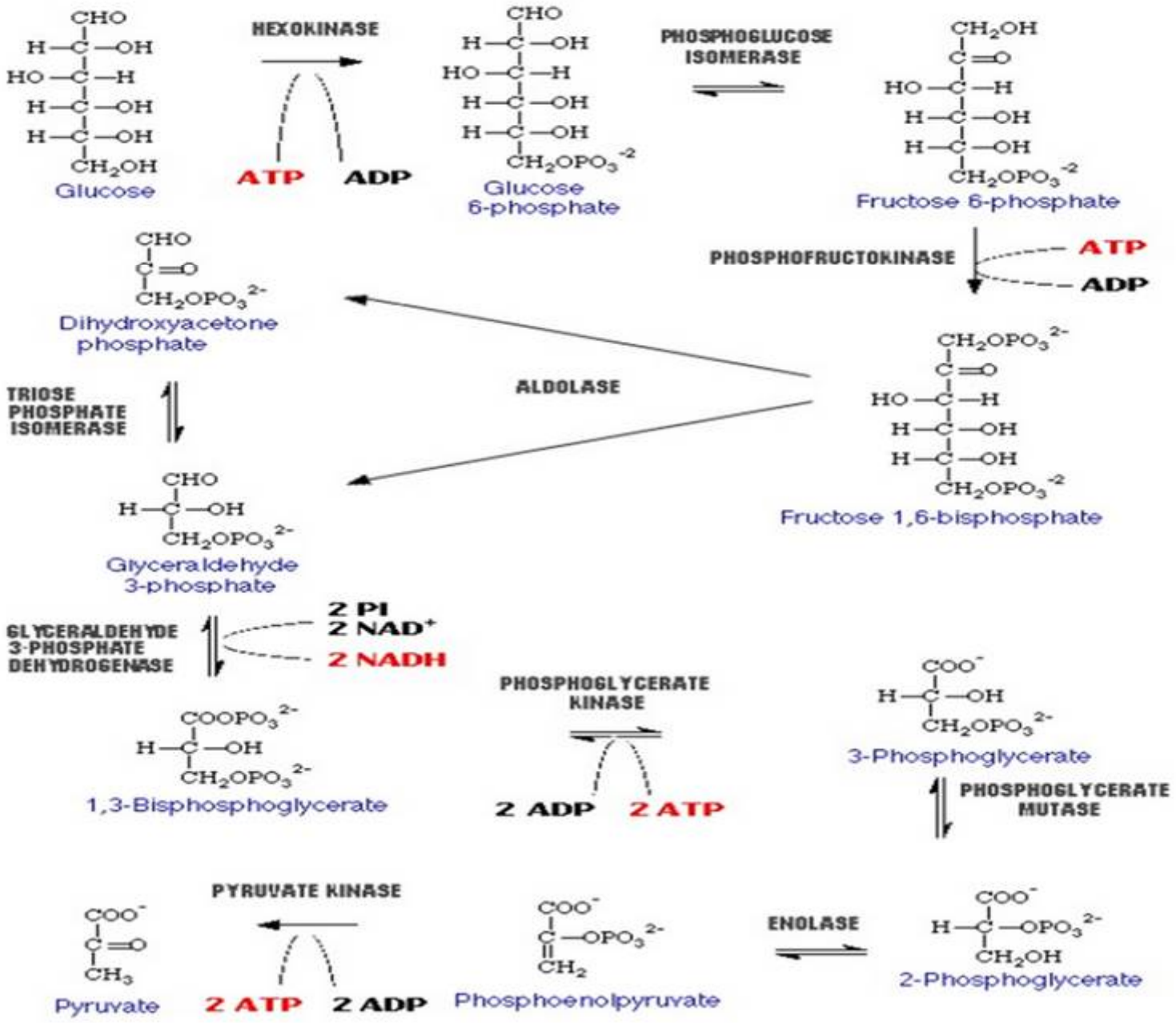

3-phosphoglycerate (3-PGA)
P
ATP
ADP
P
P
NADPH
NADP+
+ Pi
P
glyceraldehyde 3-phosphate (G3P)



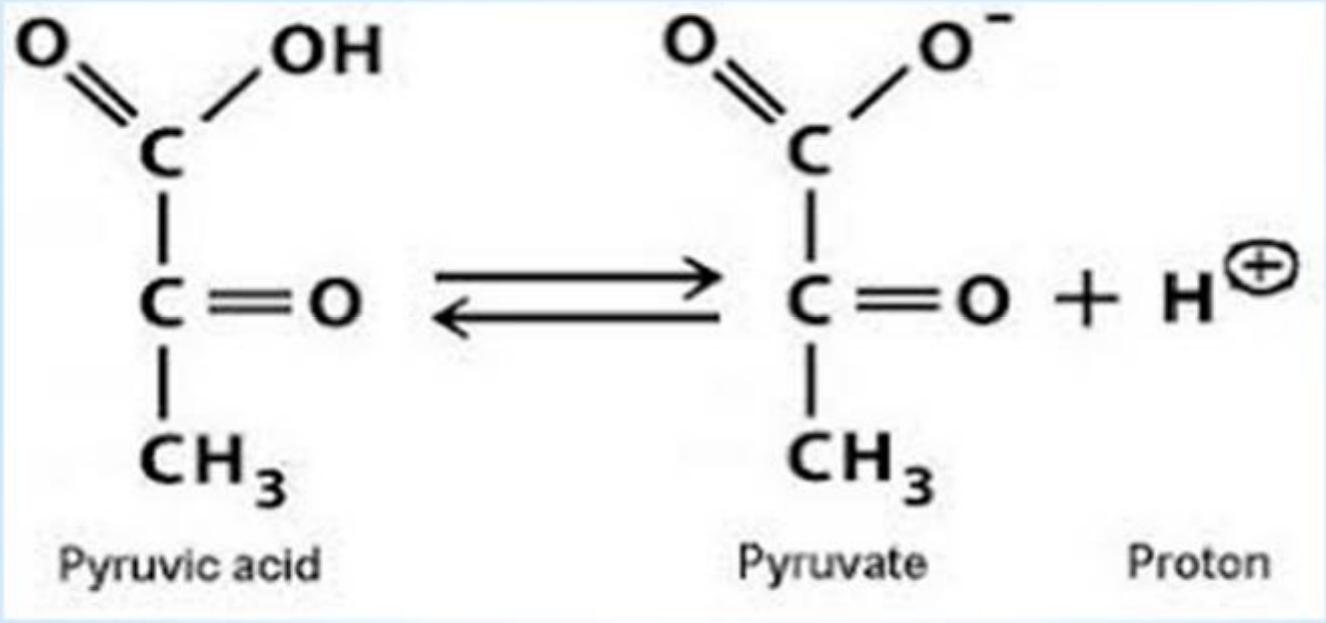
Chemical equation summarizing calvin cycle

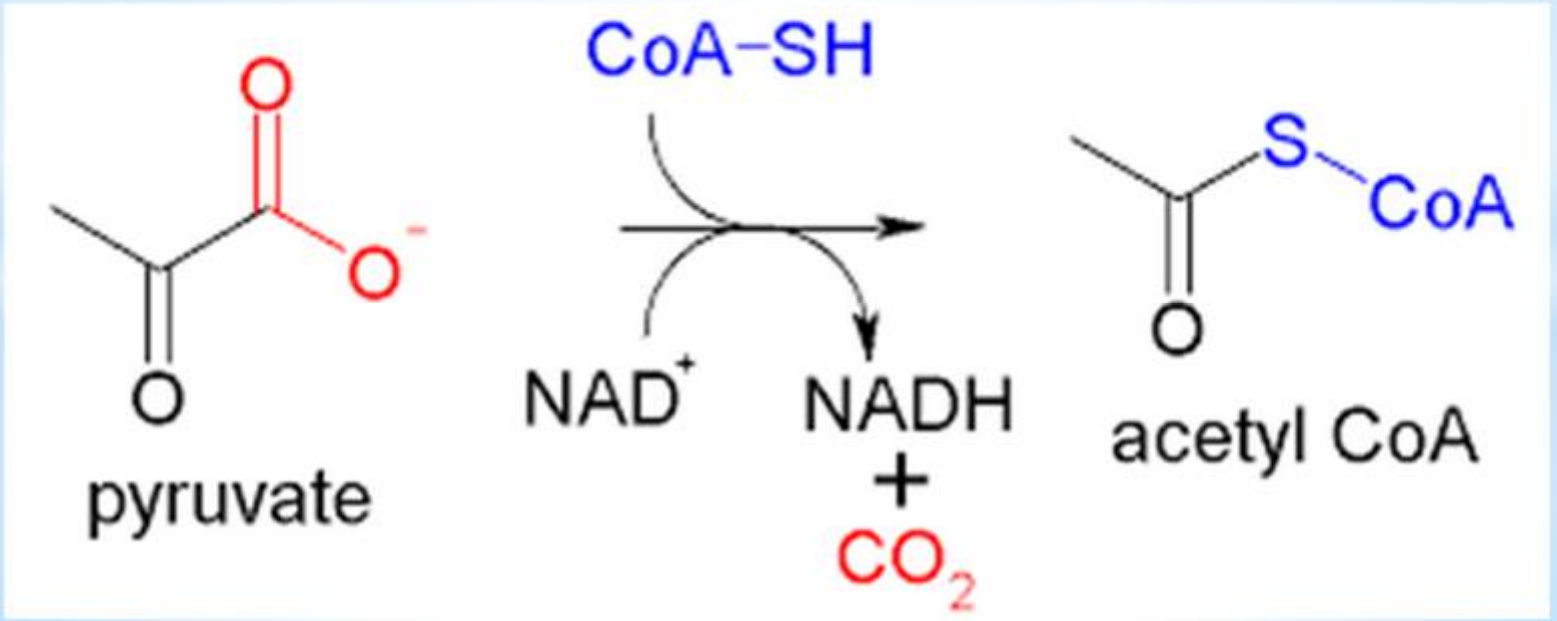
Glycolysis:

- Glycolysis represents an anabolic pathway common in both aerobic and anaerobic organisms.
- **Sugars** and **polysaccharides** are transformed into glucose or one of its phosphorylated derivatives before being processed any further.
- In the course of degradation, ATP is produced. This pathway produces energy in the form of **ATP**.
- **Pyruvate** may be regarded as the preliminary final product of the degradation.
- **Pyruvate** is fed into the citric acid cycle via an intermediate product.



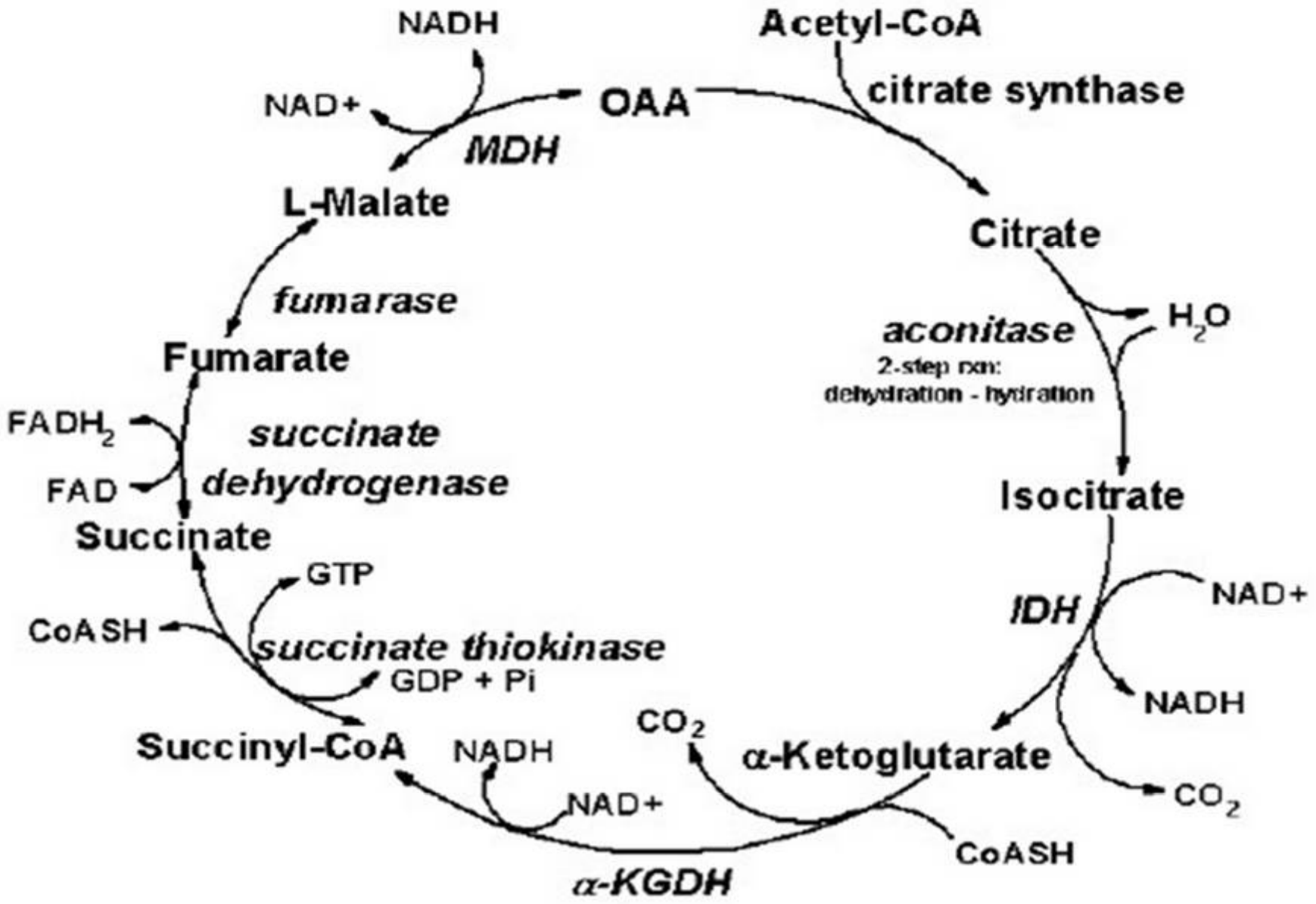
Outline of the Embden- Meyerhoff scheme of glycolysis


Pyruvic acid
Pyruvate
Proton

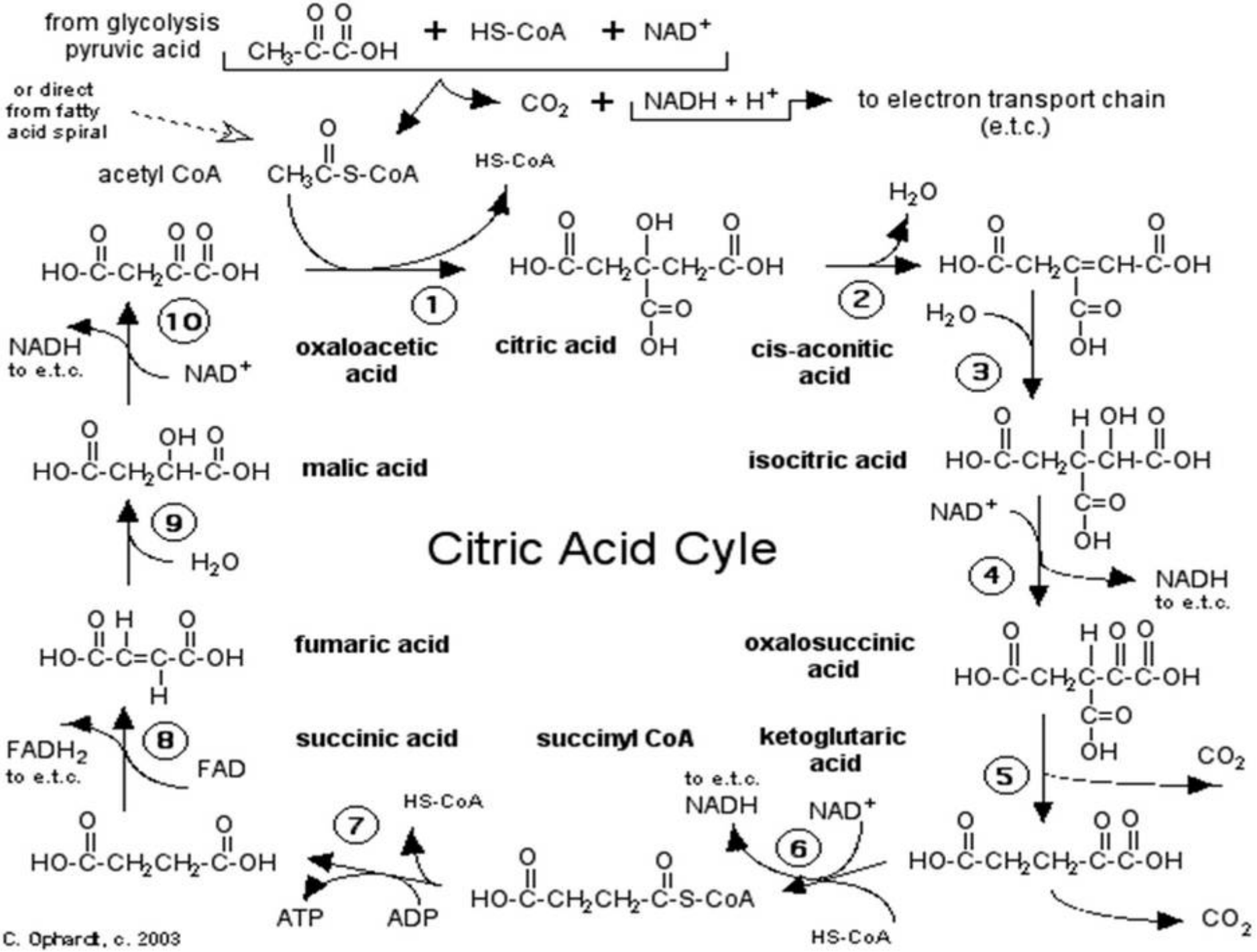

CoA–SH
pyruvate
NAD+
NADH
+
CO2
acetyl CoA

Citric Acid Cycle (Kreb's cycle):

- The citric acid cycle, also known as the tricarboxylic acid (**TCA**) cycle or the Kreb's cycle is the common mode of oxidative degradation in eukaryotes and prokaryotes It accounts for the major portion of **carbohydrate**, **fatty acid** and **amino acid** oxidation and produces at the same time a number of biosynthetic precursors .
- Each mole of NADH leads to 3 moles of ATP and each mole of FADH2 leads to 2 moles of ATP.
- Therefore, for each **mole of pyruvate** which enters the TCA cycle, **12 moles of ATP** can be generated.



Tricarboxylic acid cycle (TCA) or Krebs cycle

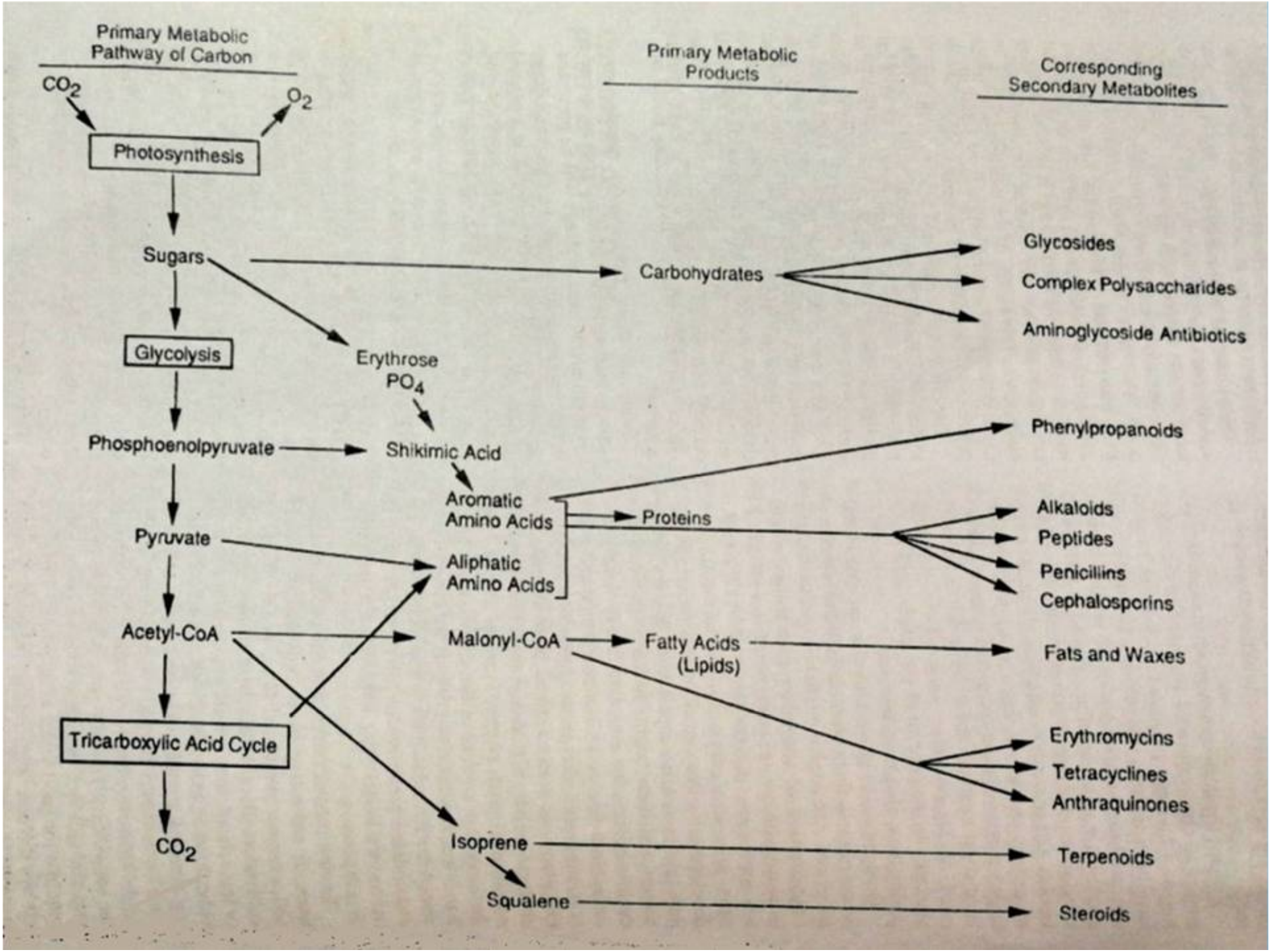

from glycolysis
pyruvic acid
CH3-C(=O)-C(=O)-OH
+ HS-CoA + NAD+
CO2 + NADH + H+
to electron transport chain
(e.t.c.)
or direct
from fatty
acid spiral
acetyl CoA
CH3C-S-CoA
HS-CoA
oxaloacetic
acid
1
citric acid
H2O
2
cis-aconitic
acid
H2O
3
isocitric acid
NAD+
4
NADH
to e.t.c.
oxalosuccinic
acid
CO2
5
ketoglutaric
acid
to e.t.c.
NADH
NAD+
6
HS-CoA
succinyl CoA
7
HS-CoA
ATP
ADP
succinic acid
FADH2
to e.t.c.
8
FAD
fumaric acid
9
H2O
malic acid
NADH
to e.t.c.
10
NAD+
Citric Acid Cyle
C. Ophardt, c. 2003

Summary equation for Krebs Cycle and the bridge reaction

$$C_3H_4O_3 + 4\ NAD^+ + ADP + P_i + FAD + 2\ H_2O$$

$$\Rightarrow$$

$$3\ CO_2 + 4\ NADH + 4\ H^+ + ATP + FADH_2$$


Primary Metabolic Pathway of Carbon
Primary Metabolic Products
Corresponding Secondary Metabolites
CO_2
O_2
Photosynthesis
Sugars
Carbohydrates
Glycosides
Complex Polysaccharides
Aminoglycoside Antibiotics
Glycolysis
Erythrose PO_4
Phosphoenolpyruvate
Shikimic Acid
Phenylpropanoids
Aromatic Amino Acids
Proteins
Alkaloids
Peptides
Penicillins
Cephalosporins
Pyruvate
Aliphatic Amino Acids
Acetyl-CoA
Malonyl-CoA
Fatty Acids (Lipids)
Fats and Waxes
Tricarboxylic Acid Cycle
Erythromycins
Tetracyclines
Anthraquinones
CO_2
Isoprene
Terpenoids
Squalene
Steroids


Thank
you!