

Efficacy of *Solanum anguivi* Lam Fruits (African bitter berry) in Lowering Glucose Levels in Diabetes Mellitus and Increasing Survival

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Abstract : The prevalence and burden of diabetes are rapidly increasing globally, stemming from changes in lifestyle and dietary habits. Although several drugs are available to treat type 2 diabetes mellitus (T2DM), many are accompanied by several side effects and are often costly. *Solanum anguivi* Lam. fruits (SALF) are bitter berries that commonly grow in the wild and are traditionally cultivated by many globally as a remedy for T2DM. This effect is likely attributable to the presence of bioactive compounds such as phenolics, flavonoids, saponins, alkaloids, and vitamin C in SALF. In this study, we investigated the morphological characteristics of different SALF accessions, and the effect of ripeness stages and thermal treatments on the bioactive compounds contents (BCC) and antioxidant activity (AA) of SALF accessions. Using the fruit fly, *Drosophila melanogaster* (*D. melanogaster*) model, we explored the potential impact of dietary SALF in preventing and treating T2DM phenotypes. Morphological characterization was conducted based on descriptors of *Solanum* species. The BCC and AA of SALF at different ripeness stages (unripe, yellow, orange, and red) and after thermal treatments were determined using spectrophotometry, HPLC, and gravimetry. Male and female fruit flies were fed a high-sugar diet (HSD) to induce a T2DM-like phenotype, while control flies were fed on SY10 medium upto 24 days. Experimental flies were exposed to HSD supplemented with 5 or 10 mg/ml SALF. The therapeutic and prevention effect of SALF in T2DM-like phenotype were investigated on weight, climbing activity, glucose and triglyceride contents, survival, and gene expression of PPAR γ co-activator 1 α fly homolog Srl and *Drosophila* insulin-like peptides. Methods in fly studies included Gustatory assay, Climbing assay, Glucose GOD-PAP assay, Triglyceride GPO-PAP assay, Roti-Quant®, and Real Time-PCR analysis. Ripeness stage significantly influenced SALF BCC and AA, and this was dependent on the accession. The unripe stage had the highest AA and total phenolics and flavonoids; orange stage was rich in saponins, while the red stage had the highest alkaloid contents. Boiling and steaming increased the total phenolics and AA upto 4-fold and 3-fold, respectively. Drying at low temperature resulted in higher phenolics and AA than the control. In the therapeutic model, the HSD-fed female flies exhibited elevated glucose levels, which exhibited a dose-dependent reduction upon exposure to SALF-supplemented diet. Female flies fed on a SALF+ HSD exhibited a significant increase in survival compared to HSD-fed and control diet-fed flies. SALF supplementation did not alter weights, fitness, and triglyceride levels of female flies in comparison with HSD-only-fed flies. The mRNA levels of Srl decreased in HSD-fed flies compared to the control-fed, with no effect observed in females exposed to HSD+SALF. Similarly, in the preventative model, SALF diet resulted in higher survival of supplemented flies compared to controls. Consumption of boiled unripe SALF may result in the highest health benefits due to high phenolic contents and antioxidant activity observed. Dietary intake of SALF significantly lowered glucose levels and increased survival of the *D. melanogaster* model. Additional studies in higher organisms are needed to explore the preventative and therapeutic potential of SALF in T2DM.

Keywords : *solanum anguivi*, type 2 diabetes mellitus, bioactive compounds, *drosophila melanogaster*, survival, antioxidant activity

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