

Effect of *Moringa oleifera* in HIV infected Patients – A Review

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the
requirements for the degree of Bachelor of Pharmacy (Hons.)

School of Pharmacy

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing a degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

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Ethics Statement

The study does not involve any kind of animal or human trial.

Abstract

The Human immunodeficiency Virus (HIV) when left untreated, can lead to a substantial risk to one's health. The life expectancy of people living with HIV has significantly increased as a result of the use of antiretroviral therapy (ART). In many developing countries, traditional medicines like *Moringa oleifera* (MO) is used as a part of their treatment in addition to ART. The goal of this review was to look into how MO affected the health of HIV patients. To evaluate the effect of MO, different health parameters were checked among HIV-infected patients. It has been found that supplementing with MO has several noteworthy advantages for HIV patients. Based on these findings, it can be inferred that adding MO supplements significantly improves the health of people living with HIV. MO can be considered as a beneficial additional therapy to ART to improve the overall treatment results for HIV patients.

Keywords: *Moringa oleifera*; HIV; Antiretroviral Therapy; Immunity.

Dedication

To my loving grandmother, the source of strength, wisdom and unconditional love in my life. She may not be here today but her love and warmth is and will always continue to guide me.

Acknowledgement

I would like to begin by thanking Almighty Allah for keeping me in good health and blessing me with the capability, strength and assistance needed to complete this project. However, this research paper would not have been completed without the support of several individuals and I would like to express my gratitude to all of them.

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List of Acronyms

MO: *Moringa Oleifera*

AIDS: Acquired Immune Deficiency Syndrome

ART: Antiretroviral Therapy

BMI: Body Mass Index

DNA: Deoxyribonucleic Acid

HIV: Human immunodeficiency Virus

HAART: Highly Active Antiretroviral Therapy

RT: Reverse Transcriptase

ART: People Living with HIV

WHO: World Health Organization

Chapter 1

Introduction

1.1: *Moringa oleifera*

1.1.1: Natural Habitat

Moringa oleifera (MO), belonging to the *Moringaceae* family, is a familiar and widespread plant (Paikra et al., 2017). Though the plant is local to India, Pakistan, Bangladesh and Afghanistan, it can be found in both subtropical and tropical regions around the world (Pareek et al., 2023). Due to its boundless medicinal and nutritional advantages, the tree is often called a “Miracle Tree” (Pareek et al., 2023). It's known by these names because of its amazing properties and benefits. MO can be a sustainable cure in combating malnutrition (Gopalakrishnan et al., 2016). Almost every part of the MO tree, including the roots, leaves, flowers, green pods, and seeds, has medicinal uses as well as applications in the functional food preparations, water purification, and biodiesel production (Saini et al., 2016). Its medicinal and nutritional properties have gained it a great deal of attention. The origin of MO is the Himalayan foothills and North west in India and Bangladesh. Its versatility has made it adaptive to different environments allowing it to be found in many countries like Thailand, Egypt, Malaysia, and many more (Brilhante et al., 2017). The commercial cultivation of MO is expanded worldwide such as in countries like America, Cambodia, Mexico, Hawai (Liu et al., 2018). MO thrives in warm temperatures, specifically among 25-35 degree Celsius (Gopalakrishnan et al., 2016). It prefers tropical climate and thrives during rainfall preferably between 1000 to 2000 mm (Trigo et al., 2020). It grows best at elevations below 600 meters (1,970 feet) and prefers well-drained, clay soils with a neutral pH from 4.5-8 (Leone et al., 2015). MO contains a wide range of vital vitamins and minerals. Additionally, it has iron, protein, fiber, and a variety of minerals that support muscle growth and bodily healing. For centuries, people have used natural products and

MO leaves in their diet to keep their skin smooth and their mental health intact as every component of the MO plant is useful (Patil et al., 2022).

1.1.2: Plant parts



Fruits



Plant



Flowers



Leaves

Taxonomy of MO

- Kingdom: *Plantae*
- Subkingdom: *Tracheobionta*
- Class: *Magnoliopsida*
- Subclass: *Dilleniidae*
- Order: *Capparales*
- Family: *Moringaceae*
- Genus: *Moringa*
- Species: *oleifera*

Figure 1: MO plant and its various parts (Paikra et al., 2017).

MO has been used in traditional medicine as well as for pharmaceutical screening for a long time (Senthilkumar et al., 2018). Even during wars, the Indian fighters used to take the leaf extract of MO to alleviate the pain and pressure of the war (Senthilkumar et al., 2018). The leaf, seeds, bark, stems and fruits of MO are enriched with amino acids, β carotene, vitamins and minerals (Massry et al., 2013). There is no doubt that MO has multiple prospects and applications in medicine, nutrition, industrial and domestic

aspects (Liu et al., 2018). It can be developed globally as a healthy, safe and functional nutriment (Liu et al., 2018).

Leaves: the vibrant green leaves of MO are enriched with vitamins, minerals and antioxidant. Leaves are the most used part of MO extending its use in the treatment of malaria, typhoid, arthritis and swelling (Leone et al., 2015). Dried leaves of MO are enriched with protein (30.0 %), amino acids as well as copper, magnesium, potassium, calcium, phosphorus, zinc, iron, and sulphur ; which add reflection to its rich nutritional value (Moyo et al., 2011).

Seed: The triangular seeds of MO are small, brown and enclosed within long seed pods. The seeds contain high nutritional value They can not only be eaten roasted, in curries, and in brewing tea but also the powdered seeds are used to purify drinking water (Massry et al., 2013). The seeds of MO are also enriched with ben oil which is a major substitute for olive oil (Liu et al., 2018).

Flower: The flowers of MO plant are white with a hint of yellow or cream in color, have a sweet fragrant and can be eaten as well (Paikra et al., 2017). Flowers are used to treat inflammation, muscle disease and hysteria (Leone et al., 2015).

Fruit: Round and small seeds guarded by fibrous pulp are present inside the pods. The fruit can be eaten like a vegetable when cooked and provide great nutritious value (Paikra et al., 2017).

1.1.3: Phytochemical Constituents

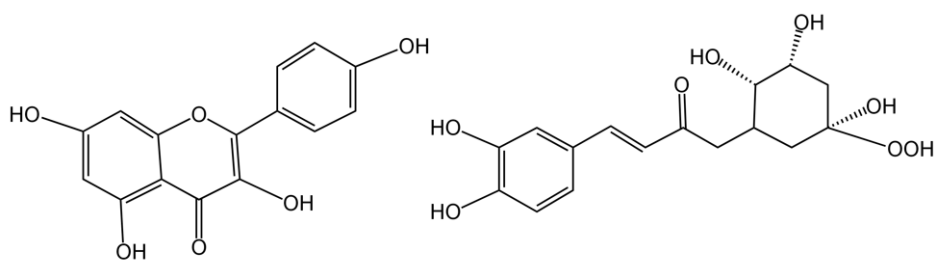
Different parts of the MO plant contain various phytochemical constituents. In the table (Table 1) provided below, the various MO components, their corresponding chemical constituents, and their respective applications are presented. This tabulated information serves to demonstrate the versatility of the plant and its utilization:

Table 1: Chemical compounds identified in MO and their therapeutic uses (Patil et al., 2022; Saini et al., 2016; Amaglo et al., 2010)

Plant part	Chemical Compounds	Therapeutic use
Seed	Cysteine, methionine, moringine, 4-(alpha-L-rhamnopyranosyloxy) benzyl glucosinolate, niazirin, niazimicin	Antihypertensive, protect the liver reducing peroxidases.
Leaf	Gallic acid, kaempferol, quercetin glycosides, flavonoid, phenolics, chlorogenic acid, phosphorus, calcium, iron, vitamins, pyroxidine	Natural remedy for various conditions such as sores, headaches when applied on the temples. Believed to have potential benefits for various health issues such as hemorrhoids, fevers, bronchitis, sore throat, eye and ear infections, scurvy, as well as regulating glucose levels.
Bark (Stem)	Vanillin, 4-hydroxymellin, octadecanoic acid and B-sitosterol	Handle delirious individuals and ocular conditions. Prevent the development of tuberculous glands in the neck. Have tumor-fighting

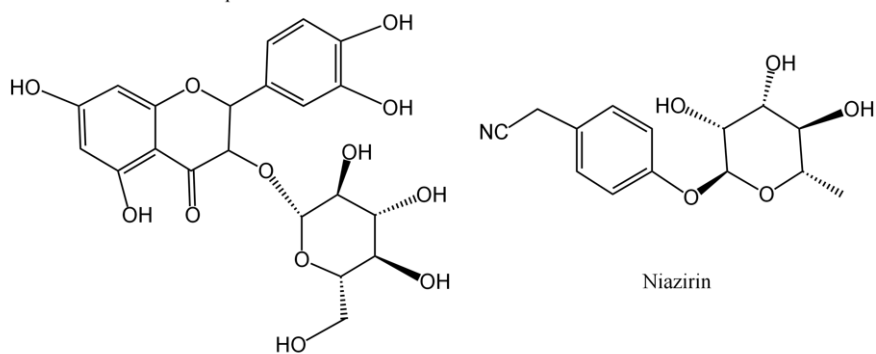
		properties, anti-tubercular activity, help in ulcer healing.
Root	Potassium, sodium, magnesium, phosphorus, and calcium	Used as a laxative, Antilithic, carminative, antifertility, function as a circulatory and heart tonic, relieve constipation, inflammations, rheumatism and lower back pain.
Flower	protein, ascorbic acid, kaemopherol, kaempferitin, quercetin, isoquercetin, and D-glucose D-mannose	Treat tumors, hysteria, muscular disorders, inflammations, and spleen enlargement. possesses the capacity to reduce triglycerides, phospholipids, and serum cholesterol.
Gum	Galactose, L-arabinose, rhamnase glucuronic acid, xylose, mannose	Possesses astringent and rubefacient properties, used in the treatment of dental carries. cure syphilis, diarrhea, fevers, digestive problems, and headaches in combination with sesame oil.

Flavonoids:



Kaempferol

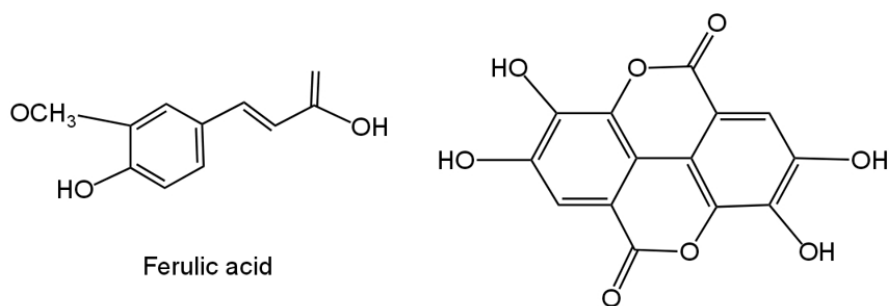
Chlorogenic acid



Quercetin-3-glucoside

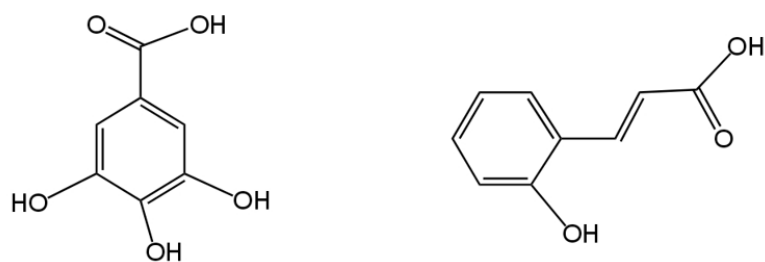
Niazirin

Phenolic acids:



Ferulic acid

Ellagic acid



Gallic acid

o-Coumaric acid

Figure 2: Structures of phytoconstituents of MO

1.1.4: Medicinal uses of MO

Throughout history, MO has been incorporated into diets of people due to its therapeutic benefit (Pareek et al., 2023). MO tends to exhibit a wide range pharmacological and medicinal efficacy against various diseases which include antidiabetic, antihypertensive, antioxidant, anti-inflammatory, anti-microbiological, anticancer, anti-epileptic, anti-asthmatic properties as well as neurological effects (Ghimire et al., 2021). The aqueous extract of MO leaves helps to control diabetes by regulating blood glucose level. MO is considered potential natural alternative to antibiotics due to its extensive range of antimicrobial properties. The roots, leaves, seeds and barks have exhibited antimicrobial action against both bacteria and fungi (Paikra et al., 2017). Due to presence of components such as polyphenols, flavonoids, vitamin C, MO is considered natural antioxidant with potential to reduce oxidative stress and related cancer (Saini et al., 2016). Chemical constituents isothiocyanate and thiocarbamate have been found in MO which contributes to the anticancer property of MO by inhibiting tumor promoters (Paikra et al., 2017). The antihypertensive effect of MO is also the outcome of components thiocarbamate and isothiocyanate (Gilani et al., 1994). Studies and researches are being conducted to explore the anti-asthmatic properties of MO. It has been found to improve the lung function in patients with bronchial asthma (Agrawal & Mehta, 2008). Methanolic extract of the leaves of MO has shown efficacy against asthma, lung inflammation and bronchoconstriction (Suresh et al., 2020). In a study by Mishra et al., 2011, the hepatoprotective properties of MO has been attributed to the methanolic and ethanolic extract of the plant roots and leaves respectively. The phenolic acids and flavonoids present in MO leaf is the source of anti-inflammatory effect of MO (Xu et al., 2019). The study also promotes the potential of MO as a natural dietary supplement for nutritional benefits. In recent years, MO has

been studied to identify its neurological properties in the treatment of diseases like dementia, Alzheimer's disease, Parkinson's disease and neurotoxicity associated indications (Ghimire et al., 2021). Bakre et al., 2013 established that MO promotes the release of GABA which allow it to contribute to the treatment of epilepsy. MO tends to have a benefitting effect on neurotoxicity in albino rats (Abdallah et al., 2021). It also provides neuroprotective action on the oxidative stress and cognitive impairment of Wister albino rats (Rahmath et al., 2015). MO has been used to treat cuts, burns and wounds (Xiao et al., 2020). Several studies have substantiated the neurological analgesic effect of MO (Rao et al., 2008; Paikra et al., 2017). In another study, ethanolic extract of MO was admistered to chromium-treated male rats where MO significantly lowered the levels of inflammatory markers and ameliorated the chromium effects on testicular local immunity (Xiao et al., 2020). The effect of MO has also been found in autoimmune disorders such as rheumatoid arthritis, atopic dermatitis, sclerosis (Xiao et al., 2020). Studies have reported the efficacy of MO in reducing joint inflammation associated with rheumatoid arthritis (Mahajan et al., 2007). In sub-Saharan Africa MO has been studied for its efficiency in the management of HIV/AIDS and due to presence of different bioactive compounds; MO extracts have been reported to have inhibitory action particularly against HIV (Saki et al., 2023).

1.2: Purpose of the study

Identifying plants with therapeutic or medicinal qualities that can be consumed by humans has received a lot of attention in recent years. Plants have the potential to provide food, medicine, and clean energy. It is necessary to look for herbs with therapeutic potential for prevention that have also been scientifically shown to be effective as an alternative treatment. Thus, the goal of this research is to examine how MO supplementation affects the well-being of adults living with HIV who are receiving antiretroviral therapy. This will enable us to assess MO's potential as a supplemental intervention to boost HIV treatment efficacy and enhance the wellbeing of those infected with the virus.

Chapter 2

HIV/AIDS

2.1: HIV and its clinical features

The genome of the enveloped retrovirus known as the human immunodeficiency virus (HIV) is composed of single-stranded RNA that targets the immune system, leading to the development of AIDS, the disease's most advanced stage (Vaillant & Gulick, 2022). HIV weakens the immune system and makes a person more vulnerable to infections, lung conditions, and some types of cancer because it targets white blood cells (Durvasula & Miller, 2014). HIV can be transmitted through bodily fluids such as blood, breast milk, semen, and vaginal secretions. It can also be passed down to a woman's offspring. Antiretroviral Therapy is an effective HIV treatment and prevention method. It involves taking a combination of HIV medicines on a regular basis and is recommended for everyone infected with HIV (Kemnic & Gulick, 2022). If left untreated, HIV can eventually progress to AIDS. The early signs of being infected with HIV include fever, aches and fatigue (Lee et al., 2009). HIV destroys the CD4 immune cells which is significant for fighting off diseases (Vaillant & Gulick, 2022). As the infection advances to the disease AIDS; patients suffer from symptoms such as thrush, yeast infections, headache, dry cough, shortness of breath, skin rashes, diarrhea, night sweats, numbness in hand or feet, chronic inflammatory diseases, swollen glands (Lee et al., 2009).

2.2: Transmission

HIV does not live outside of human cells. HIV cannot pass from one person to another unless contaminated bodily fluids is transmitted by infected cells including blood, semen, vaginal fluids, or breast milk (Durvasula & Miller, 2014). The most effective method of HIV transmission is direct touch between an infected individual's blood

supply and another person's blood, according to the Healthcare Crisis and Mental Health Services Administration of the United States. Sexual interaction is another effective mode of transmission since the mucosal linings of the anus, rectum, and vagina are easily damaged or may include infected fluids (Royce et al., 1997).

2.3: Pathophysiology

- 1. Binding:** During the primary mechanistic step, HIV attaches to receptors present on the surfaces of CD4 cells. CD4 cells are one of the types of white blood cells that send signals to the immune system when they detect that an infection has occurred.
- 2. Fusion:** After binding to the CD4 cell's outside, HIV fuses its envelope with the outside of the CD4 cell.
- 3. Reverse Transcription:** During the next mechanistic stage in the CD4 cell, HIV uses a viral enzyme, known as reverse transcriptase, to convert its RNA into DNA.
- 4. Integration:** After viral DNA has developed, HIV releases an additional viral enzyme called integrase.
- 5. Replication:** HIV is integrated into the CD4 cell DNA by the viral RNA.
- 6. Assembly:** The individual HIV pieces assemble at the cell's ends.
- 7. Budding:** The immature viruses get released from the CD4 cell and are ready to infect other cells.

A schematic representation illustrating the intricate pathophysiology of the HIV life cycle is shown in figure below (Figure 3). It provides a visual explanation of the complex processes involved in the HIV life cycle.

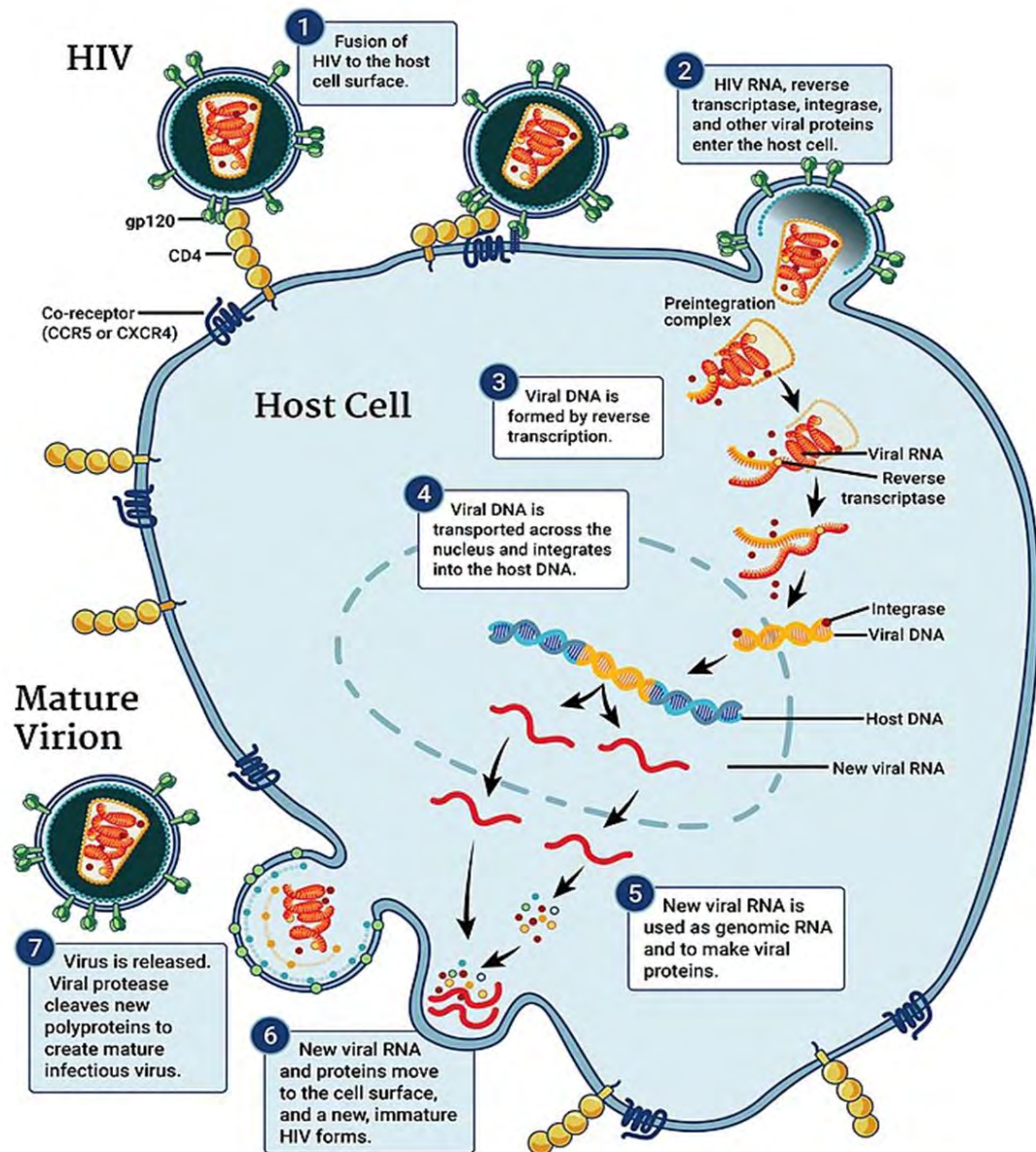


Figure 3: HIV replication cycle (Sued & Grosso, 2023)

2.4: Stages of AIDS

Below is a description of the HIV virus's progression based on data from the Centers for Disease Control and Prevention (CDC) about HIV/AIDS:

1. Stage 1 or Acute HIV infection is characterized by high blood concentration of the HIV and high contagiousness. Many people get symptoms similar to the flu.
2. Stage 2 or chronic HIV infection is sometimes referred to as clinical latency or asymptomatic HIV infection. HIV is still active and keeps proliferating within the body. During this stage, people may not feel ill or exhibit any symptoms, but they can still spread HIV. By following doctor's orders, HIV treatment can stop HIV from progressing to Stage 3 (AIDS).
3. The third stage of HIV infection, known as acquired immunodeficiency syndrome, is the most serious. Individuals suffering from AIDS have a high viral load and are highly contagious. Their compromised immune systems leave them open to opportunistic infections and other dangerous diseases. Those with AIDS usually live for three years without HIV treatment.

2.5: Treatment

ART or antiretroviral therapy refers to the medication used to treat HIV. It is a daily regimen of taking multiple HIV medications (Stanley et al., 2017). Everyone living with HIV is advised to start ART in order to improve their quality of life and lower their risk of HIV transmission. It exhibits remarkable effectiveness in managing HIV, but it cannot cure the virus. Each of the four viral processes is the target of one of the five classes of antiretroviral medications which are (Kemnic & Gulick, 2022)-

- **NRTIs (Nucleoside/Nucleotide RT inhibitors):** Once they enter cells, they are triphosphorylated into their active forms and terminate DNA chain elongation (Sarafianos et al., 2009).
- **NNRTIs (Non-Nucleoside RT inhibitors):** These drugs bind to HIV RT at an allosteric hydrophobic site and induce conformational change resulting in enzyme inhibition (Sarafianos et al., 2009).
- **Entry inhibitors:** This class of drugs inhibits fusion of HIV with host cells (Haqqani & Tilton, 2013).
- **Protease inhibitor:** Structurally complex protease inhibitors inhibit the protease enzyme activity by attaching to the active site of HIV protease (Flexner, 1998).
- **Integrase inhibitors:** These agents inhibit the DNA integrase enzyme which is responsible for integrating viral DNA into the host genome during provirus formation (Grandgenett, 2015).

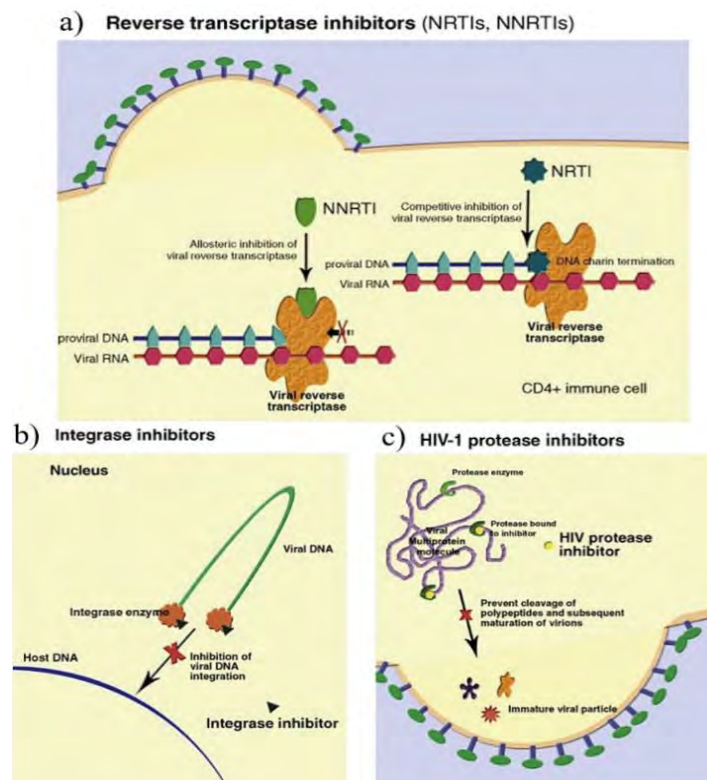


Figure 4: Mechanism of action of antiretroviral therapy drugs: (a) reverse transcriptase inhibitors (NRTIs, NNRTIs); (b) integrase inhibitors; and (c) HIV-1 protease inhibitors (Saki et al., 2023).

2.5.1: Combination treatment for HIV

HAART, or highly active antiretroviral therapy, is a drug regimen used to control and treat HIV-1. It consists of multiple medications from the antiretroviral drug class (Eggleton & Nagalli, 2023). HAART is especially recommended for patients with AIDS defining illnesses, low CD4+ cell count, or high viral load. The therapy consists of a combination of three drugs to prevent resistance. The combination typically includes at least two NRTIs and one NNRTI, integrase or protease inhibitor (Shafer & Vuitton, 1999). Common initial therapy options include Tenofovir/emtricitabine with Efavirenz or rilpivirine, Atazanavir or darunavir with ritonavir boosting, Elvitegravir with cobicistat boosting, or raltegravir (Eggleton & Nagalli, 2023).

2.6: Epidemiology

According to WHO, in 2022, around 39 million individuals worldwide were living with HIV and approximately 37,5 million of these totals were adults, and 1,5 million were minors under the age of fifteen. In addition, women and girls made up roughly 53% (Global HIV and AIDS Epidemic Statistics). D. Black and African American people are the most affected by HIV, according to an analysis of HIV diagnoses based on race and ethnicity. They accounted for 14,528 new HIV diagnoses in 2021, or 40% of all cases. Additionally, individuals who are Latino or Hispanic were also significantly impacted, accounting for almost twenty nine percent (10,467) of new diagnoses (Basic Statistics/HIV Basics / HIV/AIDS /CDC). Based on the information from Global AIDS Update 2023: Fact Sheet, since 2004, there has been a 69% decrease in AIDS-related deaths, and since 2010, there has been a 51% decrease. Globally, AIDS-related illnesses claimed the lives of about 630 000 people in 2022, compared to 2.0 million Since 2010,

there has been a 55% decrease in AIDS-related mortality among women and girls, and a 47% decrease among men and boys. In Bangladesh, HIV surveillance focuses on groups that are at high risks like injecting drug users, sex workers and Hijra individuals. According to UNFPA Bangladesh, the overall HIV prevalence has been less than 1% in all tested groups. However, there has been a rapid evolution of the HIV epidemic, particularly among injecting drug users in Dhaka city, with a significant increase in HIV prevalence over the past six years (Azim et al., 2009).

Chapter 3

Methodology

Relevant literature was selected, analyzed and summarized for this review work. The information and data for this review were compiled from relevant articles. To gather the journals connected to this topic, an electronic search has been done. In order to gather as much essential information as possible regarding the effects of MO supplementation on HIV-infected patients who are receiving ART, review articles and research papers from official websites and research databases were carried out. Utilizing well-known and reliable sources including PubMed, Google Scholar, SCOPUS and ScienceDirect, the articles for this review study were collected. Relevant articles were gathered using appropriate keywords, such as MO, clinical trials, HIV, ART, immunity. The initial search yielded 306 records, which were then narrowed down to 178 after removing duplicates and conducting initial screening. Exclusion criteria were applied to eliminate studies that were not indexed in Scopus, did not involve clinical trials, focused solely on animal trials, did not discuss MO and lacked sufficient data. After exclusion, the total number of articles for the review came down to 3. Manual searches of selected articles and their bibliographies were performed to gather additional relevant information.

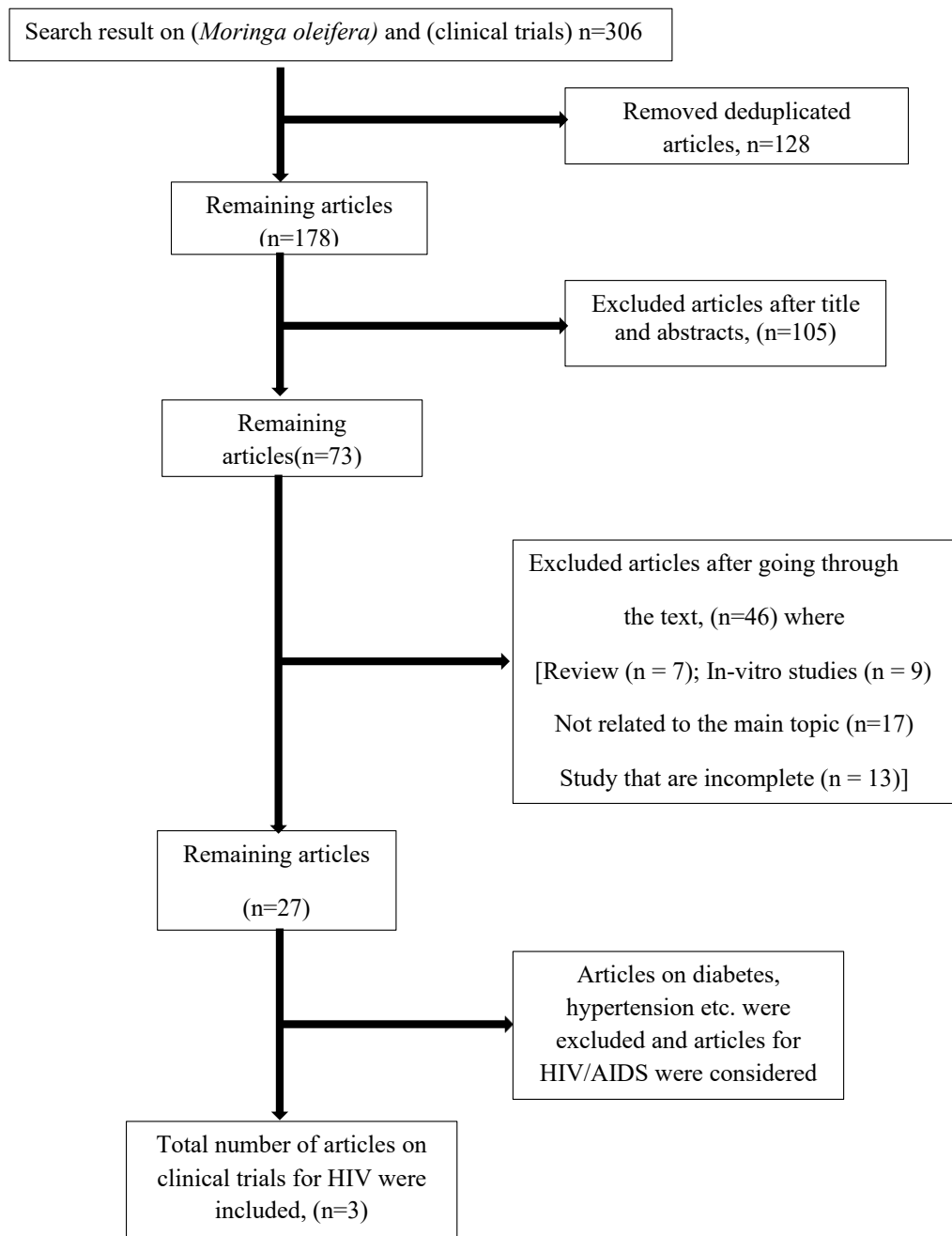


Figure 5: Sources, search strategy, and article exclusion criteria

Chapter 4

Result and Discussion

4.1: Potential of MO in HIV treatment

Given that HIV positive patients frequently struggle with inflammation, immunological dysfunction, and malnourishment, supplementing with MO has a number of potential benefits. Patients with HIV suffer from symptoms of various other diseases affecting their immune system. According to a study by Odwee et al., 2020; HIV-infected patients are reported to be malnourished due to changes in metabolism and poor absorption efficiency. MO plays a significant role in the enhancement of nutritional status in HIV-infected patients by improving the immune system as it is rich in proteins, minerals (calcium, potassium, iron), and vitamins (A, C, and E), MO is a powerhouse of nutrients (Gopalakrishnan et al., 2016). Inflammation, deteriorated immune function, hypertension, ART therapy toxicity are some of the contributors to the HIV risk factors (Deeks et al., 2013). In the pathogenesis of HIV inflammation plays a key role (Deeks et al., 2013). Hydroethanolic bioactive extract of MO leaves greatly inhibits the release of inflammatory cytokines such as prostaglandin, interleukins and nitric oxide production as well as restrain inflammatory mediators (Fard et al., 2015). The alkaloids, flavonoids, quercetin in Mo leaves also exhibit anti-inflammatory properties (Das et al., 2013). All these properties of MO play a significant role to slow down the inflammatory mechanism in HIV-infected patients improving their health condition. As discussed earlier, the antioxidant property of MO is attributed to the presence of ascorbic acid, vitamin c and flavonoids which helps to improve oxidative stress in people with HIV as well as cancer induced by oxidation (Anwar et al., 2005). presence of such components helps counteract ROS and protect cells from oxidative damage (Anwar et al., 2005). MO is widely regarded as safe to eat and is easily accessible in many parts of the world, including areas severely impacted by HIV/AIDS. It can be a useful supplement in environments with limited resources (Gambo et al.,

2022). The following table (Table 2) summarizes some clinical studies on the effect of MO in HIV –

Table 2: Summary of Clinical trials examining the effect of MO on HIV infected patients

Study Design	Participants	Study group	Response	Result	Reference
A two phase, one sequence, cross-over study was conducted.	HIV infected male and female who were >18 years old and on Nevirapine based medication for at least two weeks.	13 participants taking daily dose of MO gelatin capsule equivalent of 1.85g MO Leaf powder.	Coadministration of MO did not alter the safety profile of nevirapine.	Did not have any clinically significant impact on the way nevirapine behaves in the body.	(Monera - Penduka et al., 2017)
A single-blind, randomized, control clinical trial was conducted	60 adult patients at stable HIV/AIDS clinical staging 2,3,4 who were	Case Group: 30 patients received MO leaf powder Control group	MO tends to improve BMI and albumin levels compared to the CG group. The BMI increased by 1.9 kg/m ² in the	Significant improvement in BMI and immunity.	(Koy et al., 2017)

	undergoing ART therapy	(CG): 30 patients receiving nutritional counselling	third month and 2.0 kg/m ² in and albumin levels also increased while remaining the same in the CG group.		
A double blind, randomized clinical trial was conducted.	Male and female Participants who have CD4 counts of less than 500cells/mm ³ , are ≥ 18 years; started ART at least three months prior on a regimen of Tenofovir, Lamivudine Efavirenz.	Case group: MO leaf powder for 6 months (n=89) Control group (CG): Equivalent dose of placebo (n=88)	The study group showed no significant discrepancies in nutritional status variables (p<0.0001) such as BMI, weight. The treatment however had a significant impact on CD4 counts in Case group.	Adding MO leaves to regular diet didn't affect participants nutritional status, but it did improve their immune response.	(Gambo et al., 2022)

A study by Monera-Penduka and colleagues in 2017 investigated the potential interaction between MO leaf supplementation and nevirapine pharmacokinetics in HIV-infected adults and found that coadministration of MO leaf powder along with ART (TLE) was well tolerated by the people living with HIV (PLHIV). The enzyme CYP3A4 which is responsible for metabolism of nevirapine is inhibited by MO. However, coadministration of MO does not alter the safety profile of nevirapine. MO leaf supplementation indicates a key role by significantly increasing BMI and albumin levels of HIV-infected patients which are important parameters in context of HIV (Koy et al., 2017). MO leaf is known to contain an average of 35g/100g protein and a high amount of fat content (Koy et al., 2017). In the study, the nutrient content was found beneficial as a dietary supplement and MO leaf appears to be one of the best ways for people in limited-resource settings to supplement their diet. The MO leaf powder also contains numerous saturated and unsaturated fats, and phytosterols contributing to nutritional value of the plant. The study (Gambo et al., 2022) also indicates that MO may enhance the quality-of-life of people living with HIV in various ways. This may include better interaction with other people and intimate partners. It can foster a more positive attitude towards happier and healthier living. It can also improve the standards and aspects of social interactions and personal relationships between HIV-infected patients and their closed one. In turn, this would reduce discrimination among patients and consequently help them to deal with their depression, which are the major mental health challenges among PLHIV (Gambo et al., 2022). The MO plant presents a potential role as a low-cost and sustainable source of nutrients for PLHIV receiving ART to improve their quality of life by enhancing immune function. Another drawback of HIV is dysfunctional immune system which can be improved by MO supplementation.

Chapter 5

Conclusion

To conclude, MO as a supplement shows a significant complementary approach in managing HIV infection in adults. The studies suggest potential benefits in terms of changes in nevirapine's effects, improved body mass index, immune response, and nutritional status, including CD4 cell counts. Nevertheless, more research and studies with extended duration of follow-up periods (including large controlled trials) is needed to confirm these findings and understand the underlying mechanisms. The review has some limitations to keep in mind. Firstly, there were only a limited number of studies included, which might affect how widely we can apply the findings. Secondly, it was difficult to directly compare and aggregate the results because the studies differed in terms of design, participants, interventions, and results. Thirdly, the reliability of the review's conclusions may be impacted by the disparities in the quality and methodologies of the included studies. Furthermore, there are still a few significant questions concerning the precise MO dosages that need to be resolved. In order to determine the appropriate dosage, future trials should take into account factors such as the patient's regular energy uptake and subgroup characteristics etc. It's possible that the studies' follow-up periods weren't long enough to record long-term effects or changes over time. Finally, the studies limited general applicability stems from their localization to particular populations or regions. It's important to take into account these limitations and promote additional study in order to have a more complete understanding. However, the data indicates that supplementing with MO may be a useful strategy for managing HIV-positive patients receiving ART, with the aim of enhancing both treatment outcomes and general health.

Reference

- Anwar, F., Ashraf, M., & Bhangar, M. I. (2005). Interprovenance variation in the composition of *Moringa oleifera* oilseeds from Pakistan. *Journal of the American Oil Chemists' Society*, 82(1), 45–51. <https://doi.org/10.1007/s11746-005-1041-1>
- Amaglo, N. K., Bennett, R. N., Lo Curto, R., Rosa, E., Lo Turco, V., Giuffrida, A., Lo Curto, A., Crea, F., & Timpo, G. (2010). Profiling selected phytochemicals and nutrients in different tissues of the multipurpose tree *Moringa oleifera* L., grown in Ghana. *Food Chemistry*, 122(4), 1047–1054. <https://doi.org/10.1016/j.foodchem.2010.03.073>
- Agrawal, B., & Mehta, A. (2008). Antiasthmatic activity of *Moringa oleifera* Lam: A clinical study. *Indian Journal of Pharmacology*, 40(1), 28. <https://doi.org/10.4103/0253-7613.40486>
- Abdallah, R., Mostafa, N., Kirrella, G., Gaballah, I., Imre, K., Morar, A., Herman, V., Sallam, K. I., & Elshebrawy, H. A. (2023). Antimicrobial Effect of *Moringa oleifera* Leaves Extract on Foodborne Pathogens in Ground Beef. *Foods*, 12(4), 766. <https://doi.org/10.3390/foods12040766>
- Azim, T., Khan, S. I., Haseen, F., Huq, N. L., Henning, L., Pervez, M. M., Chowdhury, M. E., & Sarafian, I. (2009b). HIV and AIDS in Bangladesh. *Journal of Health, Population and Nutrition*, 26(3). <https://doi.org/10.3329/jhpn.v26i3.1898>

- Brilhante, R. S. N., Sales, J. C., Pereira, V. S., De Souza Collares Maia Castelo-Branco, D., De Aguiar Cordeiro, R., De Souza Sampaio, C. M., De Araújo Neto Paiva, M., Santos, J. Bakre, A. G., Aderibigbe, A. O., & Ademowo, O. G. (2013). Studies on neuropharmacological profile of ethanol extract of *Moringa oleifera* leaves in mice. *Journal of Ethnopharmacology*, *149*(3), 783–789. <https://doi.org/10.1016/j.jep.2013.08.006>
- Durvasula, R., & Miller, T. R. (2014b). Substance Abuse Treatment in Persons with HIV/AIDS: Challenges in Managing Triple Diagnosis. *Behavioral Medicine*, *40*(2), 43–52. <https://doi.org/10.1080/08964289.2013.866540>
- Das, N., Sikder, K., Bhattacharjee, S., Majumdar, S. B., Ghosh, S. K., Majumdar, S., & Dey, S. (2013). Quercetin alleviates inflammation after short-term treatment in high-fat-fed mice. *Food & Function*, *4*(6), 889. <https://doi.org/10.1039/c3fo3effect>
- Deeks, S. G., Tracy, R. P., & Douek, D. C. (2013). Systemic Effects of Inflammation on Health during Chronic HIV Infection. *Immunity*, *39*(4), 633–645. <https://doi.org/10.1016/j.immuni.2013.10.001>
- Eggleton, J. S., & Nagalli, S. (2023, July 3). Highly Active Antiretroviral Therapy (HAART). StatPearls - NCBI Bookshelf. <https://www.ncbi.nlm.nih.gov/books/NBK554533/>
- Fard, M. T., Arulselvan, P., Karthivashan, G., Adam, S. K., & Fakurazi, S. (2015). Bioactive extract from *moringa oleifera* inhibits the pro-inflammatory mediators in

lipopolysaccharide stimulated macrophages. *Pharmacognosy Magazine*, 11(44), 556.

<https://doi.org/10.4103/0973-1296.172961>

Flexner, C. (1998). HIV-Protease inhibitors. *New England Journal of Medicine* the New England Journal of Medicine, 338(18), 1281–1293.

<https://doi.org/10.1056/nejm199804303381808>

Gilani, A. H., Aftab, K., Suria, A., Siddiqui, S., Salem, R., Siddiqui, B. S., & Faizi, S. (1994). Pharmacological studies on hypotensive and spasmolytic activities of pure compounds from *Moringa oleifera*. *Phytotherapy Research*, 8(2), 87–91.

<https://doi.org/10.1002/ptr.2650080207>

Ghimire, S., Subedi, L., Acharya, N., & Gaire, B. P. (2021). *Moringa oleifera*: A Tree of Life as a Promising Medicinal Plant for Neurodegenerative Diseases. *Journal of Agricultural and Food Chemistry*, 69(48), 14358–14371.

<https://doi.org/10.1021/acs.jafc.1c04581>

Grandgenett, D. P. (2015). Multifunctional facets of retrovirus integrase. *World Journal of Biological Chemistry*, 6(3), 83. <https://doi.org/10.4331/wjbc.v6.i3.83>

Gambo, A., Gqaleni, N., & Babalola, T. K. (2022). Dietary diversity and impact of *Moringa oleifera* Lam. leaves supplemented – Diet on the nutritional status and CD4 cell counts of patients receiving antiretroviral therapy in Nigeria: A double - Blind randomized trial. *Heliyon*, 8(5), e09524. <https://doi.org/10.1016/j.heliyon.2022.e09524gopa>

- Gopalakrishnan, L., Doriya, K., & Kumar, D. S. (2016). *Moringa oleifera*: A review on nutritive importance and its medicinal application. *Food Science and Human Wellness*, 5(2), 49–56. <https://doi.org/10.1016/j.fshw.2016.04.001>
- Haqqani, A. A., & Tilton, J. C. (2013). Entry inhibitors and their use in the treatment of HIV-1 infection. *Antiviral Research*, 98(2), 158–170.
<https://doi.org/10.1016/j.antiviral.2013.03.017>
- Kemnic, T. R., & Gulick, P. G. (2022, September 20). HIV antiretroviral therapy. StatPearls - NCBI Bookshelf. <https://www.ncbi.nlm.nih.gov/books/NBK513308/>
- Koy, T., Donnen, P., Mukumbi, H., Duez, P., & Dramaix-Wilmet, M. (2017). Impact of *Moringa oleifera lam.* Leaf powder supplementation versus nutritional counseling on the body mass index and immune response of HIV patients on antiretroviral therapy: a single-blind randomized control trial. *BMC Complementary and Alternative Medicine*, 17(1). <https://doi.org/10.1186/s12906-017-1920-z>
- Leone, A., Spada, A., Battezzati, A., Schiraldi, A., Aristil, J., & Bertoli, S. (2015). Cultivation, Genetic, Ethnopharmacology, Phytochemistry and Pharmacology of *Moringa oleifera* Leaves: An Overview. *International Journal of Molecular Sciences*, 16(12), 12791–12835. <https://doi.org/10.3390/ijms160612791>
- Lee, K. A., Portillo, C. J., Coggins, T., Davis, H., Pullinger, C. R., & Aouizerat, B. E. (2009). Symptom experience in HIV-Infected Adults: a function of demographic and clinical

characteristics. *Journal of Pain and Symptom Management*, 38(6), 882–893.

<https://doi.org/10.1016/j.jpainsymman.2009.05.013>

Liu, Y., Wang, X., Wei, X., Gao, Z., & Han, J. (2018b). Values, properties and utility of different parts of *Moringa oleifera*: An overview. *Chinese Herbal Medicines/Chinese Herbal Medicines*, 10(4), 371–378. <https://doi.org/10.1016/j.chmed.2018.09.002>

Mahajan, T., & Mikuls, T. R. (2018). Recent advances in the treatment of rheumatoid arthritis. *Current Opinion in Rheumatology/Current Opinion in Rheumatology, With Evaluated MEDLINE*, 30(3), 231–237.

<https://doi.org/10.1097/bor.0000000000000496>

Massry, F. H. M. E., Mossa, M. E., & Youssef, S. M. (2013). *MORINGA OLEIFERA* PLANT "VALUE AND UTILIZATION IN FOOD PROCESSING ". *Egyptian Journal of Agricultural Research/Egyptian Journal of Agricultural Research*, 91(4), 1597–1909. <https://doi.org/10.21608/ejar.2013.166383>

Moyo, B., Masika, P., Hugo, A., & Muchenje, V. (2011). Nutritional characterization of *Moringa (Moringa oleifera Lam.)* leaves. *African Journal of Biotechnology*, 10(60), 12925–12933. <https://doi.org/10.5897/ajb10.1599>

Monera-Penduka, T. G., Maponga, C. C., Wolfe, A. R., Wiesner, L., Morse, G. D., & Nhachi, C. (2017). Effect of *Moringa oleifera Lam.* leaf powder on the pharmacokinetics of nevirapine in HIV-infected adults: a one sequence cross-over study. *AIDS Research and Therapy*, 14(1). <https://doi.org/10.1186/s12981-017-0140-4>

Mishra, G., Singh, P., Verma, R., Kumar, S., Srivastav, S., Jha, K. K., & Khosa, R. L. (2011b).

Traditional uses, phytochemistry and pharmacological properties of *Moringa oleifera* plant: An overview. *Scholars Research Library*, 3(2), 141–164.

<https://www.scholarsresearchlibrary.com/articles/traditional-uses-phytochemistry-and-pharmacological-properties-of-moringa-oleifera-plant-an-overview.pdf>

Odwee, A., Kasozi, K. I., Acup, C. A., Kyamanywa, P., Ssebuufu, R., Obura, R., Agaba, J. B.,

Makeri, D., Kirimuhuzya, C., Sasirabo, O., & Bamaiyi, P. H. (2020). Malnutrition amongst HIV adult patients in selected hospitals of Bushenyi district in southwestern Uganda. *African Health Sciences*, 20(1), 122–131.

<https://doi.org/10.4314/ahs.v20i1.17>

Paikra, B. K., Dhongade, H. K. J., & Gidwani, B. (2017). Phytochemistry and Pharmacology of *Moringa oleifera* Lam. *Journal of Pharmacopuncture*, 20(3), 194–200.

<https://doi.org/10.3831/kpi.2017.20.022>

Pareek, A., Pant, M., Gupta, M. M., Kashania, P., Ratan, Y., Jain, V., Pareek, A., & Chaturgoon, A. A. (2023). *Moringa oleifera*: An updated comprehensive review of its pharmacological activities, Ethnomedicinal, Phytopharmaceutical formulation, clinical, phytochemical, and toxicological aspects. *International Journal of Molecular Sciences*, 24(3), 2098. <https://doi.org/10.3390/ijms24032098>

- Patil, S. V., Mohite, B. V., Marathe, K., Salunkhe, N. S., Marathe, V., & Patil, V. (2022). *Moringa* Tree, Gift of Nature: a Review on Nutritional and Industrial Potential. *Current Pharmacology Reports*, 8(4), 262–280. <https://doi.org/10.1007/s40495-022-00288-7>
- Royce, R. A., Seña, A. C., Cates, W., & Cohen, M. S. (1997). Sexual transmission of HIV. *New England Journal of Medicine/the New England Journal of Medicine*, 336(15), 1072–1078. <https://doi.org/10.1056/nejm199704103361507>
- Rahmath, A., Rajan, N., Shahal, M. A., Seena, T. P., & Sreekumaran, E. (2015). Neuroprotective effect of *Moringa oleifera* in scopolamine induced cognitive impairment and oxidative stress in Wistar albino rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 6(4), 1736–1744. [https://www.cabdirect.org/cabdirect/abstract/20153277816?q=\(similar%3a20103283855\)](https://www.cabdirect.org/cabdirect/abstract/20153277816?q=(similar%3a20103283855))
- Saki, M., De Villiers, H., Ntsapi, C., & Tiloke, C. (2023). The Hepatoprotective Effects of *Moringa oleifera* against Antiretroviral-Induced Cytotoxicity in HepG2 Cells: A Review. *Plants*, 12(18), 3235. <https://doi.org/10.3390/plants12183235>
- Saini, R., Sivanesan, I., & Keum, Y. S. (2016). Phytochemicals of *Moringa oleifera*: a review of their nutritional, therapeutic and industrial significance. *3 Biotech*, 6(2). <https://doi.org/10.1007/s13205-016-0526-3>
- Sarafianos, S. G., Marchand, B., Das, K., Himmel, D., Parniak, M. A., Hughes, S. H., & Arnold, E. (2009). Structure and function of HIV-1 reverse transcriptase: molecular mechanisms

of polymerization and inhibition. *Journal of Molecular Biology/Journal of Molecular Biology*, 385(3), 693–713. <https://doi.org/10.1016/j.jmb.2008.10.071>

Senthilkumar, A., Karuvantevida, N., Rastrelli, L., Kurup, S. S., & Cheruth, A. J. (2018). Traditional Uses, Pharmacological Efficacy, and Phytochemistry of *Moringa peregrina* (Forssk.) Fiori. —A Review. *Frontiers in Pharmacology*, 9. <https://doi.org/10.3389/fphar.2018.00465>

Shafer, R. W., & Vuitton, D. A. (1999). Highly active antiretroviral therapy (Haart) for the treatment of infection with human immunodeficiency virus type 1. *Biomedicine & Pharmacotherapy*, 53(2), 73–86. [https://doi.org/10.1016/s0753-3322\(99\)80063-8](https://doi.org/10.1016/s0753-3322(99)80063-8)

Stanley, K. A., Lora, M., Merjavy, S., Chang, J., Arora, S., Menchine, M., & Jacobson, K. (2017). HIV prevention and treatment: The evolving role of the Emergency Department. *Annals of Emergency Medicine*, 70(4), 562-572.e3. <https://doi.org/10.1016/j.annemergmed.2017.01.018>

Sued, O., & Grosso, T. M. (2023). Pathophysiology of HIV and strategies to eliminate AIDS as a public health threat. In Elsevier eBoSUEDoks (pp. 339–376). <https://doi.org/10.1016/b978-0-323-91814-5.00023-4>

Suresh, S., Chhipa, A. S., Gupta, M., Lalotra, S., Sisodia, S. S., Baksi, R., & Nivsarkar, M. (2020). Phytochemical analysis and pharmacological evaluation of methanolic leaf extract of *Moringa oleifera* Lam. in ovalbumin induced allergic asthma. *South African Journal of Botany*, 130, 484–493. <https://doi.org/10.1016/j.sajb.2020.01.046>

Trigo, C., Castelló, M., Ortolá, M. D., García-Mares, F. J., & Soriano, M. D. (2020). *Moringa oleifera*: An Unknown Crop in Developed Countries with Great Potential for Industry and Adapted to Climate Change. *Foods*, 10(1), 31. <https://doi.org/10.3390/foods10010031>

Vaillant, A. a. J., & Gulick, P. G. (2022, September 20). HIV and AIDS Syndrome. StatPearls - NCBI Bookshelf. <https://www.ncbi.nlm.nih.gov/books/NBK534860/>

Xu, Y., Chen, G., & Chen, G. (2019). Antioxidant and Anti-Inflammatory Activities of the Crude Extracts of *Moringa oleifera* from Kenya and Their Correlations with Flavonoids. *Antioxidants*, 8(8), 296. <https://doi.org/10.3390/antiox8080296>

Xiao, X., Wang, J., Meng, C., Liang, W., Wang, T., Zhou, B., Wang, Y., Luo, X., Gao, L., & Zhang, L. (2020). *Moringa oleifera* Lam and its Therapeutic Effects in Immune Disorders. *Frontiers in Pharmacology*, 11. <https://doi.org/10.3389/fphar.2020.566783>

