



Echinops kebericho Root Extract: Antitrypanosomal Activities in *In vitro* and *In vivo*

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ABOUT THE STUDY

Currently, trypanocidal drugs, trypanotolerant cattle breeds, and tsetse fly vector control are used to combat trypanosomiasis. The main strategy for controlling trypanosomiasis relied on the use of trypanocidal drugs, which is being challenged by an increasing resistance problem. To combat trypanosomiasis, it is rational to look for new chemical entities that are effective against trypanosomes, safe, and affordable for disease-endemic countries. Exploration of natural and synthetic sources is therefore required to feed the pipeline of drug development for trypanosomiasis control and elimination.

Plants are potential sources of new drugs due to their abundance of secondary molecules with pharmacological effects. Exploring traditionally claimed medicinal plants for biological activity resulted in the development of a number of antiprotozoal medications.

Validation of medicinal plants for antitrypanosomal activity will guide society on the best way to use their indigenous knowledge while also providing hit compounds to feed the future pipeline for antitrypanosomal drug development. *Echinops kebericho* (Mesfin), [Amharic vernacular name: *kebericho*], is an erect perennial herb or shrub that belongs to the *Asteraceae/Compositae* family. Its numerous medicinal applications are documented in ancient medico-religious pharmacopoeias and are widely accepted by modern-day traditional professionals/specialists.

Echinops kebericho root is used to treat animal trypanosomiasis. However, there is no laboratory-based evidence that this plant is effective or safe. The goal of this study was to evaluate the antitrypanosomal effects of a hydromethanolic extract of *E. kebericho* roots *in vitro* and *in vivo* using a field isolate of *T. congolense*, the most common cause of domestic animal trypanosomiasis. The experimental mouse infection model was chosen because it provides new insight into both human and animal trypanosomiasis. The antitrypanosomal activities of *E. kebericho* roots in the current study suggested that the extract may

contain trypanocidal constituents that are active in *in vitro* and *in vivo* environments. Most trypanosomes' motility is a relatively reliable indicator of viability, and complete elimination or reduction in motility of trypanosomes when compared to the control could be used as an index of trypanocidal activity.

In vivo testing of the extract revealed a significant reduction in parasite load at 200 mg/kg and 400 mg/kg compared to the vehicle control group, despite the fact that the extract did not clear the parasite. More research is needed to determine whether the extract has a better effect when administered by injection to reduce the negative impact of limited bioavailability from the gut.

The mean Packed Cell Volume (PCV) in the untreated control group decreased until all of the animals died from infection, whereas the value in the treated groups was within the normal range. The decrease in PCV value in the untreated control group could be attributed to anemia, which is the most notable clinical and laboratory feature of trypanosomiasis.

The current study found secondary metabolites in *E. kebericho* extract, including saponins, tannins, phenol, terpenes, flavonoids, glycosides, and alkaloids. The active components in question had yet to be identified. Previous research has shown that flavonoids are effective antitrypanosomal agents against various trypanosome species. Antitrypanosomal activity of phenols and polyphenols has also been reported by inhibiting the trypanosome alternative oxidase. Alkaloids have an effect on trypanosomes by intercalating DNA and inhibiting protein synthesis. Multiple secondary metabolites may have contributed to the *in vitro* and *in vivo* activities of the *E. kebericho* extract in this study.

The current study also demonstrated that the extract is safe and tolerable, as no treatment-related toxicity signs were observed in the animals during the observation period. The hydromethanolic extract of *E. kebericho* root extract produced no significant toxic signs or death in mice after a single administration of 2000 mg/kg with an oral median lethal dose

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greater than 2000 mg/kg over a 14-day of observation period. Another study found that a hydroethanolic extract of *E. kebericho* root (up to 5,000 mg/kg) did not cause toxicity.

The current study supports the antitrypanosomal activity of a hydromethanolic extract of *E. kebericho* root and validates

traditional approach to trypanosomiasis control. It is suggested that the extract be tested *in vitro* and *in vivo* on other trypanosome species. Furthermore, the active compounds must be characterized in order to identify hits and develop lead compounds.