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ETHNOPHARMACOLOGICAL USES, PHYTOCHEMISTRY AND THERAPEUTIC POTENTIAL OF *Mucuna Pruriens*: A COMPREHENSIVE REVIEW ON CURRENT STATUS OF KNOWLEDGE

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Abstract

Background: Velvet bean scientifically named as *Mucuna pruriens* belonging to Fabaceae family is a native to tropical regions especially Asia, West Indies, Africa and many parts of America. They are excellent source of nutritional and phytochemical components which hold their potential for pharmaceutical and nutraceutical development.

Main body:

This review will apprise about the bioactive principles of *Mucuna pruriens* which holds restorative quality making it a valuable component in pharmaceutical research and therapeutic application. The bean is an wonderful source of l-DOPA (3,4-dihydroxy-L-phenylalanine) along with substantially high content of protein and starch exhibiting several medicinal and therapeutic properties. This herb is known to exhibit properties like anti-Parkinson, Anti-cholesterolemic, anti-inflammatory, anti-venom, antimicrobial, anti-diabetic, aphrodisiac, antioxidant, and many others due to its extensive phytochemical profile including high contents of alkaloids, glycosides, saponins, reducing sugars and tannins which open a boulevard of pharmaceutical applications.

Conclusion:

Diversity of active principles and significant amount of l-DOPA shows its functionality in various therapeutic areas and this study will certainly fill in the knowledge gaps of Mucuna pruriens and will help to explore potential of this plant against many other diseases like epilepsy, its application as a food resource, its nutritive and anti-nutritive or harmful principles so that it can be used as an adjunct with various therapeutic approaches.

Background:

Traditional medicine has been benevolent in treating a variety of diseases and disorders and aids in meeting the global healthcare needs. *Mucuna pruriens* is commonly known as Velvet bean because of the unique properties is commonly identified as Kawaanch in Hindi and cowitch in English and has enormous restorative and therapeutic properties. Our objective is to elucidate the therapeutic potential of this plant which will prove to be substantial in incorporation of Plant based medicines in management of various diseases.

Keywords: *Velvet bean, Medicinal plant, l-DOPA, Parkinsonism, Antioxidant, Phytochemical.*

Abbreviations:

l-DOPA	3,4-dihydroxy-L-phenylalanine
LAAD	L-aromatic amino acid decarboxylase
PD	Parkinson's disease
BBB	Blood-brain barrier
UAE	Urine Albumin Levels
HVA	Homovanillic acid
MAO	Monoamine Oxidase
COMT	catechol-*O* methyltransferase

Introduction:

Phytochemicals, Nutraceuticals and Traditional Medicinal plants have been serving a significant purpose of supporting global Healthcare needs and with this extensive support the world will eventually address high demand of such plants and herbs [1]. The medicinal plants have been utilized extensively in countries like India (Ayurvedic System of medicine), China and neighboring countries as Traditional/Chinese medicine for treatment of various diseases and disorders and especially in developing nations to support low- and middle-income strata. With a vast floristic diversity India stands out globally with approximately 54% of the country's land being used for agricultural activities like farming for Crops, Ornamental plants, and Medicinal plants and the 19% of Land is covered with Forests and other vegetation. [2,3]

Mucuna pruriens (Fabaceae-Family; Papilionaceae- sub family) is an established herbal drug for various pharmacological effects including approximately 150 species of annual and perennial legumes. The MP is commonly known as velvet bean, cowage, cowitch, Horse-eye bean or Lyon bean. In Nigeria, it is well known as "Ewe Ina" among the Yoruba's and In India, it is called as Kavach, koncha and kaunch beej.

TAXONOMY:

Table: 1- Taxonomy and related details

Kingdom	***Plantae; Planta, Planter, Vegetal, Plants***	
Sub Kingdom	*Tracheobionta, Vascular Plants*	
Division	*Magnoliophyta*	
Class	*Magnoliopsida*	
Sub-Class	*Rosidae*	
Order	*Fabales*	
Family	*Leguminoseae*	
Sub Family	*Fabaceae*	
Genus	*Mucuna*	
Species	*Pruriens*	
Commonly cited species	*M. deeringiana Merrill, M. utilis Wallich (Bengal velvet bean), M. pruriens, M. Nivea, M. Hassjoo (Yokohama velvet bean), M. aterrima Holland (Mauritius and Bourbon velvet bean), M. capitata, and M. diabolica*	[4]
Synonyms	*Carpopogon pruriens ,* *Dolichos pruriens ,* *Mucuna aterrima,* *M. atropurpurea,* *M. cochinchinensis,* *M. cyanosperma,* *M. deeringiana,* *M. esquirolii,* *M. prurita,* *M. utilis,*	[5]

	Stizolobium aterrimum, *S. deeringianum,* *S.pruriens ,* *S. pruritum,* *S. niveum,* *Negretia pruriens*	
Common Names	*Nescafé Mucuna , Fava-coceira, Cabeca-de-frade, Cowage, Cowhage, Cowitch, Velvet Bean, Bengalbean, Mauritius bean,Florida velvet bean, Itchy bean, Krame, Picapica, Chiporro, Buffalobean.*	[5]
Vernacular Names	***Hindi****- Kiwach, Daunch, Goncha, Kavach, Kawaaanch* ***Bengali****- Alkushi, bichchoti, Alkusa* ***Marathi****- Kavacha, Kuhili, Kanchkuri,* ***Gujarathi****- Kivanch, Kavatch,* ***Kannada****- Nasukunni, Nasugunni* ***Konkani****- Khavalyavali, Majram* ***Malayalam****- Naicorna, Shoriyanam* ***Oriya****- Kaincho.* ***Punjabi*** *– Kawanchi, Gugli, Kavanch* ***Tamil****- Punaikkali, Poonaikkate* ***Telegu****- Dulagondi, Pilliadagu*	[6]

GROWTH AND DISTRIBUTION OF *MUCUNA PRURIENS*:

Mucuna pruriens is a globally widespread however tropically and sub tropically indigenous plant spreading across Africa, Asia, West Indies, Pacific Islands, and United States of America. It is found in bushes, hedges, and dry deciduous and low forests throughout the Indian subcontinent covering Uttar Pradesh, Madhya Pradesh, and many more states. This traditional medicinal plant grows naturally down the lower Himalayan ranges to the entire tropical regions, enabling the residents nearby to use this plant as a medicine as well as formulation for traditional food products. [8-12]

ETHNOBOTANICAL USES OF MUCUNA PRURIENS WORLDWIDE [6, 13]

Country	Use
Brazil	Aphrodisiac, diuretic, Anthelmintic, Nerve tonic, Poison
Nigeria	Snakebite
India	Abortion, Anthelmintic, Antivenin, aphrodisiac, Cancer, Cholera, Cough, Debility, Delirium, Diabetes, Diuretic, Gout, impotency, nerve tonic, nervine, uterine stimulant, worms, tuberculosis, Dysentry, Catarrh, Dysmenorrhea, Sterility, Spermatorrhea, Snakebite, scorpion sting, fertility,
Germany	Carminative, Cholesterol, hypotensive, hypoglycemic, muscle pain, rheumatism, rubefacient, worms
Pakistan	Aphrodisiac, diabetes
Elsewhere	Anasarca, anodyne, anthelmintic, antidotal, aphrodisiac, asthma, burns, cancer, cholera, cough, cuts, diarrhea, diuretic, dogbite, dropsy, emmenagogue, insanity, intestinal parasites, mumps, nervine, paralysis, pleuritis, resolvent, ringworm, rubefacient, snakebite, sores, syphilis, tumors, vermifuge, windburns, worms

PHYTOCHEMICAL CONSTITUENTS:

The seeds of Mucuna produce predominantly a nonprotein amino acid 3-(3,4 dihydroxyl phenyl)-l-alanine (l-Dopa), which is a potent neurotransmitter precursor. The plant is reported to have many Alkaloidal constituents like Mucunadine, Mucunine, Prurienine and prurienidine which tends to have therapeutic potential. The phytochemical constituents reported in the different parts of this plant are mentioned in Table 3.

Phytochemical Constituent	Reference
Lecithin	[15]
1-methyl-3-carboxy-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinolone, **5-hydroxy tryptamine,** **5-methoxy-n,n-dimethyltryptamine-noxide,** **5-oxyindole-3-alkylamine,** **6-methoxyharman,** **Alanine,** **Arachidic Acid,** **Arginine,** **Aspartic Acid,** **Behenic Acid,** **Beta-Carboline,** **Beta -Sitosterol,** **Bufotenine,** **Calcium** **Carboline** **Choline,** **Cystine,** **Gallic Acid** **Glycine** **Glutamic Acid** **Histidine** **Iron (Inorganic)** **Indole-3-alkylamine** **Isoleucine** **Leucine,** **Linoleic Acid,** **Myristic Acid,** **N,Ndimethyltryptamine,** **N,N-Dimethyltryptamine-N-Oxide,** **Niacin (Inorganic)** **Nicotine,** **Oleic Acid,** **Palmitic Acid,** **Palmitoleic Acid,** **Phenylalanine,** **Phosphorus,** **Proline,** **Protein,** **Riboflavin (Inorganic)** **Saponins,** **Serine,** **Serotonin** **Sitosterol (Beta sterol)** **Stearic Acid,** **Stizolamine** **Thiamine** **Trypsin** **Threonine,** **Tryptamine,** **Tyrodine,** **Valine** **Vernolic Acid**	[16,17,18,19,20]
L-DOPA	[21]

L-DOPA is found to be a major constituent of this plant and especially seeds and their extracts which is predominant part of monogastric diets of people. The presence of L-Dopa, a precursor of dopamine (neurotransmitter) makes this plant a valuable assets which can be considered in treatment of diseases

like Parkinsonism and used as Ayurvedic medicine for PD and geriatric disorders. The content of L-Dopa varies from different parts of the plant depicted in table below:

Fully Matured Seeds	**3.6-4.2 Percent**
Pod- Pericarp	0.14 – 0.22 %
Leaves	0.17 – 0.35%
Stems	0.19 – 0.31 %
Roots	0.12 – 0.16%
Half Matured Seeds	Maximum L-Dopa

THERAPEUTIC PROPERTIES OF MUCUNA PRURIENS:

Mucuna pruriens is recognized throughout the world for its multiple therapeutic and restorative purposes. The farmers across the tropical and sub-tropical areas use this multipurpose plant to restore soil fertility due to its ability to fix atmospheric nitrogen (N) in soil. The therapeutic effects of *M. pruriens* are summarized in Table 4 below.

Table 4: Medicinal properties of Mucuna pruriens

Activity	**Extract**	**Therapeutic effects**	**References**
Aphrodisiac effect	Methanolic	Improvement in the mounting frequency, ejaculation latency and decrease in the mounting latency, post-ejaculatory interval and interintromission interval	[22,23,24,25]
	Seed Powder	The MP seed powder helps in rejuvenation of Harmonic balance of male reproductive hormones as well as reactivates the enzymatic activity of metabolic pathways and energy metabolic in Infertile men.	[26]
		Men found to be infertile have improved psychological stress and seminal plasma lipid peroxidaxe levels, increased sperm motility and count, and restored levels of SOD, Catalase, Gluatathione (GSH), and Ascorbic acid.	[27]
	Ethanolic	Significant upliftment during sexual activity in male rats like mounting frequency, intromission frequency and ejaculation latency.	[28]
	Seeds	Significant inhibition of lipid peroxidation, elevated spermatogenesis, and improved sperm motility after treatment with MP which also restored lipid levels, TGs, cholesterol, phospholipids, and vitamin A, C, and E and corrected fructose in seminal plasma of infertile men as compared to control.	[29]
		Improvement in hormones (Serum T, LH, Dopamine, Nor-adrenaline and Adrenaline) and reduction in FSH and Prolactin in infertile men	[30]
		Spermatogenic restorative efficacy enhancement be regulation of ROS levels, apotosis,HPG Axis, number of testicular germ cells and Mitochondrial Membrane Potential (MMP)	[31,32, 33,37]
	Extract	Significant increase in weight of sexual organs and increased levels of Testosterone in turn to ALP (Alkaline Phosphatase) activity and Protein content.	[34]
Antioxidant effect	Methanolic	Excellent Reducing power because of MP's hydrogen donating properties and also has free radical scavenging activity in dose dependent manner	[35, 36, 37, 38, 39, 40]
	Ethanolic	Anti-Lipid Peroxidation Property	[41]
Antitumor effect	Methanolic	Notable impacts on the tumor's growth and the host's duration of survival in Ehrlich ascitic carcinoma; Diminished tumor volume, densely packed cell volume, viable cell count with extended mean life duration, and mild cytotoxic impact on A549 and MCF7 cell lines	[17, 42, 43,67]

Antidiabetic effect (Hypoglycemic activity)	Ethanolic Methanolic	Dose-dependant reduction in blood glucose levels; Antidiabetic properties are most likely due to d-*chiro*-inositol and its galacto-derivatives in Mucuna pruriens	[44, 45, 46, 48, 49]
Antibacterial effect	Methanolic	Broad spectrum antibiotic properties and showed varied degree of inhibition against different organisms	[50, 51, 52, 53, 54]
Antiprotozoal effect	Methanolic	Effective control of Licthyophtirius multifilis infection in goldfish and lower mortality rate in higher doses	[55]
Anti Snake venom effect	Ethanolic Aqueous	Protective effects against Najas putatrix, Echis carinatus, and other varieties	[56, 57, 58, 59]
Analgesic and anti-inflammatory effect	Ethanolic	Increase in threshold of pain, and significant decrease in body temperature, inhibits carragenin induced edema with anti-inflammatory activity	[60, 61]
Antidiabetic Effect	Aqueous	Significantly prevented Polyuria, rise of urinary albumin levels (UAE)	[63,66]

L-DOPA – BIOACTIVE PRINCIPLES of *Mucuna pruriens*

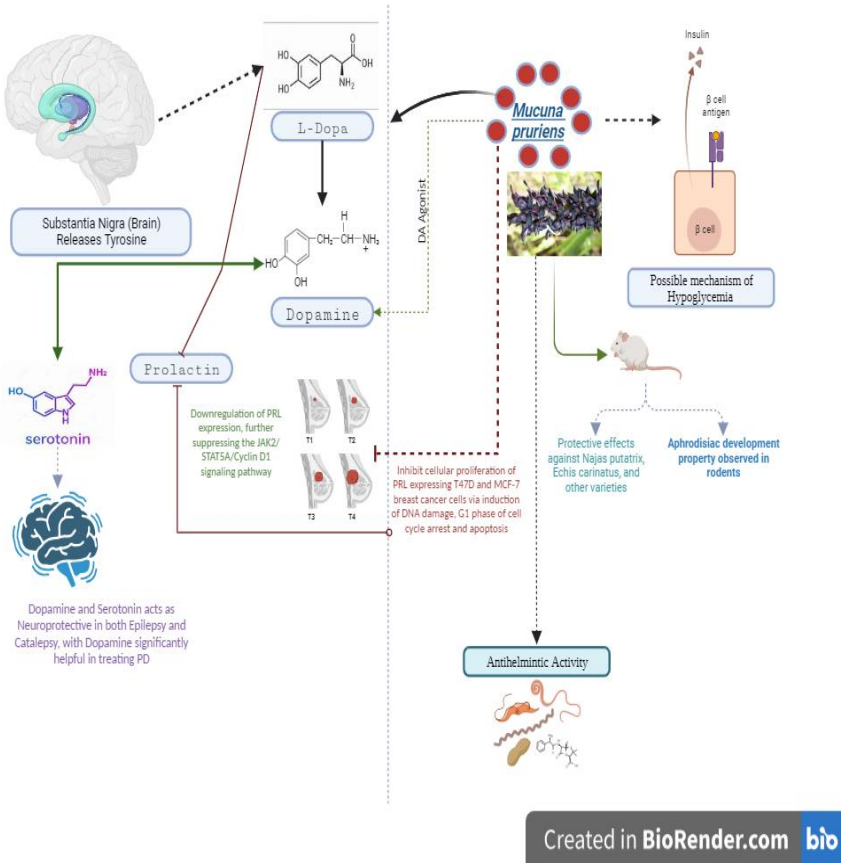
L-dopa is the principal constituent of Mucuna pruriens which is responsible for multiple therapeutic applications. The Dopamine participates in regulation of various functions in the brain (neurotransmitter), heart (an inotropic increase of cardiac output), vascular system (vessel dilator), and kidney (diuretic) and is produced from L-Tyrosine via enzymatic synthesis thereby liberating an intermediary L-dopa in circulation. L-dopa acts as a precursor to dopamine and is able to cross blood-brain barrier; however, dopamine is unable to cross BBB.

L-dopa is widely distributed throughout the body, markedly in muscles, liver, kidney and in CNS due to de novo synthesis. Majority of therapeutic attributes of L-dopa is related to the de novo synthesis and its cellular uptake in the body.

The Pharmacokinetics of L-dopa explains that distribution via oral administration includes 33% absorption via jejunum. The peak plasma concentration is being achieved within 1-3 hours of ingestion and majority of the absorbed L-dopa is converted to dopamine in the periphery, mainly in the intestinal mucosa via decarboxylation by the enzyme L-aromatic amino acid decarboxylase (LAAD). In addition to dopamine, peripheral l-Dopa is metabolized to melanin, nor epinephrine, 3-methoxytyramine, methyldopa, 3,4-dihydroxyphenylacetic acid, and 3-methoxy-4-hydroxyphenyl acetic acid (homovanillic acid or HVA).
The absorption is followed by rapid excretion of all metabolites via urine (80% of administered l-Dopa within 24 hours) leaving behind roughly 50% of metabolites consisting of dihydroxyphenylacetic acid (DOPAC) and HVA, and 10% of dopamine. In comparison, less than 30% occurs as 3-*O*-methyldopa Dopamine produced by decarboxylation of l-Dopa by LAAD in the periphery does not cross the blood–brain barrier but is further metabolized by monoamine oxidase (MAO) in endothelial cells into DOPAC [63].

Less than 1% of the administered dose crosses the blood–brain barrier into the central nervous system and the basal ganglia. In the brain's basal ganglia, dopamine is transformed into Dopa Decarboxylase, which is then subjected to enzymatic inactivation, which is facilitated by MAO and catechol-O methyltransferase (COMT). The COMT in the glial cells methylates dopamine to 3-methoxytyramine, while MAO oxidizes dopamine to DOPAC [64]. The COMT also methylates about 10% of oral l-Dopa to 3-*O*-methyldopa in the red blood cells and the liver. The COMT and MAO together convert dopamine to 3-methoxy-4-hydroxyphenyl acetic acid and HVA.

L-dopa degradation products and dopamine adduct result in oxidative stress and cause selective cytotoxicity of neuronal cells inducing pathogenesis in neurodegenerative disease like Parkinsonism. [65]



Picture 1: Potential mode of action: L-DOPA, which is derived from mucuna pruriens, helps treat Parkinsonism by converting to dopamine in the brain. Furthermore, MP increases the levels of DA by acting as a DA agonist. By causing DNA damage in the G1 cell cycle of cancer cells, MP suppresses the cellular proliferation of breast cancer cells that produce prolactin (PRL). This process is furthered by the release of prolactin into the body, which lowers the expression of PRL in cancer cells. Parkinson's illness, epilepsy, and catalepsy are all treated neuroprotectively by serotonin (5-HT) and dopamine (DA). Additionally, MP has hypoglycemic activity, possibly as a result of its action on beta cells, which releases insulin into the bloodstream. In addition to their diverse pharmacological effects, MP extracts have been shown to have anti-helmintic, aphrodisiac, antidiabetic, and antibiotic properties; however, more focused research is required to determine the underlying mechanism of action.

FUTURE PROSPECTS OF *MUCUNA PRURIENS* IN ANTIEPILEPTIC STUDIES:

Research points to the velvet bean's potential as a medication with antiepileptic properties. This plant's seeds contain a considerable amount of dopamine and 5-HT (serotonin), which has been studied for its potential to treat catalepsy and function as a neuroprotective agent in cases of epilepsy.[68,69] Mucuna pruriens has also been found to have anticonvulsant and anxiolytic qualities that are mediated by positive GABAergic neurotransmission; as a result, it may be used to treat petit mal and grand mal epilepsy, which can again be utilized to treat a variety of patient types. Traditional medications can therefore be utilized as an adjuvant in more complex pathophysiological circumstances like pregnancy, chronic kidney, or liver patients, and so forth because they have the added benefit of a superior safety profile. [70]

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