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Acacia nilotica (L.) Delile could be a potential drug combating diabetes: an evidence based and *in -silico* approach

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Background

***Acacia nilotica* (L.) Delile has long been used as a traditional anti-diabetic remedy in India, Bangladesh, Pakistan, Egypt, Nigeria etc. However, not much work has been done on the medicinal profiling of this herb. Therefore, the objective of the study was to evaluate the efficiencies of a chemically standardized extract of *A. nilotica* leaf (ANL) to ameliorate diabetes and its related complications.**

Methods

ANL was administrated orally at a dose of 50 (Low Dose) and 200 (High Dose) mg/kg body weight to alloxanized mice (blood glucose > 200 mg/dL) for 20 consecutive days. On 21st day, mice were sacrificed and different diabetic parameters were studied and compared with untreated controlled group. GC-MS and NMR were further employed to characterize different phytometabolites. In addition, several computational *in-silico* tools were assigned judicially to establish ANL as a probable anti-diabetic drug.

Parameters (units)	Control	Diabetic control	Glibenclamide	LD-ANL	HD-ANL
ACP (K.A.)	3.19±0.1	7.19±0.1^{b}	5.7±0.5$^{a\,\psi}$	6.95±0.1$^{c\,\psi}$	5.93±0.2$^{b\,\alpha}$
ALP (K.A.)	11.0±1.0	21.23±1.4^{c}	12.34±0.4$^{d\,\gamma}$	16.02±1.5$^{b\,\alpha}$	13.53±1.7$^{d\,\beta}$
AST (U/ml)	66.58±0.8	99.64±3.7^{c}	75.62±1.0$^{c\,\gamma}$	86.61±1.1$^{c\,\beta}$	76.97±3.8$^{a\,\beta}$
ALT (U/ml)	42.19±1.4	87.46±2.4^{c}	53.82±2.6$^{b\,\gamma}$	74.87±2.0$^{c\,\beta}$	72.19±13.9$^{a\,\psi}$
Creatinine (mg/dl)	0.19±0.0	0.35±0.0^{c}	0.19±0.00$^{d\,\gamma}$	0.25±0.0$^{a\,\alpha}$	0.17±0.0$^{d\,\gamma}$
Triglyceride (mg/dl)	90.36±6.4	137.83±6.9^{c}	89.07±7.7$^{d\,\beta}$	117.45±17.7$^{d\,\psi}$	112.89±25.7$^{d\,\psi}$
Cholesterol (mg/dl)	82.17±8.0	129.87±3.5^{c}	83.30±15.8$^{d\,\beta}$	133.14±44.6$^{d\,\psi}$	93.29±10.9$^{d\,\beta}$
Urea (mg/dl)	21.24±0.0	26.10±1.2^{b}	22.72±2.5$^{d\,\psi}$	22.52±1.3$^{d\,\alpha}$	24.32±1.0$^{b\,\psi}$
Uric acid (mg/dl)	1.57±0.1	2.26±0.1^{b}	1.90±0.1$^{d\,\alpha}$	2.70±0.1$^{c\,\beta}$	2.03±0.1$^{a\,\psi}$

a p<0.05; b p<0.01; c p< 0.001; d p=non-significant (p>0.05) vs group control. α p<0.05; β p<0.01; γ p< 0.001; ψ p=non-significant (p>0.05) vs diabetic control.

Table 1: Levels of various enzymatic and biochemical parameters of the serum of five experimental groups. The data represented as mean±SD; LD: Low Dose, HD: High Dose.

Results

Result reflected that ANL extract normalized blood glucose level, serum insulin level as well as glycogen level in the diabetic animals. The activities of tissue glycogen and peroxidase levels were significantly elevated which correlated with the lowering of fatty peroxides in the serum and further validated by HOMA-IR and QUICKI models. Hepatotoxicity, hyperlipidemia and nephrotoxicity were also found to be lowered in diabetic mice. Selected anti-diabetic phytometabolites, characterized through GC-MS, showed distinct drug binding-interactions with pancreatic α-amylase protein (5EMY), as figured by *in-silico* analysis.

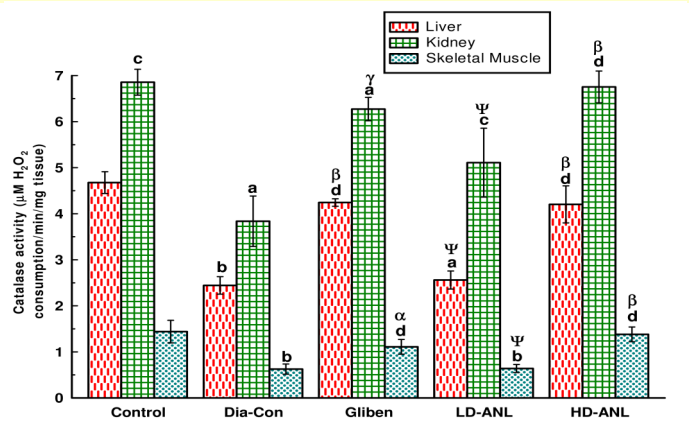

Figure 1: Catalase activity of ANL. Significance value same as shown in Table 1 foot note. LD: Low Dose, HD: High Dose.

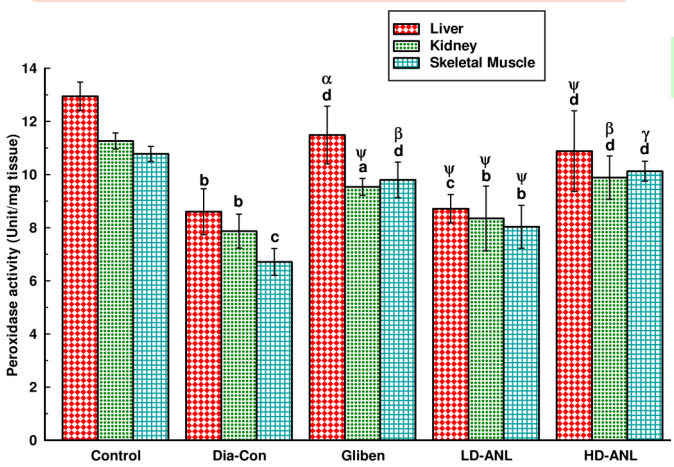

Figure 2: Peroxidase activity of ANL. Significance value same as shown in Table 1 foot note. LD: Low Dose, HD: High Dose.

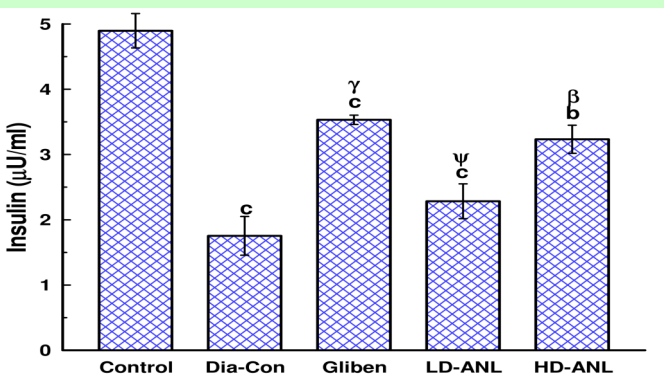

Figure 3: Represents insulin level after 20 days of treatment. Significance value same as shown in Table 1 foot note. LD: Low Dose, HD: High Dose.

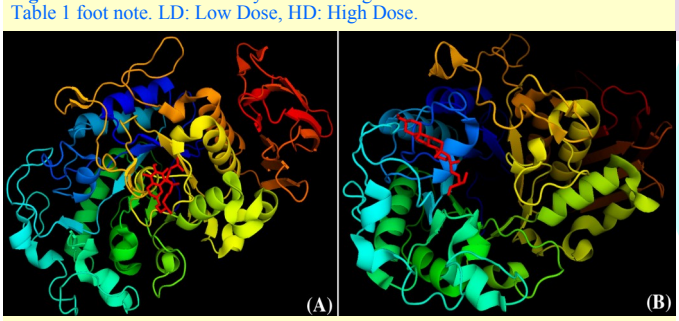

Figure 4: *In-silico* docking representation of ligands (A) α-Tocopherol and (B) Stigmasterol with pancreatic α-amylase protein (5EMY).

Conclusion

The present study with a systematic blend of *in-vivo* studies, anti-hyperglycemic modeling, phytochemical investigations and computational docking has demonstrated that ANL may possess the ability to act as a potent anti-diabetic drug.

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