In-vitro Antitrypanosomal, Antioxidant and Cytotoxicity Activities, LC-MS analysis and Molecular docking analysis of bioactive compounds from *Anopyxis klaineana* against UDP-Galactose 4`-Epimerase (GalE) of *Trypanosoma brucei*

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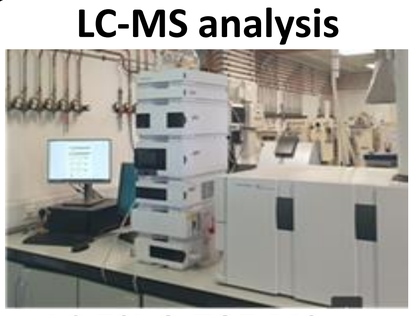
BACKGROUND

African Trypanosomiasis is a major public health concern worldwide, especially in developing countries (1). Current chemotherapies are highly toxic, resistant and ineffective. Hence, novel effective and potent trypanocides are needed. Medicinal plants have been documented to be a potential source for the development of antitrypanosomal compounds. *Anopyxis klaineana* is an ethnomedicinal plant used in west Africa to treat many ailments including protozoan diseases. In this study, we investigated the in-vitro effects of crude methanol extracts and fractions of *A. klaineana* for their antitrypanosomal activities against *Trypanosoma brucei* using Alamar blue assay. Additionally, the crude extract's antioxidant and cytotoxicity activities were also determined. The phytochemical profiling of the crude extract was determined using LC-ESI-QTOF-MS to identify major bioactive compounds present. Bioactive compounds identified were subjected to molecular docking studies against *Trypanosoma brucei's* UDP-Galactose 4`-Epimerase (TbGalE

MATERIALS & METHODS



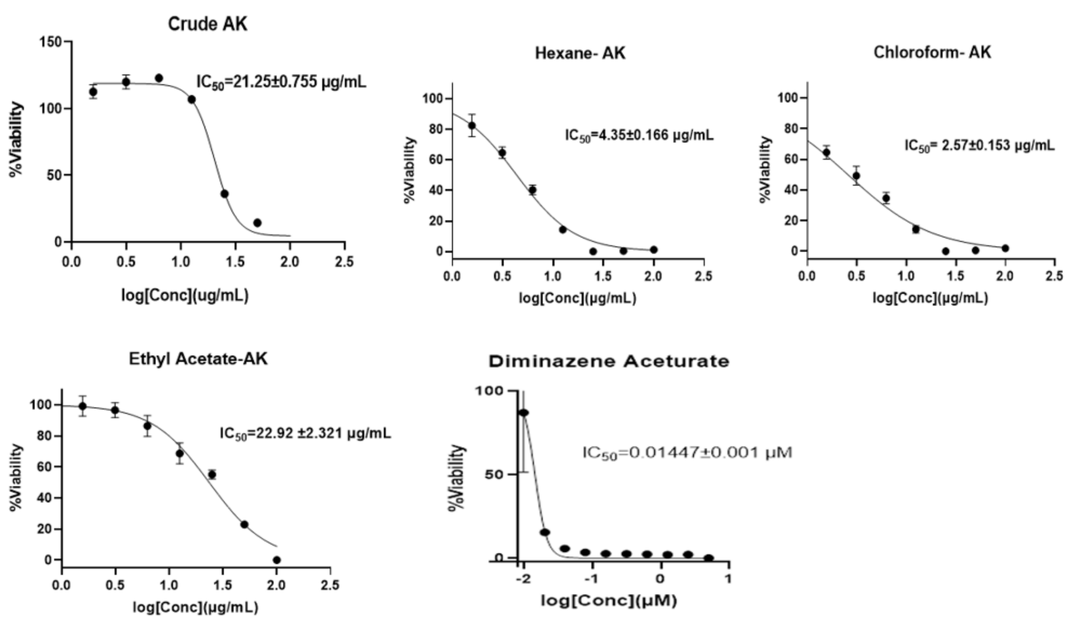
RESULTS & DISCUSSION

Invitro Anti-trypanosomal and cytotoxicity activities of *Anopyxis klaineana* stem bark extracts

Extracts	*T. b. brucei* [IC_{50}] µg/mL	HepG2 [CC_{50}] µg/mL	PNT2 [CC_{50}] µg/mL	SI [HepG2]	SI [PNT2]
AK	21.25 ± 0.755	68.0 ± 2.05	78.7 ± 2.63	3.2	3.7
Hexane fraction	4.35 ± 0.166	>100	ND	>22.9	ND
Chloroform fraction	2.57±0.153	>100	ND	>38.9	ND
Ethyl acetate fraction	22.92±2.321	>100	ND	>4.4	ND
Curcumin	ND	5.3± 0.53	5.3± 0.53	ND	ND
DA	0.01447±0.001	ND	ND	ND	ND

Data are represented as means and standard error of the mean for a triplicate experiment. The selectivity index (**SI**) is a ratio between the CC_{50} value of the human cell lines (HepG2 or PNT2) to the IC_{50} value of the *T. b. brucei*. **ND**-Not determined, **DA**-Diminazene aceturate (antitrypanosomal drug). DA and curcumin were used as positive control.

Dose-response curves of antitrypanosomal activity of extract and fractions of stem bark of *A. klaineana*



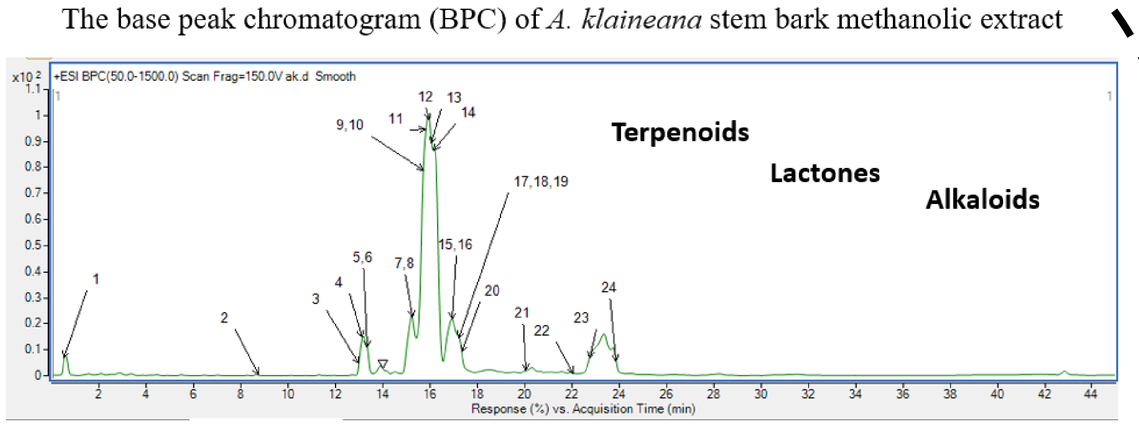
Antioxidant activity, total phenolic content, and total flavonoid content of stem bark of *A. klaineana* crude extract

Assay	AK extract	Standard
DPPH[a]	0.043±0.003	Ascorbic Acid 0.0341±0.006
FRAP[b]	35.1±0.5	NA
TPC[c]	17.3±0.3	NA
TFC[d]	290.4 ±0.2	NA

Data are represented as means and standard error of the mean for a triplicate experiment, **FRAP**-ferric reducing antioxidant power, **DPPH**- 2,2-diphenyl-1-picryl-hydrazyl-hydrate, **a**-expressed as EC_{50} in mg/ml of extract, **b**-expressed as ferrous equivalent in mM, **c**-expressed in mg gallic acid equivalent per 100g, and **d**-expressed in mg quercetin equivalent per 100g. **NA**-not applicable

LC-MS analysis

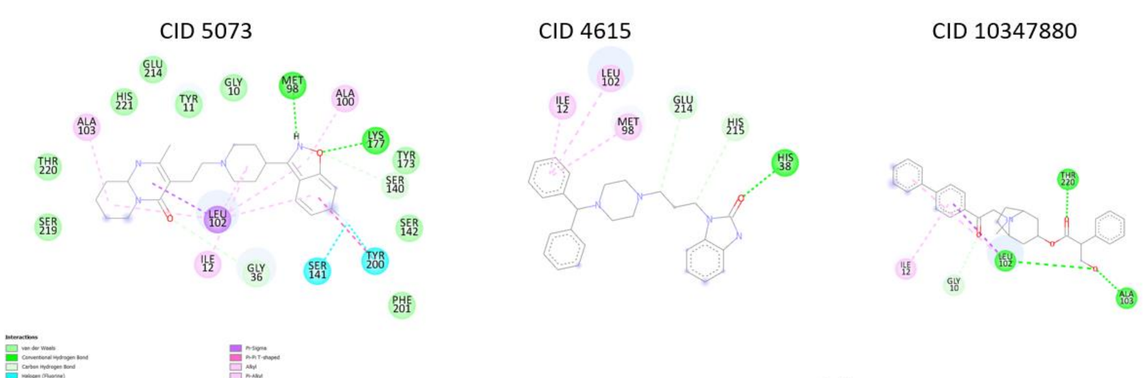
The base peak chromatogram (BPC) of *A. klaineana* stem bark methanolic extract

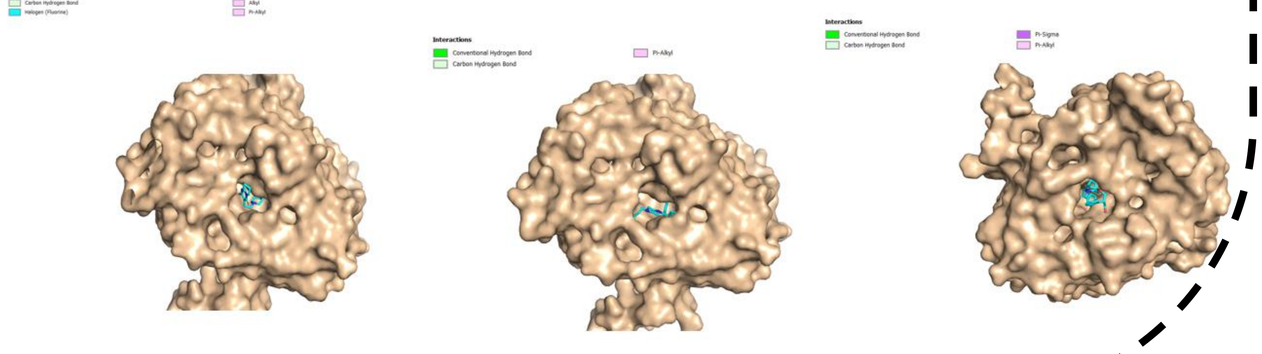


Molecular docking studies

Molecular docking results of 3 potential leads with their binding energies

COMPOUND	BINDING ENERGY (kcal/mol)
CID 5073	-10.8
CID 4615	-9.9
CID 10347880	-9.6
CID278702(*inhibitor)	-9.1





CONCLUSION

Our study indicates that *A. klaineana* has potential antitrypanosomal properties and can therefore be developed as therapeutic interventions for treating African trypanosomiasis.

FUTURE WORK

In-vitro and in-vivo investigations of potential leads to determine their potential efficacy as anti-antitrypanosomal compounds.

REFERENCE

1.Trypanosomiasis, human African (sleeping sickness) [Internet]. [cited 2023 Mar 15]. Available from: https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-(sleeping-sickness)

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