General Abstract

Herbal remedies are commonly used in developing countries for the treatment of various diseases, including constipation. The rationale for utilizing medicinal plants for the treatment of diseases rested largely on the belief that they are safe and free of side effects. However, there is limited scientific evidence on the safety and efficacy of these herbal medicines to back up their continued therapeutic application.

*Aloe ferox* Mill. (Aspodelaceae), known as Cape aloe, locally called *ikhala* is a medicinal plant used by the people of the Eastern Cape Province for the treatment of gastrointestinal problems and constipation. The plant is a perennial shrub with thick succulent leaves bearing brown thorns on the margin and bright orange flowers arranged in oval lanceolate. It occurs in all weather in bush veld, road side, gardens and undisturbed places. According to the ethnomedicinal information, *A. ferox* is used as purgative. This research project was therefore designed to evaluate its ability in the treatment of constipation and to investigate its possible toxicological property.

At the beginning of this programme, a survey of plants used for the treatment of constipation in Nkonkobe Municipality of the Eastern Cape Province was carried out using a questionnaire, which was administered to herbalists, traditional healers and rural dwellers. The study revealed 10 plant species from 8 families that are used for the treatment of constipation in the province. Four plants, *Aloe ferox* Mill, *Boophone distischa* L.f Herb, *Alepidea amatybica* Eckl and *Artemisia afra* Jacq, were repeatedly mentioned. Based on the frequency of usage, perceived efficacy and availability to the rural dwellers and the traditional healers, *Aloe ferox* was the most commonly used of the plants for the treatment of constipation. The plant was thus, chosen for the study.
The *invivo* laxative effect of the aqueous extract of *Aloe ferox* in the treatment of loperamide-induced constipation in Wistar rats was investigated at varying concentrations. The leaf extract at all the dosages investigated (50, 100 and 200 mg/kg body weight) improved intestinal motility, increased fecal volume and normalized body weight in the constipated rats. This was an indication of its laxative properties. However, the laxative property of the herb at 200 mg/kg body weight of the extract showed best efficacy and compares favourably well with senokot, a standard laxative drug. These findings have therefore, lent scientific credence to the folkloric use of the herb by the people of the Eastern Cape of South Africa as a laxative agent.

Toxicological evaluation of aqueous leaf extract of *Aloe ferox* in loperamide-induced constipation was studied at 50, 100, and 200 mg/kg body weight. The oral administration of the extracts did not show any significant effect on the liver and kidney body weight ratios as well as the kidney and liver function indices. The extracts, at all the dosages investigated, did not alter the levels of creatinine, uric acid, urea, calcium and potassium ions. Similarly, the levels of total protein, albumin, bilirubin and gamma glutamyl transferase (GGT) were not significantly different from the control. The plant extract appreciably normalized the elevated activities of alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) in the untreated constipated rats following treatment with the extract. The extract did not show a significant effect on the hematological parameters except for the increase in the lymphocyte count in the untreated constipated rats, which was attenuated after administering the herb. The available evidence in this study suggests that *A. ferox* may be safe as an oral remedy for constipation. Generally, the effect of the extract compared favourably well with senokot, a recommended drug for the treatment of constipation.
The antioxidant activities against 1, 1 diphenyl-2-picrylhydrazl (DPPH), 2,2’ – azinobis [3-ethylbenzothiazoline-6-sulfonic acid] diaminonmum salt (ABTS), hydrogen peroxide (H$_2$O$_2$), Nitric oxide (NO), lipid peroxidation and the ferric reducing agents were investigated spectrophotometrically. Alkaloids, saponins, tannins, total phenols, flavonoids, flavonols and proanthocyanidin were also determined to assess their effects on the antioxidants activity of this plant. The phytochemical content of the ethanol and acetone extracts were consistently high compared to other solvents extracts. The level of tannins was not significant (P > 0.05) as compared with other solvent extracts. The free radical scavenging activity of the extracts was high even at lower concentrations (0.025 mg/ml) except in DPPH and lipid peroxidation. The ferric reducing potential of the extracts was concentration dependent and significantly different from Vitamin C and butylated hydroxytoluene (BHT) that were used as standard drugs. The present study showed a high level of scavenging activity of the leaf extracts of Aloe ferox in all the solvent extracts. Both ethanol and methanolic extract showed potent antioxidant activities than acetone and aqueous extracts. The study indicated that the leaf extracts of Aloe ferox might be a valuable source of natural antioxidant for both medicine and food industries.

*A. ferox* leaf consists of the gel, latex and mesophyll layer; however, the main active constituents of the latex and the leaf exudate of Aloe ferox are anthraquinones, which are believed to be responsible for the laxative property. The laxative compound in Aloe ferox leaf extract was isolated and characterized by extracting the plant material in methanol and extract suspended in distilled water. Partitioning was done with n-hexane, ethyl acetate and butanol respectively and was co-spotted with the over-the-counter (OTC) laxative drugs. This led to the successive column chromatography and thin layer chromatography (TLC) of the most active ethyl acetate fraction on silica gel with benzene/ethanol/ammonia hydroxide (BEA: 90:10:1),
ethyl acetate/methanol/water (EMW: 40:5.4:5) and chloroform/ethyl acetate/formic acid (CEF: 50:40:10) as the mobile phase. The successive chromatograph and TLC afforded two compounds of $R_f$ 0.420 (blue) and 0.831 (yellow) with the over-the-counter (OTC) drugs. These compounds were not totally elucidated due to their small quantity and instability. However, hydroxyl (OH) and carboxyl groups (COOH) was established as common to the extracted compounds, which might be responsible for the biological activity recorded for the plant extract.
INTERLLECTUAL PROPERTY AGREEMENT STATEMENT
All the elderly and the traditional healers who contributed one information or the other during the preliminary investigation on the folkloric use of *Aloe ferox* were adequately financially rewarded with further verbal agreement and understanding that this research shall not be for commercial purposes but to serve as an enlightenment on the safety, toxicity and efficacy of this plant.

ETHICAL COMMITTEE APPROVAL
The study involving the use of animals in this project was carried out following the approval of the Ethical Committee on Animal Use and Care of the University of Fort Hare.

COMPLIANCE STATEMENT
No part of this study in any form has been and will be commercialized. The thesis is meant to be used for information dissemination on the medicinal potentials of *Aloe ferox* to the immediate community and the entire Eastern Cape Province of South Africa.

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Supervisor’s signature                        Student’s signature