total insulin in the body was bound to liver receptors. Other tissues as muscle transiently bind and can release insulin back into the blood.

Nutrient intake alters insulin clearance (Hennes et al., 1997). In general, glucose ingestion increases hepatic insulin uptake, the glucose-induced increase in insulin secretion may also decrease hepatic fractional extraction. Under normal physiological conditions increasing doses of glucose (10 g, 25 g, and 100 g) result in increases in insulin secretion (1.8 U, 2.7 U, and 7.2 U) with decreasing hepatic extraction (67%, 53%, 42%). Insulin clearance is reduced by oral but not by intravenous glucose administration (Meier et al., 2007).

Hepatic insulin metabolism and clearance rates are decreased in obesity and diabetes and with increases in other hormones such as Catecholamines and glutathione. In subjects with a more severe degree of Diabetes, decreased hepatic insulin removal is the primary cause of hyperinsulinemia (Bonora et al., 1983).

Despite the potential role of insulin clearance in the etiology of diabetes, little is known about the factors that are independently associated with decreased insulin removal. In the current study, by using the liver perfusion technique and isolated rat hepatocytes we will evaluate the insulin first pass metabolism in diabetic and non-diabetic rat. In addition, we will determine if the high flow rate of perfused insulin one of the factors that associated with the decreased insulin metabolism or not.

Given the importance of the liver in insulin metabolism, it is not surprising that liver disease and liver toxicity may result in a decrease in insulin metabolism, although not all studies agree. Part of this study will be evaluated the STZ toxicity of liver and if there is any decrease in insulin clearance or not. The decreased clearance is due both to reduced hepatic function and to portosystemic shunts, but not to decrease insulin-