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Research Article

Enhancement of Cluster Differentiation Antigen 4 and the Body Mass Index in Patients with HIV

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Abstract

Background and Objective: The HIV is the virus that can cause AIDS by attacking white blood cells such as T cells CD4⁺. This study aimed to determine the relationship between antiretroviral (ARV) drugs and supplements of black tea (*Camellia sinensis* var. *assamica*) powder to increase the CD4 and Body Mass Index (BMI) in patients with HIV. **Materials and Methods:** This study used a quasi-experiment. From the average number of 10 patient visits every month in the period of January to March, 2021 in the outpatient clinic for patients diagnosed positive with HIV-AIDS, seventy patients were enlisted and divided into 2 groups from 12 districts, 35 groups intervention received ARV drugs and supplements steeping black tea powder form as much as 1,505 mg, equivalent to 5-7 glasses a 1,000-1,400 mL/day for 24 weeks, while the control group of patients received ARV drugs, standard diet each house and nutrition education. **Results:** This study showed a BMI before the intervention control group's 1st week 19.31 ± 2.17 and after the intervention for 24 weeks, a BMI of 18.78 ± 2.42 . CD4 levels before the intervention, the 1st week were 380.57 ± 78.63 and after the intervention for 24 weeks, 365.74 ± 81.13 in this case either BMI or CD4 did not experience significant improvements. While the intervention group before the intervention 1st week BMI was 21.61 ± 3.32 and after the intervention for 24 weeks, 22.2 ± 3.19 or increased significantly ($p = 0.002$) and the levels of CD4 in the 1st week before the intervention, 360.91 ± 221.20 and after the intervention for 24 weeks, 425.14 ± 178.87 or increased significantly ($p = 0.003$). **Conclusion:** The ARV therapy and black tea powder significantly increased levels of CD4 and BMI HIV sufferers through the improvement of the status of T-cell immunity and body mass index.

Key words: Antiretroviral drug, black tea, body mass index, CD4, HIV, nutrition, epigallocatechin gallate

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Human Immunodeficiency Virus (HIV) has been a serious health problem since 1981, when it became a pandemic and continues to trouble people around the world. It has not only led to losses in the health field but also in the social, economic, political, cultural and demographic sectors¹. The HIV is an infectious disease that attacks the human immune system. Since the occurrence of the epidemic, more than 79.3 million people worldwide have been infected with HIV and more than 36.3 million people have died of AIDS. In 2020, an estimated 37.7 million people were living with HIV (PLWHA) with 1.5 million new cases and 680.000 million deaths caused by AIDS. The increasing numbers of PLWHA indicate the effect of antiretroviral therapy that can prolong life expectancy and is now available for many people with HIV. This can be seen clearly from the trend of the number of deaths due to HIV which continues to decline when compared with the previous years. The same trend was seen in Indonesia, with the cumulative basis reflecting the increase in the number of PLWHA, while there was a decrease in the number of new cases in 2020.

A person infected with HIV does not directly show certain signs or specific symptoms after acute infection, but the disease begins with a period with no symptoms (asymptomatic) that can last for 8-10 years. The progression of the course of the HIV disease is determined by the nutritional status of the patient. Malnutrition could occur in all phases of HIV infection, with most nutritional problems occurring along with an increase in viral load, opportunistic infections and the development of virus resistance².

The use of antiretroviral (ARV) therapy has succeeded in reducing the disease severity, but the reality in clinical services shows that HIV still causes a decrease in CD4 because the virus continues to replicate. Additionally, since the advent of the epidemic, PLWHA still experiences certain micronutrient disorders, for example, children who are HIV positive often have reduced levels of certain antioxidants, such as vitamins A, C and E. This form of malnutrition is significantly amplified due to increased levels of oxidative stress in the form of free radicals. In addition, the virus is known to mutate in some patients with HIV who have resistance to ARV therapy, so a new combination must be prescribed. Most patients are then given several ARV drugs that are known to be toxic but generally do not have serious side effects. The combination is expected to support the need for non-toxic therapy and can block HIV-1 protein³. The use of monotherapy and a two-drug combination consisting of two nucleosides should be avoided because the results of clinical trials are showing the

effectiveness of the regimen becomes lower, including levels of suppression of the virus were not optimal^{4,5}.

The above review focuses on one of the potential applications of natural catechin as a form of therapy for antivirus infection. Based on the chemical structure and molecular weight of the catechins, epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) at certain doses can block the replication of the HIV-1 virus and give 100% inhibition with 50 pM EGCG in peripheral blood lymphocyte cells. As confirmed by Hauber and colleagues, treatment in the form of EGCG catechins contained in tea elements of chemical compounds can help reduce the viral load in PLWHA⁶. According to the study conducted by comparing the 3'-azido-3'-deoxythymidine (AZT) and EGCG, which were added to the cell culture, the results concluded both EGCG and AZT act as allosteric inhibitors of reverse transcriptase and can inhibit infection of HIV⁷.

Supplements formed by steeping black tea (*C. s. assamica*) powder provide an alternative source of free radicals because it is known to contain compounds essential for the human body such as the flavins similar to or more potent than catechins, has 12 hydroxyl groups (OH), the main compound theaflavin (TF1,-3-gallate/TF2A,-3'-gallate/TF2B,-3,3'-digallate/TF3), analogues (epicatechin gallate (ECG), theaflavate A, theaflavate B, isotheaflavin-3'-o-gallate and neotheaflavin-3-ogallate), has a rate constant that can arrest higher superoxide radicals (1×10^7 /MS), prevent lipid oxidation and enhance the natural antioxidants present in the body such as glutathione-S transferase (GST), glutathione peroxidase (GPX), superoxide dismutase (SOD) and catalase (CAT)⁸.

In the study of black tea (*blesstea*) as an immunostimulant, intake of black tea the results showed that immunostimulatory activity increased. Further study is needed to see the benefits of supplements from steeping powdered form of black tea (*C. s. assamica*) for PLWHA and to determine the content of Gallocatechin, catechin, Epi Catechin, Epi Catechin error, Epi Gallocatechin, Epi Gallocatechin error, Theaflavin, Thearubigin, caffeine and tannins in the black tea which is used as an alternative source of antioxidants in overcoming autoimmune deficiency and improving BMI in patients with HIV.

MATERIALS AND METHODS

Study area: The study was carried out in January to March, 2021. Pre-test and post-test CD4 clinical examination at the Clinical Pathology Laboratory of Wahidin Sudirohusodo General Hospital, viral load examination at Hasanuddin

University Hospital and the Indonesian Ministry of Health. The Directorate General of Health Efforts at the Makassar Health Laboratory Center, while the control group of 35 HIV patients continued the ARV regimen that had been consumed and pre-test and post-test clinical examinations in the form of CD4 at the Pathology Laboratory of Bahteramas General Hospital, Southeast Sulawesi Province, including pre-measurement of BMI test and post-test for both groups.

Research design: This quasi-experimental study was conducted with random sampling to determine the relationship of supplements made from steeping black tea (*C. s. assamica*) powder with the increase of CD4 and BMI nutritional status of PLWHA, at the Bahteramas General Hospital Southeast Sulawesi Province, for 24 weeks. The study population was all patients (70 people) with HIV who visit the HIV-AIDS clinic of the Bahteramas General Hospital in Southeast Sulawesi Province. These research subjects then were randomized and the intervention group received additional supplements made from steeping black tea (*C.s. assamika*) powder as much as 1,505 grams as many as 5-7 times, with the water temperature 90°C in 1,000-1,400 mL cups/day, with the standard diet served in each household and nutrition education for 24 weeks.

Meanwhile, the control group received a standard diet at home and nutrition education, which was done at the time the patients with HIV were taking anti-retroviral therapy at the hospital every month. Both groups received antiretroviral therapy following the standard procedure of giving ARV therapy to patients with HIV. Measurements of BMI and CD4 laboratory tests were done during the 1st week of the pre-test and before treatment, then at the post-test in the 24th week. The food intake data were obtained using dietary recall every month in both groups at the time of taking the ARV therapy and consuming the black tea powder supplement.

Examination methods: The examination methods used in these studies were: (1) Test the percentage of total catechins in black tea or identification of active compounds in black tea (*C. s. assamica*) formed as a powder containing the compound EGCG, theaflavin, the rubigin, caffeine and tannins in tea supplements consisting of 15 g of black powder, at the Research Center for Tea and Quinine Gambung West Java, Indonesia, (2) Interviews/anamnesis were conducted to obtain identity data, past medical history and present and the history of the food intake with the method of guided questions and completed every month on the subject of research, (3) Examination of anthropometry to measure the height and weight. Weight measurement was done by using a digital scale (Seca, Hamburg-Germany) which has the nearest 0.1 kg

in a standing position and the height measurement was done utilizing microtoise (CMS weighing equipment, London-England) with a scale accuracy of 0.1 cm, (4) Laboratory tests CD4+T lymphocytes, pre and post test, for the intervention group testing was performed at the Central Hospital Wahidin Sudirohusodo South Sulawesi Province, while the control group underwent testing at the Bahteramas General Hospital Southeast Sulawesi Province and (5) Assessments of the supplement intake of black tea and food were done every month during the study.

Statistical methods: Wilcoxon test was used to compare the levels of CD4 and HIV sufferers' BMI before and after receiving ARV therapy and the concentration of EGCG supplements, theaflavin and tannins in 1,505 mg/day of black tea drinks, while the Kruskal-Wallis test was used to compare results between the controls and the intervention group. The relationship between the steeping black tea supplements on nutritional status was assessed using the Wilcoxon test, to determine whether the ultimate value of each variable checked after the intervention for 24 weeks had a statistically significant difference from the initial value before the intervention. The magnitude of changes in these variables was then calculated to see the delta change (the final value-initial value) and analyzed using the Wilcoxon test to determine the significance of differences between the two groups statistically.

RESULTS

A total of 70 respondents were involved in this study, which included 35 people with HIV who were treated as the intervention group and 35 patients with HIV as the control group. In both groups, an analysis was then conducted of several variables that were used as a reference in the assessment of changes due to the effect of supplementation with steeping black tea (*C. s. assamica*) in patients with HIV and to compare the number of changes in the control group.

Basic characteristics of respondents: The different characteristics of the two groups of patients with HIV was shown in Fig. 1. The mean age of adherence to counselling, complaints when undergoing ARV and black tea consumption in both groups showed no significant differences, as well as for the values of the BMI and baseline CD4 cell in the research subjects. Gender distribution in both groups also showed no significant difference. After observation for 24 weeks in both groups a significant change was found in several of the variables studied.

Table 1: Effect of ARV regimen and black tea supplementation on the increase in pre-test and post-test CD4 levels in the intervention group and the control group with HIV (n = 70)

Groups	CD4 level (Mean±SD)				*p-value
	Pre	Post	Change	Difference change	
Intervention	360.91±221.20	425.14±178.87	64.22±140.07	79.05±24.59	0.003
Control	380.57±78.63	365.74±81.13	-14.82±39.29		

*Independent Sample T-Test

Table 2: Effect of ARV regimen and black tea supplement on increasing BMI of HIV patients (n=70)

Groups	BMI level (Mean±SD)				*p-value
	Pre	Post	Change	Difference change	
Intervention	21.61±3.32	22.2±3.19	0.61±1.58	1.14±0.35	0.002
Control	19.31±2.17	18.78±2.42	-0.53±1.40		

*p: p-value significant

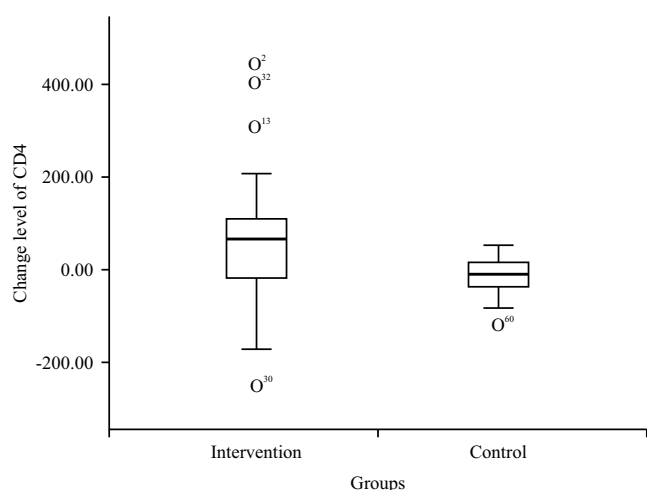


Fig. 1: CD4 condition of patients with HIV

o: Range of changes in CD4 levels and x-axis: Groups

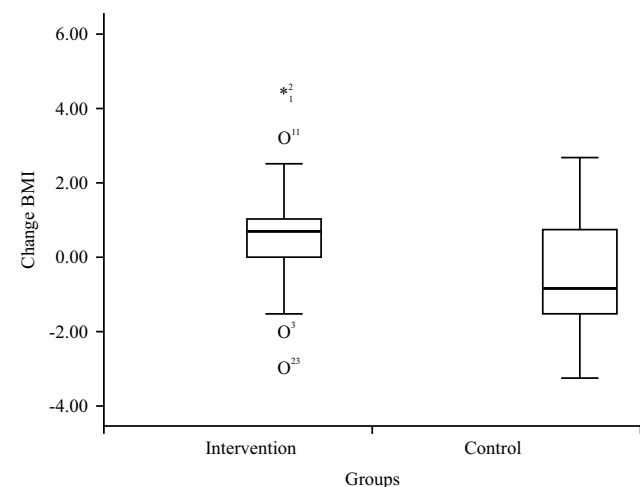


Fig. 2: Graph of body mass index of patients with HIV

*Laboratory values showed a significant difference and o: BMI change range

The magnitudes of the changes (delta changes) were shown in Table 1. Some laboratory values showed a significant difference with $p = 0.003$. The Kruskal Wallis test between intervention and control groups showed a different trend, in which the intervention group had a significant rise in CD4 levels compared with the control group.

Meanwhile, the CD4 levels in the control group showed a negative change, which indicated a decline in CD4 cells when compared with initial values. In addition to laboratory data, a significant difference with a $p < 0.05$ was also shown in Fig. 2. The Kruskal Wallis test identified a significant difference between the two groups in their BMI, which explained the increase in total energy intake in the intervention group was considerably larger, as shown in Fig. 2.

For protein intake, both groups increased, but there was no significant difference between the two groups. Meanwhile, the BMI of the control group declined. Figure 2 showed that there were significant differences in both groups, while changes in BMI in both groups showed a significant result ($p < 0.05$, Wilcoxon test) in which the intervention group had an increase in their BMI, while the control group had a decrease. To find the relationship with the supplements made from steeping black tea (*C. s. assamica*) powder analysis with Wilcoxon or Spearman Correlation Test was conducted to assess the significance of the change in value before and after treatment in both groups. Table 2 shows that the changes in the intervention group with HIV tended to increase BMI (Mean = 0.61, SD = 1.58), while the control group tended to experience a decrease in BMI (Mean = -0.53, SD = 1.40). The results of statistical analysis after the post-test obtained a significant difference in changes in the increase in BMI between the intervention group and the control group with a value ($*p = 0.002$).

DISCUSSION

Anti-retroviral therapy (ARV) aims to increase levels of T-lymphocyte cells CD4 to suppress HIV⁹. The ARVs work by blocking the ability of the virus to replicate and infect new cells, which in turn slows the progression of the disease. T-lymphocyte cell count CD4 is an indicator for the prognosis and course of HIV infection, so it is often used to monitor whether a given treatment is working or not⁹. If the therapy works, the T-lymphocyte cell count rises above CD4 $50 \mu\text{L}^{-1}$ in a few weeks and then will continue to increase 50-100/year, with an increase in BMI.

Total energy intake in patients with HIV who received antiretroviral therapy and supplements steeping black tea (*C. s. assamica*) powder increased significantly after the intervention. These findings were in contrast with the control group who only received ARV therapy, despite showing some increase but it was not statistically significant. When analyzing the magnitude of the increase in BMI at the beginning and the end between the two groups the intervention group experienced a considerable rise and had a statistically significant difference compared with the control group. The increase in total energy intake seen in the intervention group may increase the value of BMI which was statistically significant at the end of the 24 week of observation. It can be caused by the value of CD4 levels and lower BMI in the intervention group than in the control group at the time before the 1st week of treatment with improved intake, with the end measurement of the intervention group equaling or exceeding the mean BMI of the control group after treatment. This result indicated that there was an increase in the nutritional status of patients with HIV who received antiretroviral therapy and supplements steeping black tea (*C. s. assamica*) powder for 24 weeks.

There were also other significant differences: For example, the intervention group had higher levels of CD4 and lower nutritional status at baseline and the increased CD4 levels and BMI values were greater, whereas, the control group at the end of the study did not show any increase. This trend is what caused the differences in CD4 levels and nutritional status to become significantly different in both groups at the end of the intervention. The mechanism of increased levels of CD4 and BMI in this study may be associated with ARV therapy and the direct effect of black tea supplements. Support through adequate nutritional supplements can improve visceral protein levels in the body, which are used as a source of energy due to the intake of food and drink that is not sufficient during the chronic inflammatory process. At the time of the

inflammation, the body will experience an increase in resting energy expenditure that will increase the body's energy demands¹⁰.

Black tea supplementation in the intervention group contains several compounds including EGCG derivatives, flavins and tannins that are known to neutralize higher superoxide radicals and the hydroxyl group (OH). Using these as a companion to ARV therapy is expected to reduce the activity of T-lymphocytes CD, but not induce Th-1 for secreting proinflammatory cytokines, thus decreasing reactive oxygen species (ROS) levels. This indicated that the increased levels of antioxidants including micronutrient intake can suppress the activity of apoptosis in a variety of cells, opening up the formation of body fat, body mass or both, so that the levels of CD4 and BMI are increased. Cycles of inflammation resulting from unstable oxidative stress can damage the macromolecule network, including DNA and protein, which can be reduced if a person consumes food or drink that is rich in antioxidants.

One antioxidant that is referred to in this study, is related to the ability of the black tea to reduce free radicals indicated in another study's results with 1,1-Diphenyl-2-picrylhydrazyl (DPPH)¹¹, where black tea, has a much higher catechins content. In addition, the important fact is that the higher the catechins content in tea, the higher the antioxidant activity. A total of catechins in the fresh tea leaves an antioxidant catechin content which was more effective at neutralizing free radicals¹².

As a result of HIV in the body causing inadequate intake of energy, the body uses its energy reserves, such as visceral protein. If the energy intake is improved, the body will stop using its stored energy to carry out its functions. It then slowly improves serum albumin levels which were previously depleted due to being used as an energy source. This mechanism can be seen in the results of this research that found increased levels of CD4 and BMI values after administration of ARVs and black tea supplementation in the intervention group. The adequacy of food intake to meet the body's energy and protein needs to be confirmed, while this study did not conduct a deeper study on the issue.

Nevertheless, the fact that there may be a decrease in urea levels in the blood gives some idea about the reduced catabolism energy reserves of visceral protein and the beginning of a process of anabolism (as evidenced by significantly increased levels of CD4 and BMI), when the body's nitrogen balance is negative. In other words, in this case, the nutrient intake of protein was increased and adequate to start the process of anabolism¹³.

This may occur as an effect of the treatment with ARV therapy and supplements made from black tea (*C. s. assamica*) powder which were given as much as 1,505 mg in 1,000-1,400 mL equivalent to 5-7 cups/day, with water temperature 90°C and after 10 min brewing. These supplements of black tea were consumed 45 min since over time the levels of EGCG, theaflavin and tannins will become degraded. Also, they were consumed with ARV therapy resulting in significant improvements in both CD4 levels and BMI, over 24 weeks in the HIV intervention group.

According to related research by Saha and Das¹⁴, *in vivo* activity of black tea was found to be higher than most anti-oxidant-rich beverages including green tea except wine. Activities that occur on average were higher in black tea if measured *in vivo* and this is because black tea polyphenols change their structure when metabolized in the body. The antioxidant properties of black tea demonstrated the effect on increasing the activity or concentration of antioxidants¹⁵, as shown in the results of the study, indicating that the content derived from the a flavin black tea can provide a consistent effect of the antioxidants.

Increased body fat, body mass or both can increase the BMI. One study mentioned that the reduction of BMI is associated with a worse prognosis in patients with HIV¹⁶. This was due to the BMI being associated with the nutritional status and immunity of HIV patients¹⁷. These findings from this study were positively associated with an increase in CD4, which was similar to the results of the Miami intravenous drug abuse study (MIDAS) and the nutrition for healthy living (NFHL) study^{18,19}. Some other biological mechanisms that could explain the results related to BMI were: (1) HIV patients with low CD4 cell counts have a tendency to experience weight loss and (2) People with HIV with more weight can maintain their CD4 count in a higher level, with probable explanation protective effect of fat cells or adipose itself. This is because it is known that fat cells are a source of leptin circulating in the body which is in line with the amount or composition of the fat cell itself²⁰.

Several research results indicated the influence of body weight on the increase in CD4, where low weight at the start of therapy is associated with decreased CD4 counts²¹. The increase in weight after ARV treatment will improve the state of infection in the body to increase the intake and utilization of nutrients consumed in the body²². But in this study, the control group did not experience any significant CD4 increase.

One study by Womack *et al.*²³ found that CD4 cells had leptin receptors that can help CD4 cells proliferate in response to various stimuli. Decreased leptin levels were found in a state of acute starvation or hunger, including when the immune system had some deficiency as stated by Fantuzzi²⁴. Research by Faggioni *et al.*²⁵ found getting the drop in

endotoxic shock in Wistar rats with starvation provided in the form of lipopolysaccharides, namely preparations of helical cytokine leptins which are long-chain-like structures such as interleukin (IL)-6, IL-11, IL-12, leukaemia inhibitory factor and granulocyte colony-stimulating factor, obtained a structural similarity between the leptin receptor and cytokine receptors. Theoretically, leptin may inhibit the detrimental effects of cytokines whose levels were increased in patients with HIV so that the CD4 value can be increased²⁶.

On the other hand, the researchers assume the possibility of improvement occurring in the values of BMI and CD4 levels, as described by the reduction in the progression of HIV as well as the positive impact of the regularity of patient counselling obtained from the HIV-AIDS counsellors every month, as well as the intervention group receiving antiretroviral drugs at Bahteramas General Hospital Southeast Sulawesi Province, participating in meetings or discussion groups of a community of peers, exchanging information and experiencing the benefits of the consumption of drugs, supplements of black tea (*C. s. assamica*) in the powdered form regularly, including other activities that can positively affect the health conditions of HIV sufferers.

It is advisable to conduct further research to determine the mechanism of increased appetite that occurs after supplementation with black tea including identifying the components that are causing this increase. Additionally, it is necessary to do more research on the nutritional content contained in steeping black tea and the benefits of each of the substances for several of the parameters and biomarkers which were increased significantly in this study. It is also important to identify their role in the immune system to determine whether they create a decrease in viral load and/or decrease the effects of antiretroviral therapy. Overall, the global community of PLWHA needs additional nutrition education on the benefits of black tea as one of the Indonesian products for companion treatments with ARV therapy in patients with HIV/AIDS and health benefits for the wider community.

CONCLUSION

Based on the results of this study conducted on 70 patients with HIV to determine the relationship between steeping black tea (*C. s. assamica*) powder to increase the cluster differentiation 4 antigen (CD4) levels and Body Mass Index (BMI) in patients with Human Immunodeficiency Virus (HIV), it can be concluded that ARV therapy and steeping black tea (*C. s. assamica*) powder were shown to increase the levels of CD4 and BMI of HIV sufferers indicated by the statistically significant improvement of the status of T-cell immunity and BMI.

SIGNIFICANCE STATEMENT

ARV therapy and steeping black tea (*C. s. assamica*) powder are shown to increase the levels of CD4 and BMI of HIV sufferers indicated by the statistically significant improvement of the status of T-cell immunity and BMI. This study will help researchers to uncover critical areas in the care and treatment of HIV/AIDS patients. This study found a possible synergistic effect of a new combination of ARV therapy and infusion of black tea powder (*C. s. assamica*) was shown to increase CD4 levels and BMI of HIV patients as indicated by a statistically significant increase in T cell immune status and BMI.

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REFERENCES

1. UNAIDS, 2013. Case Report United Nations Programme on HIV/AIDS. Epidemic. In WHO Library Cataloguing-in-Publication Data. http://files.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UN_AIDS_Global_Report_2013_en.pdf
2. Alebel, A., D. Demant, P. Petrucka and D. Sibbritt, 2022. Effects of undernutrition on opportunistic infections among adults living with HIV on ART in Northwest Ethiopia: Using inverse-probability weighting. PLoS ONE, Vol. 17. 10.1371/journal.pone.0264843.
3. Adotey, G., A. Quarcoo, J.C. Holliday, S. Fofie and B. Saaka, 2011. Effect of immunomodulating and antiviral agent of medicinal mushrooms (immune assist 24/7™) on CD4+ T-lymphocyte counts of HIV-infected patients. Int. J. Med. Mushrooms, 13: 109-113.
4. Harris, M., B. Nosyk, R. Harrigan, V.D. Lima, C. Cohen and J. Montaner, 2012. Cost-effectiveness of antiretroviral therapy for multidrug-resistant HIV: Past, present, and future. AIDS Res. Treat., Vol. 2012. 10.1155/2012/595762.
5. Mussini, C., P. Lorenzini, A. Cozzi-Lepri, G. Marchetti and S. Rusconi *et al.*, 2018. Switching to dual/monotherapy determines an increase in CD8+ in HIV-infected individuals: An observational cohort study. BMC Med., Vol. 16. 10.1186/s12916-018-1046-2.
6. Bastianetto, S., Z.X. Yao, V. Papadopoulos and R. Quirion, 2006. Neuroprotective effects of green and black teas and their catechin gallate esters against β -amyloid-induced toxicity. Eur. J. Neurosci., 23: 55-64.
7. Li, S., T. Hattori and E.N. Kodama, 2011. Epigallocatechin gallate inhibits the HIV reverse transcription step. Antiviral Chem. Chemother., 21: 239-243.
8. Liu, S., H. Lu, Q. Zhao, Y. He and J. Niu *et al.*, 2005. Theaflavin derivatives in black tea and catechin derivatives in green tea inhibit HIV-1 entry by targeting gp41. Biochim. Biophys. Acta (BBA)-Gen. Subj., 1723: 270-281.
9. Giovannetti, A., M. Pierdominici, F. Mazzetta, S. Salemi and M. Marziali *et al.*, 2001. T cell responses to highly active antiretroviral therapy defined by chemokine receptors expression, cytokine production, T cell receptor repertoire and anti-HIV T-lymphocyte activity. Clin. Exp. Immunol., 124: 21-31.
10. Thapa, B.R. and A. Walia, 2007. Liver function tests and their interpretation. Indian J. Pediatr., 74: 663-671.
11. Nishizawa, M., M. Kohno, M. Nishimura, A. Kitagawa and Y. Niwano, 2005. Non-reductive scavenging of 1,1-diphenyl-2-picrylhydrazyl (DPPH) by peroxyradical: A useful method for quantitative analysis of peroxyradical. Chem. Pharm. Bull., 53: 714-716.
12. Musial, C., A. Kuban-Jankowska and M. Gorska-Ponikowska, 2020. Beneficial properties of green tea catechins. Int. J. Mol. Sci., Vol. 21. 10.3390/ijms21051744.
13. Bourdon, E., N. Loreau, L. Lagrost and D. Blache, 2005. Differential effects of cysteine and methionine residues in the antioxidant activity of human serum albumin. Free Radical Res., 39: 15-20.
14. Saha, P. and S. Das, 2003. Regulation of hazardous exposure by protective exposure: Modulation of phase II detoxification and lipid peroxidation by *Camellia sinensis* and *Swertia chirata*. Teratog., Carcinog., Mutagen., 23: 313-322.
15. Rietveld, A. and S. Wiseman, 2003. Antioxidant effects of tea: Evidence from human clinical trials. J. Nutr., 133: 3285S-3292S.
16. Crum-Cianflone, N.F., M. Roediger, L.E. Eberly, K. Vyas and M.L. Landrum *et al.*, 2010. Obesity among HIV-infected persons: Impact of weight on CD4 cell count. AIDS, 24: 1069-1072.
17. Bosch, R.J., K. Bennett, A.C. Collier, R. Zackin and C.A. Benson, 2007. Pretreatment factors associated with 3-year (144-week) virologic and immunologic responses to potent antiretroviral therapy. J. Acquired Immune Deficiency Syndromes, 44: 268-277.
18. Shor-Posner, G., A. Campa, G. Zhang, N. Persaud and M.J. Miguez-Burbano *et al.*, 2011. When obesity is desirable: A longitudinal study of the miami HIV-1-infected drug abusers (MIDAS) cohort. J. Acquired Immune Deficiency Syndromes, 23: 81-88.
19. Tilg, H. and A.R. Moschen, 2006. Adipocytokines: Mediators linking adipose tissue, inflammation and immunity. Nat. Rev. Immunol., 6: 772-783.

20. Smurzynski, M., A.C. Collier, S.L. Koletar, R.J. Bosch, K. Wu, B. Bastow and C.A. Benson 2008. AIDS clinical trials group longitudinal linked randomized trials (ALLRT): Rationale, design, and baseline characteristics. *HIV Clin. Trials*, 9: 269-282.
21. Crum-Cianflone, N.F., M. Roediger, L.E. Eberly, A. Ganesan, A. Weintrob, E. Johnson and B.K. Agan, 2011. Impact of weight on immune cell counts among HIV-infected persons. *Clin. Vaccine Immunol.*, 18: 940-946.
22. Kosmiski, L., 2011. Energy expenditure in HIV infection. *Am. J. Clin. Nutr.*, 94: 1677S-1682S.
23. Womack, J., P.C. Tien, J. Feldman, J.H. Shin and K. Fennie *et al*, 2007. Obesity and immune cell counts in women. *Metab. Clin. Exp.*, 56: 998-1004.
24. Fantuzzi, G., 2005. Adipose tissue, adipokines, and inflammation. *J. Allergy Clin. Immunol.*, 115: 911-919.
25. Faggioni, R., A. Moser, K.R. Feingold and C. Grunfeld, 2011. Reduced leptin levels in starvation increase susceptibility to endotoxic shock. *Am. J. Pathol.*, 156: 1781-1787.
26. Nowicki, M.J., R. Karim, W.J. Mack, H. Minkoff and K. Anastos *et al*, 2007. Correlates of CD4+ and CD8+ lymphocyte counts in High-risk Immunodeficiency Virus (HIV)-seronegative women enrolled in the Women's Interagency HIV Study (WIHS). *Hum. Immunol.*, 68: 342-349.