

Observational Study

Improvement in human immunodeficiency virus-1/acquired immune deficiency syndrome patients' well-being following administration of "Phyto V7"

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Data sharing: Technical appendix, statistical analyses, and dataset are available from the corresponding author at dr.borkow@gmail.com. Consent was not obtained but the presented data are anonymized and risk of identification is nonexistent.

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Abstract

AIM: To corroborate the capacity of Phyto V7, a complex of phytochemicals, to improve the physical well-being of human immunodeficiency virus-1 (HIV-1) infected and acquired immune deficiency syndrome (AIDS) patients not undergoing antiretroviral treatment.

METHODS: Two hundred and thirty nine HIV-1 sero-positive male and female voluntary inmates were recruited through the Uruguay National Program of AIDS. The study participants received for 90 consecutive days every eight hours two tablets (760 mg/each) of Phyto V7, containing a mix of the following phytochemicals: flavonols (Kaempferol, Quercetin), flavones (Apigenin, Luteolin), hydroxycinnamic acids (ferrulic acid), carotenoids (Lutein, Lycopene, Beta carotene) and organosulfur compounds, all from vegetal origin. The participants did not receive any antiretroviral treatment during the study. At days 0, 30, 60 and 90 (± 2 d) the participants were evaluated for body mass index (BMI), tolerance to Phyto V7 and Index of Quality of Life based on the Karnofsky scale. ANOVA, Tukey Post-test, χ^2 test and Wilcoxon Signed Rank test were used to analyze the effect of treatment.

RESULTS: One hundred and eighty nine study participants finished the study. Already after 30 d of Phyto V7 consumption, the weight, BMI and Karnofsky score statistically significantly improved ($P < 0.001$), and continued to improve until the end of the study. The mean weight gain per participant during the 90 d was

of 1.21 kg (approximately 2% of body weight). The overall increase in the mean Karnofsky score after 90 d was 14.08%. The lower the BMI and Karnofsky score of the participants were at the beginning of the study, the more notorious was the improvement over time. For example, the mean increment of Index of Quality of Life, among the participants with an initial Karnofsky score of 5 or below ($n = 33$) from day 0 to day 90, was of 35.67% (0.476 ± 0.044 vs 0.645 ± 0.09 ; $P < 0.001$). The tolerability to Phyto V7 was very good and no adverse reactions were recorded or reported.

CONCLUSION: Administration of the Phyto V7 can be an important tool to improve the well-being of HIV-1 seropositive individuals and AIDS patients, not undergoing antiretroviral treatment.

Key words: Phytochemicals; Karnofsky score; Nutrition; Human immunodeficiency virus-1; Acquired immune deficiency syndrome

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Core tip: Phyto V7 is a complex of phytochemicals and micronutrients. Phyto V7 has been found to stimulate the immune system and dramatically improve the physical well-being of terminal acquired immune deficiency syndrome (AIDS) patients. The current study demonstrates the capacity of Phyto V7 to improve the physical well-being of human immunodeficiency virus-1 (HIV-1) infected and AIDS patients not undergoing antiretroviral treatment, as demonstrated in 199 individuals. We conclude that administration of the food supplement Phyto V7 can be an important tool to improve the well-being of HIV-1 seropositive individuals and AIDS patients, not undergoing antiretroviral treatment.

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INTRODUCTION

The energy needed for physical activity and for maintaining the body weight is higher in human immunodeficiency virus-1 (HIV-1) infected individuals than in non-HIV infected individuals^[1,2]. Acquired immune deficiency syndrome (AIDS) patients spend approximately 20% to 30% more energy than healthy individuals in order to maintain their body weight, including when receiving highly active antiretroviral treatment (HAART)^[3,4]. The World Health Organization has recommended including micronutrient supplementation as an integral part of all HIV treatment programs^[5]. Micronutrient supplementation trials

demonstrated a reduced mortality and improved clinical outcomes in HIV-1 infected individuals, regardless of their clinical stage and use of antiretrovirals^[6-9].

Phytochemicals, chemical compounds that occur naturally in plants, in addition of serving as micronutrients, enhance nonspecific immunity^[10], down regulate inflammatory diseases^[11], possess radical scavenging activities^[12], and inhibit disease progression^[13-19]. For example, administration of phytochemicals reduced hepatotoxic, lithic, and hepatitis related adverse symptoms^[19]. Some phytochemicals inhibit HIV-1 protease and integrase, and inhibit viral entry to target cells^[12,20-24]. Phyto V7 is a complex of phytochemicals, which also contains micronutrients, registered as a nutritional supplement in several countries. Administration of Phyto V7 to chicks enhances their humoral immune responses against Newcastle Disease Virus following vaccination^[25]. Furthermore, its administration to human papilloma virus (HPV) affected women undergoing electrosurgical excision of cervical lesions resulted in approximately two-fold higher elimination of HPV than in the control group of women. In the group of woman receiving Phyto V7 there was an increase in the local cellular immune responses, as exemplified by much higher elevated presence of NK cells and cytotoxic T-cells (CD8⁺) in the cervical smears 90 d after the electrosurgical excisional procedure^[26]. We have also found an increase in CD4⁺ T-cells in HIV-1 infected individuals taking Phyto V7, without affecting their viral loads titers (manuscript in press). Taken together, the above findings indicate that Phyto V7 has immunestimulatory properties. Remarkably, administration of Phyto V7 to 9 terminally ill AIDS patients resulted in a dramatic improvement in their physical status^[27].

Antiretroviral treatment, which can effectively control viremia, requires high patient adherence for life. Low patient adherence results in the appearance of drug resistant viral isolates and necessitates different treatment protocols and salvage therapy options. Unfortunately, in many developing countries HIV-1 infected individuals are not treated at all. Many reasons account for that, such as inappropriate or non-existent centralized government treatment programs and elevated costs of antiretroviral treatments. One of the treatment neglected populations, in many developing countries, is prison inmates. The rates of HIV-1 infection are very high in this population^[28,29]. Prison inmates are at higher risk of HIV-1 infection due to increased intravenous drug use, unprotected sexual activity, exposure to blood during fights, and tattooing.

In the current manuscript we report the very significant improvement in the well-being of 199 HIV-1 infected prison inmates, who did not receive any antiretroviral treatment while in prison, receiving only a daily administration of Phyto V7.

MATERIALS AND METHODS

The methodological design of the study was analytical

Table 1 Karnofsky score used

10	No complaints, no signs of disease
9	Capable of normal activity, few symptoms or signs of disease
8	Normal activity with some difficulty, some symptoms or signs
7	Caring for self, not capable of normal activity or work
6	Requiring some help, can take care of most personal requirements
5	Requires help often, requires frequent medical care
4	Disabled, requires special care and help
3	Severely disabled, hospital admission indicated but no risk of death
2	Very ill, urgently requiring hospital admission, requires supportive measures or treatment
1	Moribund, rapidly progressive fatal disease processes

Table 2 Frequency of increase in the weight of the study participants over time

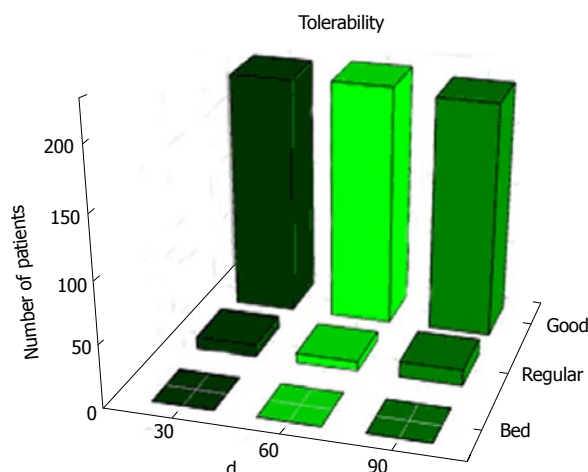
Weight	30 d		60 d		90 d	
	n	%	n	%	n	%
Decrease	27	13.6	19	9.5	12	6
Equal	65	32.7	36	18.1	24	12.1
Increase	107	53.8	144	72.4	163	81.9

and longitudinal, conducted by mid-2010 in Uruguay through the patronage of Dr. Tabaré Vazquez, President of Uruguay, by the General Direction of Prisons and the Uruguay Association of Seropositives. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was reviewed and approved by the Ethical Medical Committee of the Ministry of Health of Uruguay. HIV-1 seropositive male and female inmates were recruited from the Libertad, La Tablada and Cabilado prisons. All study participants gave their informed consent prior to the commencement of the study.

Phyto V7 was donated by the Israel Project Life Foundation and Immune Nutrition Incorporated. Phyto V7 was registered as a food supplement (Registration Number 54221) at the Division of Health Products, Department of Food. Each Phyto V7 tablet contained 760 mg of the following phytochemicals: flavonols (Kaempferol, Quercetin), flavones (Apigenin, Luteolin), hydroxy-cinnamic acids (ferrulic acid), carotenoids (Lutein, Lycopene, Beta carotene) and organosulfur compounds, all from vegetal origin.

During the study, each participant was given every 8 h two Phyto V7 tablets. At days 0, 30, 60 and 90 (± 2 d) the participants were evaluated for body mass index (BMI), tolerance to Phyto V7 and well-being. The well-being was estimated according to the modified Karnofsky scale (Table 1). Each time the doctor in charge filled the questionnaire while examining and consulting each study participant, without seeing the previous already filled questionnaires. No data regarding the viral load or immune profile of the participants could be gathered. The participants did not receive any antiretroviral treatment during the study.

The differences between weight and BMI were analyzed with Kruskal-Wallis One Way Analysis of

**Figure 1** Assessment of Phyto V7 tolerability. The assessment of tolerability is based on the medical examination and the participant's feedback and general feeling.

Variance on Ranks (ANOVA) and Tukey Post test. The proportions of levels of quality of life were analyzed with the χ^2 test. An Index of Quality of Life was defined by dividing the levels of the Karnofsky score by the maximal level (10) and applied the Wilcoxon Signed Rank Test to analyze the differences. The SigmaPlot 12 software was used to conduct the statistical analyses.

RESULTS

A total of 239 HIV-1 seropositive inmates were recruited. Forty participants did not finish the study due to various reasons, such as being transferred to other facilities and being released from prison. Thus, the data presented is of 199 participants.

As reported by the study participants, after taking Phyto V7 for 30, 60 and 90 d, the tolerability to Phyto V7 was very good (Figure 1). No adverse reactions were recorded or reported.

As can be seen in Table 2, the proportion of individuals that participated in the study in whom there was an increase in their weight was 53.8%, 72.4% and 81.9% after 30, 60 and 90 d, respectively. The increase in weight was statistically significant ($P < 0.001$). After 90 ds there was a decrease in weight in only 6% of the patients. The increase in the mean weight of the study participants can be appreciated in Figure 2B. The mean weight gain per participant during the 90 d was of 1.21 kg (approximately 2% of body weight).

In accordance with the increase in the weight, also the BMI of the participants increased over time (Figure 3A). The mean of BMI increased from 23.18 on day 0 to 23.64 on day 90, a 1.98% increase. When analyzing the mean increase in the BMI of the group of participants that had a BMI of below 21 at the beginning of the study ($n = 60$), the increase in BMI is even more impressive (Figure 3B) - the mean in BMI among this group increased from 19.69 on day 0 to 20.24 on day 90, a 2.75% increase. Similarly, when

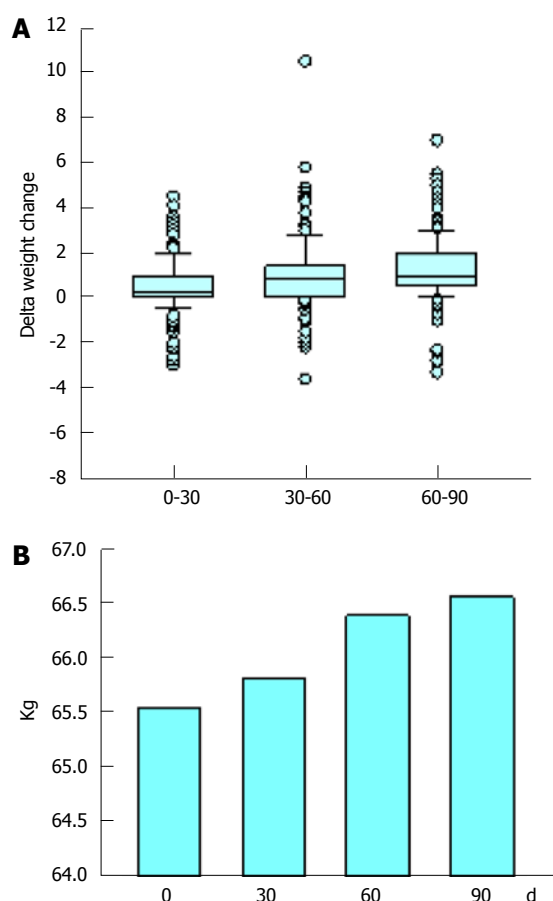


Figure 2 Participant body weight. A: Box plots describing the delta change in the weight of the study participants. The boxes represent the middle 50% of the data values. The horizontal line across the box marks the median value. The error bars show the 10th and 90th percentiles of the population. Individual data-points falling beyond these boundaries are shown as dots; B: The mean weight of the study participants.

looking into the 11 participants that had a BMI of below 19 at the beginning of the study ($n = 11$), the mean BMI increased from 18.02 on day 0 to 18.62 on day 90, a 3.04% increase.

The overall quality of life of the participants increased over time, as determined by the Karnofsky scale determinations, and as exemplified for the Index of Quality of Life in Figure 4A. The Index of Quality of Life was already statistically significantly higher at day 30 compared to day 0 (mean of 0.657 vs 0.632; $P < 0.001$). The Index of Quality of Life continued to increase with Phyto V7 consumption, from a mean of 0.657 to 0.7 and 0.721 at days 30, 60 and 90, respectively ($P < 0.001$ between each data point). The overall increase in the mean Karnofsky score after 90 d was 14.08%.

When analyzing the changes in the Index of Quality of Life among the participants that at day 0 had a Karnofsky score of 5 or below ($n = 33$), the changes in the score from day 0 to day 90 are even more impressive, *i.e.*, 35.67%, from 0.476 ± 0.044 to 0.645 ± 0.09 ($P < 0.001$; Figure 4B). The clear increase in the proportions of the Karnofsky score over time is depicted in Figure 4C. For example, the level score 8

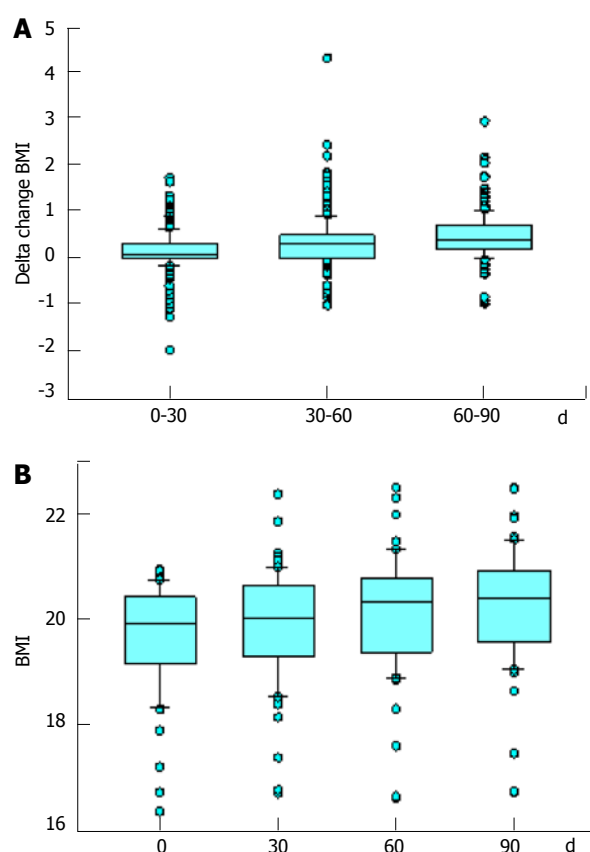


Figure 3 Body mass index of study participants. Box plots describing (A) the delta change in body mass index (BMI) of all the study participants over time and (B) the BMI of the participants who had a BMI of less than 21 at the onset of the study.

increased from day 0 to day 90 by approximately 5 fold, from 7.5% to 36.7% for all study participants. In contrast, the level score 5 decreased from day 0 to day 90 from 13.1% to 1.5%.

At day 90, approximately 73% of the study participant's felt that consumption of Phyto V7 was beneficial to them, while approximately 25% felt the same. This is in accordance with an increase in weight in 81.9% of the study participants. Two percent of the patients felt that their situation worsened during the 90 d study.

DISCUSSION

Since the institution of HAART, the number of individuals becoming ill with AIDS has declined significantly and the prognosis of AIDS patients has improved notably. However, low compliance, viral cross-resistance, and significant side effects caused by HAART, serve as reason to postpone HAART. In developing countries, wide implementation of HAART may be even more problematic due to high costs, infrastructure problems and high prevalence of other ailments such as anemia and co-infections^[30,31]. Thus, new, non-expensive, safe, easy to take alternative or complementary remedies, that can improve the patient's well-being, are very attractive for the treatment of individuals that fail HAART or antiretroviral naïve patients that can not get

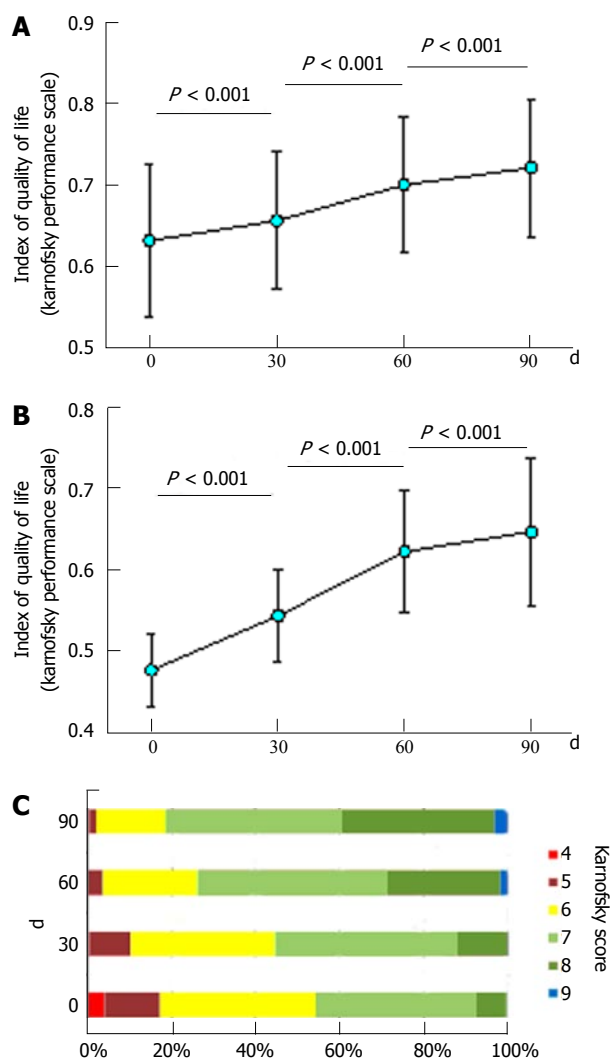


Figure 4 Quality of life of study participants based on the Karnofsky score. A: The mean and standard deviation of the Index of Quality of Life score of all study participants and of (B) participants who had a Karnofsky score of 5 or less at the onset of the study; C: The proportions of Karnofsky score at days 0, 30, 60 and 90. The *P* values of Wilcoxon Signed Rank Tests between each day are shown.

antiretroviral therapy.

Recently we published the results of a study that was conducted with 9 terminally ill AIDS patients living in a hospice^[27]. All patients had very high HIV-1 viral loads and 8 out of the 9 patients were scored as C3 according to the United States Centers for Disease Control status index. Seven out of the 9 patients were antiretroviral naïve patients. During the study they did not receive antiretroviral treatment but only received the food supplement Phyto V7. While most of the patients at the commencement of the study could not eat, stand, dress or shower by themselves, after 3 mo of Phyto V7 supplementation all patients could eat, sit down, shower, stand up and dress without help. The well-being of the patients improved dramatically, both physically and mentally. The success of this trial was the incentive to conduct the current study.

As with the terminally ill AIDS patients, the administration of Phyto V7 to HIV-1 infected, asymptomatic and

symptomatic individuals in the current study, resulted in a very significant improvement in the individuals' well-being. The weight, BMI and Karnofsky score of the study participants increased notably, especially in those who had a low BMI and low Karnofsky score at the onset of the study. Increase in appetite, weight, and individuals mood, has a positive outcome in the individual well-being. Notably 83% of the participants adhered until the end of the trial and took Phyto V7, indicating the high likelihood that they will continue using Phyto V7 also finalizing the study. Part of the positive effect of Phyto V7 can also be explained as phytochemicals having radical scavenging activities^[12], stimulating nonspecific immunity^[10], and down regulating inflammatory responses^[11]. Indeed, Phyto V7 has been shown to enhance humoral and cellular immune responses^[25,26]. It is not clear from this study if crucial parameters relevant to the progression to AIDS were affected, such as the CD4⁺ T-cell counts and viremia. However, in a another study (manuscript in press) the administration of Phyto V7 resulted in the upregulation of CD4⁺ T-cell counts without affecting viral loads, indicating that Phyto V7 has an immuno-stimulating effect and no direct antiviral effect.

Administration of a food supplement, such as the Phyto V7, is extremely inexpensive as compared to HAART. Phyto V7 is from a natural source and as opposed to antiretrovirals, does not affect directly HIV-1. Thus its uptake with low adherence would not result in appearance of drug resistant viruses. Obviously, in order to increase its efficacy, high compliance is desired. Administration of Phyto V7 may potentially postpone the need to treat HIV-1 infected individuals with HAART, postponing the potential complications associated with this treatment. It may well be that Phyto V7 can be given in conjunction with HAART resulting in better prognosis. These assumptions need to be examined in placebo controlled studies.

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COMMENTS

Background

The immune system of human immunodeficiency virus-1 (HIV-1) infected individuals decays with the progression of time until they develop immu-

nodeficiency. HIV-1 infected individuals also have increased energy needs than non-HIV infected individuals and many suffer from significant weight loss and wasting. Micronutrient supplementation is thus recommended as an integral part of all HIV treatment programs.

Research frontiers

Micronutrient supplementation improves the physical condition of HIV-1 infected individuals and acquired immune deficiency syndrome (AIDS) patients regardless of their clinical status and antiretroviral treatment, as was demonstrated in several studies. The administration of micronutrients that also enhance the immune system may be significantly advantageous to the HIV-1 infected individuals.

Innovations and breakthroughs

The food supplement Phyto V7 is a complex of phytochemicals and micronutrients. Phyto V7 has been found to stimulate cellular and antibody immune responses against viruses both in humans and in chicks. Importantly, administration of Phyto V7 to 9 terminal AIDS patients resulted in dramatic improvement in their physical well-being. The current study corroborated the significant positive effect on Phyto V7 on the physical well-being of HIV-1 infected individuals. This was demonstrated by the significant increase in the body weight and physical well-being a very large group of HIV-1 infected individuals not undergoing antiviral treatment that only received a daily dose of Phyto V7 for a period of 90 consecutive days.

Applications

Administration of the Phyto V7 can be an important tool to improve the well-being of HIV-1 seropositive individuals and AIDS patients, not undergoing antiretroviral treatment. It may well be that administration of Phyto V7 together with antiviral treatment is highly advantageous. Further studies should test this hypothesis.

Terminology

Phytochemicals are chemical compounds that occur naturally in plants. These chemicals, in addition of serving as micronutrients, have been found to enhance nonspecific immunity, down regulate inflammatory diseases, and inhibit disease progression. The Karnofsky score is a well-accepted scale used to assess the quality of life of patients. It was used by the examining physicians to address the well-being of the study participants during the study.

Peer-review

This is an interesting work with promising results in which Phyto V7, a phytochemical mix, quickly and effectively improves the weight and makes most of the HIV patients treated to feel better. For these kinds of patients it is good to be able to help them and this treatment might prepare them for a future more aggressive antiviral therapy.

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