

## The Impact of Complementary and Alternative Medication Use on Antiretroviral Plasma Concentrations and Adherence

### Abstract

**Understanding how the use of complementary and alternative medications (CAM) in HIV/AIDS, and its effect on antiretroviral (ARV) plasma concentrations, and medication adherence is critically important.** The prevalence of CAM use in the United States is increasing and is highest among patients with long-term illnesses such as cancer, arthritis, and HIV/AIDS. Common use of CAM may result in detrimental drug interactions or adverse effects, increasing the risk for immunologic and virologic failure and the development of drug resistance and/or toxicity. CAM refers to diverse therapeutic practices, based on allopathic medicine (including herbs, megavitamins, and alternative practices such as acupuncture). The risk of drug interactions in HIV-infected patients is unprecedented, as many take at least three ARV medications concomitantly for HIV and may receive other medications for supportive care and opportunistic infections. The non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs) are the basis of highly active ARV therapy (HAART) in HIV-infected patients. NNRTIs and PIs are both substrates for and modulate the cytochrome P450 enzyme system (CYP) and drug transporters, so drug interactions with these agents are often unavoidable and difficult to predict. Previous studies have identified the patient demographics of CAM use, but have not controlled for concomitant ARVs nor identified the proportion of patients taking specific CAM known to adversely affect ARV concentrations or their effects on HAART adherence. No studies to our knowledge have investigated the prevalence of these specific CAM used and the relationship between CAM use, ARV drug concentrations, and adherence to HAART.

HIV-infected patients who take at least 95% of HAART are more likely to achieve a successful virologic outcome, have a greater increase in CD4 lymphocyte count, and spend fewer days in the hospital. Although, it is still not certain which pharmacokinetic (PK) parameter best correlates with virologic efficacy, previous studies have shown that an inverse correlation exists between blood plasma ARV trough concentrations (Ctr) and HIV viral load, and dose adjustments based on Ctr can be more effective than taking the standard recommended doses.

This research project seeks to investigate the impact of CAM use in HIV-infected patients who are taking ARVs. Two Specific Aims are proposed. In **Specific Aim 1**, the association between the use of specific CAM and ARV plasma Ctr will be determined and compared to established concentrations. In **Specific Aim 2**, the association between use of CAM and adherence to HAART will be investigated by measuring adherence utilizing two different methods. This proposal is a prospective, cross-sectional, cohort study of 120 HIV-infected subjects on stable ARV therapy. Subjects will answer questionnaires regarding CAM use, patient demographics, concomitant medications, and adherence and laboratory values, concomitant disease states will be obtained from the medical chart. Subjects will be divided equally into 2 groups: those using at least one CAM and those not using any CAM. Blood for quantifying ARV Ctr will be collected. Drug concentrations will be analyzed by validated HPLC/UV methods.

This study will provide important information necessary to further determine the impact of CAM use in HIV-infected patients taking ARV medications and their implications to efficacy, adverse effects, and PK/PD. The long-term objectives of this project are to: 1) improve ARV usage by advancing the understanding of CAM use on ARV PK/PD, in order to minimize drug interactions and optimally choose effective combinations of ARV therapies and 2) design and implement a method to efficiently and effectively identify, counsel, and manage patients on high-risk CAM and traditional ARVs.