The prevalence of non-communicable diseases (NCDs) in Sub-Saharan Africa (SSA) is rising. Instead of relying on drugs, food-based approaches may be considered to help manage these chronic diseases. Sweetpotato is a cheap, easy-to-cultivate and climate-smart crop that contains substantial amounts of bioactive compounds and could be a functional food. However, the focus of sweetpotato research in SSA has been its use in alleviating hidden hunger in resource-poor populations. There is, therefore, the need to assess the sweetpotato genotypes in SSA for their use as a functional food. The objectives of this study were to characterise Ugandan-grown sweetpotato genotypes for their inherent bioactive compounds and antioxidant activities; to determine the effects of processing and *in vitro* digestion on these parameters; and to investigate their potential health-benefiting effect on symptoms of type 2 diabetes (T2D). Six (6) genotypes of sweetpotato with varying flesh colours (white, cream, pale yellow, pale orange, deep orange, and purple), harvested at physiological maturity were used for the study. The effects of peeling and standard household cooking methods (boiling, steaming, baking, frying, and microwaving) on the bioactive compounds and antioxidant activities were investigated. An *in vitro* digestion model was employed to determine the bioaccessibility of the bioactive compounds. Samples were freeze-dried for laboratory analysis, and all parameters were quantified using standard spectrophotometric methods and reported on dry weight basis. A T2D model using Wistar rats that were fed a high-fat diet followed by alloxan monohydrate administration was used to test the antidiabetic and antihyperlipidemic potential of whole sweetpotato roots at doses of 200 (SP-200), 500 (SP-500), and 1000 (SP-1000) mg/kg body weight. Metformin was used as positive control for the antidiabetic study. Body weight, blood glucose levels, lipid profile parameters and histopathological indices were evaluated. The inherent bioactive compounds and antioxidant activities in raw and cooked roots were significantly higher (P<0.05) in unpeeled than peeled roots. For raw roots, phenolic compounds were significantly higher (P=0.001) in white, cream, and purple-fleshed roots (59.67-121.04 mg GAE/g) than in yellow and orange-fleshed roots (0.89-10.89 mg GAE/g). Total alkaloids ranged between 24.05 and 233.70 µg CE/g, below the potential toxicity range of 3 - 10mg/g. All cooking methods increased phenolic compounds, flavonoids, and tannins in all genotypes, with baking increasing phenolic compounds most significantly. Significant losses of total carotenoids occurred with all cooking methods (ranging from 24.18 to 172.76 µg/g in raw sweetpotatoes *vs* 10.06 to 118.17 µg/g in cooked ones; *p* <0.001), except the deep-orange-fleshed genotype, in which frying slightly increased carotenoids from 269.81 to 304.74 µg/g. Microwaving retained 69% vitamin C in the cream-fleshed one, the highest among the cooking methods. Anthocyanins decreased with baking and frying in the purple-fleshed one but increased with the other cooking methods. The *in vitro* bioaccessibility of phenolics, flavonoids, carotenoids, anthocyanins, and antioxidant activities increased with cooking but vitamin C bioaccessibility decreased. The raw roots had a vitamin C bioaccessibility of 92%, while for cooked, it ranged between 61% (baking) and 73% (frying). For phenolics and flavonoids, peeling the roots significantly (P<0.001) increased bioaccessibility by 11% and 4%, respectively. The study revealed that the antioxidant activity of sweetpotato roots resulted from the synergistic effect of all the bioactive compounds analysed. For the animal study, body weight,blood glucose and lipid parameters varied significantly (*P*<0.05) among groups. Blood glucose normalised six days after treatment in the metformin and SP-200 groups, while in the SP-500 and SP-1000, it normalised from day 14. Compared to the diabetic control, LDL cholesterol (0.13-0.43 mmol/L) decreased by 70%, 65%, 53%, and 49% in the metformin, SP-200, SP-500, and SP-1000 groups respectively. HDL (0.56-0.90 mmol/L), total cholesterol (1.25-1.98 mmol/L), and triglycerides (0.42-1.08 mmol/L) increased with increasing sweetpotato concentration. Total cholesterol in SP-200 and SP-500 was 30% and 12% lower than the diabetic control respectively. The total triglycerides was significantly higher in the diabetic control than the other groups. Compared to the diabetic control, SP-200 decreased triglycerides by 48%, metformin by 44%, SP-500 by 29%, and SP-1000 by 21%. Based on the study results, it can be concluded that the retention of bioactive compounds in sweetpotato storage roots depends on the processing method and to obtain the most health benefits, consumers should use different cooking methods but must retain the peels. Consuming between 200 and 500 mg/kg body weight of whole sweetpotato roots per day may be recommended for improvement in hyperglycaemia and dyslipidaemia**,** but not as much as 1000 mg/kg per day as it may have antagonistic effects due to the substantial starch content.

**Keywords**: sweetpotato; bioactive compounds; antioxidant activity; cooking; bioaccessibility; antidiabetic, Uganda.