

African Traditional Medicine Use amongst People Living with HIV/AIDS in Sub-Saharan Africa in the Era of Antiretroviral Therapy

Mncengeli Sibanda*, Panjasaram Naidoo and Manimbulu Nlooto

University of KwaZulu Natal, Discipline of Pharmaceutical Sciences, Durban, South Africa

*Corresponding author: Mncengeli Sibanda, University of KwaZulu Natal, Discipline of Pharmaceutical Sciences, Westville Campus, Private Bag X54001, Durban, KwaZulu 4000, South Africa, Tel: +27725877246; E-mail: mncengelis@gmail.com

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Abstract

It is estimated that 80% of the global population uses alternative or traditional medicine. In resource poor countries, traditional health practitioners are the primary and often the only providers of health care to the majority of the population including people living with HIV/AIDS (PLWA). Globally, there are approximately 36.9 million people living with HIV and nearly 70% of these are in Sub-Saharan Africa. PLWA often use African Traditional Medicines either alone or in combination with western medicines including antiretroviral therapy.

The purpose of this review is to consider from available literature, the current trends in traditional medicine use amongst PLWA in Sub-Saharan Africa. This review also evaluates the existing research literature on the collaboration efforts between traditional health practitioners and orthodox medical practitioners in HIV/AIDS interventions. The commonly used traditional medicines in the management of HIV/AIDS as well as safety and potential Drug-herb interactions will also be considered in detail.

Keywords: African traditional medicines; AIDS; Highly active antiretroviral therapy; Traditional medicine; Drug-Herb interactions; HIV; Pluralism

Introduction

In Sub-Saharan Africa, the ratio of traditional healers to the general population is approximately 1:500, while doctors trained in “Western” medicine have a 1:40000 ratio to the rest of the population [1]. It is estimated that approximately 70% to 80% of the population in Sub-Saharan Africa uses the services of Traditional Health Practitioners (THP) [2]. Many developing countries have a pluralistic healthcare system wherein a modernised first world medical system co-exists with a variety of non-conventional health care systems such as local indigenous systems founded on traditional beliefs and practices [2].

In Sub-Saharan Africa, the use of modern medicines has never fully replaced the indigenous system, and THP continues to be consulted by the population for a variety of reasons [1]. The indigenous health system is not considered to be of a lower standard when compared to western medicine, but is thought to be desirable and necessary for treating a range of health problems that western medicine does not treat adequately. African Traditional Medicines (ATM) are a credible and convenient source of health care and dual treatment regularly takes place as a result [2]. THP thus has a crucial role to play in building the health systems in Sub-Saharan African countries [3].

HIV/AIDS has grown to pandemic proportions and has become a major health problem worldwide. Globally, an estimated 36.9 million people are living with HIV and nearly 70% of these are in Sub-Saharan Africa [4]. PLWA often use a wide range of TM products together with their Antiretroviral (ARV) in the treatment of HIV/AIDS related illnesses [5].

Although the use of Traditional Medicines (TM) is widespread, their use is not well researched, and consequently poorly regulated [6]. Limited meta-analyses of safety and efficacy exist and low-level evidence of harm identifies the potential for drug interactions with many medicines including the commonly used ARV [6].

HIV/AIDS and antiretroviral therapy (ART)

HIV/AIDS has become a major health problem worldwide with over 34 million people having died as a result of AIDS related illnesses since the beginning of the epidemic [4]. According to the 2014 UNAIDS update 69% of people infected with the HIV live in Sub-Saharan [4]. South Africa in particular, has an estimated 6.8 million people living with HIV and this represents the largest number of people living with HIV in any country in the world [7]. HIV/AIDS has worsened the demands on the health care system in Africa and has put an already overburdened system under further strain [4].

Antiretroviral Therapy (ART) using Antiretroviral drugs (ARV) is the only proven management of HIV-infection and have led to reduction in HIV related opportunistic infections and AIDS related deaths, and have thus improved substantially the quality of life in PLWA [8]. The effective distribution and uptake of ART is an essential component of any successful HIV/AIDS management strategy [8].

In 2012, Africa was leading the world in expanding access to ART with over 7.5 million people in Sub-Saharan Africa accessing the lifesaving ART [9]. South Africa alone has the world's largest ART programme, with over 2 million people estimated to have been enrolled [7].

In June 2016, the consolidated guidelines on the use of ARV for treating and preventing HIV infection were revised to recommend that ART should be initiated in all adults living with HIV, regardless of the WHO clinical stage and at any CD4 cell count and that Oral Pre-

Exposure Prophylaxis (PrEP) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches [10]. Also, the guidelines recommend fixed-dose regimen (FDC) made up of the regular three drugs used in the first-line regimen (Tenofovir+Emtricitabine (or Lamivudine)+Efavirenz) as first line treatment in order to improve adherence and retention [10]. It is envisaged that the number of people receiving ART will increase drastically in line with the new recommendations.

ATM policy and the roles of THP in the management of HIV/AIDS

The Alma-Ata International Conference on Primary Health Care in 1978 was one of the first global attempts to include THP in primary health care [11]. Subsequent to that, the World Health Organization (WHO) Traditional Medicine Strategy 2002-2005 and the current WHO Traditional Medicine Strategy 2014-2023 were published [2]. Amongst other objectives, the strategies seek to promote universal health coverage by integrating TM services into health service delivery and self-health care by capitalising on their potential contribution to improve health services and health outcomes, and by ensuring users are able to make informed choices about self-health care [2].

In 2002, SADC ministers of health established a policy which promoted the use of TM for the treatment of HIV/AIDS and associated illnesses [11]. The policy, recommended the use of *Sutherlandia frutescens* (Common name: Cancer bush) and *Hypoxis hemerocallidea* (Common name: African Potato) in the management of HIV/AIDS [11].

The Organisation of African Unity (OAU) in 2003 declared a decade of traditional medicine (2001-2010) and instituted a plan of action and implementation for traditional medicines [12]. The plan's main objective was the recognition, acceptance, development and integration/institutionalisation of traditional medicine for Malaria, HIV/AIDS and other related infectious diseases, by African countries into their public healthcare systems by the year 2010 [12].

The Association for the Promotion of Traditional Medicine (PROMETRA) is an international body whose mission it is to preserve ATM, culture, and indigenous science through research, education, development and advocacy to improve the health and well-being of Africans [13]. In its Dakar Conference in 1999, PROMETRA mapped an action plan on how the traditional healers could be involved in the fight against HIV/AIDS. Some of the recommendations were;

- An increase in the involvement of traditional healers in the prevention of HIV/AIDS.
- Use traditional healers as information, education and communication agents.
- Provide training sessions for traditional healers in AIDS education.
- Engagement of TM in the treatment of opportunistic infections associated with HIV/ AIDS.
- Exchange and referral of patients between the two medical systems [13].

Regardless of the limited evidence of the efficacy of ATM in HIV infected people many African governments passed legislation and adopted policies in the early 2000's that would incorporate Traditional Health Practitioners (THP) to be the mainstay of their health systems. In South Africa, the government established a Directorate of Traditional Medicine within the Department of Health in 2006 in

order to deal with issues relating to ATM and the professionalization of THP through the Traditional Health Practitioners Act of 2007 (THPA) [14]. The THPA promotes the training and practice of THP, and proposes the establishment of certified institutions for their training and most importantly, criminalises THP claims to "prescribe a cure for cancer, HIV and AIDS or any other prescribed terminal illness" [5]. This was a progressive step in limiting the activities of 'charlatans' who dissuade patients to adhere to the ART [14].

A 2005 Cochrane review of Herbal Medicines for Treating HIV Infection and AIDS found insufficient evidence to support the use of herbal medicines in HIV-infected individuals and AIDS patients and that the potential for any benefits needed to be studied further [15].

Antiretroviral therapy and drug-herb interactions

Typically, Drug-Drug Interactions (DDI) and Herb-Drug Interactions (HDI) may occur in at any of the stages of Absorption, Distribution, Metabolism and Excretion (ADME) phases of the pharmaceutical disposition of the drug in the human body affecting the entire pharmacokinetic profile of the drug [16]. Antiretrovirals (ARV) are categorised as Reverse Transcriptase Inhibitors (nucleoside and non-nucleoside), Protease Inhibitors, Fusion Inhibitors, Entry Inhibitors and Integrase Inhibitors. Studies have shown that most ARV are metabolised via the cytochrome P450 3A4 enzyme system (CYP3A4) and the p-glycoprotein systems [17].

Protease Inhibitors (PIs) and non-nucleoside reverse-transcriptase inhibitors in particular have a relatively narrow therapeutic index and so it is essential that the bioavailable dose is maintained at optimum level [17]. Lopinavir/ritonavir (LPV/r) is a commonly used protease inhibitor combination that is often included in some second line regimens of ART. Lopinavir, is metabolised primarily by hepatic and gastrointestinal cytochrome P450 3A (CYP3A), is 'boosted' by ritonavir through inhibition of CYP3A [16,17]. Lopinavir and ritonavir are both substrates for and inhibitors of CYP3A4, caution is warranted in the case of co-administration of LPV/r with medicinal products that are also CYP3A4 substrates or whose activity may alter CYP3A4 activity [18].

Herb-induced inhibition or induction of the cytochrome enzymes can alter the metabolism of ARVs, leading to adverse effects or lack of efficacy [18]. The concomitant intake of TM in patients using ARVs may result in lowering of plasma drug concentrations resulting in treatment failure, drug resistance and possibly death of the patient [16]. Alternatively, concomitant intake may also result in increased plasma drug concentrations resulting in drug toxicity [16].

Commonly used ATM in Sub-Saharan Africa in the management of HIV/AIDS include *Hypoxis hemerocallidea*, *Echinacea purpurea*, *Moringa oleifera*, *Taraxacum officinale* and *Lessertia frutescens* [19]. Mills et al. showed that extracts of hypoxis had significant effects on cytochrome P450 3A4 *in-vitro* metabolism and so potentially could result in sub-therapeutic plasma concentrations [18]. The nutritional herb, *M. oleifera* was been shown to inhibit 6 β -hydroxylation of testosterone by CYP3A4 and may potentially interact with ARV medication [20]. In a 2012 study, *Sutherlandia* was shown *in-vitro* to have potential for HDI in general and specifically for the ARV, Atazanavir [21,22].

The above findings were affirmed by a 2014 laboratory study of the inhibition of major drug metabolizing enzymes by *H. hemerocallidea*, *E. purpurea*, *M. oleifera*, *T. officinale* and *L. frutescens* The 2014 study

demonstrated that the ATM have the potential to interact with ARV [23].

A 2013 study on adult volunteers, by Gwaza et al. showed that hypoxis when taken concurrently with LPV/r is well-tolerated and is not associated with clinically significant changes in LPV/r pharmacokinetics [24]. Similarly, a 2012 study done in Zimbabwe showed that some commonly used ATM may not have an impact on adverse event outcomes for patients taking antiretroviral drugs with occurrence of adverse events dependent on the amount and frequency of herbal remedies taken [25]. A 2016 study on adults in South Africa taking ART and ATM concurrently found no significant differences in the CD4+ and inconclusive effects on HIV viral Load, between patients taking both ARV and ATM concomitantly and those using ARV alone [26].

Medical pluralism in the era of ART

Cant and Sharma define medical pluralism as the co-existence and use of more than one healthcare system for perceiving and treating diseases [27].

Since the early 2000's, the access to ARV across much of sub-Saharan Africa, has been enhanced through increased health budgets in most countries and especially through the support of major international donor programmes such as the Joint United Nations Programme on HIV and AIDS (UNAIDS), the Global Fund to Fight AIDS, Tuberculosis and Malaria, the US President's Emergency Plan for AIDS Relief (PEPFAR), Medicins Sans Frontieres (MSF), the Bill and Melinda Gates Foundation, as well as other domestic programmes [28]. As of March 2015, 10.7 million (41%) of people in sub-Saharan Africa living with HIV were accessing antiretroviral therapy [29]. At the same time, even the most comprehensive ARV rollout programmes will not assure that people will have confidence in the system, and it is here that the role of traditional healthcare is crucial [28].

There is evidence which shows that traditional medicines have been in existence since ancient history [2]. In Africa, ATM continued to be the only available health care option in Africa for many centuries and western medicine was only introduced through colonisation [1,2]. Western medicine is therefore a relatively new phenomenon in most of Africa and many Africans still prefer their cultural beliefs, which include consulting with THP [30]. It is widely believed that the popularity of the traditional health care system in Africa is due to the fact that amongst the African population, ATM are an acceptable, credible and convenient source of health care [30]. In addition, THP are thought to offer a more holistic, patient-centred and personalised service which also caters to social and spiritual beliefs which most Africans hold strong [28].

During the peak of the HIV/AIDS pandemic in the late 1990's, when ARVs were largely unaffordable and inaccessible, ATM were the mainstay of HIV management amongst PLWA in Africa [28]. The use of ATM was to improve the quality of life and increase life expectancy in PLWA. The advent of ARV rollout programs did not substitute ATM use amongst the population [30]. Studies show that PLWA use for ATM use to supplement dietary intake, to boost energy levels, to alleviate side effects of ART, to cure opportunistic infections, to improve immune response as well as a misguided belief that some ATM can even cure HIV/AIDS [28,30,31]. A study by Mngqundaniso et al. revealed that 4.1% of 618 PLWA interviewed at three hospitals in the KwaZulu Natal (KZN) region of South Africa believed that they could cure HIV through only the use of TM [28].

The 2008 study by Mngqundaniso et al. in KZN, South Africa on treatment naïve PLWA also found ATM had been used for HIV in the past six months by 51.3% [28]. In Uganda, a 2007 study showed that 63.5% of PLWA had used TM after HIV diagnosis and same-day, concomitant ATM and ARV use was reported by 32.8% of the patients surveyed [31]. In a tertiary hospital in Kano, Northwest Nigeria, it was found that 4.25% of the 430 patients surveyed used ARV and traditional medicine concomitantly [32]. A survey of 67 PLWA done at three ART centres in the Kumasi Metropolis in Ghana found that concomitant TM and ARV use was reported by 53.2% of the patients [33]. An astounding 98.2% of 388 patients interviewed at the Family Care Centre (FCC) ART clinic in Harare, Zimbabwe were found to be using at least one ATM concurrently with their ARV medication [25].

A 2012 cross-sectional study which involved 100 participants enrolled at ARV clinics in two South African provinces showed that 79% of PLWA has used TM prior to a diagnosis of HIV [34]. This figure was in which is in keeping with WHO estimates on ATM use [2]. The study also showed that participants were more likely to use ATM if they were from a rural province, female, older, unmarried, employed, had limited education, or were HIV-positive for less than five years [34]. This same study showed that less than 20% of participants used ATM and ARV simultaneously. A similar study done 2016 in on 281 South African patients found that 4.98% used ATM and ART concurrently [25].

Discussion and Recommendations

ATM are still widely used by the general African population and will still most likely continue to exist as an important component of African traditional culture. If properly regulated and included into the formal HIV/AIDS management programs, THP could be an invaluable resource in the primary health care management of the disease.

It is vital that PLWA inform their orthodox health care provider about their use of ATM for both HIV-related illnesses and other illnesses. Health care providers must likewise be reminded to investigate ATM use in PLWA during counselling sessions or as part of their history taking and clinical assessments. Failure to do so may expose the patient to Herb-Drug interactions with subsequent potential treatment failure or injury.

Although some data on the benefits of ATM use in PLWA exists, much more comprehensive clinical trials and meta-analyses are needed to validate preliminary results on the efficacy and safety of these alternative treatments. The biological effectiveness of ATM needs to be ascertained by further studies before their wholesale recommendation to PLWA.

In addition, the majority of the available evidence on Herb-Drug interactions are based on *in-vitro* studies. It will be vital, therefore, to conduct randomised controlled studies in human volunteers to determine the safety of ATM in PLWA who are using ART including the use of population pharmacokinetic approach in order to make the results more generalisable and to better establish a link between ARV plasma levels and concurrent ATM use.

Until the availability of more evidence, it is prudent for health professionals to continuously exercise caution when counselling patients about concomitant ATM and ART use.

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