In-vitro Biological Study of Sudanese Medicinal Plants for their Anti-diabetic and Antiretroviral Activities

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The uses of medicinal plants as a source of medicine is an inherent part of the traditional medicine practice worldwide. For example, more than 70% of physicians prescribe Kampo drugs today. On the other hand, in low- and middle-income countries traditional medicine and the use of herbal remedies is more widespread, owing to the fact that natural plants sources are abundantly available and can provide safe, stable, standardized, and cost-effective alternative to conventional drug therapy. In the Africa countries such as Sudan, diabetes mellitus, a non-communicable disease (NCD), have become the principal cause of morbidity and mortality, with an overall prevalence of 10.9% among adults, according to the International Diabetes Federation (IDF). On the other hands, a communicable disease (CD) like acquired immune deficiency syndrome (AIDS) has estimated to affect more 36.9 million people worldwide. In fact, Sudan is neighbored by countries with high rates of HIV infection, suggesting that HIV is the prospective annoying risk factor among Sudanese health sectors.

In this study, we took in our consideration the natural medicinal plant recourses value in Sudan and its possibility to help or treat Sudanese people in both communicable diseases and non-communicable diseases. First, we screened 18 Sudanese medicinal plants using for their anti-diabetic and anti-obesity activates (Chapter 1). Secondly, we evaluated 46 Sudanese medicinal plants for their increase of HIV-1 long terminal repeat (LTR) transcriptional activity (Chapter 2). Thirdly, we isolated and identified the bioactive chemical compounds from the aerial part of medicinal plant Gegeria *alta* (*G.alata*) and finally evaluated their *in-vitro* anti-diabetic and *in vitro* activity as HIV-1 latency-reversing agents (Chapter 3). The overall findings are summarized as follows:

Chapter 1. *In Vitro* Antidiabetic Activity of Selected Sudanese Medicinal Plants

Among 18 Sudanese plants extracted with either water or 70% ethanol we found:

1) Both 70% ethanol and water extracts of *Acacia nilotica*, *Ziziphus spina-christi*, *Abrus precatorius*, and *Geigeria alata* along with the 70% ethanol extract of *Martynia annua* showed potent free radical scavenging activity.

2) Both extracts of *Acacia nilotica*, *Ziziphus spina-christi*, *Geigeria alata*, and *Cyperus rotundus* showed potent α-glucosidase inhibition activity. While the 70% ethanol extracts were more potent compared to water extracts with exception of *Cordia sinensis* and *Cymbopogon proximus*, for which water extracts also showed potent enzyme inhibitory activity.

3) Similarly, water extracts of *Acacia nilotica* and *Ziziphus spina-christi* showed potent inhibitory activity against pancreatic lipase enzyme.

4) Moreover, the genotoxicity and cytotoxicity assay findings suggest that although some of the tested bioactive extracts can be cytotoxic and/or genotoxic, their use within the safe concentration limits or as pure bioactive compounds can be of great benefit therapeutically.

Chapter 2. Identification of Novel HIV-1 Latency Reversing Agents from Sudanese Medicinal Plants

Among 46 Sudanese plants extracted with either water or 70% ethanol we found:
1) Among screened extracts, five plant species were found to induce HIV-1 transcriptional activity, namely, *Acacia nilotica, Blepharis linariifolia, Geigeria alata, Dicoma tomentosa,* and *Ruta graveolens.*
2) The activity of these plant species was then reevaluated using different polarity solvents. The 70% ethanolic extracts of *Geigeria alata* and *Dicoma tomentosa* showed dose-dependent LTR activity. Whereas for their acetone extracts, the activity was significantly decreased at the highest concentrations, especially for *Dicoma tomentosa* extract which might indicate the induction of cytotoxic activity.

Chapter 3. Extraction, Isolation and Characterization of Bioactive Compounds of *Geigeria alata* and Evaluation of *in vitro* Bioactivities

1) In search of bioactive lead compounds, **Geigeria alata** which was found to have the most active plant extracts was subjected to different column chromatography MCI gel CHP20P, Sephadex LH20, ODS and silica gel to isolate and characterize the bioactive compounds. Two Flavonols (Kaempferol and Quercetin) and a chlorogenic acid derivative (3,5-Di-*O*-caffeoylquinic acid) were isolated.
2) The isolated compounds from *Geigeria alata* was investigated for the potential mammalian α-glucosidase and porcine pancreatic lipase inhibition activity. Interestingly both Flavonols (Quercetin and Kaempferol) showed potent α-glucosidase and lipase enzymes inhibition.
3) The isolated Flavonols, despite their potent enzymatic inhibition, showed cytotoxic activity in insulin-resistant HepG2 cells.
4) The isolated 3,5-di-*o*-caffeoyquninic significantly promoted the glucose uptake in insulin-resistant HepG2 cells without any significant cytotoxicity, this may be a reported anti-diabetic mechanism for the compound.
5) Although the isolated compounds did not show significant induction for the HIV-1 transcriptional activity alone, the combination with LRAs in the TZM-bl cells resulted in a significant synergistic effect of the tested compounds.

Collectively, these results suggest that *Geigeria alata* can be a potential source of bioactive compounds against both diabetes and HIV.