Contamination of Herbal Medicines with Antiretrovirals (ARVs) and Widespread use by PLWH in Nigeria

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Background

- Nigeria has an estimated 3.3 million people living with HIV, accounting for nearly 10% of global HIV burden[1].
- Use of herbal/traditional medicines is high in the general population and HIV infected individuals[2,3], but use in relation to ARV initiation is not well characterised
- Contamination of herbal/traditional medicines with antiretrovirals has not been previously studied.
- We evaluated the use of herbal medicines amongst persons living with HIV (PLWH), and undertake a country-wide analysis of herbal medicines for possible contamination with antiretrovirals (ARVs).

Methods

**a) Contamination of Herbal medications with ARVs**

- Herbal samples were collected from urban and rural sites in 8 states across Nigeria (Figure 1), using a standard protocol as follows:
  - Approach street vendors requesting traditional remedies for non-specific symptoms against a background of HIV.
  - Only herbals sold as powders or liquids were purchased; instructions for use, date, and location were recorded.
- Initial screen: each sample dissolved in water or DMSO (10mg/mL) to make a stock solution, which was diluted (1:1) in mobile phase prior to injection (10 μl) onto a Phenomenex Hydro-RP C18 column, and analysis by LC-MS/MS (Thermofinnegan-Ultra). A similar preparation of reference drug standards at two concentrations (50 ng/mL and 100 ng/mL) was also injected. Reference drugs analysed were emtricitabine, tenofovir, lamivudine, efavirenz, nevirapine, lopinavir, darunavir, ritonavir, and atazanavir (adapted from [4]
- Herbal samples which tested positive were subjected to confirmatory reanalysis as follows: higher concentrations (50 mg/mL) of stock was prepared and reanalysed as above, together with reference drug standards.
- Semi-quantitative estimation of the amount of drug present as contaminant was possible based on comparison of relative peak heights with both reference drug standards.

b) Survey of herbal medication use among PLWH:

- Clinical survey of 742 PLWH attending ARV facilities in one rural (Rural Hospital Idong) and three urban facilities (Specialist Hospital Gombe, Faith Alive Foundation Clinic Jos and Dalhatu Araf Specialist Hospital Lafia) using a structured questionnaire.
- For paediatric patients, information was obtained by interviewing their mothers.
- The data collection aimed at determining the prevalence of herbal medication use among PLWH attending Antiretroviral Therapy clinics
- Data were analysed using IBM SPSS statistics version 22.0 (IBM Corp. 2013).

Results

Figure 1 – Sample Collection Regions
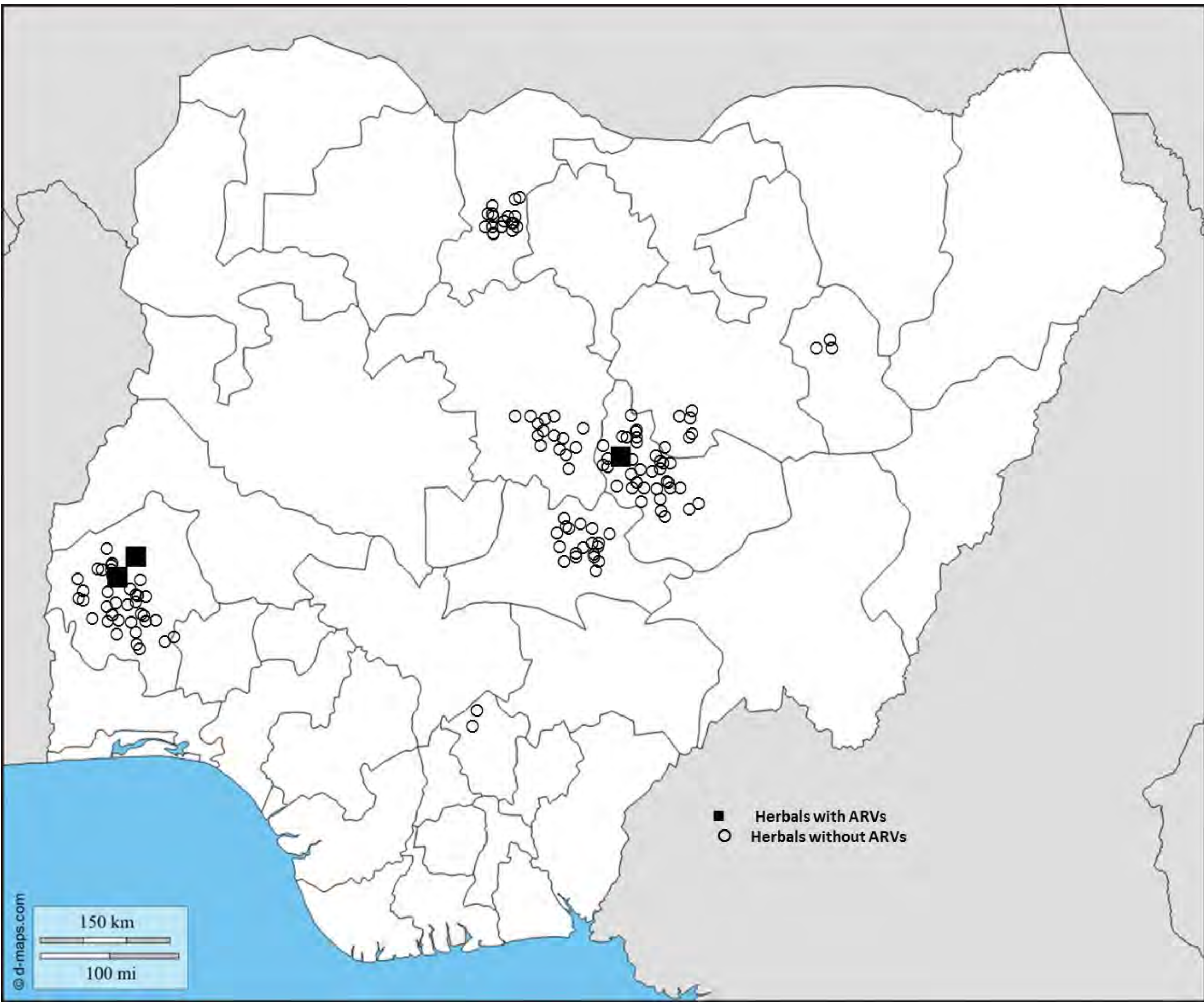
- 138 herbal samples were collected from vendors across 8 States.
- 3 (2%) samples from 2 cities (Jos and Ibadan) contained measurable antiretrovirals.
- Tenofovir and emtricitabine were detected in one sample from Jos (North-central) and two samples from Ibadan (South-west), with lamivudine also detected in one sample from Ibadan.
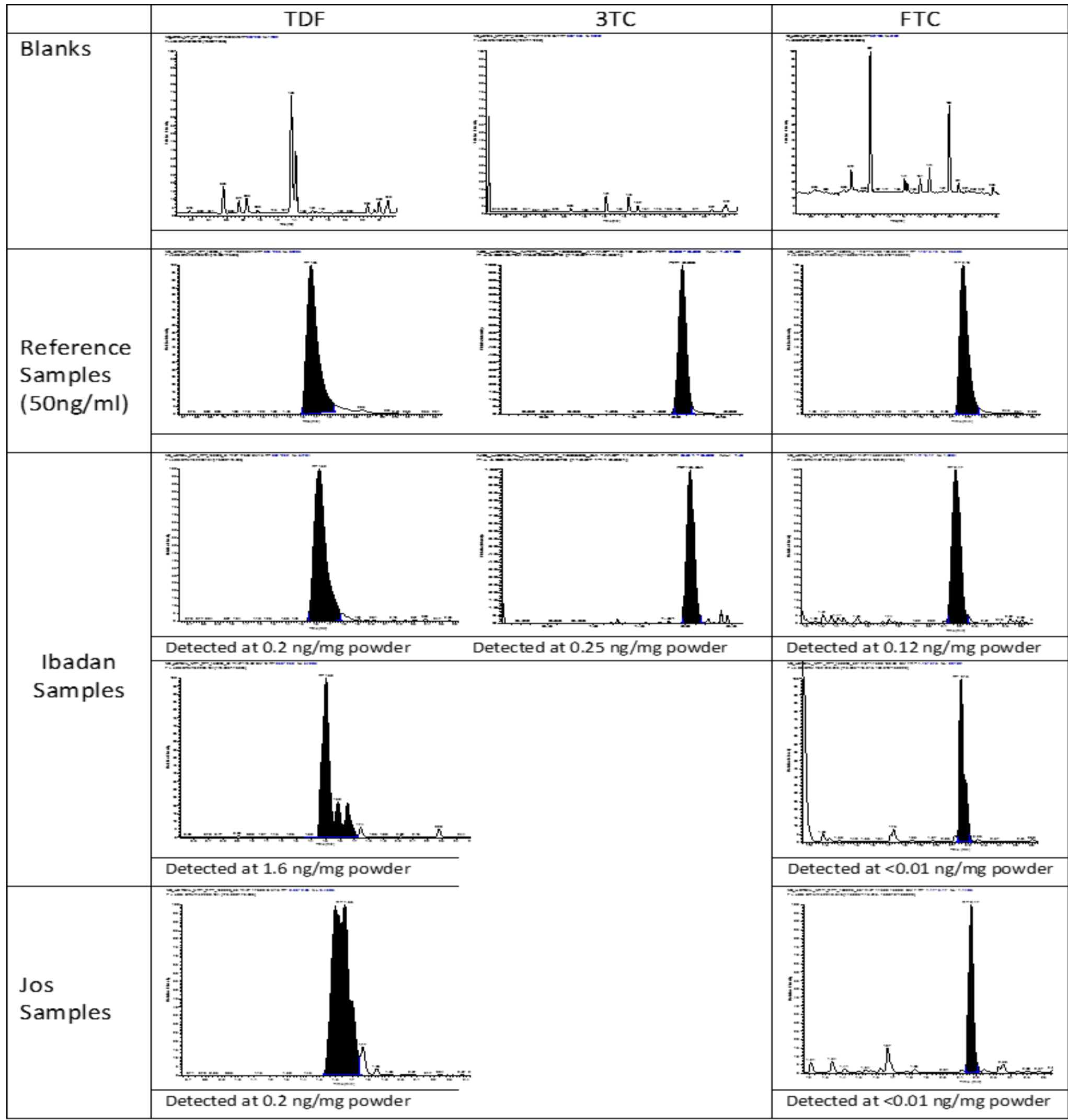
Figure 2 – Chromatograms

Table 1 – Herbal Medication Use among PLWH

Variable	Frequency (%)
Use of Herbal medications Amongst PLWH	
• Use herbal medications	310(41.8)
• Do not use herbal medications	430(58.0)
Total	**740(99.8)**
Initial herbal/traditional medicines use	
• Pre-HIV Diagnosis	150(54.9)
• Post-HIV Diagnosis	123(45.1)
Total	**273(100)**
Source of herbal medicines	
• City vendors	94(35.1)
• Village herbalist	145(54.1)
• Others	29(10.8)
Total	**268(100)**
Reasons for use of herbal medicines	
• Relieve symptoms	108(40.3)
• Achieve cure	145(54.1)
• Others	15(5.6)
Total	**268(100)**
Perceived effectiveness of herbal medication	
• No help	125(46.1)
• Moderate relieve of symptoms	89(32.8)
• Completely relieved symptoms	43(15.9)
• Cures disease (HIV) completely	14(5.2)
Total	**271(100)**

Conclusions

- We observed that use of traditional medicines was widespread (Table 1) regardless of age, gender, educational or employment status.
- In over half of cases, traditional medicine use preceded the initiation of ARVs and persisted alongside ARV use (85.2% of PLWH who use herbal medications are on ARVs).
- Despite this, herbal use was poorly recorded in ARV case notes (personal observation)
- Nearly half of patients did not perceive benefit from traditional medicines.

- Traditional healers and their medicines play an important role in supplementing and supporting treatment programmes including HIV. Often they fulfil an unmet need within the context of a system of complex cultural beliefs, and of symptom management.
- Lack of regulation and standardisation in these preparations argues strongly for further work to confirm our findings in other treatment settings, and to understand whether ARV contamination of traditional medicines has a negative impact on ARV programmes through the generation of drug resistance.

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