Dissertation Title	Evaluation of Anthocyanin Extract of Thai *Morus alba* L., on Blood Glucose Level in Diabetic Rats and Prediabetes Patients
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ABSTRACT

Mulberry (*Molus alba* L.) contains abundant anthocyanin (ANC), a natural antioxidant. The purpose of this study was to determine the ANC composition of Thai *Morus alba* L. fruits, and to assess its effect on blood glucose and insulin levels in ZDF rats and pre diabetes patients. In this study the major components of ANC were identified by high-performance liquid chromatography–electrospray ionization–mass spectrometry. ZDF and lean rats were administered with 125 or 250 mg ANC/kg body weight, or 1% carboxymethylcellulose (CMC) twice daily for 5 weeks. Neither ANC dose affected body weight. After 5 weeks of treatment, glucose levels increased from 105.5 ± 8.7 to 396.25 ± 21 mg/dl ($P < 0.0001$) in CMC-treated ZDF rats, but levels were significantly lower in rats treated with 125 (228.25 ± 45 mg/dl) or 250 (131.75 ± 10) mg/kg ANC ($P < 0.001$ vs. CMC). Administration of 250 mg/kg ANC normalized glucose levels in ZDF rats towards those of lean littermates. Insulin levels decreased significantly in ZDF rats treated with CMC or 125 mg/kg ANC ($P < 0.0001$), but not in rats treated with 250 mg/kg ANC. Histologically, 250 mg/kg ANC prevented islet degeneration compared with islets in

CMC-treated rats. We confirmed that ANC was well tolerated and had effective antidiabetic properties in male leptin receptor-deficient Zucker diabetic fatty (ZDF) rats.

In human study, the effectiveness of freeze dried mulberry fruit of Thai *Morus alba* L., on fasting blood sugar and HbA1C in pre diabetes patients were evaluated. Participants included 18 pre diabetes patients. They were divided into 2 groups (n=9). Subjects ingested either a capsule containing ANC or gelatin 750 mg. for 2 times a day. Fasting blood sugar (FBS), haemoglobin A1C (HbA1C), body weight, and body mass index (BMI) were assessed before and at intervals of 4 weeks for 12 weeks. After 12 weeks of treatment, FBS decreased significantly in pre diabetes patients treated with ANCs from 112.8 $\pm$ 5.5 mg/dl to 93.0 $\pm$ 10.45 mg/dl (p=0.0001), but not in the patients treated with gelatin (p= 0.1). Moreover, HbA1c also decreased in pre diabetes patients treated with freeze dried mulberry from 5.87 $\pm$ 0.13 % to 5.46 $\pm$ 0.37 (p=0.006) but not in the patients treated with gelatin (p=0.43). Here, we show for the first time that ANCs extracted from Thai *Morus alba* L. are an important antidiabetic agent. Furthermore, the ANC extract appeared to prevent the pathogenic lesions in diabetic islets by suppressing islet degeneration. We conclude that ANC may represent a promising class of therapeutic compounds that can be useful in type 2 diabetes prevention.

Keywords: Mulberry fruit/*Molus alba* L./Anthocyanin/ZDF rats/Glucose level/ Diabetic rats/Prediabetes patients/Islet/HbA1C/Fasting blood sugar