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A NOVEL MATHEMATICAL EQUATION FOR CALCULATING THE NUMBER OF ATP MOLECULES GENERATED FROM SUGARS IN CELLS

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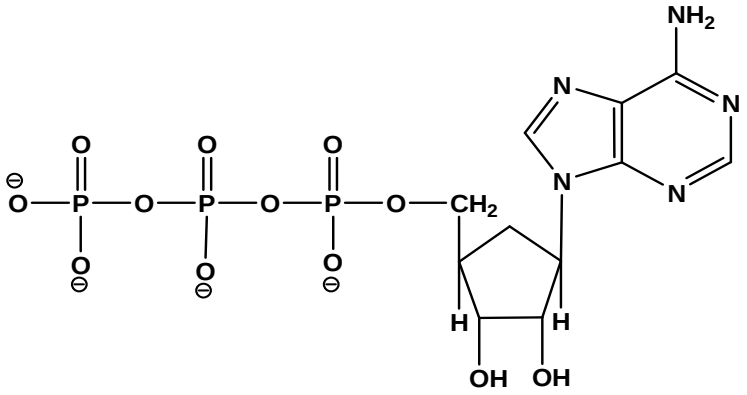
ABSTRACT

Adenosine triphosphate (ATP) is critical for all life from the simplest to the most complex. All organisms from the microscopic to humans utilize ATP as the source for their primary energy currency. This manuscript describes a novel method to calculate the number of ATP molecules generated from the consumption of any sugar (having 3-7 carbons). This calculation method based on the oxidation states of the sugar's carbons. The time needed to calculate the number of ATP molecules by this method is less than 2 minutes whereas that required by the current (regular) method is many hours and even days in some cases. In addition, the current method requires drawing all biochemical processes that the sugar undergoes upon its cellular respiration (oxidation) while our method described herein does not.

KEYWORDS: ATP, Adenosine triphosphate, Energy currency, Sugars, Oxidation state, Hexoses, Pentoses.

All living organisms obtain their energy from the surrounding environment. Photosynthetic organism utilizes the energy of sunlight, whereas heterotrophic organism utilizes the energy stored in organic nutrient molecules which is transferred by cells into the major energy currency molecule of the cell adenosine triphosphate (ATP, Figure 1).



ATP

Figure 1. Chemical structure of adenosine triphosphate (ATP).

ATP is a nucleoside triphosphate utilized by cells as a coenzyme.[1] ATP was discovered in 1929 by Karl Lohmann, and independently by Cyrus Fiske and Yellapragada Subbarow of Harvard Medical School, and was proposed to be the main energy transfer molecule in the cell by Fritz Albert Lipmann in 1941.[2] It was first artificially synthesized by Alexander Todd in 1948. This complex molecule is critical for all life from the simplest to the most complex. As well known, all organisms from bacteria to humans use ATP as their primary energy currency. The energy level that ATP carries is the precise amount needed for most biological reactions. Nutrients contain energy in low-energy covalent bonds which are translated to high energy bonds by ATP. It is the "most widely distributed high-energy compound within the human body".[3] This ubiquitous molecule is utilized to construct complex molecules, contract muscles and generate electricity in nerves. All sources of fuel in Nature and all foodstuffs of living things, produce ATP which powers every activity of the cell.

ATP functions in a cyclic manner as a carrier of chemical energy from the catabolic reactions of metabolism to the various cellular processes that require energy, such as the biosynthesis of cell macromolecules (chemical work), the active transport of inorganic ions and organic molecules across membranes against gradients of concentration (osmotic work) and the contraction of muscles (mechanical work) (see Figure 2).[4-10]

As the energy stored in ATP is delivered to these energy-requiring processes such as the low-energy phosphorylated compounds, ATP undergoes cleavage to ADP and inorganic phosphate. ADP is then rephosphorylated to ATP by high-energy phosphorylated compounds found in the cells.

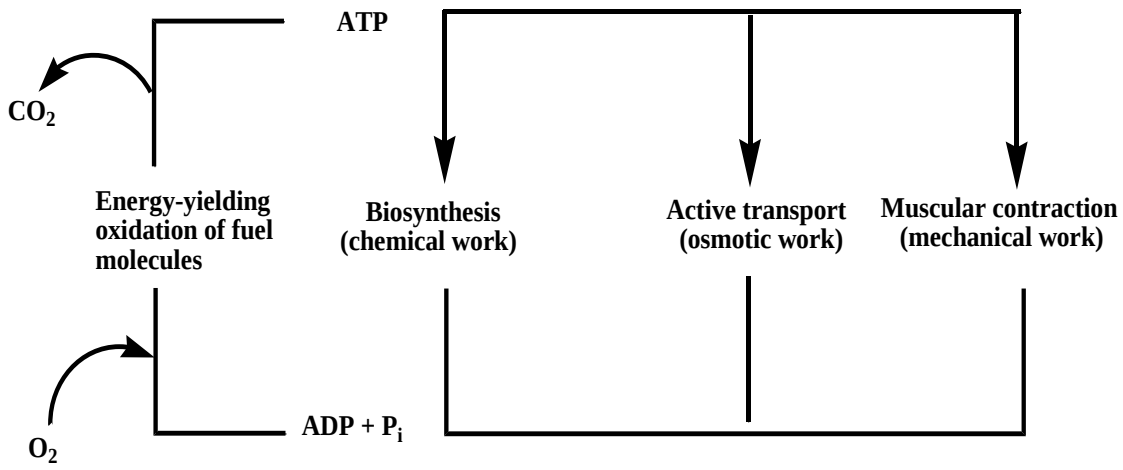


Figure 2. A schematic representation of how ATP is utilized as an energy-carrier for executing a work.

The three major mechanisms of ATP biosynthesis are: (1) substrate level phosphorylation, (2) oxidative phosphorylation in cellular respiration, and (3) photophosphorylation in photosynthesis.

ATP production requires a wide variety of enzymes, such as ATP synthase, from adenosine diphosphate (ADP) or adenosine monophosphate (AMP) and various phosphate group donors.

The source of the compounds which are utilized in the ATP biosynthesis is mainly food; complex sugars such as carbohydrates are hydrolyzed into simple sugars such as fructose and glucose, and fats which are composed of triglycerides are metabolized to provide glycerol and fatty acids. ATP production by a non-photosynthetic aerobic eukaryote takes place in the cell's mitochondria by three main pathways: (i) glycolysis, (ii) citric acid cycle/oxidative phosphorylation and beta oxidation.[4-10]

The number of ATP molecules generated in cells from sugars and fatty acids is determined on the structural features of the sugar or the fatty acid; 1 mole of glucose generates 36-38 moles of ATP , whereas 3 moles of ribose generates 95 moles of ATP via malate-aspartate shuttle or 90 moles via glycerol-phosphate shuttle. The current tool or method used to calculate the number of ATP generated from different sugars is time-consuming. It is estimated that many hours is needed to calculate the number of ATP molecules generated from any sugar since many cycles, pathways and reactions are involved.[11]

In this manuscript, we report a novel mathematical equation for calculating the number of ATP molecules generated from any sugar.

In the following paragraphs we illustrate all steps (pathways) taken into consideration when using the current accepted method to calculate the number of ATP molecules generated from glucose.

Cellular respiration or oxidation of hexoses such as glucose or fructose to CO_2 and H_2O, involves four phases: glycolysis, the prep reaction, the Krebs (citric acid) cycle, and the passage of electrons along the electron transport chain (Figure 3).[1]

The theoretical number of ATP equivalents generated through oxidation of one equivalent of glucose in glycolysis, Krebs cycle, and oxidative phosphorylation is 38. In eukaryotes, two equivalents of NADH are generated in glycolysis, which takes place in the cytoplasm. Transport of these two equivalents into the mitochondria consumes two equivalents of ATP, thus reducing the net production of ATP to 36 (Figure 3).[12]

It is worth noting that inefficiencies in oxidative phosphorylation as a result of proton leakage across the mitochondrial membrane and slippage of the ATP synthase/proton pump are believed to cause reduction in the ATP yield from NADH and $FADH_2$ to less than the theoretical maximum yield of 36.[12]

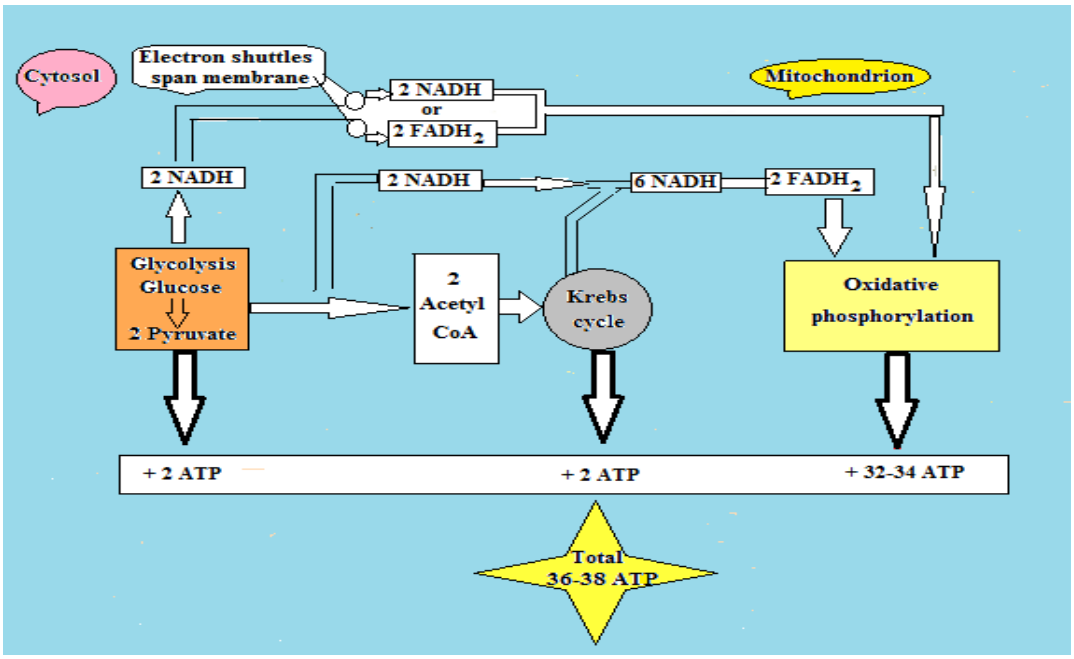


Figure 3. Schematic representation of the pathways involved in the biosynthesis of ATP from glucose.

As shown in Figure 3, in the glycolysis step, glucose is broken down to two molecules of pyruvate via a series of enzymatic reactions that occur in the cytoplasm (anaerobic). The breakdown of glucose releases enough energy to immediately give a net gain of two ATP molecules by substrate-level ATP synthesis and the production of 2 NADH.[1]

When aerobic conditions are available, pyruvate yielded from glycolysis enters the mitochondrion, where the prep reaction takes place. During the prep reaction, pyruvate loses CO_2 as a result of oxidation. NAD^+ is reduced, and CoA receives the C2 acetyl group that remains. Two NADH are resulting since the reaction must take place twice per glucose molecule.[1]

The acetyl group enters the Krebs cycle where a cyclical series of reactions located in the mitochondrial matrix take place; complete oxidation follows, as 2 CO_2 molecules, 3 NADH molecules, one $FADH_2$ molecule and one ATP molecule are formed. The entire Krebs cycle must turn twice per glucose molecule.[1]

In the cristae of the mitochondria where the electron transport chain are located, the final stage of glucose breakdown occurs. The electrons received from NADH and $FADH_2$ are passed through a chain of carriers until they are finally received by oxygen, which combines with H^+ to yield water. Electrons passage down the chain results in energy capture and storage for ATP production.[1]

In addition to passing electrons from the cristae of mitochondria complexes of the electron transport chain these complexes also pump H^+ into the inter-membrane space, setting up an electrochemical gradient. When H^+ flows down this gradient through an ATP synthase complex, ATP molecules are formed from ADP and P_i. This is called ATP synthesis by chemiosmosis.[1]

Table 1 summarizes the glucose breakdown stages as illustrated in Figure 3; out of the 36 or 38 ATP formed by complete glucose breakdown, 4 are the result of substrate-level ATP synthesis and the 32 or 34 are produced as a result of the electron transport chain. Out of NADH produced, four are the result of substrate-level ATP synthesis and the rest are produced as a result of the electron transport chain. For most NADH molecules that donate electrons to the electron transport chain, 3 ATP molecules are produced. However, in some cells, each NADH formed in the cytoplasm results in only 2 ATP molecules because a

shuttle, rather than NADH, takes electrons through the mitochondrial membrane. $FADH_2$ results in the formation of only 2 ATP because its electrons enter the electron transport chain at a lower energy level.[1]

Table 1. Summary of glucose breakdown as shown in Figure 3.

Pathway	Substrate-Level Phosphorylation	Oxidative Phosphorylation	Total ATP
Glycolysis	2 ATP	2 NADH = 4 - 6 ATP	6-8
CoA		2 NADH = 6 ATP	6
Citric acid cycle	2 ATP	6 NADH = 18 ATP 2 $FADH_2$ = 4 ATP	24
Total	4 ATP	32 ATP	36-38

On the other hand, cellular respiration or oxidation of pentoses such as ribose involves as a first step phosphorylation of ribose to ribose -5-phosphate catalyzed by ribokinase as shown in Figure 4.

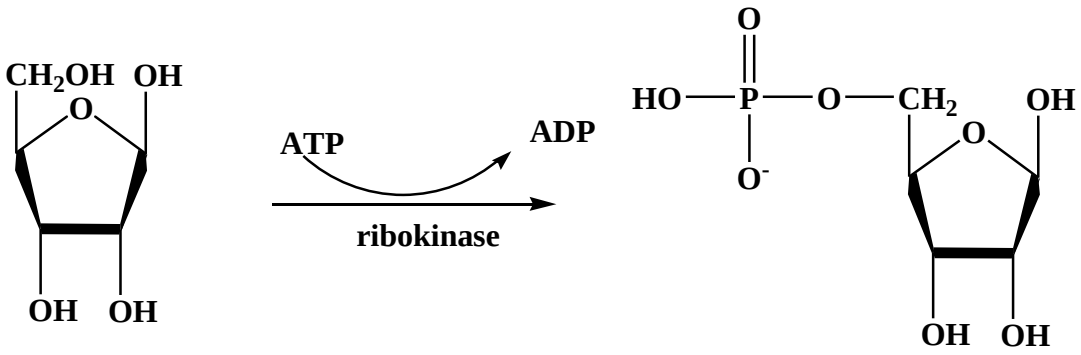


Figure 4. Phosphorylation of ribose to ribose-5-phosphate.

Once produced, ribose-5-phosphate is available for use in the pentose phosphate pathway. Ribose 5-phosphate undergoes conversion into glyceraldehyde 3-phosphate and fructose 6-phosphate by enzymatic reactions catalyzed by transketolase and transaldolase. These enzymes generate a reversible link between the pentose phosphate pathway and glycolysis by catalyzing the following three successive reactions (Equations 1-3) [11-13].

$$C_5 + C_5 \xrightleftharpoons{\text{Transketolase}} C_3 + C_7 \qquad \text{Eq. 1}$$

$$C_3 + C_7 \xrightleftharpoons{\text{Transketolase}} C_6 + C_4 \qquad \text{Eq. 2}$$

$$C_4 + C_5 \xrightleftharpoons{\text{Transketolase}} C_6 + C_3 \qquad \text{Eq. 3}$$

As a result of the above three reactions (Eq. 1-3) 3 moles of pentose yield 2 moles of hexose and one mole of triose as shown in equation 4.[11-13]

$3\ C_5 \rightleftharpoons 2\ C_6 + C_3$ Eq. 4

Therefore, the net yield from the second step in the oxidation of 3 moles of ribose-5-phosphate is shown in equation 5.

3 Ribose-5-phosphate $\rightleftharpoons$ 2 fructose-6-phosphate + glyceraldehyde-3-phosphate Eq. 5

The products from the reaction depicted in equation 5, 2 fructose-6- phosphate and glyceraldehydes-3-phosphate are converted to pyruvate through the glycolysis pathway. Fructose-6-phosphate consumes 1 ATP molecule to produce fructose-1, 6 bisphosphonate which is converted to 2 molecules of glyceraldehyde-3-phosphate.

The net amount of energy that is produced from these entities is 10 ATP, 5 $FADH_2$ and 25 NADH.

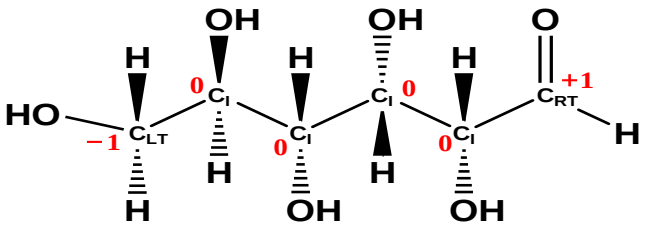
In other words we can summarize that 3 moles of ribose are metabolize to give 90 ATP moles via glycerol-phosphate shuttle whereas, 95 ATP moles are generated via malate-aspartate shuttle. Therefore, each mole of pentose such as ribose is metabolized via the glycerol phosphate shuttle to yield 30 moles of ATP.[11-13]

In contrast to the lengthy and time-consuming method described above for calculating the number of ATP molecules generated from glucose or ribose breakdown which dictates the necessity to illustrate in details all steps involved in the breakdown, the following novel method depicted in equation 6 enables to calculate the number of ATP molecules generated from any sugar within 1-2 minutes without the need to illustrate a sugar breakdown stages.

$(4+C_{LT}) + (4+C_I) \times (n-2) + (4+C_{RT}) + +2 \times n = N$ Eq. 6

Where C_{LT}, C_I and C_{RT} are the left terminal carbon, the internal carbons and the right terminal carbon, respectively (Figure 5). n is the number of carbons and N is the number of ATP molecules generated.

The calculated ATP molecules by equation 6 from any sugar are based on the oxidation states of the sugar's carbons. For simplification, we illustrate the details for calculating the number of ATP molecules generated from glucose (Figure 5).



D-Glucose

Figure 5. Chemical structure of D-glucose. The numbers in red are the oxidation states for glucose carbons.

The oxidation states for C_{LT}, C_I and C_{RT} in glucose are -1, 0 and +1 and n =6 (Figure 5). Replacing n, C_{LT}, C_I and C_{RT} with their corresponding values in equation 6 gives (4-1) + (4) x (6-2) + (4+1) + +2 x 6 = 36 (ATP molecules).

Using equation 6, we have calculated the number of ATP molecules generated from different sugars containing 3-7 carbons and the results are listed in Table 2.

Table 2. Experimental and calculated[a] ATP molecules generated from different sugars.

Sugar Name	Chemical Structure	ATP Experimental Value	ATP Calculated Value	Calculations Details By Equation 1
GLUCOSE	$C_6H_{12}O_6$	36[14]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36
FFRUCTOSE	$C_6H_{12}O_6$	36[12]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36
MANNOSE	$C_6H_{12}O_6$	36[12]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36
GALACTOSE	$C_6H_{12}O_6$	36[12]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36
TAGATOSE	$C_6H_{12}O_6$	36[15]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36
L-RHAMNOSE	$C_6H_{12}O_5$	38[15]	38	(4- 0) x 4 + (4+3) x 1+ (4-1) x1 +2x 6 = 38
L-FUCOSE	$C_6H_{12}O_5$	38[15]	38	(4- 0) x 4 + (4+3) x 1+ (4-1) x1 +2x 6 = 38
RIBOSE	$C_5H_{10}O_5$	30[11]	30	(4- 0) x 3 + (4+1) x 1+ (4-1) x1 +2x 5 = 30
GLYCERALDEHYDE	$C_3H_6O_3$	18 [14]	18	(4- 0) x 1 + (4+1) x 1+ (4-1) x1 +2x 3 = 18
DIHYDROXYACETON	$C_3H_6O_3$	18[14]	18	(4- 0) x 1 + (4+1) x 1+ (4-1) x1 +2x 3 = 18
XYLULOSE	$C_5H_{10}O_5$	30[11]	30	(4- 0) x 2 + (4-1) x 2+ (4+2) x1 +2x 5 = 30

ERETHROSE	$C_4H_8O_4$	24[12,16]	24	(4- 0) x 2 + (4+1) x 1+ (4-1) x1 +2x 4 = 24
SEDOHEPTULOSE	$C_7H_{14}O_7$	42[12,16]	42	(4- 0) x 4 + (4+1) x 2+ (4-2) x1 +2x 7 = 42
SORBOSE	$C_6H_{12}O_6$	36[12,16]	36	(4- 0) x 4 + (4+1) x 1+ (4-1) x1 +2x 6 = 36

[a]The calculated values were obtained using equation 6.

The results in Table 2 demonstrate overlapping between the calculated and experimental values of ATP generated from a sugar. Hence, the use of equation 6 for calculating the cellular respiration or oxidation of any sugar is fruitful, easy and fast.

SUMMARY AND CONCLUSION

Energy is generally released from the ATP molecule to do chemical, osmotic or mechanical work in the cell by a process that eliminates one of its phosphate-oxygen groups to yield adenosine diphosphate (ADP). Then the resulting ADP is immediately recycled in the mitochondria where it is recharged and produces ATP by four basic methods: in bacterial cell walls, in the cytoplasm by photosynthesis, in chloroplasts, and in mitochondria.

The current method used today to calculate the number of ATP molecules produced from an intake of a sugar is time consuming due to the necessity to draw all the pathways and steps involved in the degradation (breakdown) of the sugar. In contrast, the novel ATP calculations method described in this manuscript as depicted in equation 6 is very short and easy to be utilized by students and researchers alike.

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