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The hypoglycemic activity of *Lithocarpus polystachyus* Rehd. leaves in the experimental hyperglycemic rats

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ABSTRACT

Ethnopharmacological relevance: Leaves of *Lithocarpus polystachyus* Rehd. are used for the treatment of disorders such as diabetes, hypertension, and epilepsy in folk medicine of South China. The possible antidiabetic effects of the leaves were investigated in experimental type 2 and type 1 diabetic rats.
Materials and methods: Type 2 diabetic rats received orally three different extracts of *Lithocarpus polystachyus* Rehd. leaves for 4 weeks (aqueous extract [ST-1], ethanol extract [ST-2], flavonoid-rich fraction [ST-3]). At the end of the experiment biochemical parameters were tested and livers and pancreases were excised for histological study. After the comparison of the pharmacological test results of the three extracts, the one which showed the best bioactivity was further studied to confirm its antidiabetes effect on both type 2 and type 1 diabetic rats.
Results: Compared to ST-1 and ST-2, ST-3 had better effects on regulation of blood glucose, glycosylated serum protein, cholesterol, triglyceride, malondialdehyde, superoxide dismutase and attenuation of liver injury in type 2 diabetic rats ($p < 0.01$ or $p < 0.05$). ST-3 administration for four weeks also significantly reduced the fasting serum insulin and C-peptide level and improved the insulin tolerance ($p < 0.05$). In type 1 diabetic rats, ST-3 supplement for three weeks caused significant reduction in fasting blood glucose, total cholesterol, triglyceride, urea nitrogen, creatinine and liver mass, along with significantly inhibiting the decline of insulin level compared to diabetic control ($p < 0.05$ or $p < 0.01$).
Conclusion: The flavonoid-rich fraction of *Lithocarpus polystachyus* Rehd. leaves (ST-3) had better beneficial effect than that of the ethanol or aqueous extract in experimental diabetic rats, which means that the bioactivity of the herbal leaves is probably due to the presence of flavonoids. The results also strongly suggest that the antidiabetic effect of ST-3 was possibly through multiple mechanisms of action including blood lipid and antioxidant mediation. The results indicated that the aqueous flavonoid-rich fraction of *Lithocarpus polystachyus* Rehd. leaves possessed significant protective activity in type 2 and type 1 diabetes.

1. Introduction

According to the WHO definition the term diabetes mellitus (DM) covers a group of metabolic diseases characterized by elevated blood glucose levels. The two main representatives of this group are type 1 and type 2 diabetes. DM is currently one of the most costly and burdensome chronic diseases (American Diabetes Association, 2011). It is caused by inherited or acquired deficiency in insulin secretion and by decreased responsiveness of the organs to secreted insulin (Lebovitz, 2001; Janka and Michaelis, 2002). Although several drugs are available or the treatment of diabetes, adverse effects and drug resistance are of great concern. As an alternative, more and more people are seeking natural products to prevent or treat diabetes.

Abbreviations: AUC, area under the curve; BUN, urea nitrogen; C-P, C-peptide; CREA, creatinine; DM, diabetes mellitus; DMC, Diamicron; FSG, fasting serum glucose; FSN, fasting serum insulin; GSP, glycosylated serum protein; ITT, insulin tolerance test; Lep, leptin; MDA, malondialdehyde; MFM, Metformin; OGTT, oral glucose tolerance test; S.E.M., standard error of mean; SOD, superoxide dismutase; ST, Sweet Tea; STZ, streptozotocin; TC, total cholesterol; TG, triglyceride; T1DM, type 1 diabetes; T2DM, type 2 diabetes.

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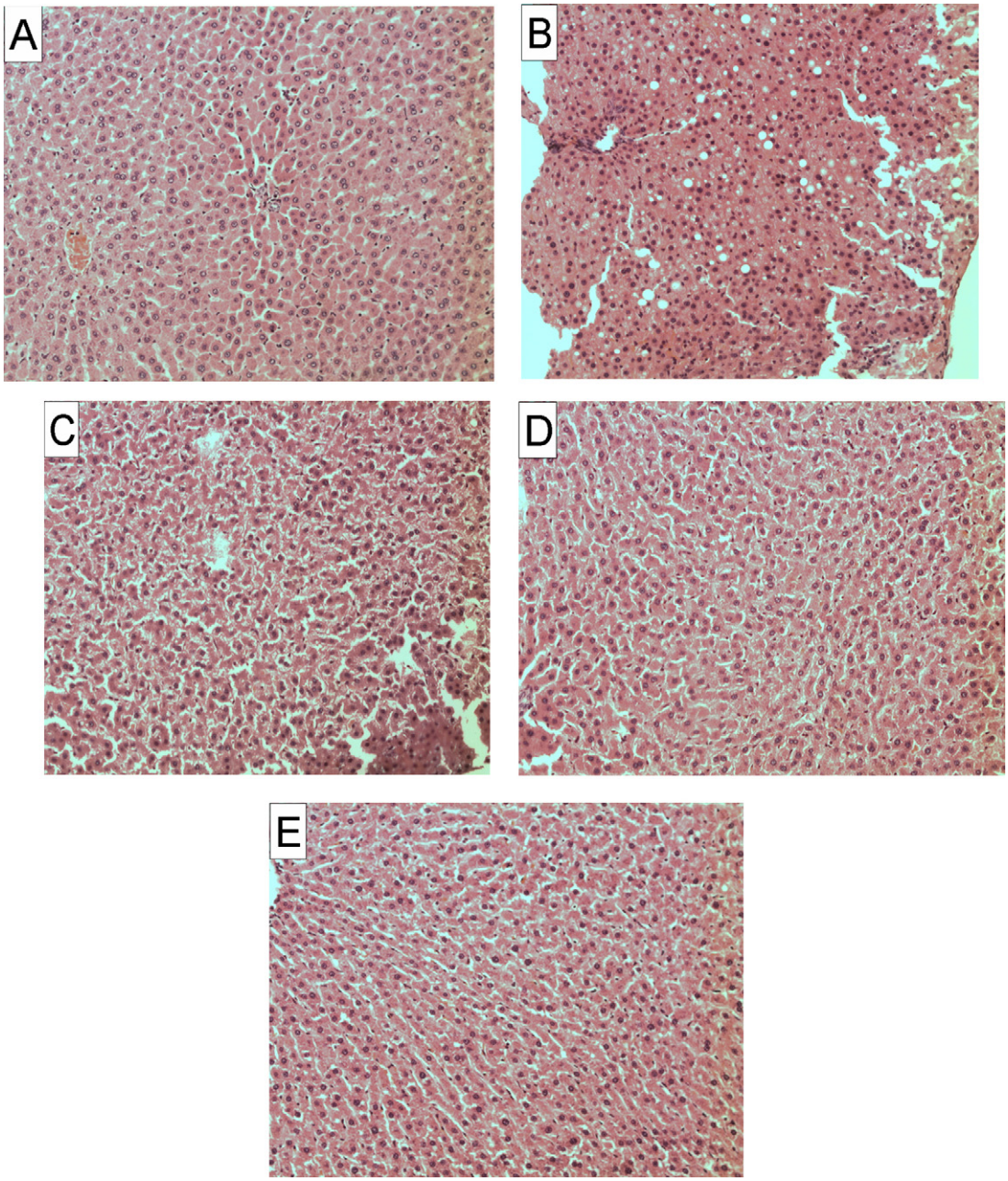

Fig. 1. Liver tissue slice from a normal control rat (A) showed the normal tissue structure. The tissue slice from high fat feeding and streptozotocin-induced diabetic rats (T2DM, B) showed abnormal retention of lipids as steatosis and edema within cells. Lipid accumulation displaced the cytoplasm and the nuclei were distorted. The tissue sections from type 2 diabetic rats that received the Sweet Tea extracts (ST-1 of 1.5 g/kg, ST-2 of 1.5 g/kg, ST-3 of 0.3 g/kg; C, D, and E, respectively) demonstrated reduced lipid deposition and cellular edema. One representative microphotograph from each of the five experimental groups was shown. Original magnification 100× and H&E staining.

Lithocarpus polystachyus Rehd. (family Fagaceae) locates mainly as a wild plant in the mountain area in southern China with a great drug resource (Institute of Botany, Chinese Academy of Sciences, 1972; Wang et al., 1999). It is popularly named "Sweet Tea" (ST) in folk and its leaves have been used as traditional herbal medicine against a variety of diseases for hundreds of years. ST is claimed to have a wide range of biological activities, such as anti-oxidative, anti-bacterial, hypoglycemic, anti-obese and anti-inflammatory (Liao and Zhou, 1994; Wang et al., 1999; Yang et al., 2007). However, very few studies have confirmed the information and measured its antidiabetic activity. Till now, there are no indications of this herbal medicine's mechanism of hypoglycemic action or whether it can improve glycemic control of type 1, type 2 or both types of diabetes. In order to further validate the beneficial effects of *Lithocarpus polystachyus* Rehd. leaves as an antidiabetic natural product, and to better understand its action, we investigated the effect of the leaves' extracts in experimental type 2 and type 1 diabetic animals.

2. Materials and methods

2.1. Kits, chemicals, and reagents

The kits of blood glucose, total cholesterol (TC), triglyceride (TG), urea nitrogen (BUN) and creatinine (CREA) were purchased from Beijing Zhongsheng Chemical Factory (Beijing, China). The