



The oral glucose tolerance test is one of the most commonly used methods to study the pathology and progression of diabetes. This test is also used to evaluate new drug candidates for treatment of diabetes. In addition to glucose, a drug's effects on various hormones, such as insulin or glucagon, are evaluated in the same study.

There are several challenges when performing oral glucose tolerance tests in rodents. Traditionally, glucose is dosed via oral gavage, and glucose or hormone levels are measured via repeated blood samples. Handling animals for gavage or during blood sampling is highly stressful, which can in turn alter blood glucose or hormone levels. Manual sampling can also be time and labor intensive, which is a concern for studies in which multiple, time-critical samples must be taken. In addition, the location from which blood is sampled can be critical. Most samples are taken from the peripheral circulation, after an orally dosed substance has already undergone first pass metabolism in the liver. For some compounds, peripheral concentrations are too low to be detected after passing through the liver, so that peripheral blood sampling is not a useful way to study their effects.

In this study, we evaluated the feasibility of performing an oral glucose tolerance test in a completely automated manner, using an implanted gastric catheter for dosing, and a portal vein catheter to sample blood before it had passed through the liver. All dosing and sampling was done via Culex® Automated Systems, without handling the animals.

Materials and Methods

Sprague Dawley rats were modified with an intragastric catheter and a portal vein catheter in a single surgery. The catheters were externalized to the scapular region and locked with taurolidine citrate. The rats were then returned to a home cage to recover for one week.

One day before the study, the locking solution was removed and the animals were placed in a Culex Automated In Vivo Sampler. The portal vein catheter was connected to the blood sampling apparatus, and the gastric catheter was connected to an Empis® Automated Dosing device. Both devices flushed the catheters with sterile saline (20 μ L and 10 μ L, respectively) every 12 minutes to maintain catheter patency. Food was withheld from the animals overnight.

Glucose was prepared as a 50% solution and administered via the Empis at 2000 mg/kg. Five pre-dose and five post-dose blood samples (300 μ L) were taken from the portal vein and automatically deposited into vials in a chilled fraction collector. Samples were immediately removed and analyzed for plasma glucose concentration.

Results and Discussion

Fasting glucose concentrations were steady in all animals at 100 mg/dl, as expected in non-diabetic rats. After the dose, glucose rose rapidly, with peak concentrations occurring at 30 minutes post-dose. Peak glucose concentration was approximately 2.5 fold greater than fasting glucose concentration. By the end of the study, two hours after dosing, glucose concentrations had returned to baseline levels.

The Culex Automated Sampler is a useful tool in diabetes research. By automating the entire study from dosing to sampling, the stressful effects of animal handling can be eliminated. In addition, automated sampling allows access to non-traditional sampling locations (such as the portal vein), which allows researchers to obtain more targeted data on compounds before they undergo first pass metabolism by the liver.

Oral Glucose Tolerance In Sprague Dawley Rats

