Research may have important implications for combating diabetes

December 11 2012, by William G. Gilroy

(Medical Xpress)—Research by University of Notre Dame biochemist Anthony S. Serianni is providing new insights that could have important implications for understanding and treating diabetes.

Serianni points out that biological compounds known as dicarbonyl sugars are produced inside the human body from the natural breakdown of the simple sugar glucose. The formation of these sugars is enhanced in diabetic patients because glucose concentrations in the blood and plasma of diabetics are significantly elevated.

"We investigated, under laboratory conditions that approximate those in the body, the degradation of a specific dicarbonyl sugar called glucosone," Serianni says. "To establish with certainty the chemical fates of the individual carbons of the glucosone molecule during degradation, we replaced some of its carbons with a rare form of carbon (denoted 13C) and applied an analytical technique known as nuclear magnetic resonance spectroscopy to observe at the molecular level how the individual 13C carbons behave as degradation occurred.

"We learned that glucosone degrades by an unanticipated reaction pathway that involves a novel rearrangement of the carbon backbone of the molecule, a process we call C1-C2 transposition."

The discovery undermines some prevailing assumptions about how sugars generally undergo degradation.

"Since sugar degradation in the body has important physiological implications—for example, by causing changes in protein structure that accompany aging and by producing highly reactive byproducts that damage cellular constituents—understanding how these molecules are transformed in the body is essential to understanding spontaneous cellular processes that are not necessarily subject to typical cellular controls," Serianni says.

The research also demonstrates a new role for phosphate as a catalyst in sugar degradation, a role that may be more common in in vitro and in vivo biochemistry than currently appreciated.

The research is a culmination of prior studies that Serianni's research group has conducted on saccharide degradation and rearrangement. In 1982, his group discovered the first stereospecific C1-C2 transposition reaction of saccharides, catalyzed by molybdate ion, that resulted in a process called C2 epimerization. This work led to new and convenient synthetic pathways for the 13C-labeling of saccharides upon which a commercial business was founded.

Serianni's lab has also promoted the use of 13C and other isotopes as tools to investigate new chemical and biochemical reactions, to probe biological metabolism and to develop new clinical and diagnostic tools and tests.

"In this sense, the glucosone work fits nicely into our overall research mission," Serianni says.

The glucosone research was described in a study that appeared in the *Journal of the American Chemical Society* and was supported by the National Institute of Diabetes and Digestive and Kidney Disease.

Provided by University of Notre Dame