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PHYTOCHEMICAL PROFILE, CARDIOPROTECTIVE EFFECTS AND SAFETY OF AQUEOUS LEAF EXTRACTS OF *Ximenia americana* (Linn.) AND *Pappea capensis* (Eckl. and Zeyh.)

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DECLARATION

I, Daniel Muthee Gaichu, duly confirm that I solely composed this work and that it has not been presented, in whole or in part, in any previous application for a degree or professional qualification in any other university.

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We confirm that the work contained herein was done by the candidate under our supervision.

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ABSTRACT

Myocardial infarction is a serious health challenge in first and low-income countries. Globally, it contributes to the largest mortality caused by cardiovascular related diseases. In 2012, MI-related deaths were about 14.1 million out of 17.5 million CVD-related deaths. Clinical management of MI remains a challenge to cardiologists because most conventional drugs provide symptomatic relief only. In addition, the synthetic therapies are linked with multiple adverse side effects and are arguably not affordable. Therefore, herbal medicines, which are widely available, with comparatively fewer side effects and are affordable, provide a more attractive therapeutic alternative. For a long time, communities such as Ambeere, Ameru and Aembu have used *X. americana* and *P. capensis* extracts to treat heart-related conditions. Regardless, the traditional use of these herbal plants in the management of heart related complications has not been scientifically validated. Therefore, this study determined quantitative phytochemical profile, *in vivo* cardioprotective and safety of aqueous leaf extracts of *Ximenia americana* and *Pappea capensis*. Wistar rats were employed for determination of cardioprotective effects, whereas Swiss albino mice were used for determination of safety profiles of the plants. Salbutamol (7.5 mg/Kg bw) was used to induce myocardial infarction. The rats were randomly divvided into 6 sets, each comprising of 5 rats. Group I (normal control) and II (negative control) rats were given normal saline and salbutamol, respectively. Group III (positive control) rats were treated with propranolol, whereas groups IV, V and VI (experimental) rats received the oral extract. Extracts dose of 50, 100 and 150 mg/Kg bw were used for cardiopreventive studies, whereas 150, 200 and 250 mg/Kg bw extract doses were used for cardiocurative studies. Biochemical assessments were carried out by evaluating the effects of the extracts on levels of cardiac function biomarkers, lipid profiles and cardiac antioxidant markers. The extract dose level used in testing for acute toxicity was 2000 mg/Kg bw, whereas sub-acute toxicity was tested at doses of 250, 430 and 750 mg/Kg bw. The LC-MS analysis showed the extracts to contain different phytocompounds, including flavonoids, phenolic acids and tannins, which are associated with cardioprotective activities. In addition, the two extracts showed dose-dependent cardioprotective activities by significantly decreasing the levels of cTnT, CK-MB, LDH-1, total cholesterol, triglycerides, LDL and MDA, and by increasing the levels of SOD, CAT, GPx and HDL in extract-treated rats as compared with negative control rats. The safety profiles results showed that there was no significant difference in the body weights, red and white blood cell indices and kidney functions of the extract-treated mice as compared with normal control mice. However, *X. americana* dose level of 2000 mg/Kg bw caused significant increase in relative pancreas weight. In addition, *X. americana* extract at dose level of 750 mg/Kg bw caused significant increase in levels of PDW, indirect- and total-bilirubin. It was concluded that the extracts possess phytochemicals associated with cardioprotective effects, have *in vivo* cardiopreventive and cardiocurative effects in rats and are generally safe in mice. Therefore, the two extracts can be a source of cardioactive agents and a safe complementary treatment of myocardial infarction at the dose levels used in the current study.