

HIV-1 Protease Inhibitory Activity of Lectin Obtained from Soybean (*Glycine max*), Betel Nut Palm Seed (*Areca catechu*), and Mung Bean Sprout (*Vigna RADIATA*)

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ABSTRACT

HIV attacks the immune system and relies on HIV-1 protease, an aspartyl protease essential for processing viral polyproteins and replication, making the enzyme a target for antiretroviral therapy. Natural lectins, known for antiviral properties, are being explored as potential inhibitors of HIV-1 protease. This study evaluated the inhibitory effects of lectins extracted from Soybean (*Glycine max*), Betel-Nut Palm Seed (*Areca catechu*), and Mung Bean Sprout (*Vigna radiata*) against HIV-1 protease. A true experimental design was used to determine each lectin's percent inhibition and IC₅₀ value. Soybean lectin exhibited the most consistent dose-dependent inhibition, reaching 47.76% at 1000 µg/mL with an IC₅₀ of 499.88 µg/mL and moderate variability (SD = 36.93), suggesting a strong interaction with the enzyme. Betel nut lectin showed minimal inhibition at low concentrations, but reached 55.05% at 1000 µg/mL, the highest of the three, though with a higher IC₅₀ (689.61 µg/mL), indicating lower potency. Mung bean lectin showed inconsistent activity at low doses, peaking at 60.21% at 750 µg/mL before slightly declining, with an IC₅₀ of 524.79 µg/mL and the lowest standard deviation. Overall, Soybean lectin showed the most consistent inhibition, while Mung bean and Betel nut lectins demonstrated potential at higher concentrations.

KEYWORDS: *Pharmacy, inhibitory activity, Lectins, HIV-1 Protease, Philippines*

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection continues to be a major global health issue. HIV is a virus that attacks the immune system, which is our body's natural defense against illness. It primarily targets CD4+ T

lymphocytes, gradually weakening immune function over time (Centers for Disease Control and Prevention [CDC], 2024; World Health Organization [WHO], 2023). Someone living with HIV who is not receiving treatment will find it harder and harder to fight off infections and diseases. If HIV is left untreated, it may take up to 10 or 15 years for the immune system to be so severely damaged it can no longer defend itself at all, often progressing to Acquired Immunodeficiency Syndrome (AIDS) (UNAIDS, 2024).

Globally, approximately 39.0 million people were living with HIV. Among 1.5 million of these cases are children living with HIV (0–14 years old) (WHO, 2023). These figures highlight how urgently ongoing efforts at prevention, treatment, and support are needed, particularly for vulnerable populations like children. Despite advances in treatment, access to care remains uneven, especially in low-resource settings where children are often underdiagnosed and undertreated (UNAIDS, 2024; WHO, 2023).

In the Philippines, there were 1,251 confirmed HIV-positive individuals reported to the HIV/AIDS & ART Registry of the Philippines (HARP) as of November 2022, contributing to a cumulative total of 108,428 documented cases since January 1984 (Department of Health [DOH], 2022). Furthermore, 288 people, of those reported in November, around 23 percent had an advanced HIV infection. There have been 43 newly recorded fatalities this year, bringing the total to 919 (Department of Health, 2022). These data reflect the continuing public health burden of HIV in the country and underscore the need for strengthened surveillance, treatment access, and prevention strategies.

Meanwhile, in Davao City, the number of HIV and Aids cases in the Davao Region from January to August 2023 is 700. Among these, 371 cases were from Davao City; 152 from Davao del Norte; 68 from Davao del Sur; 45 from Davao de Oro; 38 from Davao Oriental; and 26 from Davao Occidental (Department of Health–Davao Region [DOH-Davao], 2023). Since 1993 until August 2023, the surveillance unit has recorded a total of 6,736 HIV and AIDS cases in the region (DOH-Davao, 2023). These regional data indicate a persistent and geographically distributed burden of HIV infection, emphasizing the need for localized interventions and strengthened community-based health systems.

As the number of HIV cases continues to increase, a definitive cure remains elusive. The most severe form of HIV infection is AIDS, characterized by profound immune suppression and increased susceptibility to opportunistic

infections (National Institutes of Health [NIH], 2021). One of the major challenges in achieving a permanent cure is the virus's ability to establish latency and persist in small populations of long-lived immune cells, particularly CD4+ T cells (NIH, 2021). These concealed HIV populations, known as "latent reservoirs," consist of infected cells in a dormant state that allows the virus to evade immune detection and antiretroviral therapy, thereby complicating eradication efforts (NIH, 2021).

Studies have examined lectins and their potential therapeutic benefits. Lectins found in nature have been documented for their antiviral properties and are being investigated as potential candidates for strategies to prevent or treat viral infections (Carter et al., 2017). Numerous lectins inhibit viral replication by binding to glycoproteins present on viral envelopes, thereby interfering with viral entry and replication processes (Carter et al., 2017). This mechanism highlights their potential relevance in antiviral drug discovery, particularly for enveloped viruses such as HIV.

In this research, lectins from Soybean (*Glycine max*), Betel-nut seed (*Areca catechu*), and Mung bean sprout (*Vigna radiata*) will be extracted and used as potential inhibitors of HIV-1 protease. This study aims to investigate the inhibitory properties of plant-derived extracts and evaluate their potential to mitigate or treat HIV/AIDS. Specifically, this research seeks to assess lectins obtained from Soybean (*Glycine max*), Betel-nut seed (*Areca catechu*), and Mung bean sprout (*Vigna radiata*) as potential sources of antiviral agents that may contribute to the development of future therapeutic strategies against HIV infection.

Statement of the Problem

1. What is the percentage yield of Lectin obtained from soybean (*Glycine max*), betel nut seed (*Areca catechu*), and mung bean sprout (*Vigna radiata*)?
2. What is the percent (%) mean inhibition against HIV 1 Protease of the following: Lectin obtained from soybean (*Glycine max*); Lectin obtained from betel nut seed (*Areca catechu*); Lectin obtained from mung bean sprout (*Vigna radiata*); Positive Control (Indinavir); Negative Control (combination of hemoglobin and HIV-1 Protease)?
3. What is the Median Maximal Inhibitory Concentration (IC50) of soybean (*Glycine max*), betel nut seed (*Areca catechu*), and mung bean sprout (*Vigna radiata*) Lectin against HIV-1 Protease?

METHODOLOGY

Research Design. The study utilized a true experimental design. This study tested the inhibitory activity of lectins, proteins extracted from specific plants, including soybean, betel-nut palm seed, and mung bean, against HIV-1 protease. This constituted an intervention because the study investigated the effects of these lectins on a specific biological target: the HIV-1 protease. The quantitative data gathered from the instruments established a significant relationship among the different variables.

Research Locale. The study was conducted at the Analytical Chemistry Laboratory & Pharmaceutical Microbiology Laboratory of the University of the Immaculate Conception, Father Selga Street, Davao City, for the preparation of plant samples. The experimental assay was conducted at the Clinical Laboratory of University of the Immaculate Conception, Corner De Jesus St, Poblacion district, Davao City, This laboratory offers an ELISA machine that is essential for reading optical density of the sample.

Research Procedures. Data Collection and Authentication- The researcher collected the plant materials from Calinan, Davao City, for Soybean (*Glycine max*) and Mung bean sprout (*Vigna radiata*), while Betel-nut seed (*Areca catechu*) was collected in Benguet Products Farm, Benguet. The plant sample was collected separately & was cleaned to remove unwanted substances & any particulate matter that could cause errors throughout the study. For the plant samples to be qualified, the researcher sought the authentication of a botanist from the University of the Philippines Mindanao, College of Science and Mathematics, Department of Biological Sciences and Environmental Studies, Tugbok District, Davao City, and Bureau of Plant Industry, Davao National Crop Research, Development and Production Support Center, Bago Oshiro, Davao City.

Extraction of Lectin from the Plant Sample. The plant sample was washed thoroughly with distilled water and allowed to air-dry. Lectin from soybean (*Glycine max*), betel nut seed (*Areca catechu*), and mung bean sprout (*Vigna radiata*) was isolated using the soaking method. The soybean (*Glycine max*), betel nut seed (*Areca catechu*), and mung bean sprout (*Vigna radiata*) were pulverized and filtered through an 80-mesh sieve. The 100g pulverized soybean (*Glycine max*), betel nut seed (*Areca catechu*), and mung bean sprout (*Vigna radiata*) were soaked in 0.15 M sodium chloride for 48 hours at 4 °C and

re-filtered. Following filtration, the filtrate was centrifuged at 9000 rpm for 30 minutes, after which the supernatant was precipitated by the addition of ammonium sulfate to 100% saturation. These pellets obtained were combined and solubilized in small amounts of distilled water at 4 °C (Duong-Ly & Gabelli, 2014).

Phytochemical Test. Biuret Test. The Biuret Test is a general test for proteins. When a protein reacts with copper(II) sulfate (blue), a positive test is indicated by the formation of a violet-colored complex. To each test tube, add 2mL of 10% NaOH solution and 2 drops of 1% CuSO₄ solution while swirling. The development of a purplish-violet color indicates the presence of proteins (Yadav et al., 2024).

Ninhydrin Test. The Ninhydrin Test is a test for amino acids and proteins with a free -NH₂ group. When an -NH₂ group reacts with ninhydrin, a purple-blue complex forms. Add 5 drops of ninhydrin reagent to each test tube and heat the test tubes in a boiling water bath for about 5 minutes (Yadav et al., 2024).

Xanthoproteic Test. Phenyl rings containing an activating group can be nitrated, producing a yellow product. Add 10 drops of concentrated HNO₃ to each test tube while swirling. Heat the test tubes carefully in a warm water bath. Additionally, add a couple of drops of concentrated nitric acid to the sample (Yadav et al., 2024).

HIV-1 Protease Inhibitory Activity Assay. To prepare the assay, an HIV-1 Protease solution purchased from Interanalytical Research Services and Environmental Solutions was transferred to each lectin concentration (Singh, 2013). A 250µL aliquot of the solution was transferred to the following lectin concentrations (1000 mcg/mL, 750 mcg/mL, 500 mcg/mL, 250 mcg/mL, & 125 mcg/mL). The pre-incubated mixture was supplemented with 1000 µg of hemoglobin. This acted as the substrate to HIV-1 Protease. The reaction mixture was allowed to incubate at 37 °C for twenty (20) minutes. Its optical density (OD) was read using an ELISA Reader (Singh, 2013). The same procedures were performed for the positive & negative controls. The positive control was treated with Indinavir, which is a well-known inhibitor of HIV-1 Proteases. On the other hand, the negative control lacked inhibitors.

Data Analysis. The basis for the measurement in the reading is the

products produced from the lysis of hemoglobin. The protease inhibitory activity of Lectin obtained from Soybean (*Glycine max*) is expressed in terms of percent inhibition & is calculated by:

$$\% \text{ Inhibition} = \frac{OD \text{ of Positive Control} - OD \text{ of Negative Control}}{OD \text{ of Positive Control}} \times 100$$

Median Maximal Inhibitory Concentration (IC50). The Median Maximal Inhibitory Concentration (IC₅₀) is the concentration that inhibits the growth of 50% of the test organisms. It was done by plotting the percentage inhibition (Y) with logarithmic concentration (x). The equation of the line was obtained using linear regression.

Statistical Treatment. Mean and Standard Deviation are the basic statistical tools that was used to allow the researchers to assess whether there is a significant difference in the HIV-1 Protease inhibitory activity of Lectin obtained from Soybean (*Glycine max*), Betel-nut seed (*Areca catechu*), and Mung bean sprout (*Vigna radiata*) against HIV-1 Protease in different concentrations.

Ethical Considerations. The researcher applied for an Ethics Exemption from the REC. The University of the Immaculate Conception Research Ethics Committee (UIC-REC) assessed this to ensure that necessary elements (albeit exempt) met the required ethical features.

RESULTS AND DISCUSSION

Percentage Yield of Lectin from Extracts

Presented in Table 1 is the concentration of crude lectin extracts obtained 100g from three different plant sources: soybean (*Glycine max*), mung bean sprout (*Vigna radiata*), and betel nut seed (*Areca catechu*).

Table 1
Percentage Yield of Lectin obtained from Soybean (Glycine max), Betel nut seed (Areca catechu), and Mung bean Sprout (Vigna radiata)

Plant Sample	Weight of Extract, g	Volume of Extract, ml	Concentration, mg/ml	Percentage Yield
Soybean	100	14.0	7143	14%
Mung Bean	100	18.0	5556	18%

Betel Nut	100	18.0	3846	26%
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Results revealed that for each plant sample, 100 grams of raw material were processed to yield varying volumes of extract. The betel nut sample produced a percent yield of 26% followed by the mung bean extract that yielded 18%. In contrast, soybean extract resulted in a lowest percent yield of 14%. These differences in concentration reflect the varying efficiency of lectin extraction from each plant material and are essential for determining the potency and comparative inhibitory potential of each extract in subsequent HIV-1 protease inhibition assays. Results support the study of Lo et al.(2020) showing that after the mung bean seed coatings were dried with hot air and milled into a powder after being combined with organic acids at high temperatures and pressures. The mung bean extract yielded 13% of protein. Additionally, the study of Zamanian et al. (2024) shows that 20.0 g of betel nut was powderized that gave corresponding extract 7.7 g and 38.6%. While, another study for soybean shows that after it was powderized and dissolved in the water, it yielded to 11.97% of protein (Liu, et.al, 2023).

Percentage Inhibition against HIV-1

Results showed that among the test samples, soybean lectin exhibited a gradual and consistent increase in inhibitory activity with increasing concentration, beginning at $5.62 \pm 0.77\%$ at 125 $\mu\text{g/mL}$ and reaching $47.76 \pm 0.29\%$ at 1000 $\mu\text{g/mL}$. This trend indicates a dose-dependent inhibition pattern, suggesting the potential of soybean lectin as an HIV-1 protease inhibitor. This patternwasalsoobserved in the study by lowering intracellular which are elevated by influenzaAvirus infection, soybean extract prevented influenza A virus infection inadose-dependent manner when compared to the virus control (Kwon, 2022). Another study evaluated the Soybean extract on influenza virus adsorption inhibited the viruses in a concentration-dependent manner (Sakata et al., 2024).

Lectin extracted from mung bean sprout showed minimal inhibition at lower concentrations, with a slight negative activity observed at 125 $\mu\text{g/mL}$ ($-0.37 \pm 0.35\%$). However, a notable increase in inhibition was observed at 750 $\mu\text{g/mL}$ ($60.21 \pm 0.13\%$), although the activity slightly decreased at 1000 $\mu\text{g/mL}$ ($47.15 \pm 0.09\%$). This non-linear trend may imply a threshold effect or instability of the extract at higher concentrations, warranting further purification and structural evaluation.

Table 2
Mean Percentage Inhibition of Isolated Lectin from Soybean (Glycine max), Betel-nut seed (Areca catechu), and Mung bean Sprout (Vigna radiata)

Test Sample	Mean Percentage (%) Inhibition (n=3)									
	125µg/ml		250µg/ml		500µg/ml		750µg/m		1000µg/ml	
	%	±S	%	±SD	%	±SD	%	±SD	%	±SD
	Inhi bitio n	D	Inhibit ion		Inhibit ion		Inhibit ion		Inhibit ion	
Lectin from Soybean	5.62	0.77	13.36	2.18	31.08	3.62	47.21	0.32	47.76	0.29
Lectin from Mung Bean	-0.37	0.35	2.89	2.02	12.16	5.17	60.21	0.13	47.15	0.09
Lectin Betel Nut	-6.42	1.18	-1.35	1.39	1.88	0.53	48.04	1.69	55.05	0.17
Indinavir (Positive control)	43.39	3.09	53.57	0.34	59.28	1.21	59.09	8.63	77.45	1.74

Results confirmed the study conducted that examined the antiviral potential of mung bean extract against feline coronavirus (FCoV) which shows that mung bean extract decreased viral multiplication, downregulated spike-protein production, and successfully prevented the cytopathic impact causedbyFCoV in higher concentrations and dose-response manner. (Chou et al., 2024) Betel nut lectin displayed the lowest inhibitory effect at lower concentrations, showing negative values at 125 and 250 µg/mL, but its inhibition markedly improved at higher concentrations, peaking at 55.05 ± 0.17%at 1000µg/mL. These findings suggest that while betel nut lectin may require higher doses to achieve significant inhibition, it demonstrates promisingactivitycomparable to soybean lectin at higher concentrations. Results support the study wherein it was found that the concentrations of *Areca catechu* nut water by pulverizing and dissolving it to water, the extract shows a dose dependent inhibitory effect on Singapore Grouper Iridovirus (Li et al., 2024).

The positive control, indinavir, consistently showed the highest inhibition across all concentrations, reaching 77.45 ± 1.74% at 1000 µg/mL, thereby validating the assay’s sensitivity and reliability. Results align with previous studies indicating that plant-derived lectins possess varied inhibitory activities against viral enzymes, depending on their source, structure, and carbohydrate-binding specificities (Akkouh, 2015). The results support further investigation into plant lectins, particularly from soybean and betel nut, as

potential leads for developing novel anti-HIV agents.

**Median Maximal Inhibitory Concentration (IC₅₀)
Inhibition of Various Isolated Lectin from Soybean,
Betel-nut and Mung Bean Sprout**

Shown in Table 3 are the median maximal inhibitory concentration (IC₅₀) values of the lectin extracts from soybean (*Glycine max*), mung bean sprout (*Vigna radiata*), and betel nut (*Areca catechu*), as well as the positive control, indinavir. The IC₅₀ represents the concentration required to inhibit 50% of HIV-1 protease activity, providing a quantitative measure of each extract's potency. Each sample was tested in triplicate (T1, T2, T3), and the mean IC₅₀ values along with standard deviations (SD) were calculated.

Table 3
Median Maximal Inhibitory Concentration (IC₅₀) Inhibition of Various Isolated Lectin from Soybean, Betel-nut and Mung Bean Sprout

Test Samples	Median Maximal Inhibitory Concentration (IC ₅₀) mcg/ml				
	T ₁	T ₂	T ₃	Mean	
				IC50 (µg/mL)	SD
Lectin from Soybean	501.91	461.98	535.75	499.88	± 36.93
Lectin from Mung Bear	533.72	528.02	512.62	524.79	± 10.92
Lectin Betel-Nut	646.42	722.04	700.37	689.61	± 38.94

Among the plant samples, soybean lectin showed the lowest meanIC50value at 499.88 µg/mL with a standard deviation of 36.93, indicating are latively strong inhibitory effect and moderate consistency across trials. Result supports the study of Zhou et al. (2017) which found that soybean from Lectinhasapotent inhibitory effect against HIV infection of macrophage. SoybeanLectininhibits HIV through entry level and inducing multiple cellular antiviral factors. Further, result aligns to the study wherein protease inhibitor and hemagglutinin isolated from Chinese cultivar of black soybean have potent HIV-1reversetranscriptase inhibitory and antiproliferative activities with IC50 value mostly below 10 µM (Ye & Ng, 2011). Another study showed that Bowman-Birk inhibitors derived from Soybean could inhibit HIV reverse transcriptase with the IC₅₀ of 49µM or to equal to 387 µg/ml (Ma et al., 2018).

Mung bean lectin followed with a mean IC₅₀ of 524.79 µg/mLandnotably lower SD of 10.92, shows more consistent inhibition despiteaslightlyhigher concentration requirement. Results support the study

which shows that the cytopathic effect reduction ability of *Vigna radiata* extract indicated the IC_{50} value of 235.1 $\mu\text{g/ml}$ against feline coronavirus (Chou, 2024). In another study, mung bean sprout extract was tested for inhibitory activity against HSV-1 virus which showed an IC_{50} of 7620 mcg/ml (Hafidh, et.al, 2015). Mung bean sprout extract was also tested for antiviral effect on RSV which shows an IC_{50} of 15.62 mg/ml (Hafidh et al., 2015).

In contrast, betel nut lectin had the highest IC_{50} among the three plant extracts, averaging 689.61 $\mu\text{g/mL}$ with a higher variability ($SD = 38.94$), indicating that higher concentrations were needed to achieve 50% inhibition and that the results were less consistent. Results conform to a study which shows that *Areca catechu* extract inhibits against HSV-1 virus by interruption in HSV-1 binding to Vero cells with an IC_{50} value of 110.52 $\mu\text{g/mL}$ (Zamanian et al., 2024). In another study, it was documented that areca catechu has antiviral effect against HIV-1 Protease with an IC_{50} of 200 $\mu\text{g/mL}$ (Sun et al., 2024). The lower IC_{50} values for the plant extracts suggest that crude lectin preparations may contain components with promising inhibitory effects, although their mechanisms and selectivity require further investigation (Lv, 2015). These findings support earlier research that highlights the antiviral potential of plant-derived lectins and their relevance as candidates for antiretroviral drug development (Wang et al., 2021).

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