BIOCHEMISTRY AND MOLECULAR BIOLOGY EDUCATION
Vol. 36, No. 5, pp. 323–324, 2008

Articles

Phosphoenolpyruvate

AN END TO HAND-WAVING

Received for publication, February 28, 2008, and in revised form, March 19, 2008

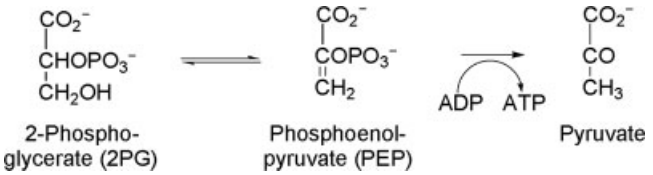
E. J. Behrman‡ and V. Gopalan

From the Department of Biochemistry, The Ohio State University, Columbus, Ohio 43210

The conversion of phosphoenolpyruvate (PEP) in glycolysis is coupled with the formation of ATP. This note discusses the origin of the energy required for ATP formation as arising from redistribution of energy in PEP when compared with its precursor, 2-phosphoglycerate.

Keywords: Phosphoenolpyruvate, 2-phosphoglycerate, free energy changes.

The transformation in glycolysis of phosphoenolpyruvate (PEP)[1] to pyruvate is coupled with the synthesis of ATP. Where does the energy for this process come from? 2-Phosphoglycerate (2-PG) is the precursor from which PEP is made by a dehydration that is catalyzed by enolase.



The standard textbooks cite the free energy of hydrolysis of PEP as about −62 kJ/mol whereas that for 2-PG is only about −16 kJ/mol. The student is left puzzled as to the origin of the "missing" 46 kJ/mol, and more specifically how a simple dehydration creates a product with dramatically different energy content than the substrate. In fact, it does not. The nearly identical-free energies of formation for 2-PG and PEP are consistent with an equilibrium constant that is near unity for their interconversion (Tables I and II). These data support the fact that the dehydration catalyzed by enolase does not convert 2-PG into the high-energy PEP. Rather, the dehydration transforms the phosphoryl group transfer potential from low (in 2-PG) to high (in PEP) due to the large value of the equilibrium constant for the formation of the ketopyruvate as opposed to the enol form (Table II, see footnote *c*). Although this distinction might appear semantic, it is essential for the student to appreciate how a mere dehydration sets the stage for the second substrate-level phosphorylation in glycolysis.

TABLE I
Equilibrium constants under standard and physiological conditions[a]

Reaction	K'^{o}_{eq}	K_{eq}
2-PG ⇆ PEP	3.6	2.3
ADP + PEP ⇆ ATP + pyruvate	9,300	250

[a] Calculated from data in D. Voet, J. G. Voet (1995) Biochemistry, 2nd ed., Wiley, New York, p. 472.

Although a number of current texts properly identify the ketonization of enolpyruvate as the dominant driving force for ATP synthesis, only Garrett and Grisham [1] point out explicitly the important point that the total energy content of 2-PG and PEP are about the same and that the energy has been merely redistributed. This was explained long ago by Fruton and Simmonds [2] and particularly well-phrased by Green and Goldberger [3]: "In the transition from 3-phosphoglycerate to phosphoenolpyruvate the total energy content of the molecule is not changed appreciably, but the energy cake is cut differently in the two molecules; the phosphoryl group in the phosphoenolpyruvate is given a larger slice than it

TABLE II
Free energies of formation and of hydrolysis

Compound	ΔG_f (kJ/mol)[a]	ΔG_{hyd} (kJ/mol)
3-Phosphoglycerate	−1500	−13[b]
2-Phosphoglycerate	−1500	−13 (est.)
Phosphoenolpyruvate	−1300	−62[c]
Pyruvate	−500	–

[a] D. E. Metzler (2001) Biochemistry, 2nd ed., Harcourt/Academic, San Diego, CA, Vol. 1, pp. 290–291.
[b] R. Barker (1971) Organic Chemistry of Biological Molecules, Prentice-Hall, Englewood Cliffs, NJ, p. 207.
[c] D. Voet, J. G. Voet (1995) Biochemistry, 2nd ed., Wiley, New York, pp. 428–432.
These authors estimate that the overall free energy of hydrolysis is made up of 16 kJ for the hydrolysis and 46 kJ for the tautomerism.

[1] The abbreviations used are: PEP, phosphoenolpyruvate; 2-PG, 2-phosphoglycerate.

‡ To whom correspondence should be addressed. Tel.: 614-292-9485; Fax: 614-292-6773. E-mail: behrman.1@osu.edu.

had in the parent molecule." By the phosphoryl group, Green and Goldberger [3] refer to the enolphosphate with the three key atoms (=C—O—P) in which the energy is localized and whose hydrolysis releases also the energy of ketonization.

We list a few rounded data in Tables I and II.

REFERENCES

[1] R. H. Garrett, C. M. Grisham (2007) Biochemistry, Thompson Brooks/Cole, Belmont, CA, p. 596.
[2] J. S. Fruton, S. Simmonds (1953) General Biochemistry, Wiley, New York, p. 433.
[3] D. E. Green, R. F. Goldberger (1967) Molecular Insights into the Living Process, Academic Press, New York, pp. 148–149.