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Evaluation of mineral content of plants used in the management of sickle cell disease

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ABSTRACT

Introduction
Sickle cell disease is a hereditary condition primarily identified in tropical areas. It is marked by significant anemia, vaso-occlusive seizures, and a heightened vulnerability to both viral and bacterial infections. Additionally, sickle cell disease is distinguished by the depletion of mineral elements during crises.

Purpose
The purpose of this investigation was to identify the mineral composition of ten plants, namely *Alchornea cordifolia, Alternanthera bettzickiana, Annona senegalensis, Cyttaranthus congolensis, Dissotis brazzae, Justicia secunda, Harungana madagascariensis, Hura crepitans, Hypoxis angustifolia,* and *Vigna unguiculata*, traditionally utilized by practitioners in the management of sickle cell disease.

Methods
In this study, the biological material consists of the leaves, bark, and seeds of ten plant species. These plants were collected in Kwilu, and the mineral composition was assessed through fluorescence spectrometric analysis. The detection and quantification of the mineral elements were done by X-ray fluorescence spectrometric method with an XEPOS fluorescence spectrometer. The analysis of the results was carried out through Excel. R Studio and SPSS software packages were used for the statistical analyses.

Results
The study identified a total of twenty-three mineral elements in each of these plants, including Potassium (K), Phosphorus (P), Calcium (Ca), Sodium (Na), Magnesium (Mg), Sulphur (S), Chlorine (Cl), as well as trace elements like Aluminum (Al), Silicon (Si), Vanadium (V), Chromium (Cr), Manganese (Mn), Iron (Fe), Nickel (Ni), Copper (Cu), Zinc (Zn), Selenium (Se), Bromine (Br), Molybdenum (Mo), Tin (Sn), Iodine (I), Barium (Ba), and Lead (Pb). Notably, Iron, Zinc, Selenium, Copper, Calcium, Magnesium, and Manganese were found to be mineral elements associated with sickle cell disease. Potassium and Calcium exhibited higher concentrations, while Lead, Tin, Bromine, Copper, and Nickel were present in trace amounts.

Conclusion
The results obtained confirm that these plants contain some mineral elements such as Fe, Zn, Mg, and Se that are useful for sickle-cell patients.

INTRODUCTION

Sickle cell disease is a genetic disorder predominantly found in tropical regions. It is characterized by hemoglobinopathy resulting from the substitution of glutamic acid with valine at the sixth position of the beta chain of hemoglobin (Bongo et al., 2017). This alteration not only affects the oxygen affinity of hemoglobin but also its solubility, particularly in low-oxygen conditions (Kitadi et al., 2020; Kitadi et al., 2021; Kitadi et al., 2022). The reduced solubility leads to the polymerization of hemoglobin, resulting in the formation of sickle cells, which is a major contributor to the various health issues experienced by individuals with SS anaemia (Masengo et al., 2021).

Symptoms can vary significantly from person to person and may fluctuate over time. Generally, the disease presents as anemia, marked by symptoms such as fatigue, dizziness, and shortness of breath. Other manifestations include increased susceptibility to infections and painful episodes due to compromised blood circulation and inadequate oxygen supply to tissues, particularly the bones (Gulbis, 2011; Bongo et al., 2017). Unfortunately, there is currently no well-defined treatment for this hemoglobin disorder. Bone marrow transplant, though a potential option, is prohibitively expensive, with costs reaching as high as $100,000, and is subject to numerous compatibility challenges. During crises, blood transfusion is commonly employed. While repeated transfusions can slow down the synthesis of hemoglobin S and decrease the frequency of vaso-occlusive attacks and superinfections, they expose patients to risks such as transfusional hepatitis and the transmission of the human immunodeficiency virus (HIV) (Sofowora, 1998).

It is noteworthy that hydroxyurea is also utilized, demonstrating established efficacy in treating sickle cell crises by increasing the production of fetal hemoglobin (HbF) and improving the erythrocyte phenotype. However, prolonged use of hydroxyurea raises concerns about its potential toxicity (Brugnara et *al.*, 2002; Panzu et *al.*, 2019).

The challenges associated with recurrent blood transfusions, the extended usage of hydroxyurea, and the substantial expenses involved in bone marrow transplantation have prompted researchers to explore alternative therapeutic approaches, including phytotherapy. In addition, this disease is also characterized by a loss of mineral elements important for the body's functioning (Kehinde et al., 2010; Soltner, 2001).

Minerals are natural chemical elements that the body uses to activate certain biochemical reactions (Bligny et al., 2005). They are part of functionally important inorganic compounds such as iron (Fe) in hemoglobin and Cytochrome or zinc (Zn) in insulin (Bligny et al., 2005, 2007). Recently, our research team has shown that certain medicinal plants used in Traditional Congolese Medicine have *in vitro* antisickling activity (Mpiana et al., 2010; Mpiana et al., 2014). However little work has been done on the mineral composition of these plants to assess their possible effect on sickle cell disease. In this respect, the development and discovery of new compounds with effective therapeutic potential for sickle cell disease remains a public health priority.

The purpose of this investigation was to identify the mineral composition of ten plants, namely *Alchornea cordifolia, Alternanthera bettzickiana, Annona senegalensis, Cyttaranthus congolensis, Dissotis brazzae, Justicia secunda, Harungana madagascariensis, Hura crepitans, Hypoxis angustifolia,* and *Vigna unguiculata*, traditionally utilized by practitioners in the management of sickle cell disease.

METHODS

Medicinal Plants

The leaves, barks, and seeds of *Alchornea cordifolia, Alternanthera bettzickiana, Annona senegalensis, Cyttaranthus congolensis, Dissotis brazzae, Justicia secunda, Harungana madagascariensis, Hura crepitans, Hypoxis angustifolia,* and *Vigna unguiculata* were collected in September 2019 and April 2020 in the five territories of the Province of Kwilu, Democratic Republic of Congo. These samples were dried in the dark at the Basic Science Laboratory of the University of Kikwit. They were then crushed to territories of fine powder.

Methods

The mineral elements were detected and quantified using the X-ray fluorescence spectrometric method with an XEPOS fluorescence spectrometer. This analytical approach allows the determination of multiple elements within the same sample. For each plant, a portion of the powder was compressed into pellets using a hydraulic press, and these

resulting pellets were introduced into the fluorescence spectrometer for analysis. Excel was employed for results analysis, while statistical analyses, including Principal Component Analysis (PCA) and Pearson Correlation, were conducted using R Studio and SPSS software packages.

X-ray fluorescence

Plant samples, initially dried at the basic science laboratory of the University of Kikwit, underwent a 24-hour drying process in an oven at 40°C to eliminate moisture. Following this step, the samples were pulverized using a ball mill to obtain a fine powder, which was stored in a desiccator. The resulting powder was utilized to create pellets through a hydraulic press for each sample. These pellets were then subjected to the X-ray fluorescence spectrophotometer for the identification and quantification of mineral elements in each plant sample.

RESULTS AND DISCUSSION

The first category of mineral elements is represented by Fe, Mg, and Cu which have concentrations ranging from a few hundred to over 5000 ppm while the second category is composed of elements with concentrations below 1000 ppm, namely Se, Mn, and Zn. All these elements are known to have a direct or indirect impact on sickle cell disease (Sungu, 2016). For these elements, the plant with the highest content was indicated by Multiple Component Analysis (PCA).

Figures 1 and 2 show the different plants with the highest content of each of these elements.

Figure 1:
Cu content in the plants

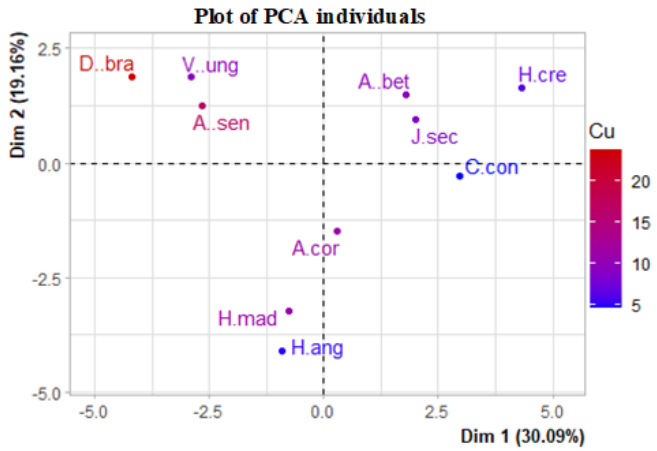
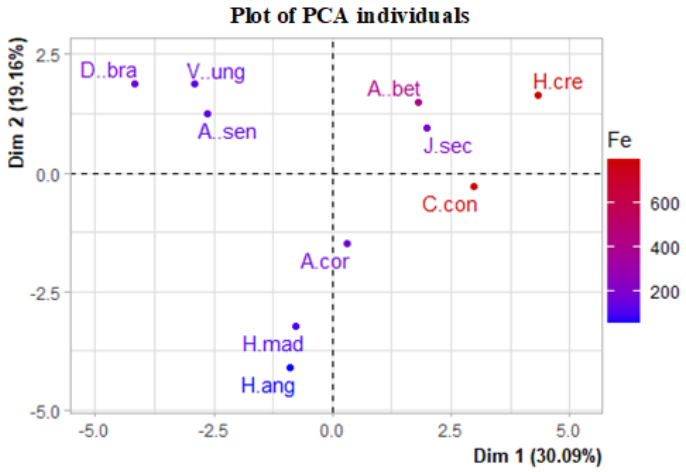


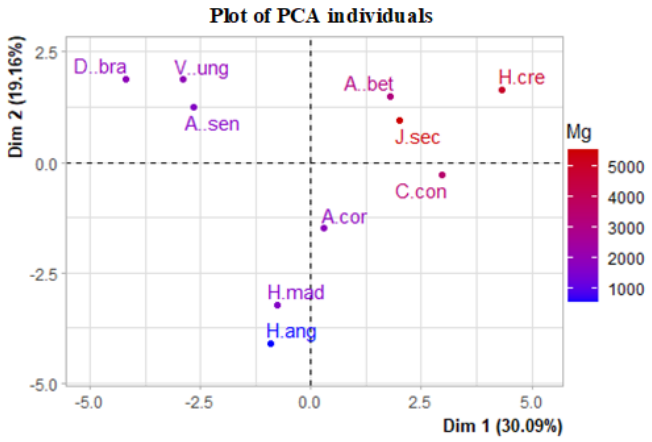
Figure 1 shows that copper content is high in *D. brazzae* while it is low in *C. congolensis*

Figure 2:
Fe content in the plants



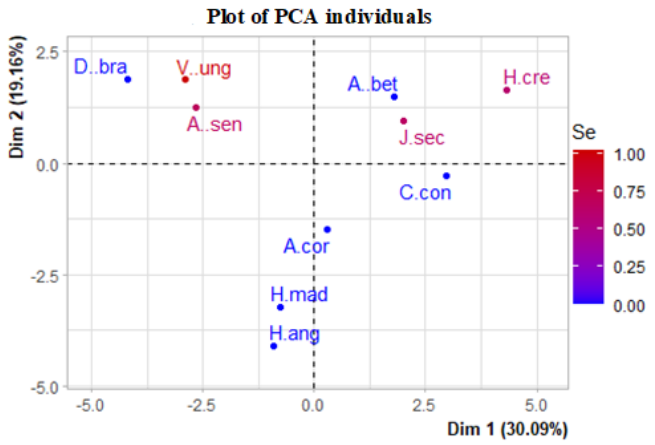
From Figure 2, it can be seen that: Fe content is high in *H. crepitans* followed by *C. congolensis* while in *H. angustifolia* it is low. This high Fe content in *H. crepitans* is the reason for the use of this plant in the management of sickle cell patients in Kwilu when the haemoglobin level in the latter decreases. We found this to be the case with guinea pigs whose haemoglobin levels were measured before and after dipping their shaved legs in a macerate of this plant. The hemoglobin content increased after this operation.

Figure 3:
Mg content in the plants



From Figure 3, it was found that the Mg content was high in *J. secunda* while it was low in *H. angustifolia*.

Figure 4:
Se content in the plants



As shown in Figure 4, Se content is high in *Vigna unguiculata* commonly known as "mbwengi" which is an important food for sickle cell patients. The same element is found at low levels simultaneously in *H. madagascarensis* and *H. angustifolia*. Se is an activator of glutathione peroxidase, an important enzyme for erythrocytes.

Figure 5:
Zn content in the plants

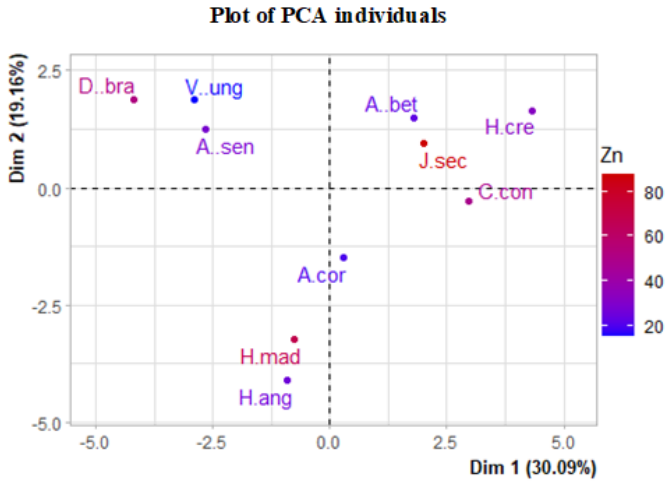


Figure 5 shows that the content of Zn, an important element for sickle cell disease, is high in *J. secunda*, a plant used by Jehovah's Witnesses to avoid transfusion (Kitadi, 2020b), while the content of this element is low in *A. cordifolia*, commonly known as "Mbunzi mbunzi". The content obtained for each of these elements confirms that obtained by X-ray fluorescence in this study.

CONCLUSIONS

The objective of this study was to determine the mineral composition of the ten medicinal plants used in traditional Congolese medicine in the province of Kwilu in the management of sickle cell disease. The results obtained confirm that these plants contain some mineral elements, and their concentration was determined.

The mineral elements measured have different contents. Iron, Zinc, Selenium, Copper, Calcium, Magnesium, and Manganese were found to be mineral elements associated with sickle cell disease. Potassium and Calcium exhibited higher concentrations, while Lead, Tin, Bromine, Copper, and Nickel were present in trace amounts. By incorporating these plants, rich in minerals such as iron, calcium, and magnesium, into the diets of sickle cell patients, it is possible to help alleviate the nutritional deficits often associated with this disease, while offering additional benefits for the overall health of individuals. This study opens the way to new complementary therapeutic approaches that could be integrated into public health programs aimed at improving the quality of life of patients suffering from this disease. However, further research would be desirable to determine the optimal doses, administration modalities, and possible side effects of these plants.

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Ethical Approval: Nil required

Conflicts of Interest: None declared.

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