# In-vitro Antitrypanosomal Activities of the stem bark of *Entadrophragma angolense (Meliaceae)*

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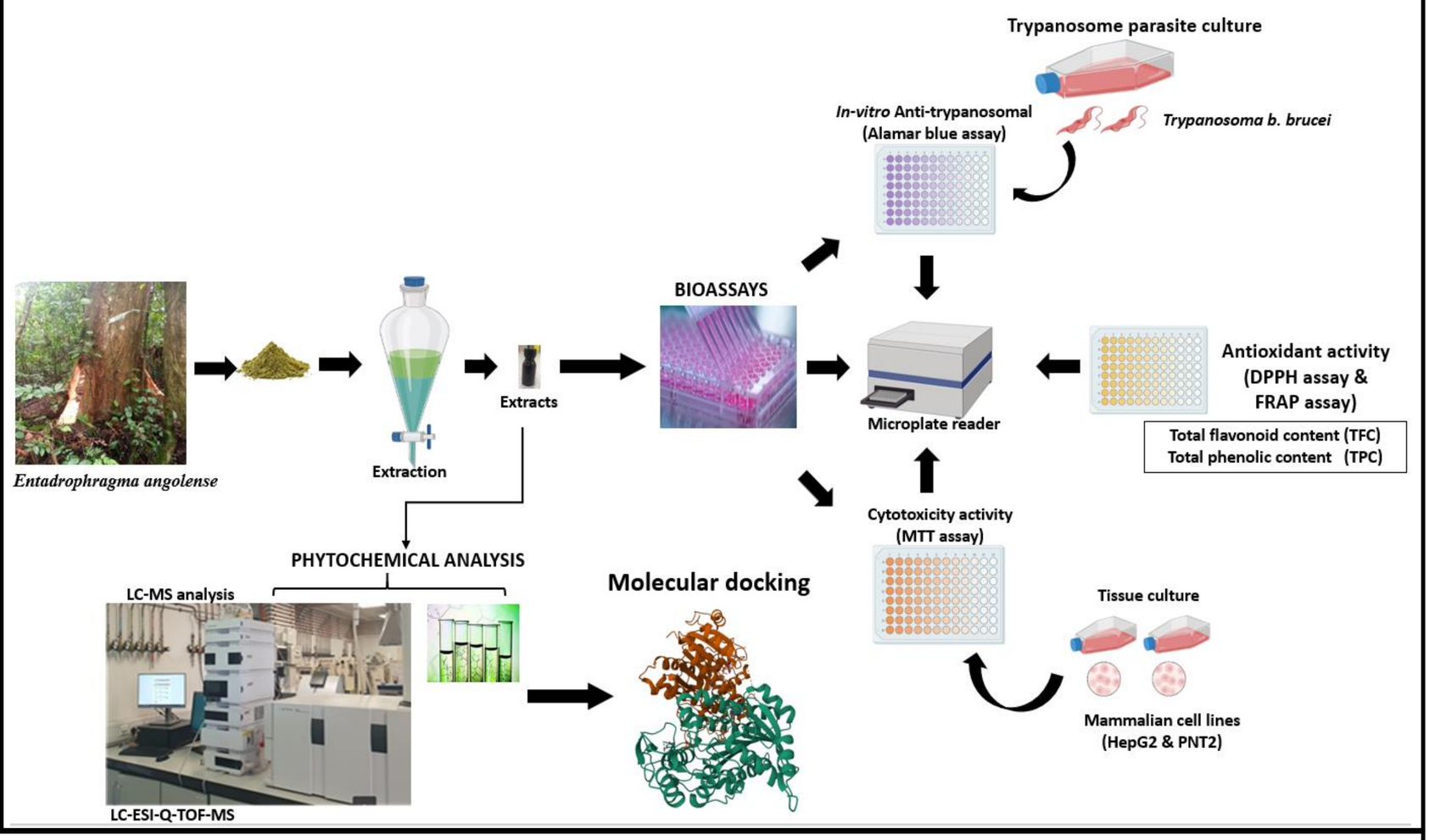
## INTRODUCTION

African Trypanosomiasis continues to be a major public health concern worldwide, especially in developing countries with thousands of new infected cases yearly (1). They are associated with high significant morbidity and large economic impacts. Currently, there are no vaccines to combat this disease, and current chemotherapy regimens are highly toxic, ineffective, and resistant. Hence, novel and potent trypanocides are urgently needed. Medicinal plants have been documented to be a potential source for the development of antitrypanosomal compounds. Amongst such is *Entadrophragma angolense* , an ethnopharmacological plant used in West Africa to treat several ailments including protozoan diseases (2). In this present study, we investigated the potential antitrypanosomal properties of *E. angolense* and its possible development as a therapeutic intervention for treating African trypanosomiasis. *In-vitro* effects of crude extracts and fractions of stem bark of *E. angolense* were tested against *Trypanosoma brucei* using Alamar blue assay. Additionally, the crude extract's antioxidant (FRAP and DPPH) 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.

## MATERIALS & METHODS



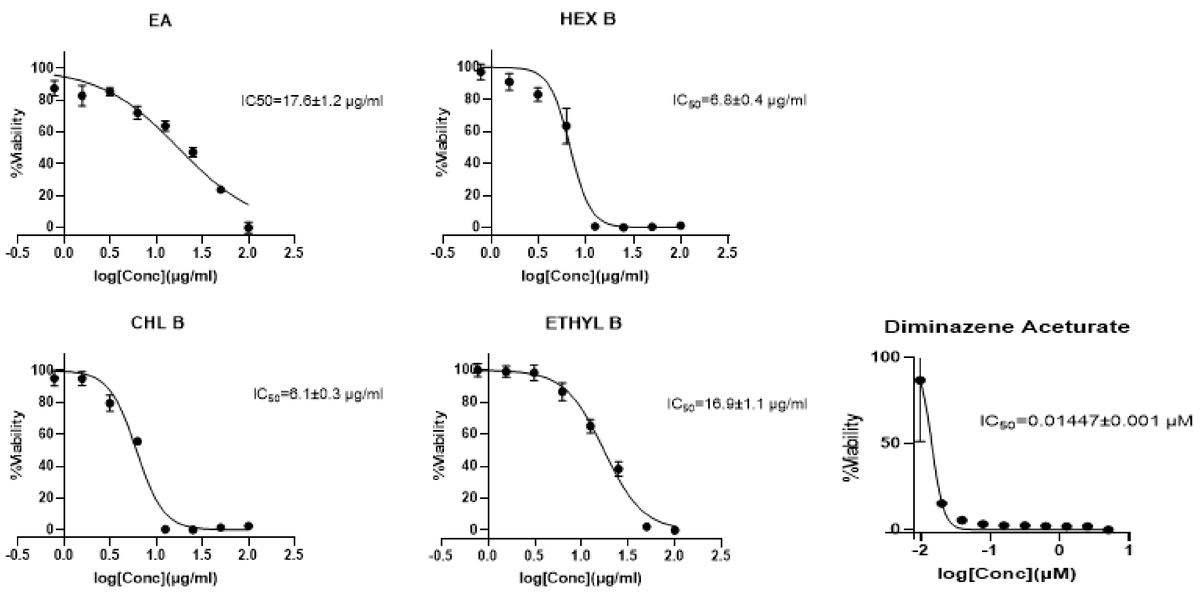

## RESULTS & DISCUSSION

**Invitro Anti-trypanosomal and cytotoxicity activities of *E. angolense* stem bark extracts**

| Extracts | *T.brucei brucei* [$IC_{50}$] µg/mL | HepG2 [$CC_{50}$] µg/mL | PNT2 [$CC_{50}$] µg/mL | SI [HepG2] | SI [PNT2] |
|---|---|---|---|---|---|
| **EA** | 17.55±1.199 | 235.4 ± 0.30 | 548.3 ± 0.09 | 13.41 | 31.24 |
| **Hexane** | 6.8±0.400 | ND | ND | ND | ND |
| **Chloroform** | 6.1±0.300 | ND | ND | ND | ND |
| **Ethyl acetate** | 16.9±1.1 | ND | ND | ND | ND |
| **Curcumin** | ND | 5.3± 0.07 | 5.3± 0.07 | 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.brucei brucei*. ND-Not determined, DA-Diminazene aceturate (antitrypanosomal drug). DA and curcumin were used as control.

Dose-response curves



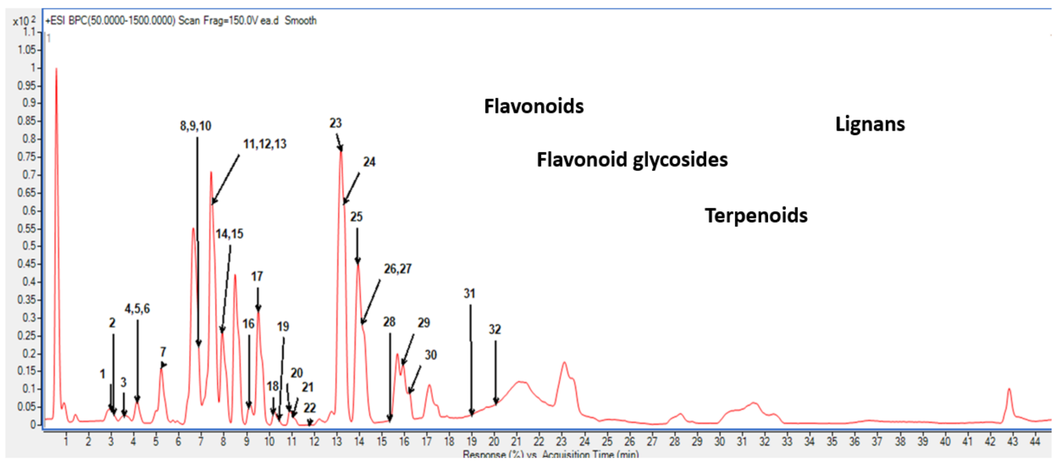

**Antioxidant activity, total phenolic content, and total flavonoid content of *E. angolense* stem bark extract**

| Assay | EA extract | Standard |
|---|---|---|
| DPPH[a] | 0.47±0.06 | Ascorbic Acid 0.0341±0.006 |
| FRAP[b] | 13.5±0.3 | NA |
| TPC[c] | 7.6±0.2 | NA |
| TFC[d] | 531.1±0.04 | 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, **TPC**-total phenolic content, **c**-expressed in mg gallic acid equivalent per 100g, and **TFC**-total flavonoid content, **d**-expressed in mg quercetin equivalent per 100g. **NA**-not applicable

### LC-MS analysis

The base peak chromatogram of *E. angolense stem bark* methanol extract

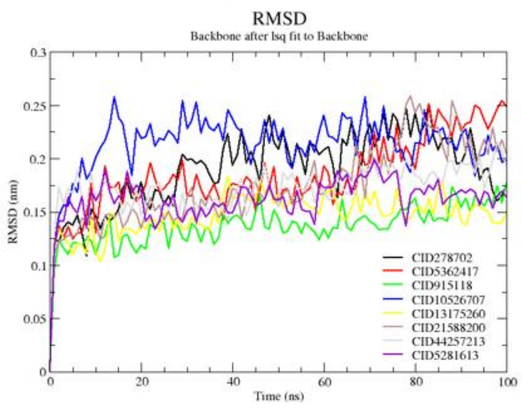



### *In-silico* studies

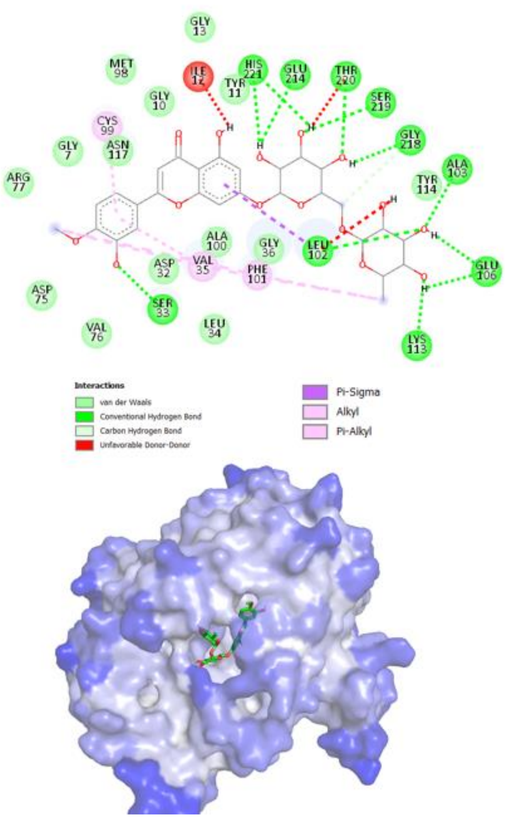
**Molecular docking results of 8 potential leads with their binding energies**

| COMPOUND | BINDING ENERGY (kcal/mol) |
|---|---|
| CID 5281613 | -11.4 |
| CID 9151181 | -11.2 |
| CID 131751171 | -10.3 |
| CID 131752602 | -10.2 |
| CID 10526707 | -10.1 |
| CID 4425213 | -9.9 |
| CID 5362417 | -9.3 |
| CID 21588200 | -9.1 |
| **CID278702(*inhibitor)** | -9.1 |

**Molecular dynamics simulations**




**CID 5281613**




## CONCLUSION

Our findings for the first time have demonstrated that *E. angolense* has potential antitrypanosomal properties through both invitro and in-silico approaches.

*E. angolense* can therefore be developed as therapeutic interventions for treating African trypanosomiasis.

## ACKNOWLEDGEMENT

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This work was carried at the Department of Parasitology, Noguchi Memorial Institute for Medical Research, Ghana

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