Pharmacological Effects of Active Compound of *Tinospora crispa* (*Batawali*) on Immunomodulation and Carbohydrate Metabolism in STZ-Induced Diabetic Rats

Review of the literature

The deficiency of insulin secretion and the weakened response of body to insulin are fundamental causes of this disease, which result in postprandial or fasting hyperglycemia (Boyko *et al.*, 2007; Tfayli *et al.*, 2009). In nowadays, the number of diabetic patients is being wildly increased while the control of diabetes with fewer side effects remains a big challenge. Therefore searching herbal product with antidiabetic activity possessing fewer side effects receives considerable publicity and provides an opportunity to cure this disease.

*Tinospora crispa* is indigenous to the Indian subcontinent and has been used in Ayurveda for several centuries. It had been used as traditional medicine in rural society to treat fever, cholera, snake bites, rheumatism and fever due to malaria (Dweck and Andawali 2006). Tinospora crispa has shown to have an antihyperglycemia effect by augmenting the release of insulin (Noor and Ashcroft 1998). Its antimalarial activity (Rahman *et al.*, 1999), antibacterial (Zakaria *et al.*, 2006), anti-inflammatory (Sulaiman *et al.*, 2008) and anti-oxidant properties (Rahman *et al.*, 1999) are also recorded. Recent study by Chantong *et al.*, 2008. This study was designed to measure the cytotoxicity and antioxidant properties in different type of T. crispa crude extracts. The current study is undertaken to establish the antidiabetic activity of *Tinospora crispa* active compound against STZ-induced diabetic rats.

Objectives
To investigate the phytochemical properties of *Tinospora crispa* active compound.

- Determination of the main active component in *Tinospora crispa* extract and its possible role as an anti-diabetic activity in *vivo* and *in vitro*.
- The stimulatory activity of *Tinospora crispa* on immune response through *in vivo* and *in vitro* studies.
- To study mechanisms of action of selective fraction via carbohydrate metabolic key enzymes, gene expression and cell cycle analyses and effects on the apoptotic machinery.
- Cytotoxicity effects of *Tinospora crispa* active compound in cultured lymphocytes cell lines

**Experimental design**

Thirty rats were divided into five equal groups as follows:

(i) **Control group**: Rats of this group received of normal saline (vehicle/kg body weight per rat per day for 30 days by gavage).

(ii) **Diabetic group**: Rats will be made diabetic by an single intramuscular injection of streptozotocin (50mg/kg bw per rat).

(iii) **Tinospora crispa supplement group**: The rats will be forcefully fed with active compound of *Tinospora crispa* at the dose of (standardization) mg/kg bw per rat per day for 30 days by gavage.

(iv) **Diabetic plus Tinospora crispa supplement group**: The diabetic rats will be forcefully fed with active compound of *Tinospora crispa* at the dose of (standardization) mg/kg body weight per rat per day for 30 days by gavage.

(v) **Diabetic plus glibenclamide supplement group**: The diabetic rats will be forcefully fed with glibenclamide at the dose of 20 mg/kg body weight per rat per day for 30 dys by gavage.

**EXPERIMENTAL DESIGN**
Petroleum ether extraction
Methanol extraction
Ethyl acetate extraction

Selected extraction & fraction

In vitro studies

Lymphocytes cell, Rat insulinoma cell

Non Oxidative stress-induced cells
Oxidative stress-induced cells

STZ, H$_2$O$_2$

Cell viability, Cytotoxicity effect and Cytoprotection effect.
1) MTS assay
2) LDH assay

Cell Death Study

Apoptosis (Flow cytometry)

K562, Jurkat T cell
Rat insulinoma cell

1. Caspase 3, 2. Caspase 8,
3. Caspase 9

1. Annexin V
2. Propidium Iodide
Expected outcome:

- Possesses immunostimulatory effect in in vivo and in vitro studies.
• Improved the production of cytokines.
• Reduced serum glucose levels and increased the body weight of STZ-induced diabetic.
• No toxicity in lymphocytes
• *Tinospora crispa* extracts as possible anti-diabetic in therapeutic usage.
• Isolate and purify the active components that possess the anti-diabetic activities to formulate a new drug.

**Time schedule of activities giving milestones**

- **Year:** Collection of literature will be taken up. Procurement of plant material, isolation of active compound, and biological activity of plant, procurement of the chemicals, and planning of experiments with regard to the preliminary studies will be taken up.
- **Year:** In this year, the first phase will be to develop STZ-induced diabetes and this will be followed by detailed study of various biochemical parameters will be taken up. Submission for publication

**References:**


