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Gymnema sylvestre Extracts Stimulate Insulin Secretion *In Vitro* and *In Vivo*: A Potential Phytopharmacological Therapy for Type 2 Diabetes

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Gymnema sylvestre Extracts Stimulate Insulin Secretion _In Vitro_ and _In Vivo_: A Potential Phytopharmacological Therapy for Type 2 Diabetes

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Plant-derived extracts have been used to treat Type 2 diabetes mellitus (T2DM) for several millennia, and the Santals in east-central India have used *Gymnema sylvestre* leaves as a folk-medicine for centuries. We have now investigated the potential anti-diabetogenic effects of an ayurvedically prepared *Gymnema sylvestre* virgin isolate extract (designated OSA for *Om Santal Adivasi*; U.S. Patents # 6,949,261, # 6,946,151). *In vitro* studies using human islets and the insulin-secreting MIN6 cell line demonstrated that OSA (0.06-2mg/ml) induced a concentration-dependent stimulation of insulin secretion (0.5mg/ml OSA: 745±71% and 807±84% 2mM and 20mM glucose-stimulated secretion respectively, n=10, $p<0.001$). OSA-induced insulin secretion was rapidly reversible on removal of OSA, and was at least partially dependent on an influx of extracellular calcium (0.2mg/ml OSA: 368±32% 2mM glucose response; 237±22% in absence of calcium, n=6, $p<0.05$). Clinical studies in non-obese patients with T2DM confirmed the insulin-releasing effect of OSA. Thus, daily ingestion of OSA (1000mg/day) for 60 days resulted in significant elevations in basal serum levels of insulin (24.3±2.8 vs 32.1±1.9mU/L, n=11, $p<0.01$) and C-peptide (298±42pM vs 448±48, $p<0.01$). The increased circulating insulin after OSA treatment was accompanied by significant reductions in fasting blood glucose (9.8±0.5mM vs 7.6±0.53, n=14, $p<0.01$), and by reductions in the post-prandial glucose excursions (16.1±1.1mM vs 13.6±1.1, $p<0.01$). OSA treatment also reduced cholesterol by 13% and triglycerides by 26%. These clinical data suggest that OSA may offer an effective therapy for insulin-deficient T2DM. Moreover, the *in vitro* studies suggest that at least one mechanism of action of OSA is in directly stimulating insulin secretion. OSA may therefore offer a safe sole therapy for T2DM or an adjunct to conventional oral hypoglycemic drugs.