International Journal of Advance and Applied Research
www.ijaar.co.in
ISSN – 2347-7075 Impact Factor – 7.328
Peer Reviewed Bi-Monthly
Vol.11 No.5 May – June 2024

Formulation And Evaluation Of Mucuna Pruriens Tablets Containing Levodopa For Parkinson's Disease Management

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DOI - 10.5281/zenodo.11467942

Abstract:

This study focuses on formulating levodopa tablets utilizing extracts from Mucuna pruriens seeds, a natural source of levodopa. The formulations were prepared with different concentrations of the seed extract to determine the optimal dosage form. The tablets were formulated using excipients aimed at enhancing levodopa stability and bioavailability. Physicochemical parameters, including tablet hardness, friability and disintegration time were evaluated to ensure formulation uniformity and integrity. In vitro studies were conducted to assess the formulation and dissolution characteristics of Mucuna pruriens tablets containing levodopa, intended for the management of Parkinson's disease (PD).In vitro dissolution studies were performed to assess the release profile of levodopa from the tablets under simulated physiological conditions. The results demonstrated sustained and controlled release of levodopa from the tablets, indicating their potential for extended drug delivery. These findings suggest that the formulated Mucuna pruriens tablets possess desirable dissolution characteristics, which could contribute to enhanced therapeutic efficacy and patient compliance in the treatment of PD.

Keywords: Levodopa, Mucuna Pruriens, Parkinson's Disease, Tablet Formulation, Herbal Medicine, Stability, Invitro Studies, Dissolution, Excipient.

Introduction:

Natural Source of Levodopa: *Mucuna pruriens*, also known as velvet bean, contains high levels of levodopa, the precursor to dopamine. Levodopa is the primary medication used to manage motor symptoms in Parkinson's disease by replenishing dopamine levels in the brain. *Mucuna pruriens* provides levodopa in its natural form, potentially offering advantages in terms of bioavailability, tolerability and sustained release compared to synthetic levodopa preparations.[1]

Bioavailability and Pharmacokinetics: Studies have suggested that levodopa from *Mucuna pruriens* may have superior bioavailability and pharmacokinetic properties compared to synthetic levodopa formulations. This could lead to more consistent and prolonged delivery of

levodopa to the brain, potentially reducing motor fluctuations and improving symptom control in Parkinson's disease patients.[2]

Neuroprotective Effects: In addition to levodopa *Mucuna pruriens* contains various bioactive compounds such as antioxidants, flavonoids, and alkaloids, which may exert neuroprotective effects. These compounds have been shown to protect dopaminergic neurons from oxidative stress, inflammation and other mechanisms implicated in the pathogenesis of Parkinson's disease. By preserving dopaminergic function, *Mucuna pruriens* may not only alleviate symptoms but also slow disease progression.[3]

Traditional Use in Ayurvedic Medicine: *Mucuna pruriens* has a long history of use in traditional medicine systems such as Ayurveda for the management of neurological disorders, including Parkinson's disease-like symptoms. Traditional healers have recognized its therapeutic properties and have used it to improve motor function, reduce tremors and enhance overall well-being in patients with movement disorders.[4]

Potential to Mitigate Side Effects: Some studies suggest that *Mucuna pruriens* may have fewer side effects compared to synthetic levodopa preparations. This includes a potentially lower risk of motor fluctuations, dyskinesias and gastrointestinal disturbances commonly associated with long-term levodopa use. Patients may experience improved tolerability and adherence to treatment with *Mucuna pruriens*.[5]

Complementary and Integrative Approach: *Mucuna pruriens* offers a complementary and integrative approach to Parkinson's disease management, allowing patients to potentially reduce reliance on conventional medications or use it in conjunction with existing therapies. Integrating *Mucuna pruriens* into treatment regimens may provide additional benefits and broaden therapeutic options for individuals with Parkinson's disease.

Overall, exploring *Mucuna pruriens* as an alternative therapy for Parkinson's disease aligns with the growing interest in natural remedies, personalized medicine and holistic approaches to healthcare. Further research is needed to elucidate its efficacy, safety, optimal dosing regimens and long-term effects in Parkinson's disease patients[6]

Materials and Methods:

Materials:

Active Ingredients – *Mucuna pruriens* seed extract containing Levodopa

Excipients – HPMC, Magnesium Stearate, Talc, etc

Method of Preparation

Extraction of *Mucuna Prurines* Seeds : Cold Maceration Method: The seed powder of the *Mucuna pruriens* was extracted with cold maceration technique. Cold maceration method gives maximum extraction of Levodopa from *Mucuna pruriens* seed powder.

Formulation of *Mucuna pruriens* seed extract Tablets

Each tablet containing 500mg of *Mucuna pruriens* seed extract were prepared by direct compression method using round shape punch and die set. The final weight was made 550 mg by adding other excipients.

Mucuna pruriens seed extract as active Pharmaceutical ingredient, Gum Acacia, PVP, and HPMC are used as binder in the different concentration, starch, and lactose is used as the diluent. Magnesium carbonate is used as adsorbent and talc is used as the Lubricant. Composition of ingredient used for the formulation is shown in the beloa table 1. Batches were prepared with varying the concentrations of binders.

Tablet No 1: Formulation Tablet

Ingredients	Quantity (mg)
Mucuna pruriens seed extract	500
HPMC	40
Mg sterate	5
Talc	5

Evaluation Parameters:

Tablet Thickness: The thickness of the tablets was determined by using Vernier caliper. Three tablets were used, and average values were calculated.[7]

Hardness: Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.[7]

Weight Variation: To study weight variation twenty tablets of the formulation were weighed using a digital balance and the test was performed according to the official method. The specification for weight variation of tablets as per USP was mentioned in Table no 2. Twenty tablets were selected randomly and weighed individually to check for weight variation.[7]

Table No 2: Specification for weight variation of tablets as per USP

Average Weight of Tablets (mg)	% Difference
130 or less	10
From 130 to 324	7.5
More than 324	5

Friability: The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed and transferred into Friabilator. The friabilator was operated at 25 rpm for 4 minutes. The tablets were weighed again. The % friability was then calculated by:

% Friability = Initial Weight – Final Weight/ Final Weight X 100 (Percentage friability of tablets less than 1% is considered acceptable.)[7]

Disintegration Time: Disintegration time test was carried out according to USP specification. 6 tablets were placed in a disintegration tester filled with distilled water at 37±0.200C. The tablets were considered completely disintegrated when all the particles passed through the wire

mesh. Disintegration times recorded are mean of two determinations.[7]

Assay and Calibration Curve for Levodopa in *Mucuna pruriens* seed exract:

In-house *Mucuna pruriens* seed extract tablets were punched and used for assay. Weigh accurately 10 tablets and crushed in mortar and pestle, weigh the tablet powder equivalent to 5 mg of Levodopa in 10 ml volumetric flask then add 5 ml diluents 0.1 M Hydrochloric acid and sonicate for 10 min; make up the volume with 0.1 M Hydrochloric acid (Conc. = 500 µg/ml). Pipette out 0.5 ml of above solution in 10 ml volumetric flask then add 5 ml 0.1 M Hydrochloric acid and mix for 10 min; make up the volume with 0.1 M Hydrochloric acid. (Conc. = 25 µg/ml)[8]

Fourier Transform Infrared Spectroscopy (FTIR):

FTIR analysis was conducted to verify the possibility of chemical bonds between drug and polymer. Samples were scanned in the range from 400-4000 cm^{-1} and carbon black reference (Model-Bruker Alpha-II). The detector was purged carefully by clean dry helium gas to increase the signal level and reduce moisture.[9]

In Vitro Drug Release Study:

This test was carried out using dissolution test apparatus containing specified volume of 900 ml 0.1N HCL and the temperature were maintained at 37±0.5oC. The tablets are directly placed in a medium and immediately the paddles were started at the specified rate (75 RPM). Within the time interval specified (15, 30, 45, 60, 90, 120, 180, and 210 min) an aliquot of 5 ml sample were withdrawn and replaced with equal volume of fresh dissolution medium. The samples were filtered and added 5 ml of 0.1N HCL. These samples are analyzed at 280 nm by UV Spectrophotometer for levodopa and further calculation is carried out to get drug release. The drug released data were plotted. The procedure was repeated for each sample.[8]

Result and Discussion:

Levodopa Content in *Mucuna pruriens* Seed Extract (As per IP):

Content of Levodopa in *Mucuna pruriens* seed *extract* was analysed by using UV Spectroscopy at wavelength 280 nm in 0.1 *M hydrochloric acid.*

The sample solution was prepared by using 30 mg of *Mucuna pruriens* seeds extract containing levodopa was dissolved in 0.1 M HCl to produce 100 ml and dilute 10 ml to 100 ml with 0.1 M HCl. i.e. (30 µg/ml)

The prepared sample solution when examined in the UV Spectroscopy the absorption was found to 0.085.

The specific absorbance of levodopa is 141, when calculated using Beer's Law; A = abc

The concentration was found to be 6.02 µg/ml

Percentage yield = Practical yield / Theoretical yield x 100

Percentage yield = 6.02 µg/ml / 30 µg/ml x 100

Percentage yield = 20. 06 % of Levodopa in *Mucuna prurines* seeds Extract

Linearity and Range:

In the concentration range of 10-30µg/ml at 280 nm, the analytical parameter linearity was found to be linear and proportional in a relationship. The regression coefficient was found to be 0.999. The analytical parameter range is the difference between the upper and lower concentration limits. The range was found to be 10-30µg/ml. The correlation coefficient was found to be 0.999 which is well within the acceptance criteria.

Table No 3: Linearity Results

Concentration (µg/ml)	Absorbance
0	0
10	0.140
15	0.215
20	0.281
25	0.358
30	0.430

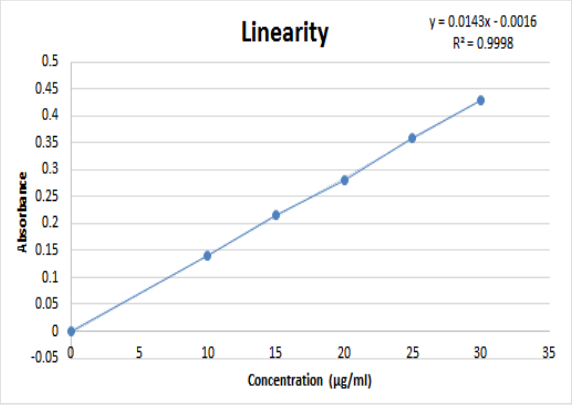

Fig no 1: Calibration curve for Levodopa

Table no 4: Linear Regression Analysis of Calibration Curves for *Mucuna pruriens* seed extract

Parameters	Values
Linearity Range µg/ml	10-30µg/ml
Regression Coefficient (R^2)	0.999
Regression Equation	y = 0.0143x - 0.0016

Fourier Transform Infrared Spectroscopy (FTIR):

The FTIR analysis was implemented to assume the compatibility of assorted excipients blend with the pure drug. Spectral examination was executed using FTIR to explore the generation of new compound or any chemical change in the functional portion of the ad-mixtures among the blends. Infrared spectroscopy as utilized in pharmaceutical investigation for its authentication and structure elucidation of drug Infrared spectroscopy is one of the methods used for the authentication of the compound.

The FTIR spectra of pure extract is shown in Fig 2 and pure drug and HPMC in fig 3

1. Amine group (-NH2): Primary & secondary amines and amides usually appears as a broad peak around 3500-3100 cm^{-1} due to N-H stretching vibrations. For pure drug it showed maxima at 3385.81 and HPMC at 3407.53.

2. Aliphatic C-H bonds: Peaks in the region of 3000-2850 cm^{-1} due to symmetric and asymmetric stretching vibrations of C-H bonds in alkyl groups,

the drug showed the maxima at 2924.44 and for drug with HPMC at 2924.06

3. Aromatic ring: Characteristic peaks around 1680-1600 cm^{-1} due to C=C stretching vibrations. The maximum peak observed for drug appeared at 1631.34 and for drug with HPMC at 1630.41 respectively.

4. C-O stretching: The C-O stretching vibration occurs as a medium to strong peak around 1000-1300 cm^{-1}. For pure drug observed maximum peak showed at 1384.02 and drug with HPMC showed peak at 1384.07 respectively.

5. Alkyl halide C-X bonds: The stretching vibrations of the carbon-halogen bond typically occur at lower wavenumbers. For C-Cl carbon-chloride stretches appears around 785-540 cm^{-1}.

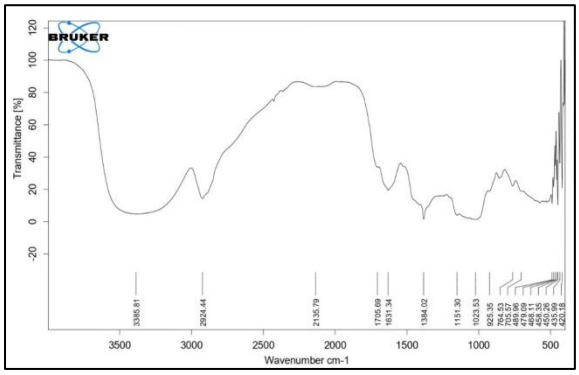

Fig. 2: FTIR Spectra of *M. pruriens* Seed Extract containing Levodopa

Table 5: Data Interpretation of FTIR Spectra

Sr. No.	**Functional Group**	**Frequency region (cm^{-1})**	**M. pruriens Seed Extract containing Levodopa**	**Drug with HPMC**
1	Amine group (-NH2): Primary & secondary amines and amides (Stretching)	3500-3100	3385.81	3407.53
2	Aliphatic C-H bonds symmetric & asymmetric (stretching)	3000-2850	2924.44	2924.06
3	Aromatic ring C=C (stretching)	1680-1600	1631.34	1630.41
4	C-O bonds (stretching)	1300-1000	1384.02	1384.07
5	Alkyl halide (C-Cl) bonds (Stretching)	785-540	764.53	766.55

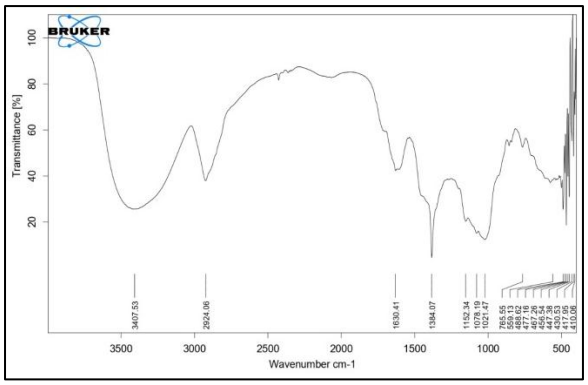

Fig. 3: FTIR Spectra of drug with HPMC

Table no 6: Results of Post Formulation Study

Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Average wt. of Tablet	Drug content (equivalent % of Levodopa)	Disintegration time
4±0.25	3.88±2	0.235	550±5	95.53±0.5	12.45±1.30

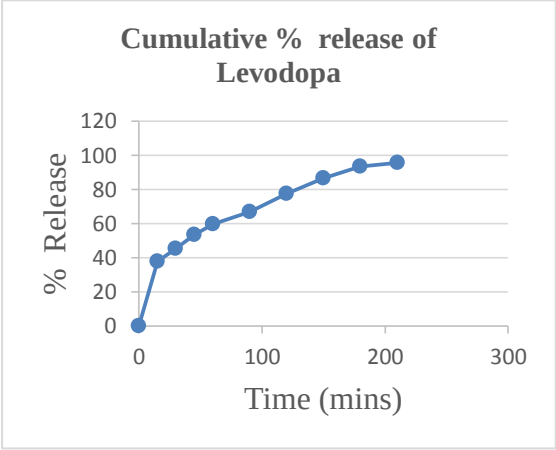

Fig No 4: In Vitro Drug Release Study

Summary and Conclusion:

The study focuses on formulating tablets containing extract from Mucuna pruriens seeds, which are known to be rich in levodopa, a key component in the management of Parkinson's disease. The primary objective was to enhance the delivery of levodopa through tablets, aiming to improve treatment efficacy and patient adherence.

The extraction of the Mucuna pruriens seed extract was carried out using the cold maceration technique. The resulting extract was then analyzed using UV spectroscopy to determine its levodopa content, which is crucial for assessing the therapeutic potential of the formulation.

Various formulations of tablets were prepared and evaluated to optimize drug release kinetics and ensure dosage uniformity. Parameters such as drug release profile, assay, and other quality attributes were systematically assessed to identify the most suitable formulation.

Through optimization efforts, an ideal formulation (referred to as the optimized formulation) was developed, exhibiting desirable drug release characteristics.

Furthermore, post-compression evaluation was conducted to assess the physical and chemical properties of the tablets. The results indicate that the tablets meet the required quality standards, confirming their feasibility for large-scale production.

In conclusion, the study demonstrates the successful formulation and evaluation of tablets containing Mucuna pruriens seed extract for the management of Parkinson's disease. These tablets offer a promising alternative for delivering levodopa, potentially improving treatment outcomes and patient acceptance. Further clinical studies are warranted to validate the efficacy and

safety of these extended-release tablets in real-world settings.

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