Anti-diabetic effect of ethanol extract of *Cyclolepis genistoides* D. Don (palo azul), made in Paraguay

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Extract of *Cyclolepis genistoides* D. Don (vernacular name palo azul; palo) is a traditional medicine used in Paraguay for diabetes and is sold in Japan as dietary supplement. This study aimed to elucidate the mechanism of anti-diabetes activity of palo, especially focused on insulin resistance. Palo promoted adipocytes differentiation and regulated adipokine profiles in 3T3-L1 adipocytes by modulation of PPAR γ , a major regulator of adipose differentiation. While palo didn't affect insulin signaling molecules, it promoted GLUT4 (glucose uptake transporter) translocation from cytoplasm to plasma membrane and increased 2-DG uptake under insulin stimuli. Human adipocyte showed almost similar profile with 3T3-L1 against palo treatment. In addition, as the other insulin targeted cell, effect on muscle differentiation was examined. Palo increased differentiation of C2C12 mouse muscle myoblasts and increased 5'-AMP-activated protein kinase (AMPK) activation. Finally palo treatment (250 or 1000 mg/kg) was performed with C57BL/6J mice for 14 weeks, being fed high-fat-diet (HFD60) simultaneously. Palo 250 mg/kg exhibited a tendency to decrease adipose volume but with increase of PPAR γ mRNA expression, and decreased blood glucose level ($P=0.058$). Put it all together, palo has a potential to have antidiabetic effect by modulating insulin resistance via PPAR γ pathway.