

Action Center 12

1. An in vitro system to synthesize palmitate with purified fatty acid synthase was developed. The acetyl-CoA was supplied as $C^3H_3CO_2SCoA$; the other components, including malonyl-CoA were unlabeled. Given this experimental set-up, how many tritium atoms will be found in palmitate that is synthesized by this method?

Tree. Acetyl-CoA is initially incorporated and becomes the last two carbons of palmitate.
2. An in vitro system to synthesize palmitate with purified acetyl-CoA carboxylase, fatty acid synthase, and all necessary components and cofactors was developed. The bicarbonate ion used was labeled with ^{14}C , but the remaining components were unlabeled. Where would ^{14}C be found in palmitate?

There will be no ^{14}C in palmitate. The bicarbonate that is initially incorporated is lost as CO_2 .
3. A normal, well-fed animal is given an intravenous injection of radioactive acetate labeled with ^{14}C in the methyl carbon. Several hours later the animal is sacrificed, glycogen and triacylglycerols (TAGs) are isolated from the liver, and the distribution of radioactivity is determined. (A) Would the levels of radioactivity in the two isolated materials be roughly the same? Why or why not? (B) Draw the structure of a resulting, representative TAG and indicate where the labeled carbons would appear.

(A) The level of radioactivity will be higher in TAGs. Animals do not have net synthesis of carbohydrates from acetate. Some acetates will be converted to TCA cycle intermediates and can be incorporated in glycogen through gluconeogenesis, but there will be far more ^{14}C in TAGs.

(B) There will be a radioactive label on every other carbon of the fatty acid. I.e. Glycerol- $OCO-C^{14}H_2-CH_2-C^{14}H_2-CH_2-C^{14}H_2...$
4. How many ATPs could ultimately be produced per molecule of 14:1 (Δ^9) that was metabolized completely to CO_2 and H_2O ? Assume 2.5 ATPs per NADH and 1.5 ATPs for every $FADH_2$ after oxidative phosphorylation.

7 Acetyl-CoA - 70 ATP's (10 per acetyl-CoA (1 GTP, 3 NADH, 1 $FADH_2$))
5 $FADH_2$ (one less $FADH_2$ than NADH, because there is already a double bond present) - 7.5 ATP's
6 NADH - 15 ATP's
92.5 ATP's
2 ATP's are initially consumed to activate the fatty acid
Net: 90.5 ATP's
5. Assume that 12% of the body mass of an 200 pound person is made up of glycogen. (Note that this is very unrealistic.) What is this person's total fuel reserve (in kcal) in the form of glycogen? Assume 4 Cal/g for carbohydrates.

12% of 200lbs = 24lbs = 10,866g (2.2046 lbs = 1kg)
10,866g * 4cal/g = 43,544kcal (1 dietary calorie = 1kcal)

6. Given your answer to the previous problem, how long (in days) would the glycogen reserves be able to support a person if 2000 Cal per day were required to sustain life?

43,544 Cal / 2000 Cal/day \approx 22 days

7. Camel humps contain fat, which camels then use to produce metabolic water. How many liters of water can a camel produce from 1kg of fat? Assume that the fat is all tristearoylglycerol (3 stearic acid (18:0) + glycerol). To simplify this problem, do not worry about the metabolism of the liberated glycerol.

18:0 \rightarrow 9 acetyl-CoA + 8 NADH + 8 FADH₂ - 8 H₂O

Per acetyl-CoA: acetyl-CoA + 2H₂O + Pi + GDP + 3 NAD + FAD \rightarrow 2 CO₂ + CoA + GTP + 3NADH + FADH₂ (net: 2 H₂O per acetyl-CoA)

3 H₂O are used to hydrolyze stearic acid from glycerol

Net: 75 H₂O per tristearoylglycerol

Molecular weight of tristearoylglycerol = 890 g/mol

1000g / 890g/mol = 1.12 mol

1.12 mol * 75mol (H₂O) * 18 g/mol (H₂O) * 0.001 L/g of H₂O = 1.5L H₂O

8. Predict the effect of an overdose of insulin on brain function in a normal person. Insulin overdose will dramatically lower the glucose levels in the blood. Since glucose is absolutely essential as a source of energy for brain cells (they cannot use fatty acids for energy metabolism), low levels of glucose can lead to very serious conditions and even death.

9. Pancreatic beta cells express a receptor for fatty acids. Fatty acid binding to the protein appears to stimulate insulin secretion. Does this phenomenon make metabolic sense?

The body uses fatty acids as fuel for energy production. Because of this, it makes sense to stimulate the insulin secretion as a signal to store energy.

10. Pi activates PFK-2 in cells. Explain what would happen if a mutated form of PFK-2 had a dramatically decreased affinity to Pi?

PFK-2 could no longer efficiently convert fructose-6-phosphate to fructose-2,6-bisphosphate. Since fructose-2,6-bisphosphate is one of the key activators for glycolysis, gluconeogenesis would be favored by cells containing this mutation.

11. Describe the effects of cAMP in liver cells.

cAMP binds to protein kinase A. PKA activates several other proteins by phosphorylation, one of which is phosphorylase. Phosphorylase promotes the conversion of glycogen to G6P. G6P is then converted to glucose and excreted from the liver into the blood stream.

12. After several days of starvation, the capacity of the liver to metabolize acetyl-CoA via the citric acid cycle is greatly diminished. Explain.

After days of starvation, most TCA cycle intermediates (including oxaloacetate) are used up by other metabolic reactions to serve as sources of energy. Since these intermediates are required for TCA cycle breakdown of acetyl-CoA, the capacity of the liver to metabolize acetyl-CoA is diminished. The body will regenerate those intermediates from glycerol breakdown and catabolism of proteins.