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Glucose: A Little Goes a Long Way

by

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Abbreviations: (AGE) Advanced Glycation Endproducts, (DETAPAC) Diethylenetriamine-pentaacetic acid, (IR) Infrared Spectroscopy, (NMR) Nuclear Magnetic Spectroscopy, (MS) Mass Spectroscopy, (SOD) Superoxide Dismutase

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ABSTRACT: Glucose is a simple sugar with a varied chemistry. It is an essential molecule for most aerobic species, but too much glucose can be harmful, even deadly, to a cell. Glucose contains primarily hydroxyl groups, which are responsible for the majority of the chemistry the molecule undergoes. Glucose is not a free radical itself, but it is able to produce free radicals, such as $O_2^{\bullet -}$ and $\bullet OH$ through autoxidation reactions, under the proper reaction conditions. Glucose has also been shown, in high concentrations, to inhibit antioxidant enzyme activity.

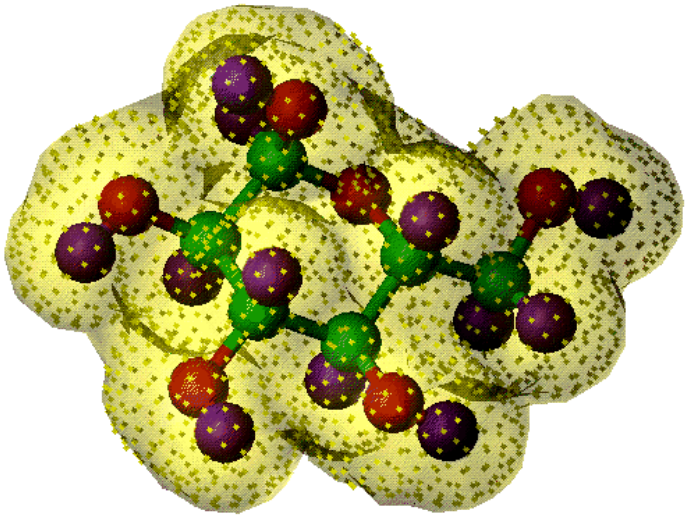


Figure 1
Carbon λ: Oxygen λ: Hydrogen λ

INTRODUCTION

Glucose is an extremely diverse molecule. Not only is it the primary energy source for most organisms, but it can also be toxic to cells if it is allowed to accumulate in high concentrations. Glucose is a small, simple sugar (Figure 1) or monosaccharide (a sugar that can not be broken down by aqueous acids into smaller molecules) and a member of the carbohydrate family. Carbohydrates, which come from animal and plant sources, are named for the chemical make-up of the molecule, a carbon hydrate. The empirical formula for a carbohydrate can be written as $C_x(H_2O)_y$. Glucose, the most common carbohydrate, is an aldehyde made up of six carbon atoms.

GLUCOSE THE MOLECULE

Glucose contains alcohol, ester (in the ring form) and aldehyde (in the linear form) functional groups, which are responsible for the majority of the chemistry that glucose undergoes. Because of the abundant alcohol groups, glucose is a polar molecule and is readily soluble in polar solvents such as water. Some of the physical characteristics of glucose, such as melting point, solubility and density, are listed in Table I.

PHYSICAL CHARACTERISTICS OF GLUCOSE	
Appearance	White, crystalline
Formula Weight	180.16 g / mol
Melting Point	150°C
Density	1.5620 g / cm^3 (at 18°C)
Solubility	
Water	Very Soluble
Ethanol	Slightly Soluble
Ethyl Ether	Insoluble
Pyrimidine	Soluble

Table 1. Physical properties of glucose [2].

Glucose can adopt three configurations. The linear form of glucose can react with itself to form either a five or six membered ring (Figure 2). At equilibrium (in aqueous solutions), the six-membered ring interconverts between its two stereoisomers, α and β (approximately 1 / 3 in the α form and 2 / 3 in the β form), with a very small amount of the linear form [9]. The five-membered ring form is not often found.

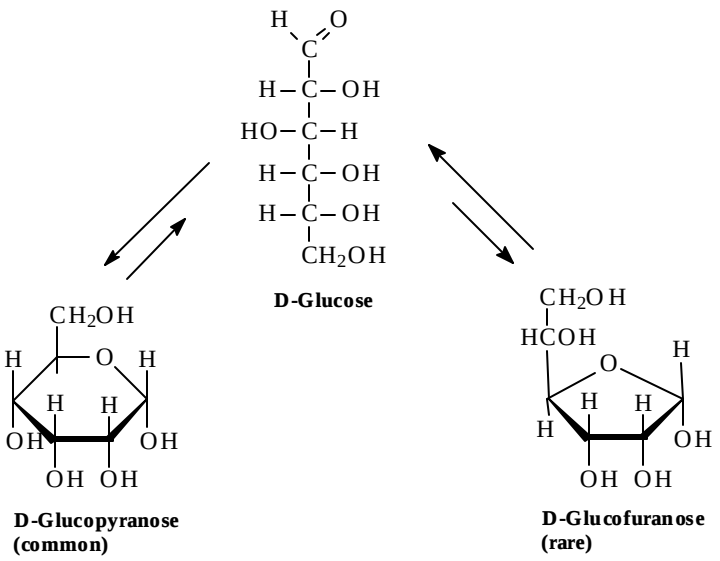


Figure 2. The three different configurations of glucose [9].

IR Spectrum

Since glucose is an organic molecule, IR spectroscopy can be used to verify identity and check purity. The IR spectrum shows peaks corresponding to the different functional groups, specifically the alcohol and aldehyde group(s). The spectrum (Figure 3) shows two broad peaks in the 3300-3400 cm^{-1} range, which is characteristic of an alcohol. Another peak is seen at approximately 1050 cm^{-1}, this peak represents the C-O bonds [10].

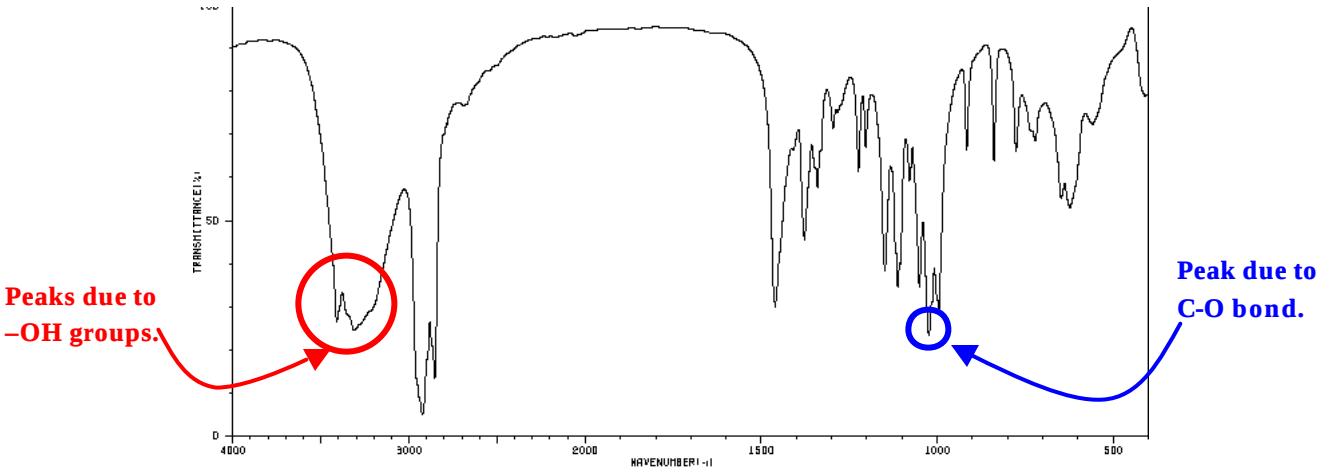


Figure 3. The IR spectrum of glucose. [13]

NMR Spectrum

^{1}H or ^{13}C labeled glucose can be used to obtain a NMR spectrum (Figure 4). NMR is a extremely useful tool for molecules of this size. It can determine purity,

verify identity and in some cases isoform. Alcohol-adjacent and ethers (-O-C-H) generally have absorptions in the range of 50-80 δ for ^{13}C NMR and 3.5-4.5 δ for ^{1}H NMR. The range for alcohols (-C-O-H) is variable and can extend from 2.5 through 5.0 δ [10]. Ethers are generally found in the same range as most alcohols, 3.5-4.5 δ. The chemical shift depends greatly on the local environment of each hydrogen, neighboring hydrogens can cause peak splitting and peak shift.

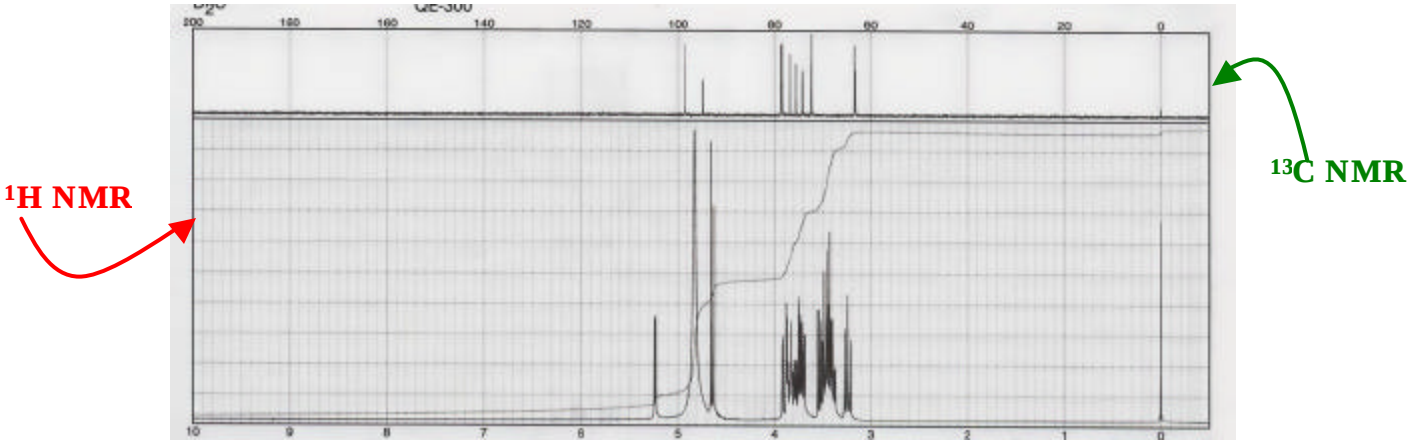


Figure 4. The 13C and ^{1}H NMR spectra of glucose. The different peaks represent hydrogen atoms that reside in different environments within the molecule[11].

Mass Spectrum

Mass spectroscopy can be used by studying the fragmentation pattern of a molecule. Alcohols can undergo two different types of fragmentation; α cleavage (when the bond is broken between the carbons nearest the oxygen of the hydroxyl) or dehydration (the loss of water and formation of an alkene radical). The charged species, which result from the reactions, are seen on the spectrum (Figure 5).

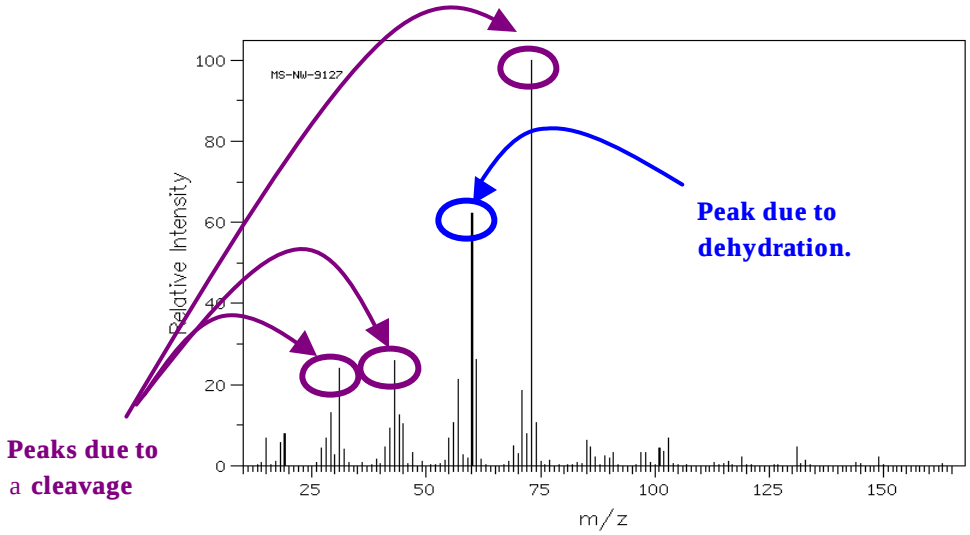
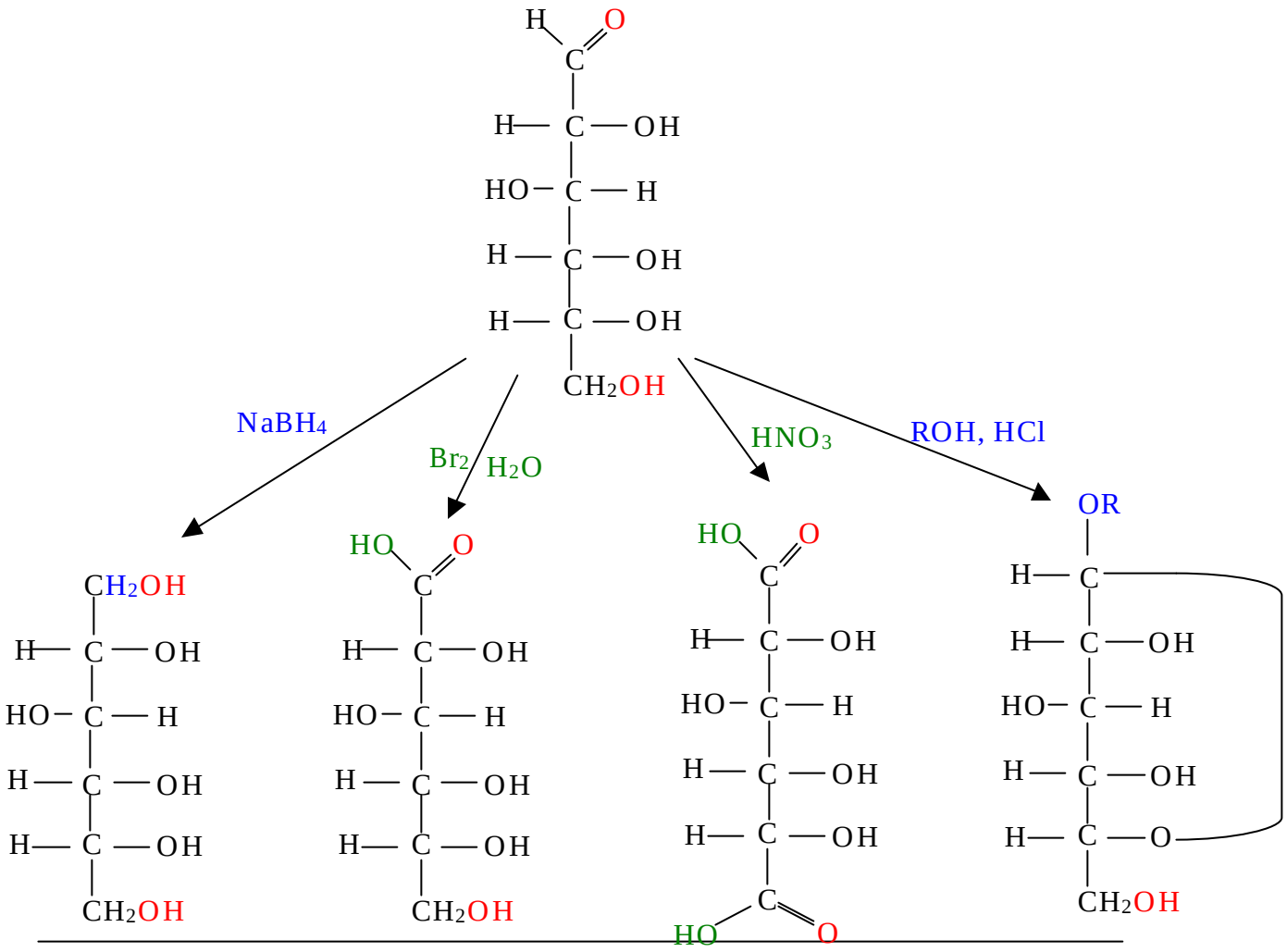


Figure 5. The mass spectrum of glucose. [13]

THE MANY FACES OF GLUCOSE

Glucose can be easily oxidized under several different conditions. If an oxidizing agent, such as bromide, is used, an aldonic acid is formed. If a stronger oxidizing agent,



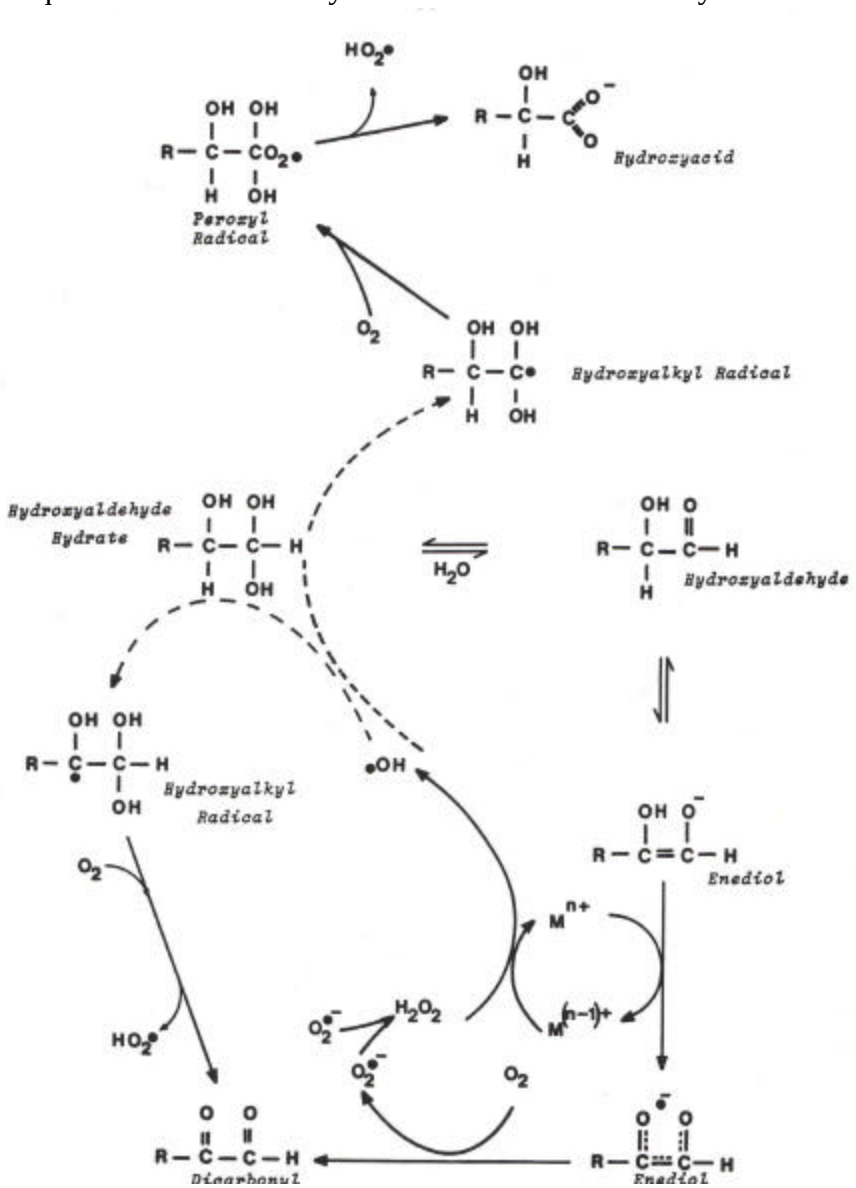
such as nitric acid, is used, an aldaric acid is formed. Glucose can also be reduced by treatment with an agent such as sodium boron hydride. The molecule will be reduced to an alditol (Figure 6).

Figure 6. Possible oxidation reactions glucose undergoes under various conditions [10].

Aerobic oxidation of glucose, the primary energy source for most aerobic organisms, entails the complete combustion of a molecule of glucose to carbon dioxide and water (Equation 1).

$$C_6H_{12}O_6 + 6\ O_2 + 36\ P_i^{2-} + 36\ ADP^{3-} + 36\ H^+ \rightarrow 6\ CO_2 + 36\ ATP^{4-} + 42\ H_2O$$ **Equation 1** [9]

There are several stages of glucose metabolism. The first stage, glycolysis, involves the production of pyruvate and small quantities of ATP. Pyruvate is then oxidized by O_2 to CO_2. This process takes place in the mitochondria and through chemiosmotic coupling generates the remaining 34 molecules of ATP produced from glucose. The complete combustion of glucose to water and carbon dioxide yields 36 molecules of ATP[9].



Autoxidation of glucose is the process by which it enolizes. This process entails the reduction of oxygen, producing oxidizing intermediates, such as $O_2^{\bullet-}$, $^{\bullet}OH$, H_2O_2,

and α-ketoaldeydes (Figure 7). These molecules can damage important biomolecules such as proteins and lipids. The oxidizing intermediates formed by autoxidation are proposed to be a cause for some of the structural damage seen in diabetes. This reaction is often catalyzed by transition metals, and even with the catalyst, the reaction is very slow. These ketoaldehyde products may attach to proteins, in a process is called labile glycation. Protein fragmentation and labile glycation due to glucose autoxidation can be reduced by the use of a chelating agent, such as DETAPAC [5].

Glucose can also undergo glycation directly, where the glucose molecule covalently bonds to a protein to form a Schiff base. These molecules can then undergo rearrangement to form an Amadori adduct. Amadori adducts can then decompose to form deoxyglucones, which are considerably more reactive than the sugar they are derived from (Figure 8). These highly reactive ketoaldeyhdes go on to react with other proteins to form **A**dvanced **G**lycation **E**ndproducts (AGE) or Maillard products [12]. The Maillard products lead to the "browning" of the protein, the protein also becomes fluorescent and crosslinked. Glycation is a reversible process. When glycation follows autoxidation, also called glycoxidation, the products tend to be more permanent modifications such as protein crosslinking. Hemoglobin glycation is commonly used clinically to monitor the blood sugar level over several weeks. The amount of hemoglobin glycation can help doctors and patients monitor glycemic control, or the lack thereof.

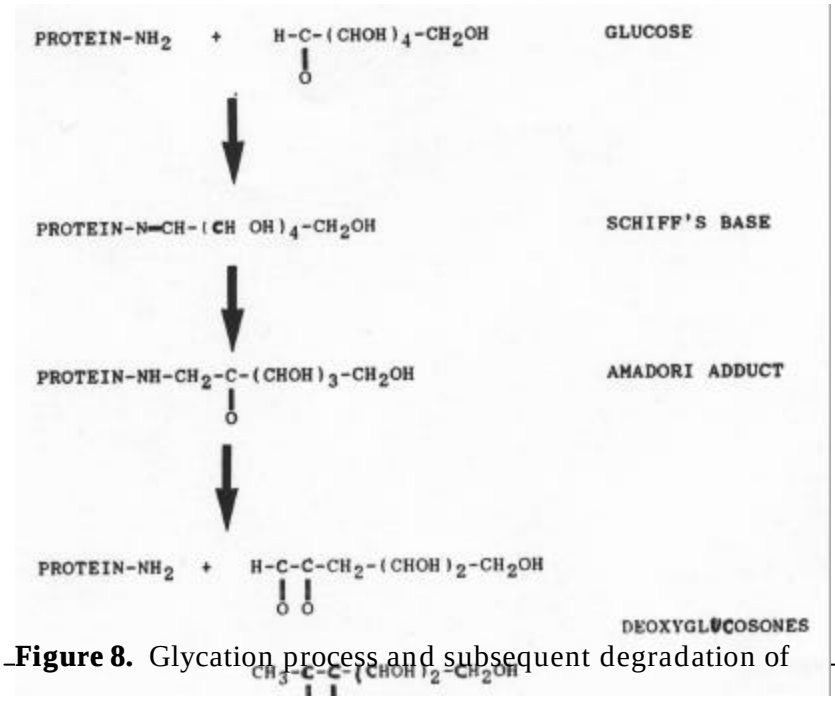


Figure 8. Glycation process and subsequent degradation of

An increase in the concentration of glucose contributes to an enhanced activity of the two enzymes used in the polyol pathway, aldose reductase and sorbitol dehydrogenase. With the increased activity of these two enzymes, the

concentration of both sorbitol and fructose increase. This increased activity also causes the NADPH:$NADP^+$ ratio to decrease and the NADH: NAD^+ ratio to increase [4]. The change in these ratios can cause changes throughout various systems in the cell. The increase in the NADH:NAD+ ratio, also called hyperglycemic pseudohypoxia, may cause an increase in free radical production which may lead to ischemia. It may also cause a reduction in glycolysis, which results in reduced pyruvate levels [8]. The reduction in the amount of NADPH may cause an inhibition in enzymes which are NADPH-dependent and may also lead to a shortage of the NADPH available for the many pathways in which it is involved.

A high level of glucose is thought to hamper the activity of antioxidants, including superoxide dismutase. A study was done in which varying levels of glucose were mixed with Cu,Zn-SOD. In this study, a decrease in the activity of the enzyme was found at higher levels of glucose [4]. Various antioxidants such as SOD and catalase have been studied in different types of tissue and in diabetic animals. Conclusive or consistent results have yet to be obtained.

CONCLUSION

Even though glucose is not a free radical, its chemistry is intertwined with that of free radicals. In many cases it can be considered a free radical precursor. Glucose is an extremely important molecule in energy production. However, in excessive concentrations, it can be toxic to the cell in many ways. It is known that too much glucose is related to the many symptoms of diabetes, such as cataracts and cardiopathy. It can also be speculated, that if allowed to get out of control, glucose might contribute to the aging process.

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