

**Shifts in African Traditional Herbal medicine (THM):  
Relevance for HIV/AIDS, as Foremost Among *New Diseases*, and Impacts of Stigma  
and Culture Change:  
A Review**

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**Abstract**

African herbal medicine is as ancient as humankind, and was categorised into organised healing systems since before ancient Egyptian times, around 3000 BC and earlier. African herbs became popularised in Europe, following colonisation of Africa by European nations. Contemporary inroads of African modernisation processes include dramatic culture shifts around understanding the nature and definitions of wellbeing and cure, and the use of ‘medicine’ and ‘healing’ to effect health improvements. Viewing endemic disease in the face of extensive poverty, pressure is exerted by international communities and African national governments to ensure greater reliance on conventional biomedicine, while traditional healing cultures are now often portrayed as ineffective, over-simplistic, superstitious and potentially dangerous, or conversely as exclusively ‘magical’ and disconnected from everyday reality. Despite this, African herbal products have supplied a lucrative global marketplace, to an extent where some species are now threatened. Ongoing interest in the use of herbs is evidenced by popular articles and scholarly research. Significant value is accorded to African indigenous herbal medicine to treat ‘new’ diseases, including HIV/AIDS (as a current lead cause of mortality for adults in Africa). This paper discusses issues pertinent to herbal use in the context of HIV/AIDS treatment, including environmental impacts, and focuses on relevant shifts in the social and cultural contexts of herbal medicine practice in Africa.

**Introduction**

This literature-based paper will introduce the idea that serious and newly emergent transmissible diseases may be helped in part by recourse to traditional herbal medicines (THMs). It specifically references HIV/AIDS,<sup>1</sup> as the foremost example (WHO 2014, pp. 59-61; WHO 2016; Morens & Fauci 2013) among a number of other strongly medicalised zoonotic infectious conditions identified in **Africa** in recent decades. These include Ebola, Lassa and Marburg haemorrhagic viruses, mosquito-borne Zika and Chikungunya viral diseases, and *Bacillus cereus* ‘new anthrax’ (see: Butler 2012 (re the emergence of such new diseases); O’Hearn *et al* 2016 (re surveillance); Leligdowicz *et al* 2016 (re Ebola); Brosh-Nissimov 2016 (re Lassa); Pavlin 2014 (re Marburg); Gyawali, Bradbury & Taylor-Robinson, 2016 (re Zika); Chaleem *et al* 2016 (re Chikungunya); and unfortunately no reference was found describing *B cereus* anthrax aside of unscholarly

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<sup>1</sup>Human Immunodeficiency Virus (HIV) is an infective ‘retrovirus’ organism that causes reduction in immune cells, particularly CD4+ T-lymphocytes. Acquired Immune Deficiency Syndrome (AIDS) is a serious and fatal late-stage multiple disease presentation resulting from profoundly compromised immunity and deteriorating health, after long-standing or rapidly progressing HIV infection.

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media ‘hype’ on the internet). The idea of using THMs for new diseases is of great relevance in African countries, where disease severity and spread is associated with widespread poverty (see: Kelly *et al* 2013 (re Lassa and post-war housing problems); Barter *et al* 2012 (re TB and poverty); Bhutta *et al* 2014 (re global burden, and Infectious Diseases of Poverty (IDoP)); Salcito *et al* 2014 (re multinational corporations and HR management of infectious disease); and So & Ruiz-Esparza 2012 (re relevant technology)).

HIV/AIDS is now the leading cause of adult deaths in Africa, often in combination with tuberculosis (TB), despite suggestions of declining HIV-associated mortality at a global level (AFP/Africa Check 2014; IHME 2016; Wang *et al* 2016). This paper describes treatment approaches for and by Persons Living With HIV/AIDS (PLWHA) in Africa, specifically in terms of understanding the divergent strategies of biomedicine and ‘traditional medicine’, in the specific guise of plant-based treatment. The manner in which these distinct systems are believed to take effect generally relies on differing cosmologies, cultural assumptions, and perspectives about health and healing.

In particular, the paper briefly outlines the HIV/AIDS disease and epidemic, and details its management by biomedicine. It then engages, by way of contextualisation, with pertinent contemporary issues affecting the use of THM for HIV/AIDS, including socio-cultural experiences of HIV/AIDS disease and stigma, the shifting social roles of traditional herbal practices in Africa, and the relevance of socio-economic and environmental changes. Later sections of the paper provide a summary of a number of studies focused on particular African medicinal plants, whose findings offer potential support for the use of THM to assist in care and treatment of HIV-infected persons. Although the original plan was to present a literature review of African plant research with potential to help HIV-positive persons, it was only possible to include a briefer summary of relevant literature about herbal research, due to time constraints.

### **Author’s position**

My interest in the use of African traditional medicine for HIV/AIDS was triggered by a part of the literature review for my recent PhD research, about complementary and alternative medicine (CAM) use in Victoria, Australia (Holmes, 2015). This literature was concerned with the determined use of traditional healing and CAM by PLWHA in both African and western countries, which is often experienced and portrayed as a type of behavioural ‘deviance’, in that it shies away from medical expectations (such as: Pawluch, Cain, & Gillett 2000; McDonald & Slavin 2010; Musheke, Bond & Merten 2013; Ekwunife, Oreh, & Ubaka 2012).

### **Brief historic background**

African herbal medicine is as old as humankind, and was already categorised into organised healing systems since before ancient **Egyptian** times, around 3000 BC and earlier (Abou El-Soud 2010). Archaeological evidence of herbal medicine use from the **Middle East** (in northern Iraq) is dated at about 60,000 years (Saad, Azaizeh & Said 2005). **North African**, Middle Eastern and Mediterranean herbal medicine usage has longstanding cross-over and similarities, and may be grouped for simplicity.

African herbs became popularised in western Europe due to ancient trade around the

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Mediterranean, and the Red and Arabian Seas (including with the historic seafaring nations of Phoenicia, Cypress, Greece, Egypt and India) and waves of colonisation of African countries in more recent centuries by European nations. While this process led to a widespread commercial use of many African medicinal and food plants over time, in later centuries it was irrevocably bound up with the history of slavery, and contributed to massive exploitation and poverty in African nations.

Across millennia, traders and colonisers arriving in Africa brought common food items and spicy or fragrant plants, that were incorporated into native African fare as foods and medicinal staples. At the same time, the African diaspora carried their traditional knowledge of food and medicinal plants to countries throughout the world. As the oldest land mass inhabited by human ancestors, Africa shared its knowledge of the methods of using foods and medicinal plants with its neighbours – particularly in the Middle East and Mediterranean regions – since ancient times, and established many generations of traditional healing practice.

### **Issues of modernisation, HIV/AIDS and appropriate healthcare**

In the post-colonial era, contemporary modernisation processes in Africa include dramatic culture shifts and trends of change in dealing with health, such as questions around how wellbeing and cure are best understood. Commentators observe the relative accessibility and affordability of different forms of ‘medicine’ and ‘healing’, and argue over whether diverse healing methods are appropriate to effect health improvements, based on stakeholder opinions. The HIV/AIDS epidemic poses an urgent pressing concern, on a global scale (Kanta, Unnati & Ritu 2011), having caused millions of adult and child deaths in Africa alone in the course of the past three decades. As mentioned in opening, HIV/AIDS now represents the leading cause of adult mortality in Africa, particularly in combination with TB, a recognised ‘disease of poverty’. HIV/AIDS is inadequately treated with prescribed medications in resource-poor areas.

HIV/AIDS is now endemic in much of Africa, and co-exists with problems of extensive poverty, post-colonial governance issues, and ongoing conflicts. Pressure is exerted by concerned international organisations, national governments and African communities to try to ensure the possibility of greater reliance on conventional biomedicine, to address the spiralling epidemic nature of this problem. Compounding this further, from biomedical and public health perspectives, traditional healing practices that derive from tribal cultures and agriculture-to-market communities are often portrayed as ineffective, over-simplistic and superstitious. Conversely, they may be represented as potentially dangerous, contaminated, or exclusively based on ‘magical’ concepts, and disconnected from a modernist view of everyday reality.

Despite this, African herbal products continue to remain in popular use, providing a clear majority of African people with regular healthcare, and supplying a lucrative global herbal marketplace. Commercialisation and over-consumption has occurred in some regions to the extent that numerous species are listed as threatened or endangered, through excessive harvesting. An ongoing global interest in African THMs is evidenced in part by a recent explosion of popular articles and scholarly research on the topic, and significant value is accorded to herbal medicines that could potentially help treat ‘new diseases’, particularly HIV/AIDS.

### **The character of AIDS deaths and the spreading HIV epidemic**

AIDS-related deaths characteristically involve either ‘AIDS-defining’ disease, in countries of higher economic status (mainly cancer, liver cirrhosis or hepatitis, and pneumonia) (Lewden *et al* 2005), or other Opportunistic Infections (OIs), or both. The profile of PLWHA who die from AIDS is improving overall, with longer survival, evidence of less reduced CD4+ T-lymphocyte immune cell counts, some preserved immunity, and reduced viral presence (Valdez *et al* 2001). HIV-positive cancer deaths often occur in smokers (Lewden *et al* 2005).

In low to middle income countries, and racially diverse communities in developed countries, AIDS-related OIs most frequently cause death from pneumonia, often TB-related, which results in impaired lung function and acute respiratory failure (Kumarasamy *et al* 2010; Iroezindu 2016). Various studies (McCabe *et al* 1997; Hirani *et al* 2011) suggest HIV infection contributes to compromised lung function, and significantly increases rates of potentially fatal infectious pneumonia-type lung disease due to TB or other pathogens, and disabling chronic obstructive pulmonary disease (COPD). Currently the highest risk globally for developing active TB infection and related lung disease is HIV infection. The incidence of HIV-TB co-infection is extremely high in Africa, representing three quarters of its global occurrence, and causing many thousands of deaths annually (Seeling *et al* 2014; AFP/Africa Check 2014).

Looking at the HIV/AIDS epidemic from a biological standpoint, some optimism may be drawn from understanding that the strength of new viral diseases becomes attenuated over time, and across the course of sequential waves of epidemic infection.<sup>2</sup> From this perspective, it could be expected that the rate of fatalities and serious illness associated with HIV/AIDS will lessen in severity over time, as a ‘natural’ outcome. This concept is not widely discussed, due to the severity of the disease warranting an interventionist approach. Despite the possibility of viral attenuation and increasing human immunity to HIV, the recently increased lifespan of HIV-seropositive individuals – mainly attributed, in published literature, to Anti-Retroviral (ARV) treatment (for example, see: Hirani *et al* 2011, p.1656) – is swelling the pool of HIV-infectious persons. It will thereby likely contribute to an accelerated spread of the epidemic, both in USA and **sub-Saharan Africa** (Vellozzi *et al* 2009). To substantiate this concern, a meta-analysis of viral markers in newly HIV-positive diagnosed persons in USA and Europe, (Herbeck *et al* 2012), shows regular decreases over time of measured CD4+ T-lymphocytes (which are reduced by HIV virus), and an increase over time of HIV viral load in blood serum. This finding suggests an increasing virility of newer HIV strains, and likely further spread of the epidemic. The authors also state however that a year-by-year analysis indicates “convergence toward a virulence optimum...[suggesting] the rate of virulence evolution has slowed, perhaps approaching an optimum and stable virulence” (Herbeck *et al* 2012). This parallels the biological model of co-evolution of virus and host, that moves toward an increased level of host immunity and viral attenuation, until a plateau is reached, representing an optimum infection rate that ensures viral continuation. In summary, from any realistic perspective, HIV/AIDS is ‘here to stay’.

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<sup>2</sup> Virgin (2007, pp.369-371, citing research by Fenner and colleagues) explains the concept of viral attenuation by referring to the example of epidemic myxomatosis, introduced into wild rabbits in Australia in the 1950s. This disease showed a well documented decline in virility and rabbit fatalities caused, in a short period of time, alongside a co-evolution of rabbit immunity.

### **A conventional biomedical approach to treating HIV/AIDS**

Biomedical management of PLWHA requires encouragement of patient engagement with conventional care and treatment. Phases include: (1) blood testing to establish a diagnosis (reliant on a sero-positive finding of HIV infection), followed by; (2) referral and enrollment in a drug treatment program; (3) prescription of pharmaceutical ARV agents (also called anti-retroviral therapy (ART) or highly active anti-retroviral therapy (HAART)); (4) monitoring for adherence to prescribed medication regimes and for regular attendance at appointments, or hospitalisations for health crises; and (5) an aim of achieving a reduced viral presence or ‘viral load’ in the body, as measured by periodic blood testing (Kay, Batey & Mugavero 2016).

Antiretroviral drugs are geared to preventing the ‘growth’ (multiplication) of HIV. They may have several functions such as killing the virus, thus limiting viral load, or slowing its entry into cells. ARVs do not completely eliminate HIV from the body, or totally cure HIV/AIDS (AIDS Infonet 2014). However, a multi-faceted treatment approach, including management of psychological stress, promotion of general health, immunity, hygiene and psycho-social wellbeing, and early diagnosis and access to recent combination ARV treatments (cARVs or cARTs) (Lewden *et al* 2007) purportedly now enables PLWHA to achieve a life expectancy of around 80 years in developed countries, similar to those without HIV.

### **Method of investigation**

This paper does not incorporate a formally structured review of literature, but summarises presenting issues around ongoing use of THMs in Africa among persons with HIV-positive status. It presents social and cultural ramifications of the disease and of ongoing THM reliance, and provides a brief overview of research of relevance to evaluating the worth of African herbal medicines for this context.

Background information was compiled using extensive online searching in 2016, mainly via PubMed and Google. This was enhanced by reference to scholarly anthropological and HIV-focused journals, in order to describe representative socio-cultural studies concerned with lived experience of HIV/AIDS, among PLWHA in African communities.

An increasing number of journal articles discuss THM use for HIV/AIDS, especially in low-income countries. The later sections of this paper focus on such research about African herbs and traditional medicine. THM offers enormous potential to support PLWHA, either to fortify general wellbeing, or to help address co-morbid conditions and bolster the effects of ARV drug therapy.

To this end, an initial basic search was conducted in EBSCO database in July 2016 (repeated August 2016), for search terms (‘herb medicine’ AND ‘HIV/AIDS’ AND ‘Africa’), requesting full-text articles in English, published 1985 to 2016. This search yielded 350 items, which were saved to an Endnote database, and grouped into relevant themes. Further searches were conducted from October 2016 to January 2017 in PubMed, the Cochrane Database of Systematic Reviews, the BioMed Central (BMC) open access database of journal publications, and via the Directory of Open Access Journals (DOAJ), and African Journals Online (AJOL), for open-access full-text journal articles in English, of relevance to presenting themes in the paper. This ‘review’ should

not be considered comprehensive however, as all search returns and relevant published articles were ultimately not able to be screened for inclusion.

Resulting topics discussed in the subsequent sections of this paper are: (1) problems of ARV coverage, (2) social and community aspects of the HIV/AIDS experience in Africa, (3) ongoing use of THMs by PLWHA in Africa, (4) a summary of some African antiviral herbs and traditional plant medicines offering potential to help treat HIV/AIDS, and (5) further potential of plant antioxidants.

### **‘Findings’ – 1. Social issues raised in published literature**

#### **Problems of medication and limited access or ‘coverage’**

Population coverage with ARV treatment has improved in recent years. Nevertheless, even in developed countries such as USA, while some well-funded research organisations claim almost 100% coverage (IHME 2016; Wang *et al* 2016), others describe the rate of viral reduction resulting from or associated with ARV treatment in HIV-positive patients quite conservatively, at about 30% (Kay *et al* 2016), with the vast majority of HIV-positive persons in USA not adequately managed. Problems include low rates of early diagnosis, racial disparities in accessing care and treatments, particularly affecting African Americans, state-based differences in treatment funding, inadequate retention of clients in PLWHA-focused care programs, and patchy adherence to prescribed ARVs (Kay *et al* 2016).

Such coverage, representing the extent of population access to ARV treatment, is much less again in **African countries** (IHME 2016; Wang *et al* 2016), despite vastly greater HIV/AIDS epidemics than those in USA and other high-income countries. Pharmaceutical drugs, including ARVs, often remain unaffordable for consumers in Africa at the dosage rate prescribed by medical personnel (Merten *et al* 2010; Thomas 2008; Stanifer *et al* 2015; Granado *et al* 2009). Furthermore, many HIV-positive people in Africa experience difficulty accessing clinical services, or delay seeking medical diagnosis and treatment, presenting for diagnosis only when their CD4 cell counts are already low and immune health is compromised (Gesese *et al* 2016; Geng *et al* 2011; Audet *et al* 2014).

Consultation with traditional healers prior to HIV diagnosis has been shown to delay presentation to a medical clinic by a matter of about one month up to several months in **Mozambique** (Audet *et al* 2014). Educational training about biomedicine may not effectively dissuade people from seeking treatment provided by traditional healers, or encourage traditional healers to refer patients to medical clinics. Audet, Salato, Blevins *et al* (2013) also published conflicting information, about education influencing referrals by traditional healers, but found that unfortunately, of the patients thus referred to biomedical clinics, very few (only 3.5%) were then tested for HIV. Cochrane reviews suggest mass media promotion of HIV testing effectively increases its uptake in the short-term (Vidanapathirana *et al* 2005), while voluntary home-based testing is also an effective strategy (Bateganya, Abdulwadud, & Kiene 2010), circumventing stigma and travel cost attached to clinic-based testing.

In **Ethiopia**, **Kenya**, **Uganda**, **Tanzania** and **Zimbabwe**, medium to high experience of

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stigma, male gender, and lack of knowledge of HIV/AIDS disease, low educational attainment, and TB co-infection or other illness, tobacco smoking, loss of ambulatory function, rural distance, unemployment, shared accommodation, single-room housing, young or older age group, single marital status, and lack of spousal HIV disclosure, are all factors that variously correlate with delayed presentation for HIV diagnosis, as is acquiring HIV through sexual contact rather than by another means (Gesese *et al* 2016; Kigozi *et al* 2009; Beyenne & Beyenne 2015; Aniley *et al* 2016; Geng *et al* 2011; Nyika *et al* 2016). The level of reduced CD4+ count considered 'late' at first diagnosis varies between studies, however, which confuses these findings somewhat (cf. Beyenne & Beyenne 2015; Aniley *et al* 2016; Geng *et al* 2011). Having an illness appeared to delay rather than to hasten HIV-testing in Harare, **Zimbabwe** (Nyika *et al* 2016). Of further concern, the presence of TB, and tobacco smoking, may mask early HIV-related health conditions. Tobacco smoking is shown to activate and 'stress' normal immune functions and cause immune exhaustion, including of CD4+ cells, particularly impacting health for HIV-infected persons, among whom smoking is very common (Valiathan *et al* 2014). Female gender may also correlate to a relative inability to access services providing HIV diagnosis and treatment, likely due to rural distance, farming work commitments, and language barriers; this suggests an extra group of late presenters and non-presenters to clinics, and non-participants in study cohorts (Geng *et al* 2011, p. 9; Audet *et al* 2014). Factors contributing to *earlier* diagnosis include family and community support and encouragement, greater education, knowledge of HIV/AIDS or being provided with information about it, higher income, belief in the value of medical intervention, and attending a clinic for antenatal care (Beyenne & Beyenne 2015; Nyika *et al* 2016).

Very late presentations for diagnosis are reducing in frequency in some African countries coincident with improved funding for ARVs. Globally this amounts to an astonishingly high estimated medical cost and expenditure, from internationally donated funds, of US\$10,000 minimum per individual patient in resource-poor areas, who has been commenced on ARV drugs (Geng *et al* 2011, p. 2). While such funds may arrive in the hands of pharmaceutical companies, health professionals, and governments, this spending does not amount to improvements in available income or general life quality for community members, who often remain very poor by western standards. For example, Kigozi, *et al* (2009, p. 4) reported that 80% of HIV-positive study subjects at a regional **Ugandan** urban hospital had a monthly income equivalent to US\$60 or less. Audet *et al* (2014) found few HIV-positive participants in rural **Mozambique** had completed more than 3-4 years of primary school education, or received any monthly income at all. Based on websites accessed in November 2016, the estimated direct retail cost to purchase ARV treatment for one year, online, without subsidisation, ranges between US\$230 up to about \$13,000, depending on source and type of drugs, number of drugs and amount or dosage consumed, and choice of branded or generic products, with generics from companies such as Cipla, Sun Pharma and others being vastly cheaper.

Early commencement of ARV treatment is linked to reduction in HIV disease and opportunistic infections (Low *et al* 2016), and should, therefore, be actively promoted and funded by government health departments. Nevertheless, ARVs do cause adverse drug reactions in a substantial minority of consumers (Weldegebreal, Mitiku & Teklemariam 2016), who are more often women (Riedl & Casillas 2003). Such effects include 'lipodystrophy', peripheral neuropathy, numbness or tingling, pain, liver toxicity,

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visual disturbances, anaemia, bad taste, nausea and vomiting, diarrhoea, itching, skin rashes, dizziness, heart palpitations, and polyuria (Weldegebreal *et al* 2016; Ammassari *et al* 2001; Agu & Oparah 2013). A small percentage of deaths occur as a direct result of ARV treatment (Valdez *et al* 2001; Lewden *et al* 2005). This high level of toxicity compromises patients' life quality, contributing to reduced adherence to treatment and often leading to treatment failure and worsening disease (Weldegebreal *et al* 2016; Ammassari *et al* 2001). Furthermore, use of ARVs or HAART does not always correlate with improved survival (Dickson *et al* 2007), and a sub-group of HIV-infected patients develop a condition of resistance to ARV drugs and/or multiple drug resistance while taking ARVs (Recksy *et al* 2004).

In light of the persistent use of THMs in Africa, their accessibility and cultural appropriateness, and problems raised in this passage, this author suggests THMs can support general wellbeing for PLWHA, and thereby enhance ARV treatment outcomes. *A systematic review of ten studies in African countries showed that 'task-shifting' from doctors to non-doctors, including nurses and trained community-health field workers, caused no appreciable differences in HIV patient deaths after a year, and no evidence of differing immunological and virological outcomes based on provider type (somewhat favouring nurse-care over doctors) (Kredo et al 2014). Across studies, there was some improvement or no change in patient numbers lost to follow-up, while costs of travel were reduced, and satisfaction with non-doctor care was greater. Consequently, given the enduring popularity of traditional providers, it may be realistic, wherever culturally acceptable, to train and fund willing THM practitioners, who could test patients for HIV, and dispense suitable generic-brand ARV medications alongside traditional treatments.*

### **Social and community aspects of African HIV/AIDS experiences**

An in-depth appreciation of socio-cultural contexts of HIV/AIDS experiences in Africa is also required. While achieving good ground in providing pharmaceutical treatments for PLWHA, biomedical protocols often unintentionally overlook the social aspects and context of HIV/AIDS sufferers' life experiences (Merten *et al* 2010), thereby neglecting the importance of community-based components of care and the significance of cultural meanings. Nevertheless, an increasing number of ethnographic and qualitative studies explore these facets of the HIV/AIDS experience.

For example, an ethnographic study by Wyrod (2011) describes how normative expectations of gendered behaviour render HIV-positive status problematic for men, in an urban community in Kampala, **Uganda**, due to the impact of negative stigma around a perception of 'failed' masculinity. This occurred largely due to loss of opportunities for affected men to earn a living as sole breadwinner for their family, as well as through shame associated with HIV/AIDS-related deaths, of a wife or other female sexual partner, and sometimes children. Wyrod describes the in-built structural nature of gendered norms as reinforcing the difficulties HIV-positive men experience – both prior to and subsequent to blood tests and diagnosis – and reducing their ability to maintain participation in a support group. This group, in any case, was limited in duration and resources, locally provided, and self-managed by group members.

Another study conducted interviews with diverse healthcare professionals who work with HIV and TB co-infected patients in **Namibia**, an upper middle income country in



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sub-Saharan Africa (Seeling *et al* 2014). It revealed insufficient staff numbers and services provision, as well as inadequate training and knowledge. These problems presented in addition to complex cultural and socio-economic barriers for patients in the community, that included stigma, religious beliefs, and fear of indirect treatment costs, all further compromising access to treatment (Seeling *et al* 2014).

A review by Tsoka and Mwanri (2014) serves to highlight the multi-dimensional character and socio-cultural location of various types of stigma that occur around HIV-positive status in **Malawi**, a rural-agricultural nation in south-eastern Africa. Stigma affected both women and men, and impacted workplace relations through discrimination, social exclusion and the internalisation of self-blame. Stigma was perceived to be generated mainly through cultural expectations, including moral teachings associated with religious beliefs, portrayal of AIDS arising only through 'illicit sex', lack of knowledge about the disease and fear of contagion, and gender-based behavioural norms (Tsoka & Mwanri 2014).

An interview-based study by O'Brien (2013), of HIV-positive persons from low socio-economic locations in urban Harare, **Zimbabwe**, notes that gendered understandings, against a traditionally patriarchal cultural backdrop, and the 'spiritualisation' of disease and suffering through religious ideation which culminates in the portrayal of HIV as "a predicament for the sexually deviant" (p. 37), both strongly influence self-perceptions, culturally-mediated interpretations, and lived experiences of HIV/AIDS. O'Brien observed (2013) HIV-related stigma in Zimbabwe was entrenched as a form of structural violence, occurring due to state ideologies and institutions that tend to oppress women by upholding traditional views about the limited social or economic status women could hope to achieve. It thereby contributes to misinformation, lack of knowledge, gendered blaming, and fear of witchcraft.

An anthropological study by Thomas (2008) explains the shifting nature of health roles in **Namibia**. Thomas explores narratives of stigma and a culture of blame around HIV/AIDS, that have emerged from socioeconomic changes, and an erosion of traditions of morality leading to violations of behavioural taboos. Thomas describes the prohibitive cost of accessing THM from traditional healers, in a context where poorer people struggle with cultural alterations that occur through the pressure to accept modernisation (2008). They are helpless to participate fully in an expected level of health-directed behaviours, whether modern or traditional, due to unaffordability in both cases.

Several of these aforementioned studies (Wyrod 2011; Tsoka & Mwanri 2014; O'Brien 2013) describe how having multiple sexual partners remains common for men, and culturally tolerated, even among those known to be HIV-positive. In contrast, infidelities or promiscuity by women (or abortions (Thomas 2008)) may be viewed as tantamount to prostitution, and are socially punished by accusations and shaming. There is therefore an effective *double* stigma that compromises the socio-cultural standing of women, linked both to gender identity and HIV-positive status.

While surveys (cf. Hughes *et al* 2012; Audet *et al* 2013, 2014) occasionally cite traditional healers or self-directed THM use as a cause of reluctance to seek medical treatment, or delays in obtaining diagnostic blood tests on the part of HIV-positive

persons, Seeling *et al*'s (2014) study suggests this is less of an obstruction to treatment-seeking behaviour than either fear of stigma and discrimination, or Pentecostal religious beliefs (also: Zou *et al* 2009). Over half of religious survey respondents in **Tanzania** (Zou *et al* 2009) believed HIV infection occurs as a punishment from God, and a third felt it was due to not following the word of God, with both these categories correlating with shame-related stigma around HIV. Over 80% believed HIV could be cured by prayer irrespective of their willingness to undergo ARV treatment.

Campbell, Skovdal and Gibbs (2011) disclose however that, while churches contribute to moralising (such as disincentivising condom use), pressuring women, shaming, and stigma, they may also be instrumental in creating social spaces that help to destigmatise HIV in **Sub-Saharan Africa**, and can assist in promoting HIV prevention and caring for AIDS-affected persons. Tsoka and Mwanri (2014) and O'Brien (2013) nevertheless reiterate that religious ideas and moral stigma may compromise medication adherence and access to health networks, while O'Brien suggests (2013, p. 46) that traditional healers in fact often provide or mediate a pathway to greater acceptance of biomedicine and enhanced willingness on the part of patients to seek HIV testing and medical treatment (also evident in: Audet *et al* 2013, 2014).

## **'Findings' – 2. Relevance of African THM for HIV/AIDS**

### **Ongoing traditional herbal medicine use, for HIV/AIDS in Africa**

THM remains a central and substantial part of regular healthcare throughout Africa, as is widely illustrated by findings of numerous recent studies. For example, a comprehensive study in urban and rural parts of northern **Tanzania**, by Stanifer *et al* (2015), found cultural associations with THMs that were in widespread use by 56% of respondents of all income levels. These participants mainly identified as Christian, or less often Islamic, in terms of religious orientation. THMs were considered safe, and were used as first-line treatment for common symptoms and ailments, chronic diseases, reproductive problems, and malaria or other febrile illnesses. Most participants had a primary school level education, although some were trained professionals including medical doctors, who also used THMs frequently.

Stanifer and co-authors' (2015) study participants valued THMs more highly when they perceived the quality of biomedical care they accessed was low, due to communication problems between consumers and providers, or was expensive, with lengthy wait times, or they had limited understanding of biomedicine. Some viewed biomedical treatment as ineffective, inappropriate, unproven or from unknown sources, excessively toxic or chemical, or 'foreign' and thus representing of a form of ongoing colonisation. While participants willingly 'doctor shopped', seeking biomedical care particularly if THM treatments failed, many placed a very high value on elders' health advice and family traditions of healthcare. Reliance on and favouring THM persisted even among those who needed to use hospital services often. THM was thought 'credible' compared to biomedicine, as it required no scientific proof, due to a widespread awareness and promotion of many testimonials of successful healing and personal experiences of improved well-being. Traditional beliefs regarding causation in health and disease were influential, including notions of 'evil spirits', both to explain conditions like epilepsy and mental illness, and overtly 'physical' chronic or acute sicknesses (Stanifer *et al* 2015).

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THMs are also in common use for adjunctive ‘non-medical’ treatment of specific HIV-related illnesses. The meaning of THM and other non-biomedical treatments for PLWHA has been widely discussed in publications for over a decade, in both developed and developing country contexts. In western countries, including Australia and USA, PLWHA’s frequent reliance on CAM of many types to self-manage symptoms, reduce stress, help deal with stigma, and boost overall wellbeing, has been reported by consumers to also promote a sense of their being able to resist an ‘uncritical’ dependence on ARVs, and an enhanced autonomy in making decisions about their health (McDonald & Slavin 2010; Thomas *et al* 2007; Foote-Ardah 2003; Pawluch *et al* 2000). PLWHA occasionally continue using THMs against medical advice, or to reduce impacts of drug side-effects. Thus ‘traditional’ modes of healing are linked at times with negative stigma associated with HIV-positive status, due to an overriding biomedical emphasis on drug consumption designed to reduce impacts of HIV, and an avoidance of ‘unproven’ therapies. However, Audet and co-authors (2014, p. 2) point out that there are *many* traditional healers working in some African countries (such as **Mozambique**), compared to the number of medical doctors and nurses available, who are few. This circumstance raises the issue of THMs contributing to reduced adherence to biomedically-prescribed ARVs, and gives rise to expressed concerns regarding possible drug-herb interactions (Hughes *et al* 2012; Awortwe *et al* 2014).

Such a concern was expressed for instance by the authors of a small study in urban and rural **South Africa**, which found 79% of respondents sourced through HIV clinics used THMs prior to HIV-diagnosis; this reduced to 16%, of almost entirely self-prescribed THMs, among HIV-positive persons taking ARVs (Hughes *et al* 2012). This cohort also relied on family support, spiritual care and prayer. Those using THM after HIV diagnosis mainly consumed herbal or compound mixtures, most popularly “*ubhejane* which is believed to effectively treat all bodily conditions” or another “mixture that was believed to heal all conditions (*zifozoneke*)” (Hughes *et al* 2012, pp. 472, 482, italics added). THM users were wealthier than non-users, and tended not to disclose THM use to medical workers for fear of punitive reactions. Some believed THMs “could counteract the effects of witchcraft” (Hughes *et al* 2012, p. 482).

An interview-based study in **Kenya** (Nagata *et al* 2011) with traditional herbalists, mothers and PLWHA, sought knowledge about medicinal plants suited for treating HIV/AIDS and a purportedly similar local-classified sexually-transmitted wasting disease, *chira*. In contrast to Hughes *et al* (2012), Nagata *et al* (2011) describe extensive ongoing coincident ARV and THM consumption (among 63% of PLWHA interviewed), including self-treatment of *chira* and HIV/AIDS symptomatology. They mainly used leaves or other medicinal or food plant parts, for chewing, or decocted for internal medicine or external washing. Herbs include *Allium spp.* (known as ekitungu; *A. porrum*, used by 88%), bitter orange (machunga/ichunga; *Citrus aurantium*, used by 81%), pawpaw (poipoi/ipa pau; *Carica papaya*, used by 72%) and lemon (endim; *Citrus limon*, by 67%). Among 40 African native and naturalised THMs, Nagata and colleagues (2011) list Neem (mwarubaine; *Azadirachta indica*, used by 40%), garlic (ekitungu saumu; *Allium sativum*, used by 24%) and several other plants considered potent against HIV.

Similarly, a cross-sectional study in two AIDS treatment centres in **Uganda** (Namuddu *et al* 2011) found a relatively high percentage, 34% of participants, coincidentally used

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both THMs and ARVs (in this case HAART). THM was most frequently used by those who had consumed ARVs for less than 4 years, or who experienced side effects from ARV drugs (Namuddu *et al* 2011). Commonly known herb medicines and mixtures were taken to treat problems of ‘constant fever’, cough, pain associated with HIV, itching, low energy, anaemia, frequent illness, reduced immunity, appetite changes, diarrhoea, and sweating (with some of these symptoms tallying closely with side-effects of ARV drugs). The herbs used included guava leaf (amapeera), mango leaf (miyembe), *Aloe vera*<sup>3</sup> (kigagi), hibiscus (bazukuza bafu), bitter leaf (mululuza/olubirizi; *Vernonia amygdalina*), avocado (ovakedo), and parts of African trees or shrubs (including mpafu tree: *Canarium schweinfurtii*; red-hot poker tree/lucky bean tree (jilikiti: *Erythrina abyssinica*); entanda tree (mwooloola: *Entada abyssinica*); musisiya/mugavu (*Albizia coriaria*); mazukizi (*Dicliptera laxata*) and kamyuye (*Hoslundia opposita*).

These herbal plants were usually obtained from registered herbalists, or grown in gardens. Over 96% of the THM-ARV coincident users reported improvements in wellbeing from herbal treatments (Namuddu *et al* 2011, p. 4). On this basis, it may be argued that THM use that ameliorates drug side effects could improve adherence to ARVs. Namuddu *et al* also cite (2011, p. 7, reference #5) a Chinese study demonstrating improved anti-viral effects among THM-ARV coincident consumers. They state furthermore that the percentage of PLWHA in their cohort using both THM and ARV may be an underestimate of the true prevalence, due to pressure from medical staff for patients to not consume THM, resulting in reluctance to disclose such use.

In light of the foregoing, it seems apparent that efforts directed to developing public and biomedical health services for HIV/AIDS in African countries ideally should incorporate the work of traditional healers, and could gainfully facilitate healthful uses of traditional plant-based medicines, and related psycho-spiritual aspects of healing. All these remain important for many African people.

### **Studies of antiviral traditional herbal medicines for HIV/AIDS**

Numerous recent ethnographic surveys and reviews list common use African plants, including many with antiviral properties, some of which are believed to improve health for HIV-positive persons (such as: Kloos *et al* 2013; Chinsebu & Hedimbi 2009; Kanta *et al* 2011). Chinsebu and Hedimbi’s (2009) literature survey cites laboratory research demonstrating specific ways in which 46 medicinal herbs or their constituent chemicals act against HIV, in reducing infectious spread, preventing the virus from penetrating body cells, or hampering viral replication at various stages after infection is established. Kloos *et al* (2013) name herbs recognised for antiviral properties, and used for HIV/AIDS in **Ethiopia**, including *Combretum paniculatum*, *Dodonea angustifolia*, *Bersema abyssinica*, *Ximenia americana*, *Aconkanthera schimperi* and *Euclea schimperi*, and in **South Africa** and **Zimbabwe**, including *Azadirachta indica*, *Moringa oleifera*, *Sutherlandia frutescens* and *Hypoxia hemerocallidea*.

Tabuti *et al* (n.d.), describe a current project in **Uganda**, involving interviews with traditional healers and cultivation of herbs useful for HIV/AIDS. To date healers had documented 302 plants, usually prescribed as complex mixtures, which they used to treat HIV/AIDS and related OIs. The researchers’ aims included establishing the effectiveness

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<sup>3</sup> Note: Many *Aloe spp.* are listed as endangered in CITES Appendix I.

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and safety of THM for HIV/AIDS, disseminating medicinal herb seedlings, sourcing plants suited to ARV drug development, conserving endangered species, and promoting commercial use.

Tshibangu *et al* (2004) investigated the effect of five THMs in 33 HIV-positive study subjects in **South Africa**. The plants remained unnamed (coded by letters) for publication purposes, on account of the collection and administration of herbs being considered a sacred ritual. Herb medicines were prepared and given to participants by a Lady Mokwena and her assistant, in the form of burnt plant ash, shaved dried wood chips, or powdered or decocted plant material, and were taken before meals, or mixed with food, or drunk as a water-based extract. Despite 3 deaths due to advanced AIDS at the start point of the study, adverse effects were not otherwise encountered during an 8-month program of treatment. The authors contrasted this with the extreme risk of severe and potentially fatal toxic reactions to certain ARV treatments such as nevirapine.

In summary, Tshibangu *et al* (2004) claim many general and specific virucidal benefits from THM treatments, such as appetite and general weight gain, disappearance of lesions, better energy, and other markers of improved overall health, substantially increased CD4+ cell counts and dramatic decreases in viral load, as verified by numerous clinical tests. They describe a close alliance between indigenous THM practitioners and western doctors, and call for more such collaborations and university teaching of THM, suggesting THMs are excellent in combination with ARVs, to improve the health of HIV-positive persons. Nevertheless, a caution should be noted, as numerous African tree species commonly used for medicinal wood or bark chips or resin, including 5 types of mahogany (*Khaya spp.*), sandalwood (*Osyris lanceolata*), several types of dragon's blood trees (*Dracaena*, *Pterocarpus*, and other *spp.*), the African almond or cherry tree (*Prunus africanus*), and others, are presently endangered or vulnerable, as listed on the IUCN Red List and in CITES Appendices.

While studies investigating antiviral activity and overall effect of THM for PLWHA are few, and this research is at an early stage, some optimistic anecdotal evidence emerges from participant narratives in anthropological and qualitative health research. Musheke, Bond and Merten (2013) describe a qualitative study of self-care practices among HIV-positive participants in urban Lusaka, **Zambia**, who avoided treatment with ARVs, in some cases for years. Common-use herb medicines reported for this group include garlic, ginger, *Aloe spp.*<sup>4</sup> (locally *tembusha*), plus “[*Moringa oleifolia*, *Ngetwa* from Tanzania, crocodile fats, Chinese herbal remedies, *stametta* (aloe mixed with vitamins and herbs) and some [packaged] herbs” labelled with a ‘Back to Eden’ brand (Musheke *et al* 2013, p.4). Quoted narratives cite the use of guava leaf, lemon leaf or garlic, or lemon and honey, for cough, and *moringa*, ginger or *tembusha*, often home-grown, to invigorate the body and stimulate immunity, including by respondents who believed herbs improve health and raise CD4 cell count (pp.5, 8, 9) without noticeable side effects. Another plant called *paliba kantu* (translates as ‘there is no problem’, and elsewhere called feverbush or stomach-bush, *Dicoma anomala*),<sup>5</sup> was prepared as a decoction. Enhanced nutrition practice was another recurring theme, as respondents added pounded groundnuts (*sashila*

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<sup>4</sup> See #3 re *Aloe spp.*; *Ngetwa* appears as a packaged brand name herbal product on the internet; IUCN lists African dwarf crocodiles as a vulnerable species.

<sup>5</sup> A close species, *D. pretoriensis* is listed as critically endangered, and possibly extinct, on IUCN Red List.

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or *kusashila*) to leafy vegetables, to improve overall nourishment and wellbeing.

Laboratory-based and clinical research about African THM often incorporates a more pessimistic outlook, and is biomedically oriented. A literature study (Mills *et al* 2005a) briefly describes current use of *Hypoxis hemerocallidea* and *Sutherlandia frutescens* from **southern Africa** as antioxidant and immune stimulant herbs for HIV/AIDS. These plants were traditionally used, respectively, for urinary infection, tumours, heart weakness and nervous conditions, and for gastro-intestinal disorders, chronic fatigue, and infected and inflammatory conditions. Mills *et al* (2005a) report that *S. frutescens* is particularly non-toxic, although isolated plant chemicals from both plants may have caused reactions in trial subjects. A study of *H. hemerocallidea* in HIV/AIDS patients is cited (Terreblanche *et al* 2005a), which was terminated due to apparent bone marrow suppression. While inadequate research has been conducted that might verify the plants' physiological activities, Mills and co-authors' main expressed concern is that an existing publication (Mills *et al* 2005b) recognises that the herbs potentially interact with HIV-drug metabolising enzymes in the body. Thereby they may cause herb-drug interactions, and purportedly could diminish the medication effects of drugs or lead to drug toxicity.

Awortwe *et al* (2014) found *H. hemerocallidea* displayed the most active herb-drug interactivity, among **South African**-grown or sourced plants used for HIV/AIDS that were laboratory-tested on enzymes. The other plants were *Echinacea purpurea*, *Lessertia frutescens* (see next), *Taraxacum officinale* (dandelion), *Moringa oleifera* and *Pelargonium sidoides*. From a herbalist perspective, *H. hemerocallidea* may in fact be a potent healing agent. However, it originates in grasslands of South Africa that are presently threatened by urban developments, and could become rapidly endangered by commercialisation and over-harvesting. Two similar *Hypoxis* species are listed in the IUCN Red List, one as endangered and another with inadequate data.

In a small study of *S. frutescens* (syn. *Lessertia frutescens*) in healthy **South African** participants, Johnson *et al* (2007) found no adverse effects, but statistically significant improved appetite, respiration, and important parameters of normal blood health. Koffuor *et al* (2014) showed two herbs, *Betula alba* and *S. frutescens*, both significantly reduced viral load in HIV-positive clinic patients in **Ghana**. Dane Africa and Smith (2015) however, caution against using *S. frutescens* as an anti-neuroinflammatory substance for HIV infection because, based on laboratory research in human cell culture, it demonstrated pro-inflammatory effects and increased migration of affected monocyte cells across a simulated blood-brain barrier. Three closely related species of *Lessertia* from South Africa are listed as endangered, or insufficient data, on IUCN's Red List.

A study by Bepe *et al* (2011) in **Zimbabwe** found somewhat lower quality of life scores for HIV-positive patients taking THMs and ARVs, compared to ARVs alone, implying this was linked to the herbs use. The herb consumers group were marginally older in age, better educated, and had taken ARVs for longer periods (p. 7). The patient group that was 'assessed for QoL' however had different socio-demographic characteristics (p. 8). The length of the study is not documented (in Bepe *et al* 2011) and no distinction is made between self-sourced or practitioner-prescribed herbs.

Bepe *et al* (2011) claimed adverse events were infrequent, with peripheral neuropathy marginally more common, and abdominal pains and skin rash occurring more often

among THM consumers. Of these, peripheral neuropathy is recognised as a common side effect of ARV drugs, and may also be linked to abnormal weight problems due to pharmaceutical drugs consumption (termed ‘lipodystrophy’); skin rashes also occur through ARV usage (cf. Mudzviti *et al* 2012, p. 3). Some HIV-positive patients take herbs with an aim of counteracting drug side effects, or if faced with health problems. They may have a lower quality of life due to such effects, or a worse overall health profile. While Bepe *et al* (2011, p. 5) state that the herb *Moringa oleifera* causes abdominal pain, they acknowledge that ARVs nevirapine and efavirenz both also cause abdominal pain. Studies such as this may expect to demonstrate potential for interactivity between herbs and drugs, and aim to discourage herbs use, but often do not take other relevant factors into account, such as type and source of THMs consumed, reasons for taking THM, cultural significance of THM and its influence on treatment, drug side effects, and QoL scores attributable to factors other than medication or herb effects.

Another study in **Zimbabwe** (Mudzviti *et al* 2012) found 381 of 388 (98.2%) HIV-positive patients enrolled in the trial took at least one type of herbal medicine concurrently with consumption of ARVs, suggesting THMs are of signal importance and widely considered effective. Herbs most commonly used (by 10.6 to 72.7% of participants), in order of highest to lowest frequency, were: *Allium sativum* (garlic), *Bidens pilosa*, *Eucalyptus globulus* (Australian blue gum), *Moringa oleifera*, *Lippia javanica*, *Peltoforum africanum*, *Aloe vera*, *Dicoma anomala*, Murunguyane, *Hypoxis hemerocallidea* and *Symphytum officinale* (comfrey). Findings of the study (Mudzviti *et al* 2012) indicated that consumption of *Musakavakadzi* and *Peltoforum africanum*, two indigenous herbs, significantly reduced adverse ARV drug-related reactions, which were frequent and often severe. The authors discuss patient reasons for consuming THMs, including efforts to alleviate discomfort caused by ARV.

### **Antioxidant therapy as a promising part of antiviral treatment**

The antioxidant potential of herbal medicines to support patients with HIV/AIDS may be explained in part by referring to research by Asokan *et al* (2015). These authors conducted detailed trials in India, and found that a polyherbal formulation had immunomodulatory action in HIV-positive subjects, and in blood serum studies, related to the degree to which the HIV virus penetrated cells. Antioxidants are known to be responsible for maintaining tissue integrity in the body, including the cell walls. Extracts of the commercialised **South African** cactus *Hoodia gordonii* have demonstrated a level of inhibition of HIV-1 (reverse transcriptase, and protease) and antioxidant activity, in laboratory tests (Kapewangolo *et al* 2016). However this study has been reported, effectively as a promotion for further commercialisation of the herb, without mentioning that all *Hoodia spp.* are listed as protected in CITES Appendix II. This listing is due to the sensitive desert habitat and limited range of *Hoodia* plants, and impacts on and likely further depletion of these species, due to over-harvesting for profit that occurred due to bioprospecting efforts by European pharmaceutical companies, and widespread sale of the processed herb as a weight-loss supplement in western countries.

While discussing therapeutic agents that target steps in the Ebola virus life cycle, Lai *et al* (2014) state that high-doses of the common naturopathic antioxidant supplement N-acetylcysteine (NAC) may help prevent a cytotoxic inflammatory-response trigger caused by accumulating virus-associated glycoproteins in the endoplasmic reticulum

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(one of the widely known cellular organelles within body cells). Assuming adequate protein nutrition, supplementary NAC<sup>[6]</sup> serves as a precursor that promotes the body's endogenous synthesis of glutathione, an important antioxidant responsible for maintaining oxidative balance within cells, and moderating various nervous system functions and pro-inflammatory pathways (Wu *et al* 2004; Dean, Giorlando & Berk 2011). NAC (and glutathione) thereby helps prevent inflammation and oxidative stress that causes cellular damage, and protects normal body functions. It is also used to reduce drug, lead and mercury toxicity (cf. Aremu, Madejczyk & Ballatori 2008), to drain respiratory mucus, and help lung disease (Ramos, Krahnke & Kim 2014, p.146), to enhance pregnancy retention in women suffering habitual miscarriage (Amin, Shaaban & Bediawy 2008), and to assist in treating viral infections. This includes HIV, where it replenishes depleted glutathione levels (Roederer *et al* 1992; Akerlund *et al* 1996; De Rosa *et al* 2000; Muller *et al* 2000), although not clearly in association with ARV therapy (Treitinger *et al* 2004).

Following these leads, the potential of many THMs and nutrients known for powerful antioxidant functions could be explored to support treatment and wellbeing of PLWHA. Common and widely accessed herbal and nutrient antioxidants used in CAM include green tea, alpha-lipoic acid, beta-carotene and vitamin A, vitamins C and E, minerals including zinc, and many edible phytochemicals obtained from whole plant foods, often colourful fruit and vegetables (Better Health 2012). Existing evidence for such use is limited but promising. Wiysonge *et al's* (2011) systematic review of African studies found no evidence of vitamin A supplementation decreasing mother to child transmission of HIV, or leading to improvements across several indicators of maternal or infant health, however it did increase infant birthweights to HIV-positive mothers. Another review found vitamin A reduced mortality in HIV-infected children (Humphreys *et al* 2010), while a third suggests that, despite vitamin A decreasing HIV-associated child mortality, it did not slow HIV disease progression in adults (Irlam *et al* 2010). More research is needed about roles of nutrient and herbal antioxidants in moderating HIV.

## Conclusion

HIV/AIDS causes millions of fatalities, on a global scale, particularly in Africa, and remains inadequately addressed by treatment with prescribed medications in resource-poor areas. This paper has reviewed African experiences of HIV/AIDS disease and treatments, and discusses pertinent contemporary issues of relevance to traditional herbal medicines use for HIV/AIDS, including relevant shifts in the status and socio-cultural contexts of herbal medicine practice in Africa. It then briefly provides a summary of plant-based research that prospectively may assist HIV-positive persons to preserve their health, and advocates for positive aspects of continued African herbal medicines use, with due caution regarding awareness of endangered species. As suggested above, based on this information, greater effort could be made to incorporate the work of traditional healers into funded health systems. Also, there is a need to conduct further detailed review research to establish what exactly has been learned to date about the use of THMs for HIV/AIDS treatment and support in Africa, particularly in human studies.

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<sup>6</sup> Note: some authors (e.g. Dean et al., 2011) caution against high dosages of NAC, which may be toxic for sensitive persons. Low doses are said to be anti-epileptic, but very high doses may cause seizures.



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