Clinical relevance and use of traditional, complementary and alternative medicines for the management of HIV infection in local African communities, 1989-2014: A review of selected literature

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Abstract

Conventional medicine has long benefited from traditional medicinal knowledge through pharmaceutical innovations. Management of HIV infection may benefit from the African indigenous medical knowledge through a transparent collaboration between practitioners of biomedicine and African traditional medicine. This review summarises studies investigating African traditional medication therapies with clinical relevance to management of HIV and related opportunistic infections and to assess their findings in HIV-infected individuals.

An advanced search was conducted online in Sabinet, to identify articles with historical background on the topic for South Africa and Africa. The search was then broadened to include peer reviewed English and French language literature published in the period from 1989 to 2014 in the following databases: Medline (PubMed) via EbscoHost, Science Direct, AMED, Cochrane Library, and Google scholar. After potential relevant articles were identified; the selection criteria were narrowed to include medication therapies with an effective impact on clinical indicators of HIV disease progression (viral load and CD4 count), treatment of opportunistic infections, and improvement in quality of life. We identified ten studies reporting results either on increase of CD4 count or decrease in viral load; four studies reported improvement on quality of life and HIV related symptoms. The usefulness of African traditional medicines in the management of HIV infection has been demonstrated by the improvement of CD4 count, reduction of viral load and or amelioration of quality of life in HIV-infected individuals but these improvements have not yet led to products that can be used at a massive scale for the management of HIV. This may be due to the fact that clinical trials that are needed to ensure product development have not been conducted. There is an urgent need for more research.

Keywords: African traditional, complementary, alternative medicine, HIV, AIDS, clinical studies, evidence, health benefits, risks.

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Introduction

Combination antiretroviral therapy was introduced in 1996 in the Western world (Moore et al, 2003). Long before its advent the World Health Organization (WHO) encouraged efforts to include traditional healers in responses to human immunodeficiency virus and acquired immune deficiency syndrome (HIV/AIDS) (WHO, 1989; King, 2000).

Traditional use or knowledge refers to –

'the *customary utilisation or knowledge of indigenous biological resources by an indigenous community, in accordance with written or unwritten rules, usages, customs or practices traditionally observed, accepted and recognised by them, and include discoveries about the relevant indigenous biological resources by that community; while traditional knowledge, for example, may imply old knowledge that has been passed on through generations, and is often related to time. Indigenous knowledge may refer to the knowledge of peop1 le of a geographical area, who may hold traditional knowledge but also have evolved technologically advanced knowledge"* (South African National Department of Environmental Affairs, 2012).

According to the WHO *"traditional Medicine(TM) is a comprehensive term used to refer both to traditional medicine systems such as traditional Chinese medicine, Indian Ayurveda and Arabic Unani medicine, and to various forms of indigenous medicine. In countries where the dominant health care system is based on allopathic medicine, or where TM has not been incorporated into the national health care system, TM is often termed 'complementary, 'alternative" or "non-conventional" medicine (*WHO,2002a). The terms complementary and alternative medicines also refer to "a *broad set of health care practices that are not part of a country's own tradition, or not integrated into its dominant health care systems (WHO, 2002b).* Conventional medicine is generally known as the westernised mainstream medical treatment; the National Centre for Complementary and Alternative Medicine in America defines complementary and alternative medicines (CAM) as *"a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine" (*Yates et al, 2005).

Although conventional medicine is disease centred, as opposed to the holistic characteristic of traditional, complementary and alternative medicines, all these different types of medicines may find a common ground in the use of medicinal plant extracts. Conventional medicine has long benefited from traditional medicinal knowledge through pharmaceutical innovations. To briefly name a few, artemisinin and lovastatin were extracted from medicinal plants or natural products *Artemisia annua*, and oyster mushrooms and red yeast rice respectively (Shetty, 2010). Based on epistemic relativism which suggests that knowledge is bound to time and culture (Macionis and Plummer, 2008), this review seeks to explore treatment modalities based on African traditional medicine or complementary and alternative medicines (CAM) with clinical relevance to the management of HIV and related opportunistic infections in the period from 1989 to 2014 in local African communities.

The United Nations estimated that 34 million people were HIV positive in 2012; sub-Saharan Africa accounted for the majority of this population with 23.5 million people infected, and South Africa had the largest number of HIV infections with 5.6 million infected people

residing within the borders of the country in the same year (Joint United Nations Programme on HIV/AIDS (UNAIDS) report, 2012). The last decade (2001-2010) saw many developing countries, including South Africa, implementing public antiretroviral programmes. But more or less 46% of those currently eligible for combination antiretroviral therapy, also known as highly active antiretroviral therapy (HAART), did not have access to it in 2012 and the vast majority was in the low-and –middle income countries with a high burden of the HIV epidemic (UNAIDS, 2012).

In contrast to poor accessibility to conventional medicine, between 70% to 95 % of the general population in Africa, Asia, Latin America and Middle East reportedly rely on traditional and herbal medicines to fulfil their health care needs and concerns; nonetheless in some developed nations such as Canada, France, Germany and Italy more than 70% of the general population have resorted to the use of traditional medicine under the titles of complementary, alternative and non-conventional medicines (Robinson and Zhang, 2011). Individuals with the most serious and debilitating medical conditions such as cancer, chronic pain, HIV and AIDS tend to be the most users of such practices (Bodeker et al, 2005). Despite the success of combination antiretroviral treatment and limited evidence on safety and efficacy of complementary and alternative medicines, many HIV –infected individuals in the developed world have used the latter practices (Littlewood and Vanable, 2008). On the African continent people diagnosed with HIV infection had consulted a traditional health practitioner prior to conventional antiretroviral therapy and sometimes after joining antiretroviral programme (Awodele et al, 2012; Mbatha et al, 2012; Namuddu et al, 2011; Nagata et al, 2011; Peltzer et al, 2008).

To determine our current state of knowledge on treatment modalities under traditional, complementary and alternative medicines in local African communities, this review summarises studies investigating non-conventional medication therapies with clinical relevance to HIV and related opportunistic infections management and to assess their findings in HIV infected individuals.

Methods

Data sources

With the help of a senior subject librarian in health sciences, an advanced search was conducted online in Sabinet, to identify articles with historical background on the topic for South Africa and Africa. The search was then broadened to include peer reviewed English and French language literature published in the period from 1989 to 2014 in the following databases: Medline (PubMed) via EbscoHost, Science Direct, AMED, Cochrane Library, and Google scholar. A variety of searches was conducted using a combination of the following keywords: HIV, AIDS, clinical studies, African traditional, complementary, and alternative, medicine; management, treatment modalities, healing, natural products, ethno medicines, parallel, non-conventional, clinical studies, observational, randomized, Africa, and South Africa. In addition, abstracts of

international AIDS conferences and potentially relevant articles were identified from the reference lists of some publications. We also conducted an offline search of books and official documents from the South African National Department of Health (NDOH), Department of Environmental Affairs and Department of Science and Technology. An attempt was made to identify unpublished studies through research space.

Study selection

All duplicate articles, titles expressing comments, news, letters, opinion pieces and advertisements were rejected. Articles based on African traditional medication therapies with clinical relevance for the management of HIV and related opportunistic infections were retained. The UNESCO report refers to medication therapies, under traditional, complementary and alternative medicines (TCAM), as the use of herbal medicines and or medicines based on animal parts and or minerals. Non-medication therapies refer to manual (massages), physical (qigong, Tai ji quan), mental (meditation, hypnosis) and spiritual therapies (magico-religious) or a combination thereof (yoga), while mixed therapies combine medication and non-medication therapies (United Nations Educational, Scientific and Cultural OrganizationUNESCO, 2012). According to the selection criteria 108 potential articles were identified; the selection criteria were narrowed to include medication therapies with an effective impact on clinical indicators of HIV disease progression (viral load and CD4 count), treatment of opportunistic infections, and improvement in quality of life. Emphasis was on randomized controlled, non-randomized, and observational studies involving collaboration between biomedical trained healthcare workers and African traditional healers in the management of HIV infection.

Data extraction and analysis

From these publications, variables for the review were as follows: country, year of study, types of TCAM, participants with HIV infection, increase in CD4 count, decrease in viral load, treatment of opportunistic infections, improvement in quality of life, and use of conventional antiretroviral therapy for comparison where applicable.

Review findings

Articles found were grouped under main two themes: African traditional medicines and CAM administered under the supervision of biomedical health care providers; and self-administered traditional medicines during HAART era. We identified a total of 14 studies based on African traditional medication therapies, with at least ten studies reporting results either on increase of CD4 count or decrease in viral load (VL) while the other four studies reported improvement on quality of life and HIV related symptoms. Low levels of adherence to HAART have been reported amongst HIV patients using both self-administered traditional, complementary and alternative medicine and prescribed antiretroviral therapy.

African traditional medicines and CAM administered under the supervision of biomedical health care providers (1989-2014)

In early 1989 an informal WHO consultation group noted the usefulness of traditional Chinese medicine remedy in addition of one of the African plants, *Polyporus umbellatus, Cordyceps sinensis*, and *Paeonia obovate* where 17 individuals in Tanzania had amelioration of HIV related symptoms (WHO,1989). More recently, clinical studies supporting safety in humans have shown antibacterial and potent anti-HIV-1 properties of the root extracts of an indigenous South African plant, *Pelargonium sidoides*, licensed in Germany as the herbal medicine EPs®7630 or Umckaloabo® (Helfer et al, 2014). Similar clinical studies conducted in African local communities are described below (Table 1).

Table 1 Studies reporting the use of African traditional medicines in patients under the supervision of biomedical health care workers (1989-2014)

Author, year of Publication	Year of study	Country	Study design	Participants	Treatment, patients(n)	Control(n)	Outcome
Mtullu, 2005	1991-2005	Tanzania	Obs.	HIV+, with CD4 counts≥200	Mixture of 4 unnamed herbal plants(n=650)	HIV+ with CD4 count ≤200	↑CD4 in herbal treated patients
Homsy et al, 1999	1992-1994	Uganda	Obs.	HIV+, with herpes zoster	unnamed herbal medicine (n=44)	acyclovir tablets (n=28)	↓super infection, less keloid formation
UNDP-UNFPA, 2005	1994-1999	Ghana	Obs.	HIV+	unnamed herbal medicine (n=35)	No	80% improved quality of care and life
Taylor et al, 2008	2001	Zimbabwe	Quality of life, self-administered	HIV+ (n=254)	Unnamed traditional medicines (n=155)	-unnamed HAART (n=69)	↑61% QOL in TAC vs 39% in WM
Bashengezi,1995	1988	Zaire (DRC)	Observational	HIV+	300 mg dried extract of Uvaria brevistipitata (n=268)	No	Symptomatic remission in 60% of subjects ↑ CD4
Gbodossou, Prometra, 2002	1999-2002	Senegal	Obs.	HIV+	Mixture of 5 herbal plants, Metrafaids (n=62)	No	↑71% CD4 counts, ↓54% VL
Matsabisa, 2004	2002-2004	South Africa	double blind randomised, parallel group, placebo controlled trial	HIV+	unnamed herbal medicine (n=200)	placebo	↑199% CD4 counts, ↓79% VL, 23% weight gain
Tshibangu et al., 2004	2001-2002	South Africa	Descriptive prospective follow up	HIV+	Powder, suspension of unnamed herbal medicine (n=33)	No	↓85.4% VL ↑226% CD4 count

Elujoba, 2005	2005	Nigeria	Obs.	HIV+, with skin rashes	black soap with powered herbal medicines (n=20)	No	↓85% skin infections in 10 days
Sia, 2012	2006-2008	Burkina Faso	Double-blind randomised	HIV+	FMG341 (n=60)	HAART (AZT, 3TC, EFV)	↓VL, ↑ CD4 counts
Mokondjimobe et al, 2012.	2007-2009	Gabon, DRC, Congo, Libya	Multicenter obs. Cohort	HIV+	100 mg Fagaricine twice daily, commercial extract of Zanthoxylum heitzii(n=75)	No	↓52% of p24 in the blood, ↑ 50-100% CD4 counts at baseline 200
Onifade et al, 2013	2010	Nigeria	Obs. prospective	HIV+	Nigella sativa concoction (n=1)	No	↑CD4 counts ↓VL in 6 months
Onifade et al, 2013	2011	Nigeria	Obs.	HIV+	A-Zam(n=6)	No	↓VL
McClelland et al, 2004	1998-2000	Kenya	Randomised	HIV+ women	Multivitamins	Placebo	↑CD4 count

a. Legend: VL=viral load, ↓=decrease, ↑=increase, Obs=observational, p24=capsid protein

b. Percent (%) given as per publication

Self-administered traditional medicines during HAART era among HIV-infected patients

A certain number of studies were conducted among HIV –infected patients who used traditional, complementary and alternative medicines with prescribed highly active antiretroviral therapy (HAART) in different African communities (Table 2).

Table 2: Studies reporting use of TCAM with HAART among HIV-infected patients in different African communities.

Author, year of publication	Year of Study	Country	Study design	Participants (n)	Prevalence and types of TCAM used with HAART	HAART (n/ %)	Outcome
Babb et al, 2007	2003	South Africa	Cross sectional, interview	HIV+(n=44)	23%(7/30):TM hypoxis spp, aloe vera	Not reported	-
Malangu, 2007	2004-2005	South Africa	Cross sectional, interview	HIV+(n=180)	4.4%TM (hypoxis tea), 3.3% CAM (sex booster, medicated soap), 1.7% OTC (senokot)	Not reported	-
Langlois-Klassen, 2007	2004	Uganda	Cross-sectional	HIV+(n=137)	29.4% (40/137), TM (Vernonia amygdalina, aloe)	D4T, 3TC, NVP(triiomune 30 mg)	Rapid relief of symptoms
Peltzer et al, 2008	2007-2008	South Africa	Cross sectional	HIV+(n=618)	Use of herbal therapies (29.6%),	Not reported	-
Peltzer et al, 2010	2007-2008	South Africa	Prospective	HIV+(n=735)	7.9% use of herbal medicines after 6 months post ARV initiation	Not reported	Reduced adherence to HAART with TCAM
Nagata et al, 2011	2009	Kenya	Cross-sectional, interview	HIV+(n=67)	63% of those on ART (49/67) used herbal medicines	Not reported	Relief of symptoms
Namuddu et al,	2008	Uganda	Cross	HIV+(n=401)	96.3% on HAART	Not reported	Better health

2011			sectional		(130/135)		
Peltzer et al, 2011	2007-2008	South Africa	Prospective	HIV+(n=735)	0.6% use of TCAM after 20 months on HAART	Not reported	-
Lubinga et al, 2012	2010	Uganda	Cross sectional	HIV+(n=334)	46.4% (155/334) used Aloe vera, vernonia amygdalina	Not reported	↓Adherence to HAART in concomitant use (19.4%)
Awodele et al, 2012	2011	Nigeria	cross-sectional survey	HIV+(n=354)	Jobelyn [Sorghum bicolor plant leaves (13.8%)], Garlic (10.3%), Ginger (17.2%) and Aloe vera (10.3%).	55% on AZT, NVP, 3TC combination	8.2% use HAART, marginal improvement in CD4 count

a. Legend: QOL=quality of life, ↓=decrease, ↑=increase; TM=traditional medicine, CAM=complementary and alternative medicines, OTC=over-the-counter, TAC=traditional care site, WM=western care centre, AZT=zidovudine, 3TC=lamivudine, NVP=nevirapine, D4T=stavudine,

b. Percent (%) given as per publication

Discussion

Based on published studies, there has been limited clinical research on African Traditional Medicine with the gold standard of randomized controlled trials among HIV-infected patients from 1989 to 2014. Observational clinical studies that met our review criteria were identified. Brandful (2005) discusses key indicators to assess the ability of herbal medications to treat or manage HIV/AIDS cases which should include: improvement of the immune status (CD4+ count) of the patient, elimination of the virus, attenuation of the virus, elimination of symptoms, reduction of opportunistic infections, and minimal side-effects.

In the studies reviewed, modest CD4 counts increases were noted in the Nigerian and Tanzanian settings (Awodele et al., 2012; Mtullu, 2005). Improvement of quality of life and amelioration of HIV related symptoms were demonstrated in other studies as well (Namuddu et al., 2011; Nagata et al., 2011; Homsy et al., 1999; Elujoba, 2005; Langlois-Klassen, 2007). However, these findings differ from Chinese studies that showed dramatic improvements in CD4 cell counts as reported by Kaiser and Donegan (1997).

Moreover, given the fact that concomitant use of traditional medicines with highly active antiretroviral therapy results in poor adherence to conventional antiretroviral treatment (Owen-Smith et al., 2007; Peltzer et al, 2010; Lubinga et al, 2012) and the risks of herbal medicines-antiretroviral medicines interactions (Borrelli and Izzo, 2009; Muller and Kanfer, 2011), there is a need for initiatives to promote collaboration between traditional healers and biomedical trained health care workers. Furthermore the evidence of improvements in CD4 cell counts and reduction in viral load should foster the need for more collaborative research initiatives (Bashengezi, 1995; Gbodossou, 2002; Matsabisa, 2004; Tshibangu et al., 2004; Mokondjimobe et al., 2012).

Further research is needed because very little is known about the interactions due to concomitant use of commonly prescribed antiretroviral medicines, for example, stavudine or tenofovir combinations, with most of the African traditional medication therapies taken by HIV – infected patients. Many in vitro studies may shed light on the potential for interactions, but very few clinical studies support the evidence of the rich biodiversity of plants with immuno-

restorative, antiretroviral properties and those with reduced adverse allopathic drug events (Eto, 2013).Muller and Kanfer (2011) argue that notably, only one clinical ATM-ARV PK interaction study has been conducted, albeit Africa and Southern Africa in particular has the highest incidence of HIV/AIDS in the world.

Conclusion and implications for future research

The usefulness of African traditional medicines in the management of HIV infection has been demonstrated by the improvement of CD4 count, reduction of viral load and or amelioration of quality of life in HIV-infected individuals but these improvements have not yet led to products that can be used at a massive scale for the management of HIV. This may be due to the fact that clinical trials that are needed to ensure product development have not been conducted. There is an urgent need for more research.

Contribution of authors

MN conceived, drafted the paper, and accepted the final version of the article. PN reviewed the draft and contributed for intellectual content.

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