Prevalence and patterns of *Moringa oleifera* use among HIV positive patients in Zimbabwe: a cross-sectional survey

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Abstract

Supplementation of conventional medicines with herbs is increasing globally, including among people infected with HIV. Yet there is little data systematically describing the prevalence and patterns of this supplementation and on which counseling scripts can be based. *Moringa oleifera* is an herb found in the tropics and sub-tropics commonly used for medicinal and nutritional purposes. This survey determined the prevalence and patterns of use of *M. oleifera* among HIV positive patients. The study was a cross-sectional survey. HIV-infected adults were enrolled from an opportunistic infections clinic of a referral hospital. Using a previously piloted researcher administered questionnaire; patients who reported to the clinic over three months were interviewed about their use of herbal medicines. The focus was on *M. oleifera* use, and included plant part, dosage, prescribers and the associated medical conditions. Sixty-eight percent (68%) of the study participants consumed *M. oleifera*. Of these, 81% had commenced antiretroviral drugs. Friends or relatives were the most common source of a recommendation for use of the herb (69%). Most (80%) consumed *M. oleifera* to boost the immune system. The leaf powder was mainly used, either alone or in combination with the root and/or bark. *M. oleifera* supplementation is common among HIV positive patients. Because it is frequently prescribed by non-professionals and taken concomitantly with conventional medicine, it poses a potential risk for herb-drug interactions. Further experimental investigations into its effect on drug metabolism and transport would be useful in improving clinical outcome of HIV positive patients.

Keywords

*Moringa oleifera*, HIV; herb; interaction; complementary

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Introduction

The World Health Organization estimates that 80% of the world's population complements conventional therapy with traditional folk medicinal therapies in some aspect of their health care and the most popular of these are herbal therapies. In Africa, a wide range of traditional herbal medicines are used as part of therapy by the majority of HIV positive people. Several SADC countries support the use of Sutherlandia and Hypoxis obtusa (African Potato) for HIV management. 

Herbal medicine use may replace or complement conventional medicines, usually on a self-selection basis, since herbs are available over the counter. Moringa oleifera is commonly advocated for use in HIV positive people in the tropics and sub-tropics as a nutritional supplement and immune booster. Through the Ministry of Health and Child Welfare the staff of the District Hospitals and Rural Health Centers in Zimbabwe were introduced to Moringa cultivation and the nutritional benefits for severely malnourished children as well as TB and HIV positive patients. This herb is rich in vitamins and nutrients including beta carotene, potassium, calcium, magnesium, sulphur, iron and phosphorus and has a high protein and carbohydrate content. The hypotensive, hypocholesterolemic, hypo-glycemic, anti-ulcer, antibacterial, anti-inflammatory, antispasmodic and diuretic activities of M. oleifera have been demonstrated in laboratory studies.

Even though there is evidence to support M. oleifera’s health benefits and nutritional value, little is known about the effects when taken in conjunction with conventional medical therapies such as antiretroviral drugs. When herbs are taken concomitantly with anti-retroviral drugs, there is a potential for clinically significant interactions. Several studies have shown that garlic, St John’s wort, grapefruit juice and other herbs interact significantly with antiretroviral drugs. Herbs contain a mixture of naturally occurring chemicals, which when absorbed may also cause enzymes and transporters that act on drugs to be inhibited or induced. This may raise or lower conventional drug plasma levels which will result in toxicity or sub-therapeutic drug concentrations, drug resistance and treatment failure.

Since the risk of interaction increases with the number of concomitantly administered drugs and herbs, the risk of harmful interaction is particularly high in tropical Africa where treatment for opportunistic infections is the most frequent point of entry for admission to antiretroviral therapy (ART) programs, and where people traditionally supplement conventional medicines with a wide variety of herbal medicines. In order to build useful evidence for the safe use of herbal medicines concomitant to conventional drugs, research should be focused on specific relevant and popular herbs.

It is in this context that we conducted a cross-sectional survey to determine the prevalence and patterns of M. oleifera use by HIV positive people in Harare, Zimbabwe, to establish evidence of its importance among HIV positive patients.
Materials and Methods

The sampling frame was all HIV-infected adults presenting to the opportunistic infection clinic of the largest referral hospital situated in Harare, the capital city of Zimbabwe. Participants had to be already enrolled in the national antiretroviral program. Participants were selected as a convenience sample of patients who came to the clinic during April to June 2006 on one afternoon a week. Assuming that 79% of HIV positive people in Zimbabwe used traditional herbs, the required sample size was calculated to be 255 for 5% precision and 95% confidence level.

This research was carried out in compliance with the Helsinki Declaration. Ethical approval was granted by the University of Zimbabwe Ethics Committee and all participants gave oral and written informed consent before they were interviewed.

An interviewer-administered, previously piloted questionnaire was used to interview participants. Participants were asked about their age, sex, religion, level of education, drug history, consumption of herbal medicines, and specifically about M. oleifera plant parts consumed, dosage, indications and prescribers.

Statistical analysis was performed using STATA® 11.0. Categorical data was generated from the questionnaire responses. The Pearson’s χ² test was used to examine and assess possible associations between herbal consumption and other socio-demographic factors such as age, sex, religion and level of education.

Results

The acceptance rate was 97% and in the course of the study 263 men and women were recruited. 19% had not, at the time of interview, commenced ARV therapy. Table 1 describes the participants by gender, age, religion and educational level. The mean age was 39 years and the participants were more likely to be females than males (P=0.04). The proportion of participants who reported to have used M. oleifera within the last six months was high in this population (68%). Comparisons between self-reported users and non-users showed no statistically significant difference in age or educational status. Herbal medicine use appeared to be less common among apostolic believers, which was not the case for other religious affiliations. The most common reason for using M. oleifera was as an immune booster (80% of respondents). Other indications were digestive disorders, nutritional disorders, hypertension, immune suppression, diabetes and arthritis. Dosages given for these indications were not specific to a particular condition. The dose of M. oleifera taken ranged from a pinch to one tablespoon and varied with the part of the plant that is used. The leaf powder was mainly used, either alone (41%) or in combination with the root and/or bark (37%). In almost 70% of cases the herb was recommended or supplied by a friend or relative.

Discussion

A wide array of herbs is consumed as medicines in different parts of the world. Several studies have shown that concomitant intake of specific herbal medicines like St John’s wort
and garlic with antiretroviral drugs can result in herb-drug interactions that may lead to treatment failure, drug resistance and toxicity.\textsuperscript{12,13,17} It is important to know the prevalence and patterns of use for the herbs used in order to focus research efforts; tailor adherence counselling messages for local settings; and reduce the potential risk of herb-drug interactions.

This survey suggests that a large proportion of HIV-positive people enrolled onto the national ART roll-out program at Zimbabwe's largest referral hospital augment their conventional therapy with traditional herbal therapies that include \textit{M. oleifera}. First-line drugs included in the ART program include nevirapine, an extensively metabolized, low water-solubility drug that is prone to major interactions mediated by both transporters and metabolizing enzymes. In-vitro studies have shown that leaf extracts of Moringa oleifera inhibit CYP3A4 enzymes which metabolize a large proportion of drugs, including antiretroviral drugs.\textsuperscript{15,18} The potential for interaction between \textit{M. oleifera} and antiretroviral drugs therefore needs to be carefully monitored so that appropriate recommendations and advice can be given to those at risk. These results suggest that a high potential exists among HIV-positive Zimbabweans for \textit{M. oleifera} interactions with antiretroviral medications.

Immune boosting was the major reason cited for using \textit{M. oleifera among the study group}, suggesting that \textit{M. oleifera} is consumed daily or with every meal, thus increasing the risk for potential herb/drug interactions. Furthermore, relatives and friends were the common source of recommendation for use of \textit{M. oleifera} as opposed to healthcare professionals or support group counselors. These relatives and friends are unlikely to be knowledgeable about the potential risks of herb/drug interactions of the herbs they are advising patients to take.

While the sampling technique may have been a limitation in this study, the results are consistent with other studies that found that herbal medicine use in HIV clinics and among HIV-positive people is high.\textsuperscript{19-21}

\textbf{Conclusions}

There is a high prevalence of \textit{M. oleifera} use among HIV positive people attending public clinics in Zimbabwe. The patterns of use increase the risk of \textit{M. oleifera} interacting with any conventional drugs that may be taken concomitantly. Research focused on the effects of \textit{M. oleifera} on antiretroviral drug transport, metabolism and plasma profiles is needed in order to assess the specific risk of clinically significant herb-drug interactions in this community. This would enable accurate and evidence-based adherence counseling to patients, which could potentially reduce the likelihood of interactions.

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References

1. WHO. Traditional Medicine. Fact sheet no. 34, 2008. Available from: http://www.who.int/mediacentre/factsheets/fs134/en/
2. Ozsoy M, Ernst E. How effective are complementary therapies for HIV and AIDS? A systematic review. Int J STD AIDS. 1999; 10:629–35. [PubMed: 10582628]
3. Peltzer K, Preez N, Ramlagan S, Fomundam H. Use of traditional complementary and alternative medicine for HIV patients in KwaZulu-Natal, South Africa. BMC Public Health. 2008; 8:255. [PubMed: 18652666]
4. Langlois-Klassen D, Kipp W, Jiangri G, Rubaale T. Use of traditional herbal medicine by AIDS patients in Kabarole District, western Uganda. Am J Trop Med Hyg. 2007; 77:757–63. [PubMed: 17978084]
5. Giraldo, R. Southern african development community (SADC) meeting on nutrition and HIV/AIDS, November 28 and 29, 2002, Johannesburg, South Africa. Available from: http://www.robertogiraldo.com/eng/papers/ReportOfSADCMeeting.html
6. Ncube, D. Moringa and other highly nutritious plant resources: strategies, standards and markets for a better impact on nutrition in Africa. Accra, Ghana: 2006. Moringa programmes in Binga District (Zimbabwe).
7. Anwar F, Latif S, Ashraf M, Gilani AH. Moringa oleifera: a food plant with multiple medicinal uses. Phytotherapy Res. 2007; 21:17–25.
8. Seshadri S, Nambiar VS. Kanjero (Digera arvensis) and drumstick leaves (Moringa oleifera): nutrient profile and potential for human consumption. World Rev Nutr Diet. 2003; 91:41–59. [PubMed: 12747087]
9. Cáceres A, Saravia A, Rizzo S, et al. Pharmacologie properties of Moringa oleifera 2: Screening for antispasmodic, antiinflammatory and diuretic activity. J Ethnopharmacol. 1992; 36:233–7. [PubMed: 1434682]
10. Nambiar VS, Bhadalkar K, Daxini M. Drumstick leaves as source of vitamin A in ICDS-SFP. Indian J Pediatr. 2003; 70:383–7. [PubMed: 12841398]
11. Barry M, Gibbons S, Back D, M F. Protease inhibitors in patients with HIV disease. Clinically important pharmacokinetic considerations. Clin Pharmacokinet Pharm Res. 1997; 32:194–209.
12. Di YM, Li CG, Xue CC, Zhou SF. Clinical drugs that interact with St. John’s wort and implication in drug development. Curr Pharm Des. 2008; 14:1723–42. [PubMed: 18673195]
13. Gurley BJ, Hubbard MA, Williams DK, et al. In vivo effects of goldenseal, kava kava, black cohosh, and valerian on human cytochrome P450 1A2, 2D6, 2E1, and 3A4 phenotypes. Clin Pharmacol Ther. 2005; 77:415–26. [PubMed: 15900287]
14. Lee LS, Andrade ASA, Flexner C. Interactions between natural health products and antiretroviral drugs: pharmacokinetic and pharmacodynamic effects. Clin Infect Dis. 2006; 43:1052–9. [PubMed: 16983620]
15. Monera TG, Wolfe AR, Maponga CC, et al. Moringa oleifera leaf extracts inhibit 6β-hydroxylation of testosterone by CYP3A4. J Infect Dev Ctries. 2008; 2:379–83. [PubMed: 19745507]
16. Köhler GI, Busse R, Hoopmann M, et al. Drug-drug interactions in medical patients: effects of in-hospital treatment and relation to multiple drug use. Int J Clin Pharmacol Ther. 2000; 38:504–13. [PubMed: 11097142]
17. van den Bout-van den Beukel CJ, Koopmans PP, van der Ven AJ, et al. Possible drug-metabolism interactions of medicinal herbs with antiretroviral agents. Drug Metab Rev. 2006; 38:477–514. [PubMed: 16877262]
18. Wrighton SA, Stevens JC. The human hepatic cytochromes P450 involved in drug metabolism. Crit Rev Toxicol. 1992; 22:1–21. [PubMed: 1616599]
19. Bepe N, Madanhi N, Mudzviti T, et al. The impact of herbal remedies on adverse effects and quality of life in HIV-infected individuals on antiretroviral therapy. J Infect Dev Ctries. 2011; 5:48–53. [PubMed: 21330740]

20. Dhalla S, Chan KJ, Montaner JSG, Hogg RS. Complementary and alternative medicine use in British Columbia—a survey of HIV positive people on antiretroviral therapy. Complement Ther Clin Pract. 2006; 12:242–8. [PubMed: 17030295]

21. Faragon JJ, Purdy BD, Pi PJ. An assessment of herbal therapy use, adherence and utilization of pharmacy services in HIV clinics. J Herbal Pharmacother. 2002; 2:27–37.
Table 1
Socio-demographic characteristics of participants by *M. oleifera* use

|                      | M. oleifera usage 68% (n=179) | Users 32% (n=84) | Non-users | P   |
|----------------------|--------------------------------|------------------|-----------|-----|
| Mean age             | 39.3±9.5 years                 | 39.9±8.5 years   | 0.5826    |     |
| Gender               |                                |                  |           |     |
| Male                 | 30% (53)                       | 13% (11)         | 0.040     |     |
| Female               | 70% (126)                      | 87% (73)         |           |     |
| Religion             |                                |                  |           |     |
| Non-apostolic Christian | 79% (142)                       | 77% (65)         | 0.038     |     |
| Apostolic Christian  | 12% (21)                       | 21% (18)         |           |     |
| Traditional          | 4% (7)                         | 0% (0)           |           |     |
| Other                | 5% (9)                         | 2% (1)           |           |     |
| Education level      |                                |                  |           |     |
| No School            | 2% (3)                         | 2% (2)           | 0.80      |     |
| Primary              | 24% (43)                       | 23% (19)         |           |     |
| Secondary            | 66% (119)                      | 70% (59)         |           |     |
| Tertiary             | 8% (14)                        | 5% (4)           |           |     |