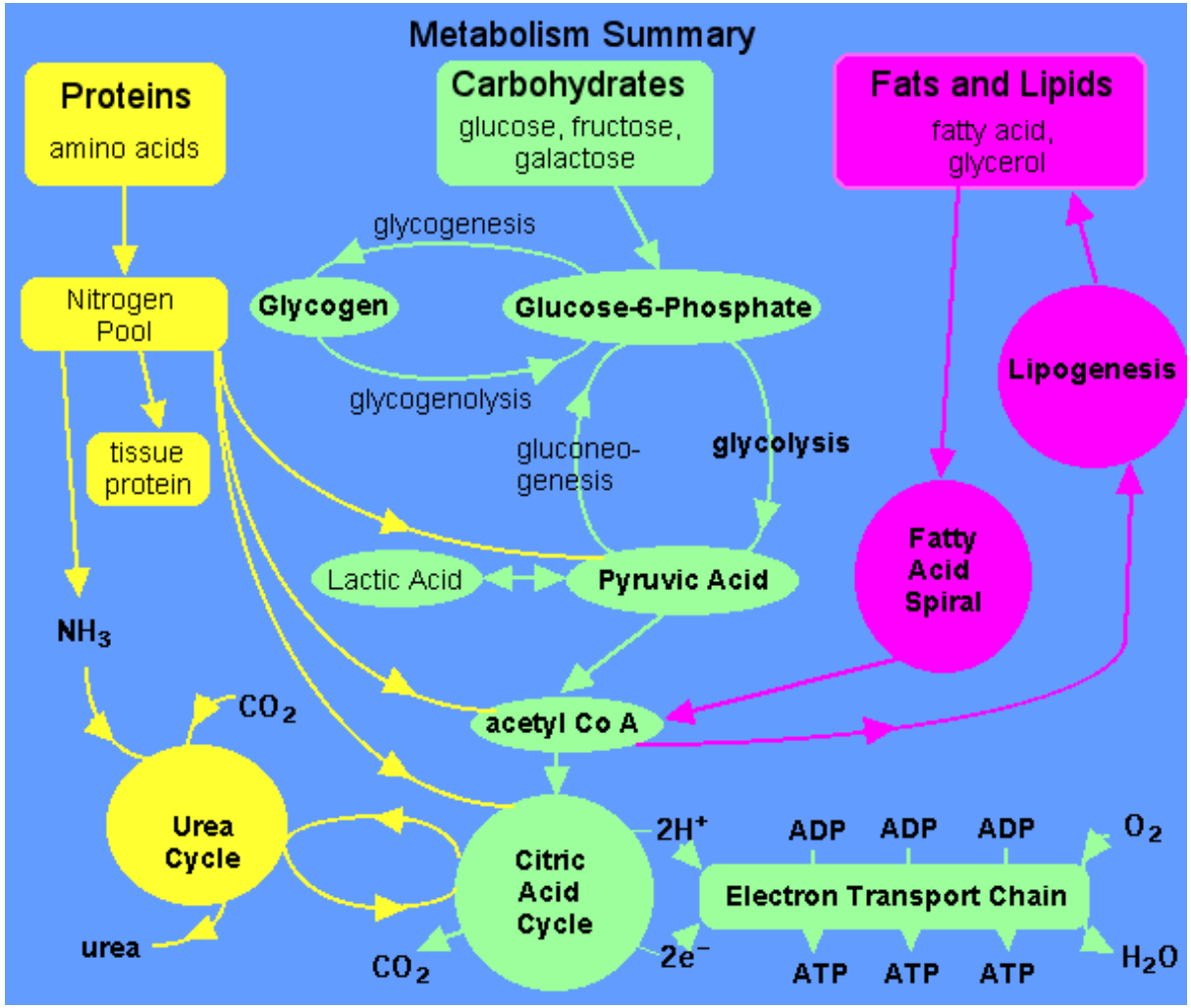
Chapter 13
Carbohydrate Metabolism

Metabolism of Foods

Food is broken down into carbohydrates, lipids, and proteins and sent through catabolic pathways to produce energy.

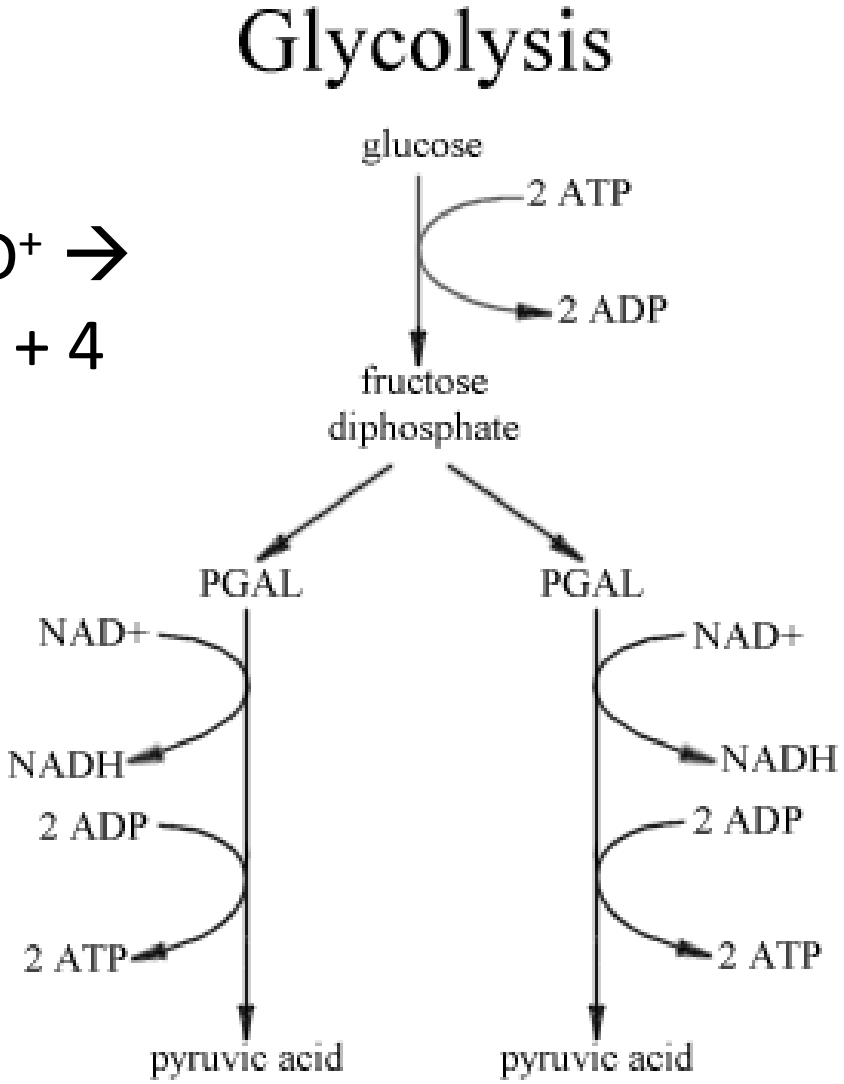


Glycolysis

glucose + 2 P_i + 2 ADP + 2 NAD^+ → 2 pyruvate + 2 ATP + 2 NADH + 4 H^+ + 2 H_2O

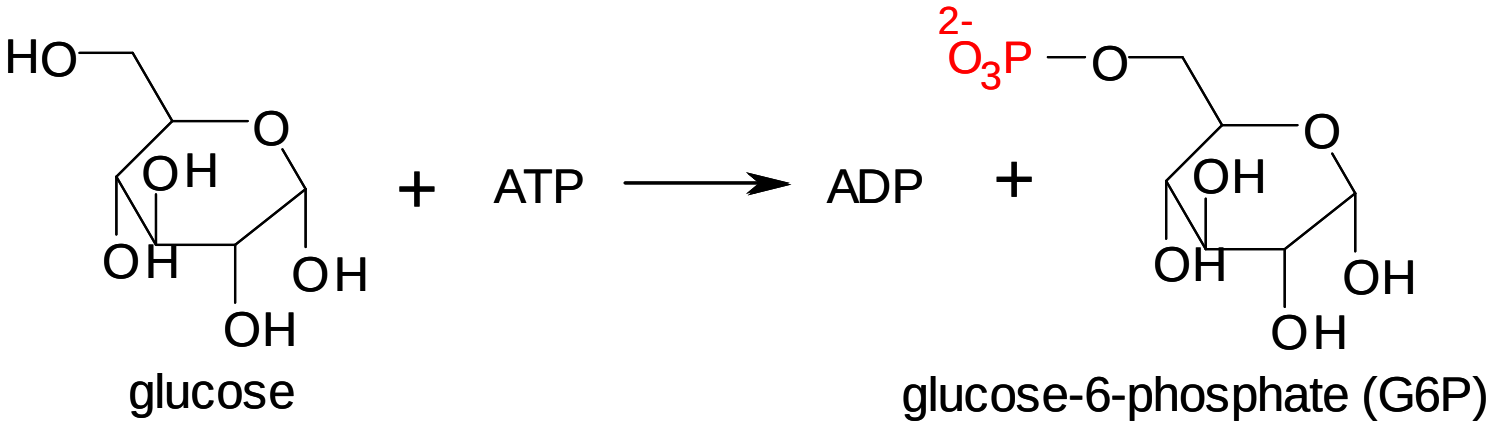
Ten-step pathway

<u>Net Gain</u>: 2 mols ATP per 1 mol glucose



Step 1: Phosphorylation to G6P

A phosphate group from ATP transfers to glucose.

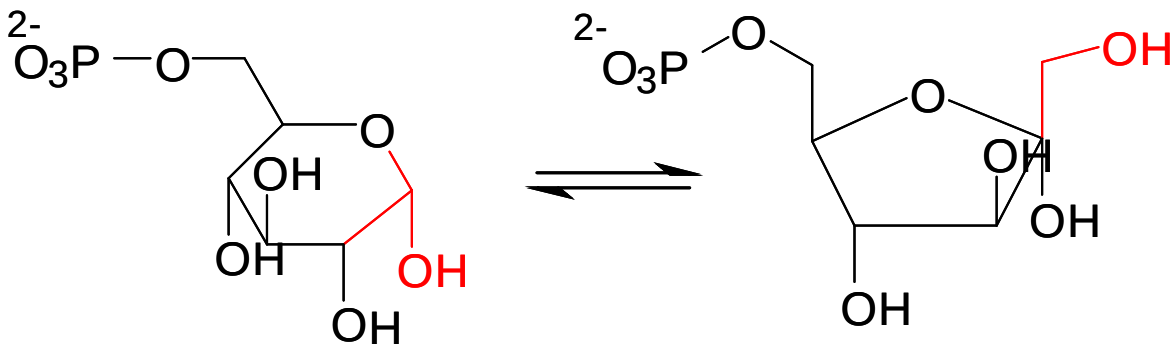


Catalyzed by hexokinase/glucokinase.

Step 1 serves to keep the concentration of glucose low.
G6P traps the glucose.

Step 2: Isomerization to F6P

G6P isomerizes to fructose-6-phosphate (F6P).

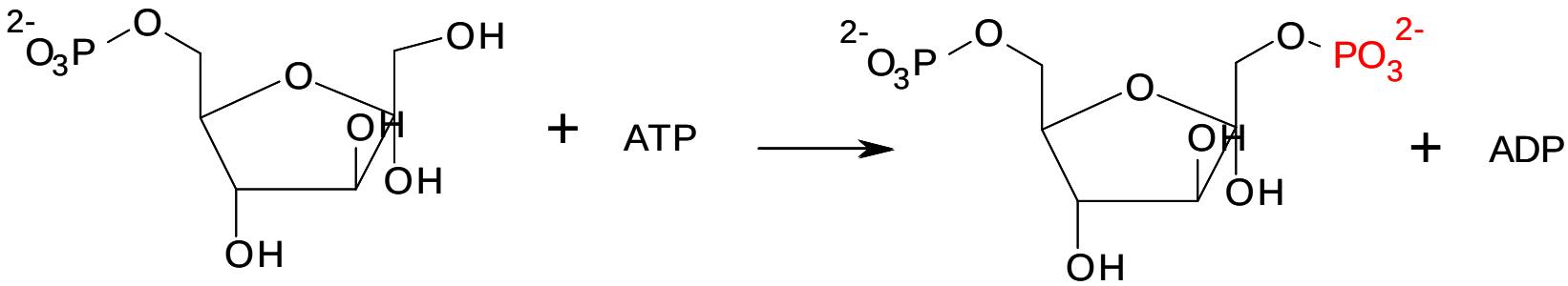


glucose-6-phosphate (G6P) fructose-6-phosphate (F6P)

Catalyzed by phosphoglucose isomerase.
Reaction is fully reversible.

Step 3: Phosphorylation to FBP

A second ATP molecule enters and transfers a phosphate group to fructose-1,6-bisphosphate (FBP).



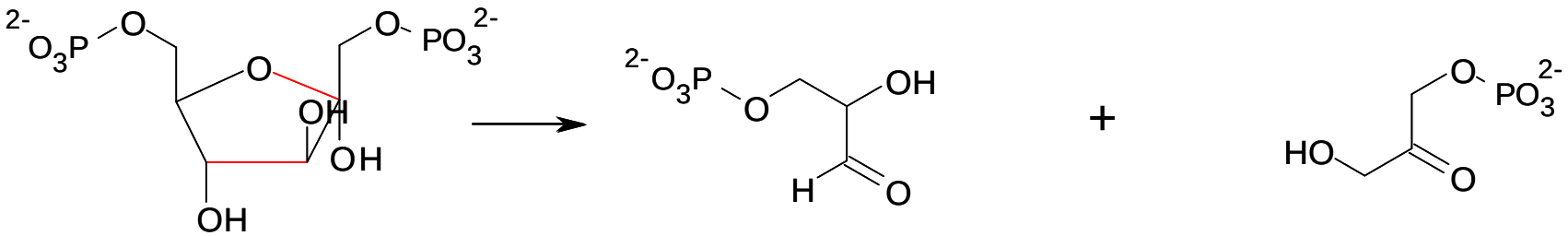
fructose-6-phosphate (F6P)

fructose-1,6-bisphosphate (FBP)

Catalyzed by phosphofructokinase.
Inhibited by high concentrations of ATP and citrate; activated by high concentrations of ADP and AMP.

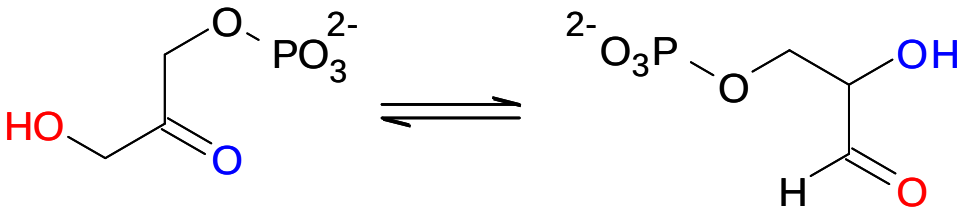
Step 4: Cleavage to DHAP and GADP

FBP (six carbons) is cleaved into two trioses.



fructose-1,6-bisphosphate (FBP) glyceraldehyde 3-phosphate (GADP) dihydroxyacetone phosphate (DHAP)

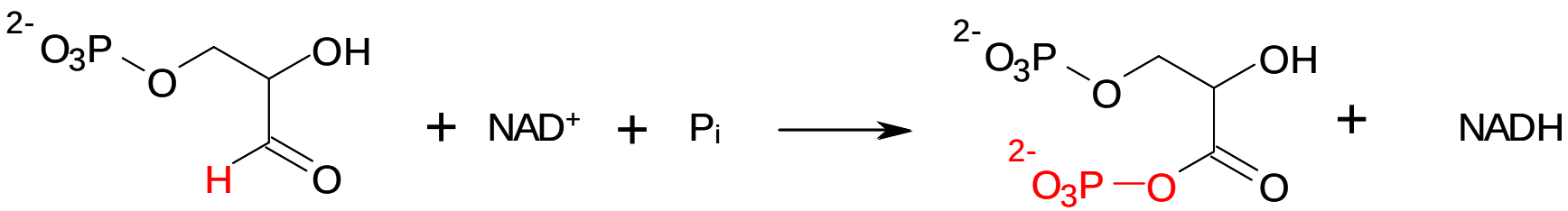
Catalyzed by fructose biphosphate aldolase (ALDO).
DHAP can convert to GADP.



DHAP GADP

Step 5: Oxidation to 1,3-BPG

GAP is oxidized to 1,3-bisphosphoglycerate (1,3-BPG). A second inorganic phosphate is added.



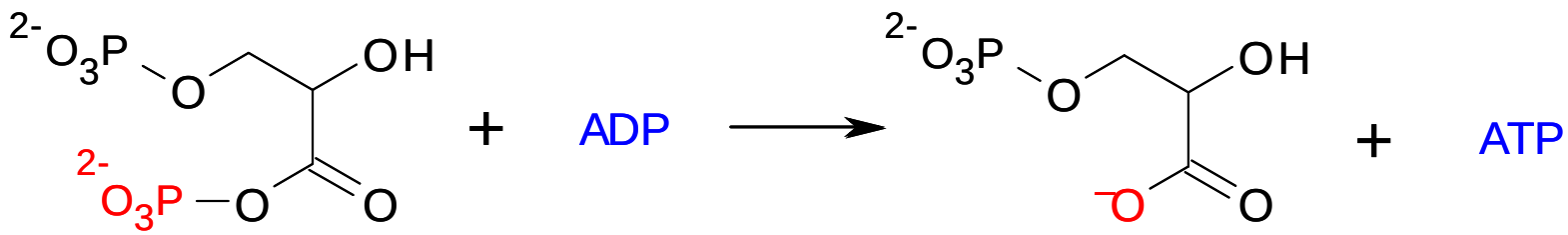
glyceraldehyde 3-phosphate (GADP)

1,3-bisphosphoglycerate (1,3-BPG)

Catalyzed by glyceraldehyde phosphate dehydrogenase (GAPDH).

Step 6: Transfer of Phosphate

The phosphate on the carboxyl group is transferred to an ADP molecule.



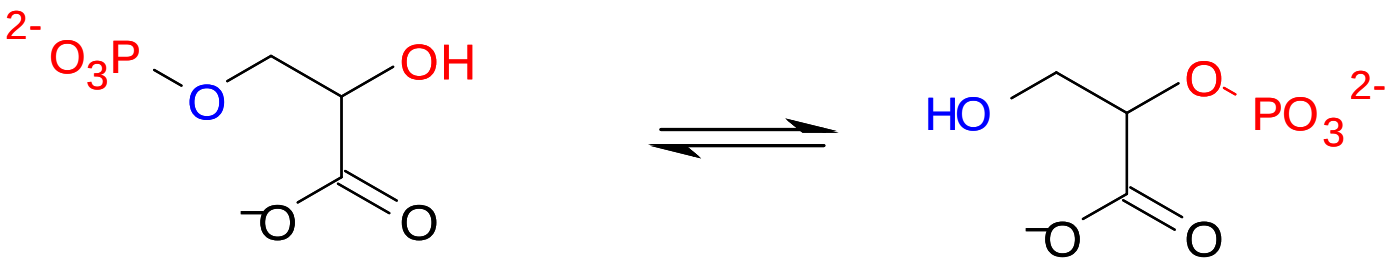
1,3-bisphosphoglycerate (1,3-BPG)

3-phosphoglycerate (3PG)

Catalyzed by phosphoglycerate kinase (PGK).

Step 7: Isomerization to 2PG

3PG is isomerized to 2-phosphoglycerate (2PG).

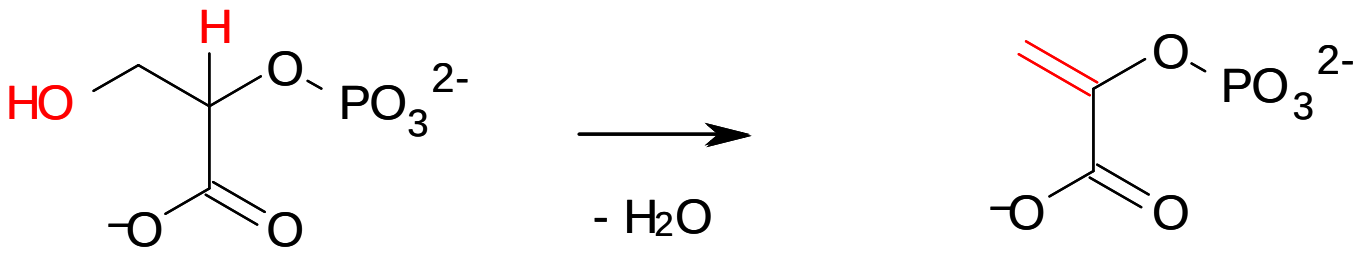


3-phosphoglycerate (3PG) 2-phosphoglycerate (2PG)

Catalyzed by phosphoglycerate mutase (PGM).

Step 8: Dehydration to PEP

PGM is dehydrated to remove the alcohol to form phosphoenolpyruvate (PEP).

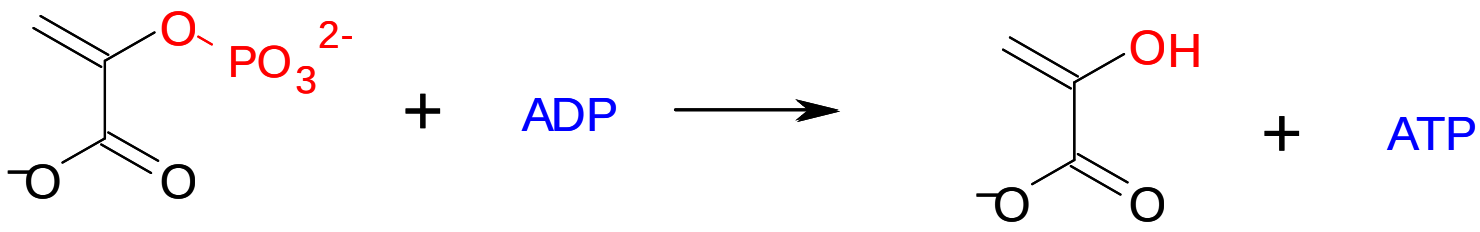


2-phosphoglycerate (2PG) phosphoenolpyruvate (PEP)

Catalyzed by enolase.

Step 9: Removal of Phosphate

Phosphoenolpyruvate loses its last phosphate.

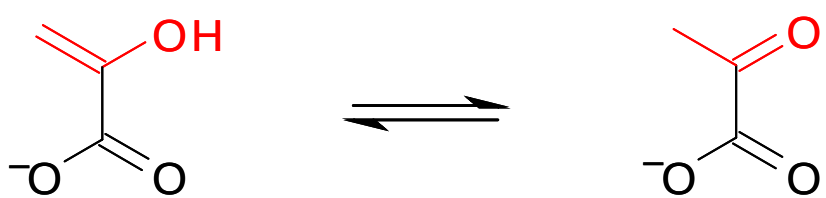


phosphoenolpyruvate (PEP)

pyruvate (enol)

Catalyzed by pyruvate kinase (PK) and regulated by the ratio of ADP/ATP present.

Pyruvate tautomerizes to pyruvic acid.

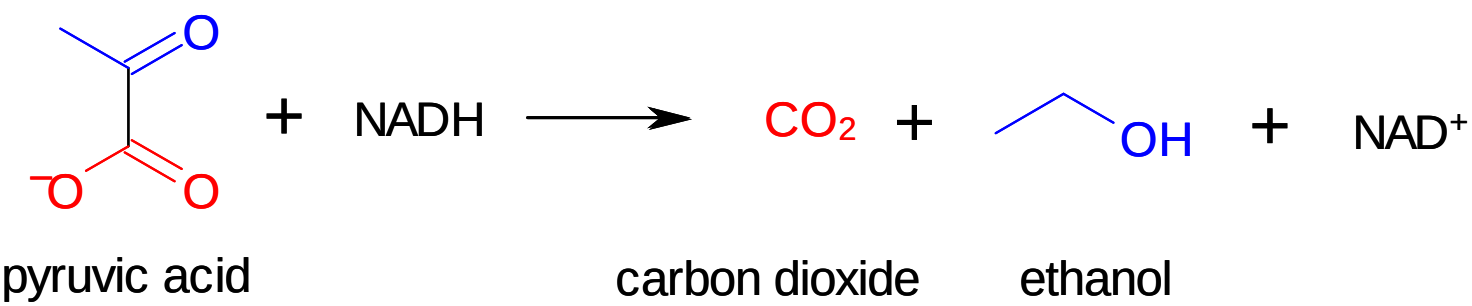


pyruvate (enol)

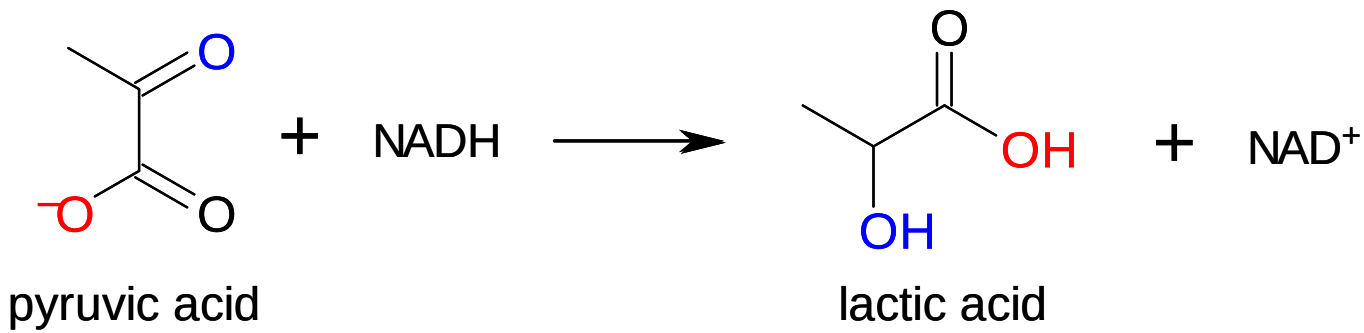
pyruvic acid (keto)

Fate of Pyruvate

Alcoholic fermentation produces ethanol and CO_2.



Homolactic fermentation produces lactate.



Summary of Glycolysis

<u>Overall Reaction</u>:

$$\text{D-glucose} + 2\ NAD^+ + 2\ ADP + 2\ P_i \rightarrow$$
$$2\ \text{pyruvate} + 2\ NADH + 2\ H^+ + 2\ ATP$$

<u>Energy Gain (per glucose)</u>:

2 NADH + 2 H^+

2 ATP

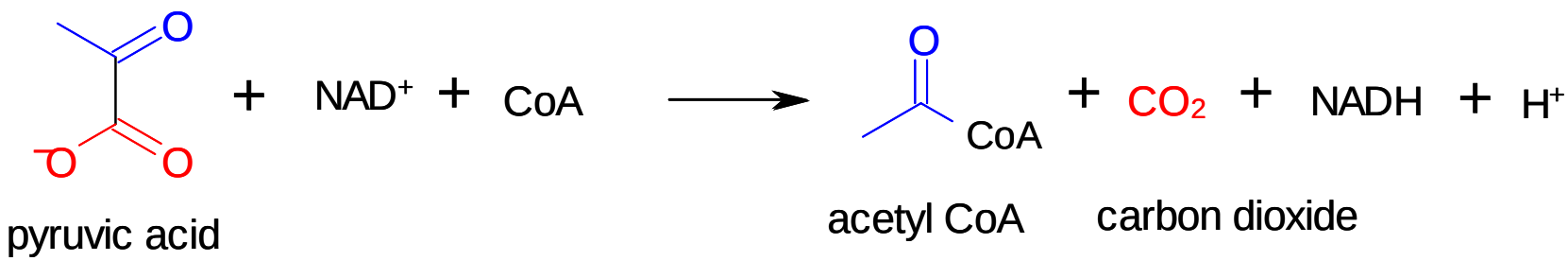
- Other monosaccharides (fructose, galactose) can enter the glycolysis pathway at intermediary points.
- Occurs in nearly all living organisms.
- Produces pyruvate.

Energy Yield from Glycolysis

Activation (Steps 1-3)	- 2 ATP
Phosphorylation (Step 5)	+ 4 ATP (from 2 NADH + H^+)
Dephosphorylation (Steps 6, 9)	+ 4 ATP
TOTAL (cycle):	**6 ATP/1 glucose**

Oxidative Phosphorylation

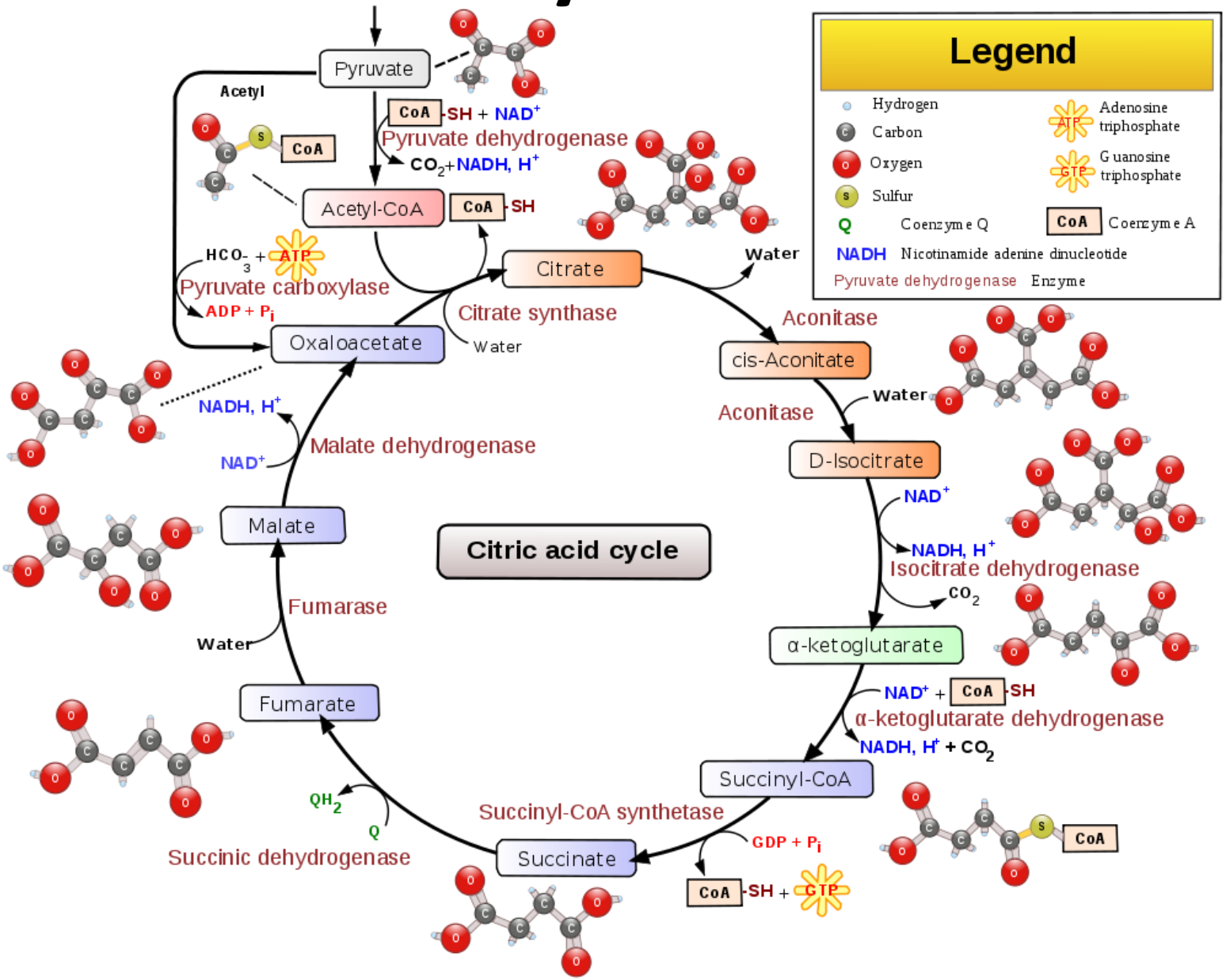
Oxidative phosphorylation produces acetyl CoA.



<u>Energy Gain</u>**:** 2 ATP per pyruvate (from NADH + H^+)

TOTAL: 4 ATP/1 glucose (2 pyruvate/1 glucose)

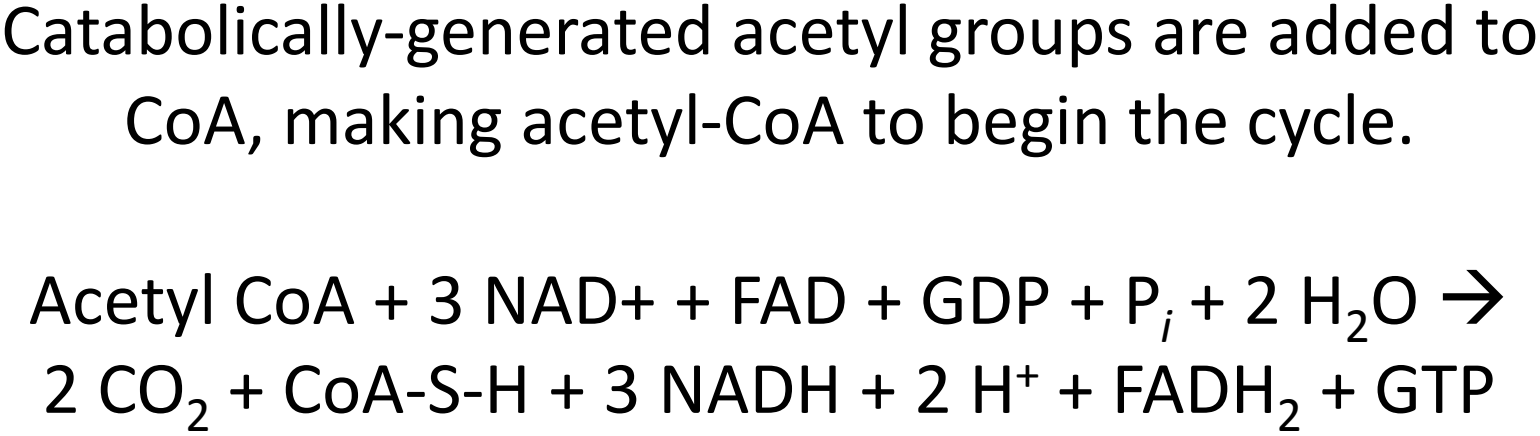
The Citric Acid Cycle



Preliminary Stages

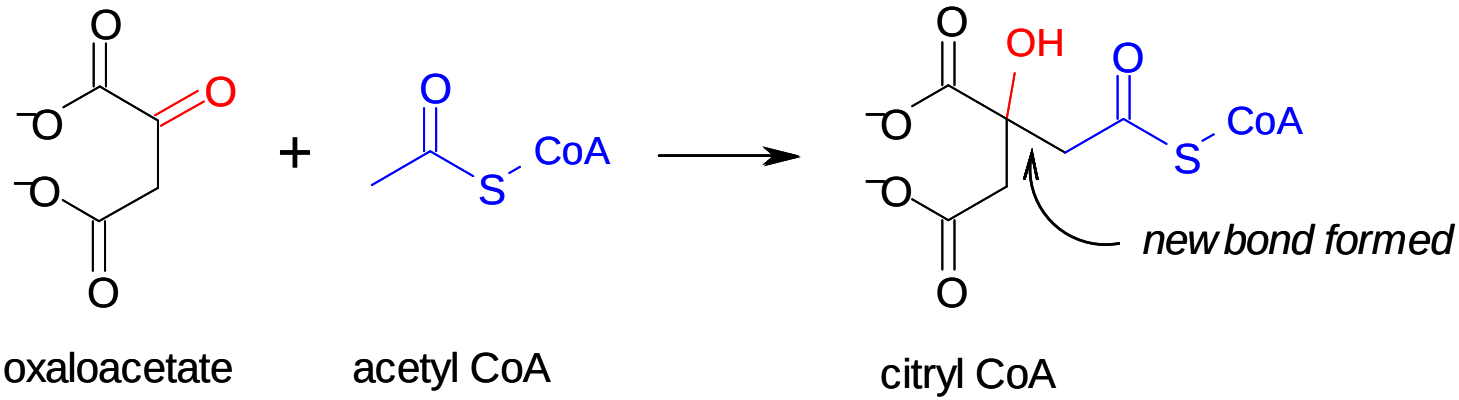
The Citric Acid Cycle (tricarboxylic TAC, Krebs) converts food into carbon dioxide, water, and usable energy.

Catabolically-generated acetyl groups are added to CoA, making acetyl-CoA to begin the cycle.

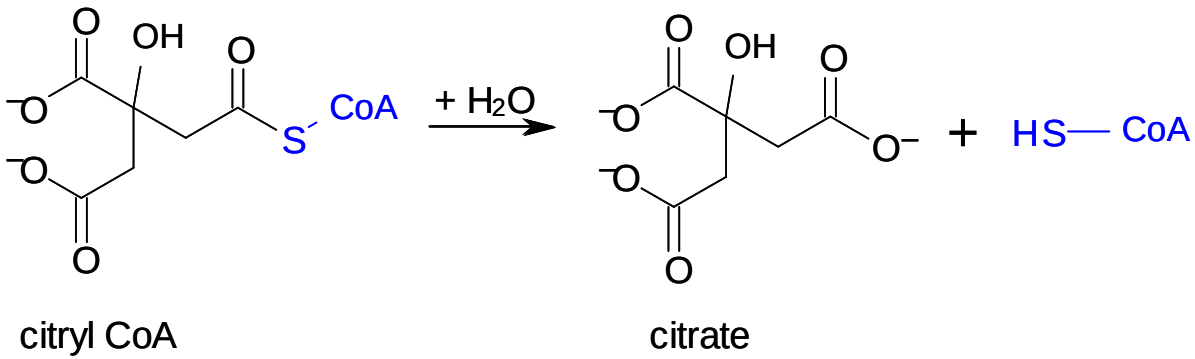


Step 1: Synthesis of Citrate

Acetyl-CoA (2 C) adds to oxaloacetate (4 C) to generate citryl CoA (6 C).

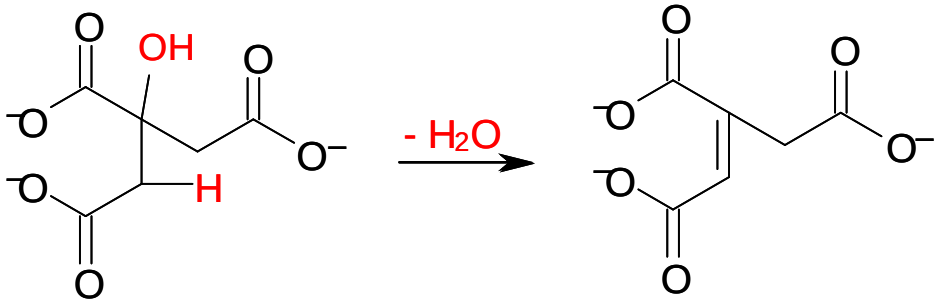


A hydrolysis reaction regenerates free CoA.



Step 2: Isomerization to Isocitrate

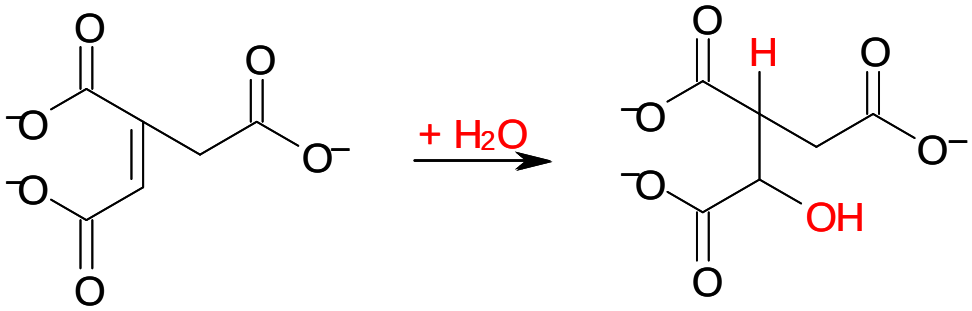
Citrate is dehydrated.



citrate

cis-aconitate

cis-aconitate is re-hydrated.

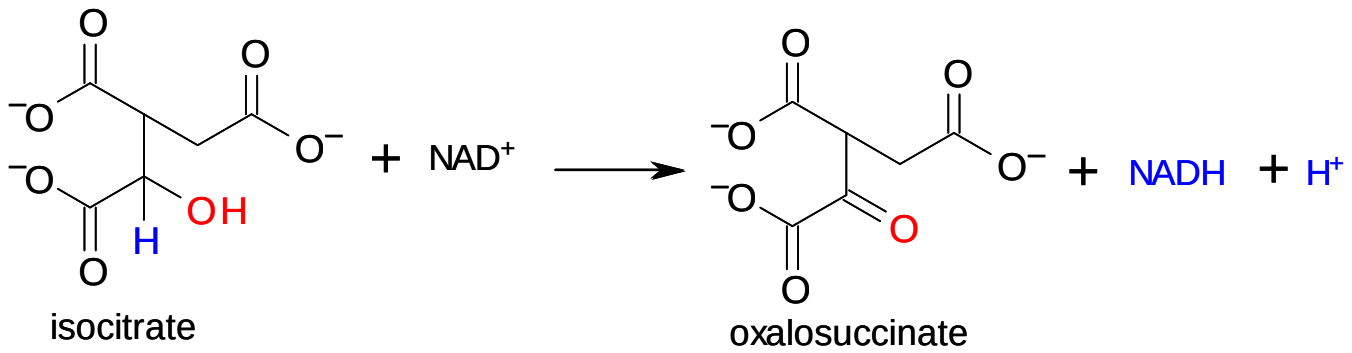


cis-aconitate

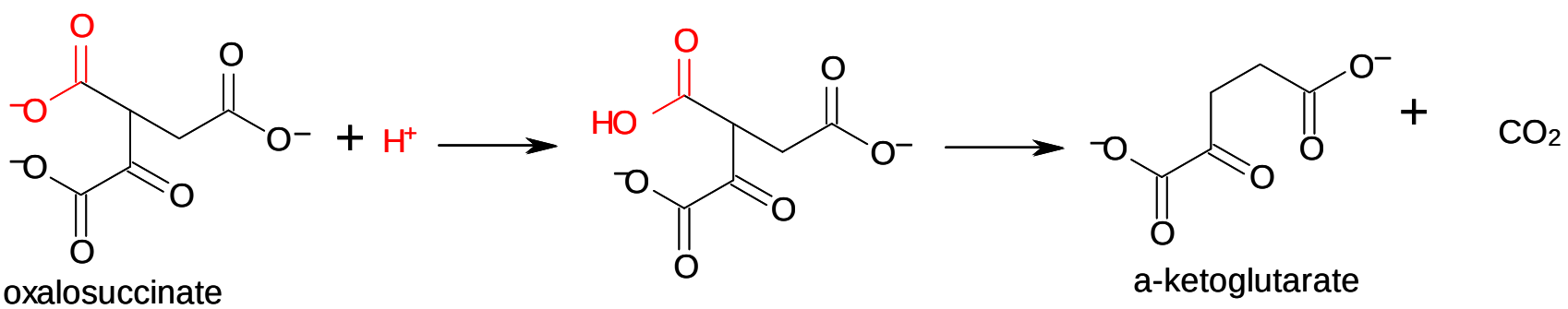
isocitrate

Step 3: Oxidative Decarboxylation

Isocitrate is oxidized by NAD^+.

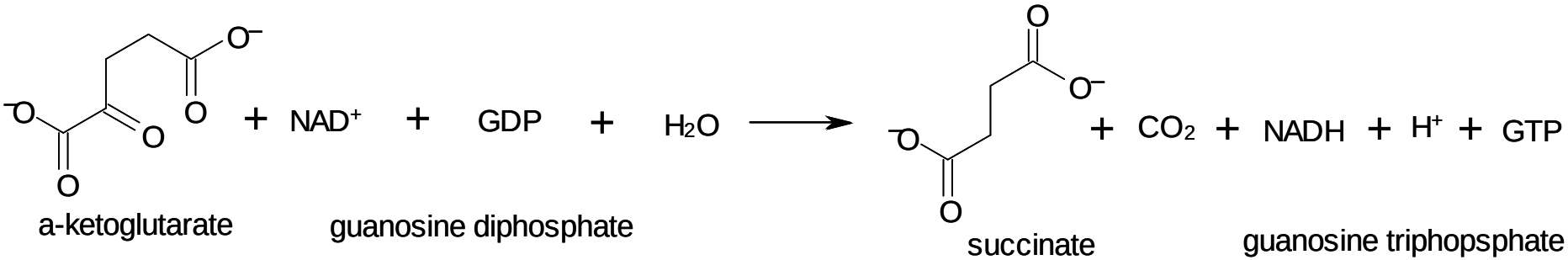


Oxalosuccinate is decarboxylated.



Step 4/5: Oxidative Decarboxylation

A complex system removes another equivalent of CO_2 from α-ketoglutarate.

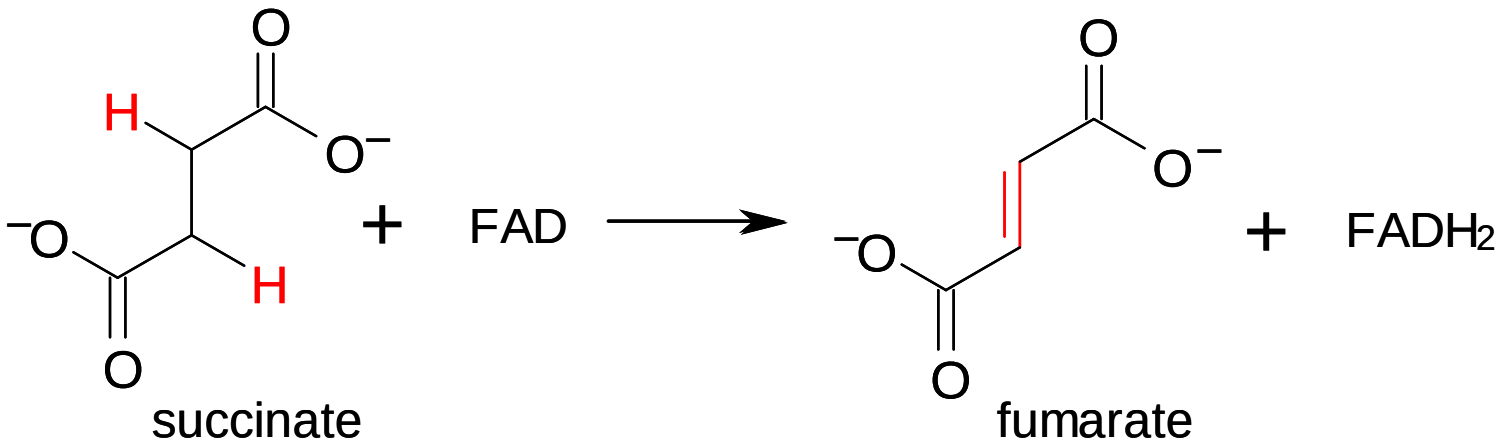


The decarboxylation of α-ketoglutarate is complex. GTP is another energy-storage molecule (guanine replaces adenine).

The CO_2 produced in Step 3 and Step 4/5 is exhaled.

Step 6: Oxidation to Fumarate

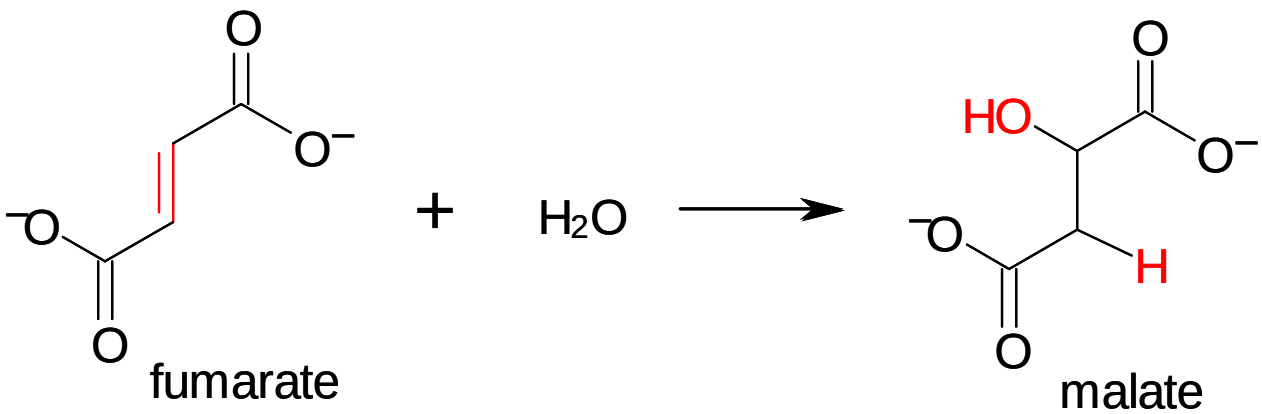
Succinate (4 C) is oxidized by FAD. The double bond form is the *trans* isomer.



Succinate dehydrogenase catalyzes the reaction. FAD is reduced to $FADH_2$.

Step 7: Hydration to Malate

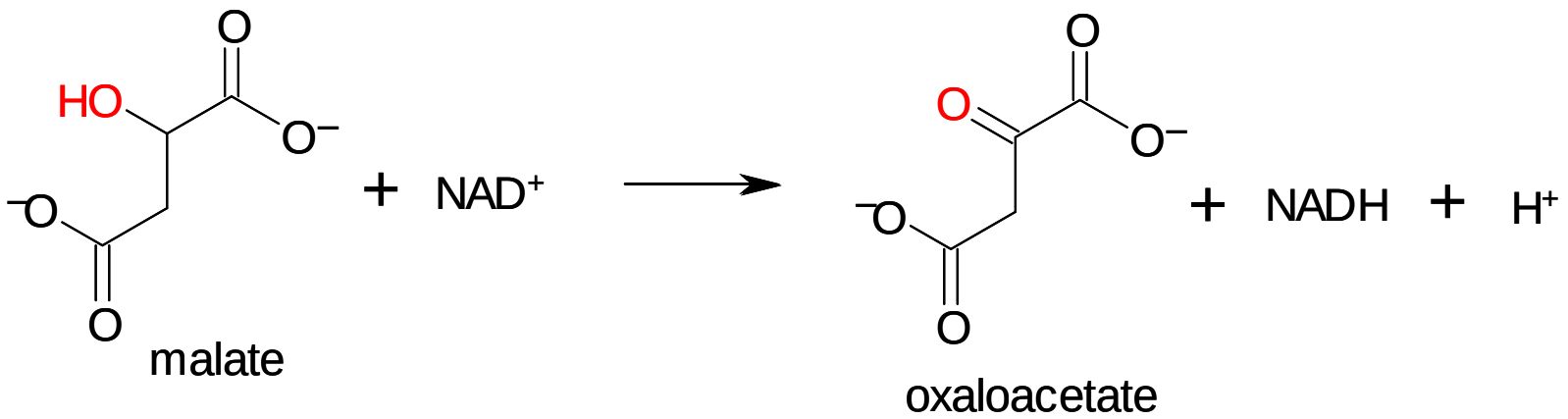
The double bond in fumarate is hydrolyzed.



Fumarase catalyzes the hydrolysis.

Step 8: Oxidation to Oxaloacetate

NAD^+ oxidizes the alcohol on malate to a ketone.



Oxaloacetate is generated and can begin Step 1 in the Citric Acid Cycle again.

Summary of the Citric Acid Cycle

<u>Overall Reaction</u>:

Acetyl CoA + 3 NAD+ + FAD + GDP + P_i + 2 H_2O → 2 CO_2 + CoA-S-H + 3 NADH + 2 H^+ + $FADH_2$ + GTP

<u>Energy Gain (per glucose)</u>:

8 NADH (pyruvate)
6 CO_2 (pyruvate)
2 ATP (GTP)
2 $FADH_2$

- 1 glucose = 2 pyruvate (glycolysis) = 2 acetyl CoA
- Oxaloacetate (4 carbons) adds an acetyl group (2 carbons) from acetyl CoA, then loses 2 CO_2 molecules (2 carbons) to regenerate oxaloacetate (4 carbons).

Energy Yield from Citric Acid Cycle

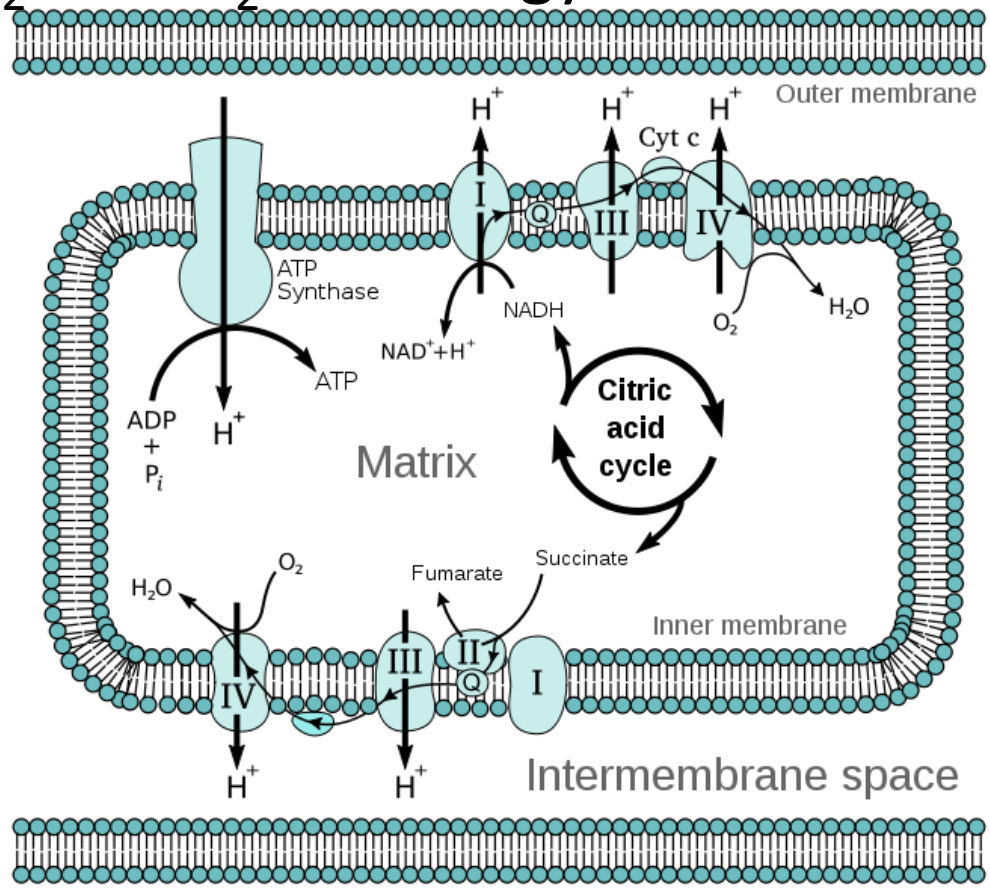
Pyruvate Oxidation (prior)	+ 2 ATP (from 1 NADH + H^+)
Decarboxylation (Steps 3-5)	+ 5 ATP (from 1 GTP, 2 NADH + H^+)
Oxidation (Steps 6, 8)	+ 5 ATP (from $FADH_2$, NADH + H^+)
TOTAL (cycle):	**12 ATP /1 pyruvate**
TOTAL (overall):	**24 ATP/1 glucose**

Electron Transport

When H^+, electrons, and oxygen are combined, water and energy are produced.

$$4\ H^+ + 4\ e^- + O_2 \rightarrow 2\ H_2O + \text{energy}$$

NADH and $FADH_2$ carry H^+ and e^- to the mitochondria in a cell to be combined with O_2 inhaled via the respiratory system to produce energy.



Summary of Electron Transport Chain

The H^+ move through proton-translocating ATPase which catalyzes the conversion of ADP to ATP and H_2O.

NADH and $FADH_2$ are oxidized back to NAD^+ and FAD respectively so that they can go back to participating in the citric acid cycle.

Energy is provided to convert ADP to ATP.

Energy Production

From the citric acid cycle:

1 acetyl group = 3 NADH + 1 $FADH_2$ + 1 GTP
(equivalent with ATP in energy production)

From the electron transport chain:

1 NADH = 6 protons = 3 ATP
1 $FADH_2$ = 4 protons = 2 ATP

In total:

1 acetyl group = 9 ATP + 2 ATP + 1 ATP = 12 ATP

$$C_2 + 2\ O_2 + 12\ ADP + 12\ P_i \rightarrow 12\ ATP + 2\ CO_2$$

Glucose Metabolism

Glycolysis	
Activation	- 2 ATP
Phosphorylation	+ 2 NADH
Dephosphorylation	+ 4 ATP
Pyruvate Synthesis	
Oxidation	+ 2 NADH
Citric Acid Cycle	
Oxidation	+ 2 NADH
Decarboxylation	+ 2 GTP, 2 NADH
Oxidation	+ 2 $FADH_2$, 2 NADH
Electron Transport Chain	
- 10 NADH	+ 25 ATP
- 2 $FADH_2$	+ 3 ATP
TOTAL:	**+ 32 ATP/1 mol glucose**

Energy Efficiency

Glucose oxidation:

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + H_2O$$

$$\Delta G = -\ 686\ \text{kcal/mol}$$

ATP synthesis:

$$32\ ADP + 32\ P_i \rightarrow 32\ ATP + 32\ H_2O$$

$$\Delta G = +\ 234\ \text{kcal/mol}$$

Efficiency:

(234 kcal/686 kcal) x 100 = **34.1 % efficient**