Research Proposal 1: The Glycaemic Control, Anti-inflammatory and Antioxidant Potential of Momordica charantia in Addressing Obesity and Metabolic Disease (750 words)

https://www.findaphd.com/phds/project/the-anti-inflammatory-and-antioxidant-potential-of-herbal-supplements-identifying-tissue-targets-in-addressing-obesity-and-metabolic-disease-phd-funded/?p131309

Metabolic syndrome encompasses diabetes mellitus, hypertension and obesity, and is considered a global epidemic (Saklayen, 2018). Both obesity and hypertension trigger vascular inflammation and oxidative stress followed by endothelial dysfunction and atherosclerosis (Virdis, 2016). Momordica charantia (M. *charantia*), also known as Bitter Gourd is a vegetable plant traditionally used in Ayurvedic medicine (Jia *et al.,* 2017). Emerging evidence suggests that M. *charantia* has anti-inflammatory and antioxidant effects and has the potential to be developed as a therapeutic intervention for Type 2 Diabetes Mellitus (T2DM) and its related complications (Peter *et al.,* 2019). My research proposal aims to examine M. *charantia's* efficacy to improve glycaemic control, inflammation and antioxidant capability.

Compared to a placebo, M. *charantia* significantly reduced fasting plasma glucose, postprandial plasma glucose level and glycosylated haemoglobin A1c (HbA1c) in T2DM patients (Cortez-Navarrete *et al.,* 2018). Only two studies have evaluated the effect of M. *charantia* administration on insulin secretion in human participants, and different indexes to assess insulin secretion and sensitivity were used (Cortez-Navarrete *et al.,* 2018; Lim *et al*., 2010). The present research project proposal could feature a double-blinded placebo-controlled randomised trial examining the effect of M. *charantia*'s influence on key health outcomes such as changes in HbA1c, fasting blood sugar, serum cholesterol and weight. Additionally, this study could add to the literature on M. *charantia's* influence on insulin secretion and sensitivity, using a variety of indexes (Matsuda index, Insulinogenic index and Stumvoll index). Variety of follow up time and dosage exist in M. *charantia* research (Peter *et al.,* 2019). This paper could contribute to gaps in the literature by manipulating the dosage, follow up period and improving dietary reporting.

Chronic systemic inflammation has a clear association with obesity and accumulation of lipids in the hepatocytes causes redox imbalance and triggers fat oxidation (Marrocco *et al.,* 2017; Minihane *et al.,* 2015). Consequentially, inflammatory responses comprising of up-regulation of pro-inflammatory cytokines including TNF-a and C-reactive protein (CRP) are apparent in these populations (Buzzetti *et al.,* 2016; Byrne & Targher, 2015). In rodent studies, mice fed diets supplemented with M. *charantia* observed decreased pro-inflammatory cytokines IL-1, IL-6 and TNF-a and increased anti-inflammatory cytokine IL-10 production (Chao *et al.,* 2014). Furthermore, the expression of proteins NF-kB, iNOS and COX-2 were significantly inhibited (Chao *et al.,* 2014; Lee *et al.,* 2020). May et al., (2018) observed significant improvements in knee osteoarthritis, analgesic score, body weight, BMI and fasting blood glucose in T2DM patients following 3 months of supplementation with a M. *charantia* supplement. The present research proposal could feature a double-blinded placebo-controlled randomised trial examining M. *charantia*'s influence on key anti-inflammatory and pro-inflammatory markers in T2DM patients.

Techniques used could include serum blood samples and analysis via enzyme-linked immunosorbent assay (ELISA) kits.

Hyperglycaemia, a typical symptom in T2DM patients, generates reactive oxygen species (ROS), which cause cellular injury (Tiwari *et al.,* 2013). T2DM patients typically suffer from oxidative stress-induced alterations including increased lipid peroxidation (LPO), increased protein oxidation, impaired glutathione metabolism, low catalase activity and reduced superoxide dismutase activity (McLennan *et al.,* 1991; Tiwari *et al.,* 2013). LPO is a significant risk factor for developing atherosclerosis (Wohaeib and Godin, 1987). Treating hyperammonemic rats with M. *charantia* extract inhibited LPO and increased the expression of anti-oxidation enzymes (Lu *et al.,* 2014; Poovitha and Parani, 2020). Pre-treatment with M. *charantia* extract for 25 days downregulated LPO and replenished endogenous antioxidant enzymes such as superoxide dismutase, catalase and non-protein sulfhydryls and total protein in rats (Raish, 2017). As part of this research project, I propose to conduct a double-blinded placebo-controlled randomised trial study investigating the antioxidant effects of M. *charantia* on human plasma and oxidative stress in the body - making key observations on components such as superoxide dismutase, glutathione metabolism and LPO.

Standardisation of dietary intake is an important practical consideration when assessing the effectiveness of a bioactive supplement. Participants may habitually consume foods containing bioactive ingredients that may influence the outcome of the intervention, for example, curcumin. Blinding of intervention is often difficult because herbal supplements have a distinct taste. For example, M. *charantia* is very bitter, however, the use of capsules may help to mask the taste. Additionally, in T2DM patients accompanying medicines may also influence the effect of the intervention. Due to the long follow up periods required to accurately assess HbA1c (Hirst *et al.,* 2014), participant attrition is likely and must be considered when recruiting participants. Participant safety is also a concern as gastrointestinal symptoms such as abdominal discomfort and diarrhoea may be apparent following herbal supplementation (Peter *et al*., 2019).

Word count: 750

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