Gongronema latifolium lowers blood glucose via pancreatic islet cell regeneration and insulin sensitization

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Introduction

Diabetes

Diabetes Mellitus (DM) refers to a medical condition marked by hyperglycemia due to loss of control over blood glucose homeostasis.

As projected in 2013 by the World Health Organization (WHO), DM is expected to become the 7th leading cause of death in 2030.

According to the Malaysian Ministry of Health, there were more than 3 million Malaysians with DM in 2011.

Gongronema latifolium

Traditionally, the leaves of the African shrub *Gongronema latifolium* (Apocynaceae) were cooked as a vegetable soup and eaten as such for diabetes [1].

Although recent reports [2-3-4] have confirmed that *G. latifolium* possessed antihyperglycemic activity, its use in the treatment of DM, as well as its mechanisms of action, remain vaguely understood.

While Ugochukwu & Babady [5] attributed an insulin-like activity to *G. latifolium* ethanolic extract, Adebajo et al. [6] reported that the extract rather acted by increasing insulin release.

These conflicting and shallow reports justify our quest for detail understanding of the anti-diabetic action and possible mechanism of action of *G. latifolium* extracts.

Objectives and Aims

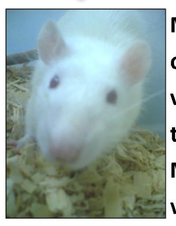
- To establish that *Gongronema latifolium* extract (GL) effectively decreases blood glucose levels upon sub-chronic use in diabetic rats.
- To investigate the effect of GL on the pancreatic tissue and insulin-secreting Langerhans islets.
- To assess the insulin-sensitizing potential of GL through *in-vitro* tests on isolated rat abdominal muscle.

Materials and Methods

Collection
- *Gongronema latifolium* was collected from Yakhur, Cross River State, Nigeria, under the supervision of the Department of Biochemistry at the University of Calabar.

Transport
- GL shade-dried leaf powder was properly packaged to arrive at the Department of Pharmacology, Universiti Sains Malaysia via courier within 7 days.

Extraction
- The powder was extracted in Soxhlet apparatus (at 60°C and at ratio of 1:5 to 1:10 of raw material/solvent) for three days. The extract was filtered and evaporated to dryness at 40°C using a rotary evaporator.



Male *Sprague-Dawley* (SD) rats, weighing initially between 180g-220g, were obtained from the Animal Research and Service Centre, Main Campus, Universiti Sains Malaysia (USM), Penang. Diabetes was induced by a single intraperitoneal (IP) injection of streptozotocin (STZ) (Sigma-Aldrich, St. Louis, MO, USA) at a dose of (55 mg/kg) to rats fasted for 12 hours. Rats with FBG within 15.0-20.0mMol/L were included in the study.

Table 1: *Animal Grouping: Sub-chronic treatment in diabetic rats (n = 6)*

Group	Treatment
TG1	250mg/kg BW of *G. latifolium* extract
TG2	500mg/kg BW of *G. latifolium* extract
TG3	1000mg/kg BW of *G. latifolium* extract
Diabetic Control (DC)	10ml/kg BW of distilled water
Positive Control (PC)	500 mg/kg BW of metformin
Non-diabetic Control (NC)	10ml/kg BW of distilled water

At the end of the sub-chronic treatment, the rats were sacrificed and dissected. The fixed pancreatic tissues were sectioned (5-micron thickness) and the sections were specifically stained for β-cells by the Aldehyde Fuschin procedure, and examined using a Leica MZ6 optical microscope (Leica Microskopie und Systeme, Germany) equipped with a Leica Qwin (Leica Imaging Systems, Cambridge, England).

Glucose uptake by isolated abdominal muscle was measured according to [7] with modifications [8].

Statistical significance was investigated using version 21 of the IBM-SPSS statistical program (IBM Corp., Armonk, NY). One-way ANOVA was used followed by Dunnett's Test as a Post Hoc Test.

Results and Discussion

This paper investigated the antihyperglycemic activity of *Gongronema latifolium* upon subchronic treatment. The results confirmed the antihyperglycemic activity observed earlier in [5]. As indicated by our findings, and in agreement with [2], unlike metformin, *Gongronema latifolium* was found to act directly on the pancreas to induce the regeneration of a tissue that appeared well structured, and Langerhans islets that appeared well defined and larger in area compared to the diabetic control

In 2012, GL extract was reported to decrease glucose levels by increasing insulin release from the pancreas and acting directly on the β-cells [6]. Hence, the insulin sensitizing effect of GL extract observed in this study might be one of the mechanisms by which *Gongronema latifolium* exerts its antihyperglycemic effect.

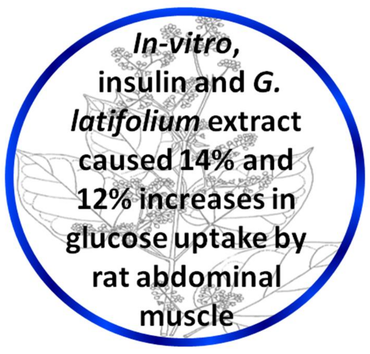


Figure 1: Sub-chronic (14 days) treatment with *Gongronema latifolium* extract in STZ-induced diabetic rats (n = 6). Values are expressed as the mean ± SEM, * = P < 0.05; ** = P < 0.01; *** = P < 0.001 vs DC.

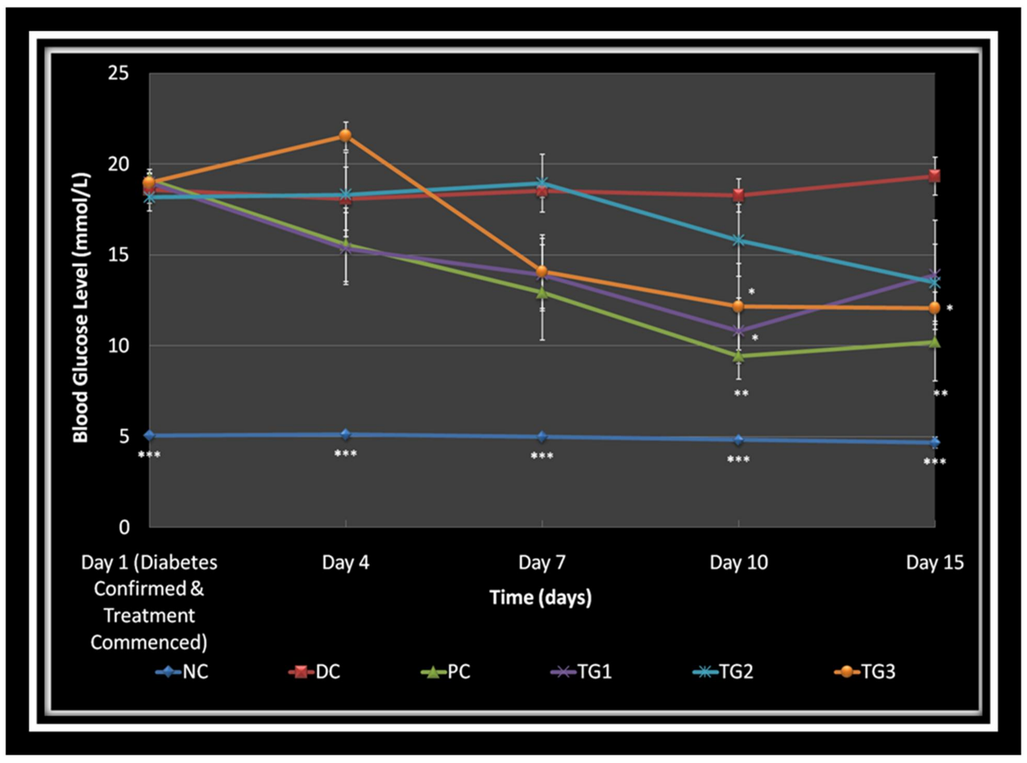


Figure 2: Langerhans islets under 40x magnification following the 14-day treatment.

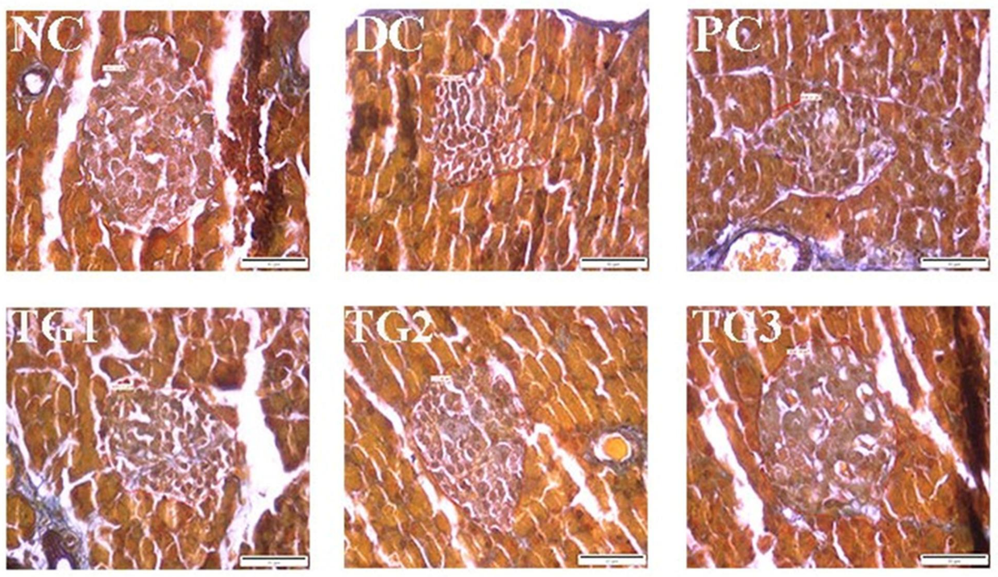


Table 2: Effect of ethanolic extract of Gongronema latifolium (GL) on glucose uptake by isolated rat abdominal muscle when incubated in the presence/absence of 1 IU/ml of insulin, expressed as mg glucose/g tissue (number of observations: n = 5).

Control	Insulin (1 IU/ml)	GL (1 mg/ml)	Insulin + GL
285.2 ± 10.81	328.52 ± 9.43	319.87 ± 29.41	392.54 ± 34.16

Conclusion

In conclusion, *Gongronema latifolium* proved to exert significant blood glucose lowering effects with daily sub-chronic treatment in diabetic SD rats from day 10. The extract seemed to exert a regenerative effect on the pancreas, restoring up to 80% of damaged insulin-producing Langerhans islets. *In vitro* tests indicated that the antihyperglycemic effect of the extract could be partially attributable to an insulin-sensitizing activity. Further research is required, however, to determine whether the regeneration seen on the level of the pancreatic Langerhans islets in this study would be transient or permanent with/without continuous treatment.

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