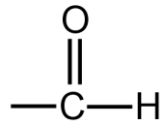
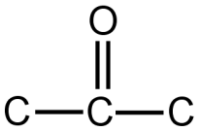
Chapter 2

Web Text Box 2

Testing for Sugar in Diabetes

Since diabetes was first described, and it was realized that it could be controlled to a greater or lesser extent by a carefully planned diet, there has been considerable interest in finding sensitive ways of detecting glucose in the urine and blood of diabetics. Early tests used for urinalysis were based upon Fehling's Test. The sample is heated with an alkaline solution of Cu^{2+} SO_4^{2-} (copper sulphate). A red precipitate of Cu_2O is generated if an aldehyde or a ketone is present.

An aldehyde is any compound that contains a  group. As we show in book figure 2.7 on page 24, glucose interconverts between two oxygen-containing ring structures via an open chain form that is an aldehyde.

A ketone is any compound that contains a  motif. Acetoacetic acid (figure on book page 22) is an example. All monosaccharides are like glucose in that they spend a fraction of their time in an open chain form, either an aldehyde or a ketone. Thus Fehling's test will detect any monosaccharide.

Although all monosaccharides spend a fraction of their time in an open chain form, a greater fraction of their time is spent in one or other oxygen containing ring form. This is why in book figure 2.8 on page 24 we show each monosaccharide in its preferred ring structure. Formation of the glycosidic bond locks the monosaccharide on one side of the bond into the ring form. In all the more complex molecules in the book that contain sugar residues (polysaccharides, nucleotides, nucleic acids…) the sugar residues are locked in a ring structure.

A variation on Fehling's Test called Benedict's test was used in the first kits to detect urine glucose - the writer remembers his diabetic grandfather boiling up urine with a test tablet twice a day. The blue color of the copper ions meant that there was a range of yellows and oranges available depending upon the amount of the sugar (and so of the red copper oxide). As diabetes

was an illness that allowed exemption from military service in many countries eating something that caused sugars to be excreted in the urine (for instance, apricots were said to produce the sugar arabinose in the urine) became a method for dodging the draft.

Better and more specific tests were developed for glucose and the non-specific copper tests became a thing of the past. Glucose oxidase is an enzyme that is highly specific for glucose and forms the basis of very sensitive tests. The enzyme oxidizes glucose using oxygen which is converted to hydrogen peroxide (while the glucose gets converted to a cyclic ester that hydrolyses to glucuronic acid). The hydrogen peroxide can be used to generate a color change and this can be seen by eye, for example on a plastic urine test strip, or by spectrophotometer. Glucose oxidase is reasonably stable and can be isolated from the bread mold *Aspergillus niger*. It is important that blood glucose is kept within the normal range in diabetics and test strips, as well as more accurate assays with the same underlying chemistry, helps the patient and their doctor to achieve this.