GLYCOGEN METABOLISM

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Contents

1. Introduction

Glucose can be obtained from three primary sources: diet, degradation of glycogen (glycogenolysis) and gluconeogenesis (synthesis of glucose from glycogen). Glycogen is a readily mobilized storage form of glucose [Figure 1]. Most of the glucose residues in glycogen are linked α-1,4-glycosidic bonds with an occasional, 1 in 10, α- 1,6-linkage.

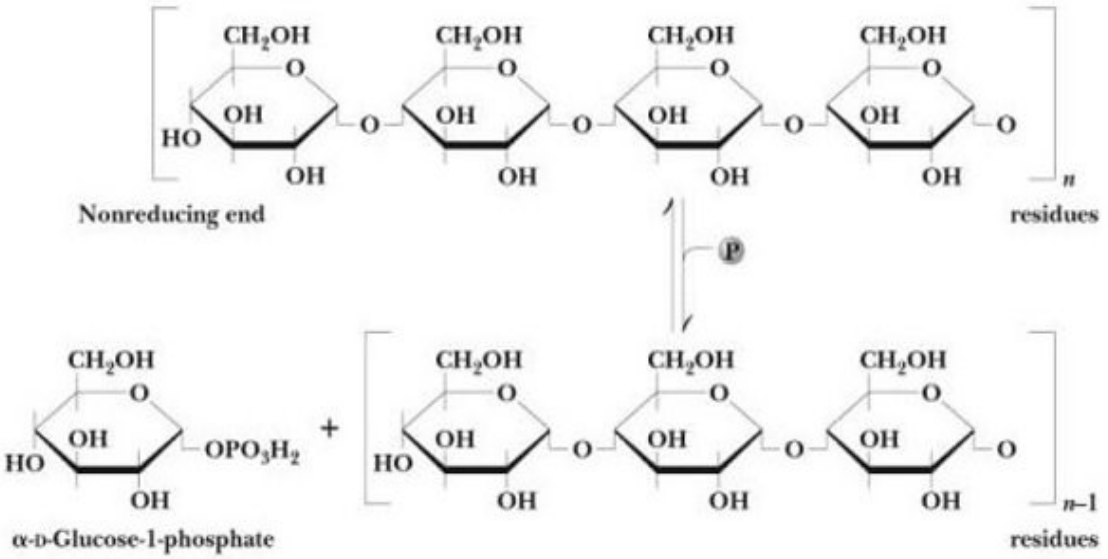

Figure 1:

2. Glycogenolysis

Glycogen is degraded by a phosphorylase enzyme sequential removal of glycosyl residues from the non-reducing end combining with orthophosphate to produce monomeric glucose-1-phosphate [Figure 1]. Though this reaction is reversible *in vitro* the phosphorolysis proceeds far in the direction of glycogen breakdown *in vivo*. The

cleavage of glycogen to glucose-1-phosphate has advantages over a simple hydrolysis to glucose since the latter would have to be subsequently phosphorylated at the expense of ATP to enter the glycolytic pathway. Furthermore the generated glucose-1-phosphate, ionized under physiological conditions, cannot diffuse out of the muscle cell whereas glucose can. Glycogen phosphorylase requires the coenzyme pyridoxal phosphate, which creates a Schiff base with a lysine residue at the active site. Since water must be excluded from the active site in order to avoid hydrolysis the 5'-phosphate group of the coenzyme serves as a general acid-base catalyst. Both the glycogen substrate and the glucose-1-phosphate have the same α-configuration suggesting a nucleophilic attack of the orthophosphate oxygen to a glucosyl carbonium ion intermediate from the same side as that of the leaving glycogen moiety. The orthophosphate donates a proton to O-4 of the departing glycogen chain simultaneously acquiring a proton from the pyridoxal phosphate.

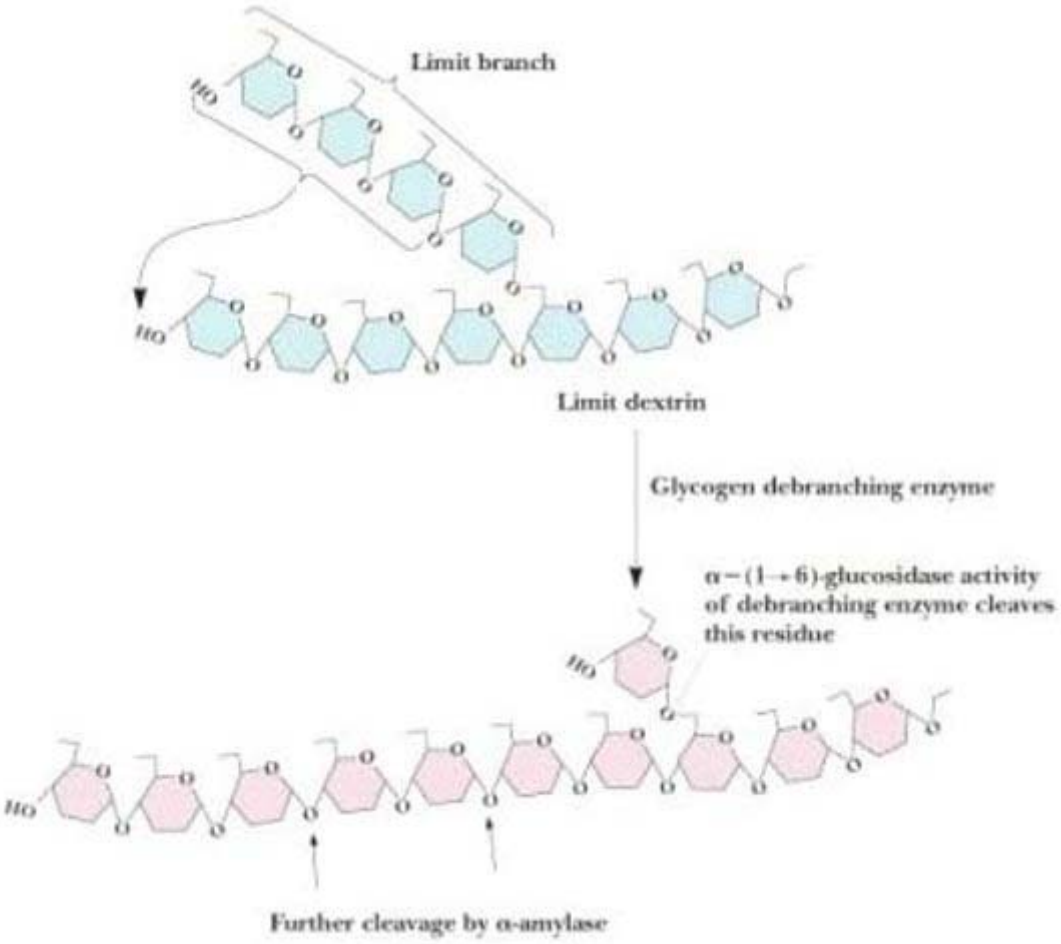

Figure 2:

The α-1,6-glycosidic bonds do not get degraded by this phosphorylase enzyme. When only four glycosyl residues remain before a 1,6 branch a transferase enzyme moves three of these residues on to an adjacent chain leaving the remaining residue to be removed via a α-1,6-glucosidase [Figure 2]. The now linear chain is susceptible to the action of the phosphorylase once again. Glucose-1-phosphate is converted into glucose-6-phosphate

by phosphoglucomutase. The enzyme, which has a phosphorylated serine at its active site, donates this phosphoryl group to the hydroxyl at position 6 thus forming glucose-1,6-biphosphate. This intermediate transfers its C-1 phosphoryl group to the serine residue at the active site resulting in glucose-6-phosphate and regeneration of the phosphoenzyme.

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