International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Inexpensive Happy Hormone "Dopamine"-A Safe Antiangiogenic Drug & Enhancing Dopamine Levels By Mucuna Pruriens

Ayesha Sultana[1], K. Saraswathi[2]

[1]Department of Pharmaceutics, Guru Nanak Institutions Technical Campus-School of Pharmacy, Khanapur, Ibrahimpatnam, R.R District, Hyderabad, Telangana, India

[2]Deparment of Pharmacology, Guru Nanak Institutions Technical Campus-School of Pharmacy, Khanapur, Ibrahimpatnam, R.R District, Hyderabad, Telangana, India

Abstract: ***The research reveals that Dopamine blocks the formation of blood vessels in tumors by inhibiting the action of vascular endothelial factor and prevents the side effects associated with currently used chemotherapeutic agents. The aim of this work is to show the role of Dopamine as safe anti angiogenic agent, treating and enhancing Dopamine naturally by the tablets prepared from the powdered seed extracts of Mucuna pruriens by Wet granulation method. The tablets prepared were evaluated for pre and post compression parameters and they were within permissibe limits as per the standards. Experiments were carried out in mice and were divided into four groups. Group A-Control group, Group B-Disease induced (tumor) but no treatment, Group C-Disease induced and treatment by Standard I.V dose of Dopamine, Group D-Disease induced ,it is treated with test dose of tablets of Mucuna pruriens. The tumors were induced by Benzopyrene, formation of tumors were confirmed by checking the parameters of electrolyte levels, haematology values and liver function test .The mice treated with standard dose exhibited weight gain because of retention of urine which leads to accumulation of Uric acid. Swelling and Pain is also observed at the site of injection. Mice treated with test dose showed no side effects, as Mucuna pruriens contains L-Dopa which readily crosses Blood Brain Barrier enhances Dopamine levels naturally, significantly in very economical and easy approach. The In –vitro release of formulation(F3) showed 92% drug release.***

Keywords: Benzopyrene , Dopamine, Vascular Endothelial Factor, Mucuna pruriens

1. Introduction

Dopamine controls the Brain rewards and in this research it is used to treat Cancer. Brain has 100 billion neurons and only 20,000 carry dopamine in 4 major tracts .The VTA(Ventral tegmental area) contains large number of Dopamine neurons in brain. Dopamine boosters Mucuna pruriens (MP) enhances dopamine levels. Dopamine is monoamine acting as neurohumoral transmitters at the post – ganglionic sympathetic nerve endings and certain regions within the brain. This is present in highest concentration in the terminal axonal processes of specific neurons where they are synthesized and stored in vesicles within the varicose axon terminals. This naturally occurring precursor of noradrenaline acts on dopaminergic and other adrenergic receptors. Currently two classes of postsynaptic dopamine receptors have been described: D1-like (D1 and D5) and D2-like (D2,D3,D4). Presynaptic receptors or autoreceptors for Dopamine are present in the brain. Dopamine is also alpha and beta adrenergic receptor agonist. Mainly D1 receptors helps in dilatation of blood vessels. Dopamine is most abundant in corpus striatum a part of the extrapyramidal motor sytem concerned with the co-ordination of movement, and high concentrations also occur in certain parts of frontal Cortex, limbic system and hypothalamus, it is the best food sources of the amino acid L-dopa, also called Levodopa , L-dopa is a direct precursor to dopamine, a powerful neurotransmitter in your brain .Dopamine doesn't cross the blood brain barrier so it cannot be taken or administered directly for therapeutic results. Dopamine boosters Mucuna pruriens (MP) naturally contains 5% of L-Dopa it enhances Dopamine levels and the Psycological stress, depression associated with cancers can also be treated. It also nourishes tissues and fluids of body. The Mucuna pruriens seeds contain 20%proteins, 59%carbohydrates, 10% fiber, 7% crude lipids, tetra hydro iso quinoline alkaloid, beta-carboline, D-chiro inositol and psychoactive substances.

2. Objective

The objective of this research is to treat cancer in very economical and easy approach. Dopamine prevents the formation of blood vessels in tumors and helps in the treatment. It also restores healthy neuron synapses and minimizes the toxicities associated with chemotherapeutic agents.

3. Mechanism of Action- Dopamine

It inhibits vascular endothelial growth factor (VEGF) or vascular permeability Factor (VPF).VEF'S create new blood vessels including in tumors , dopamine prevents the formation of blood vessels in tumors and helps in treatment of cancers.

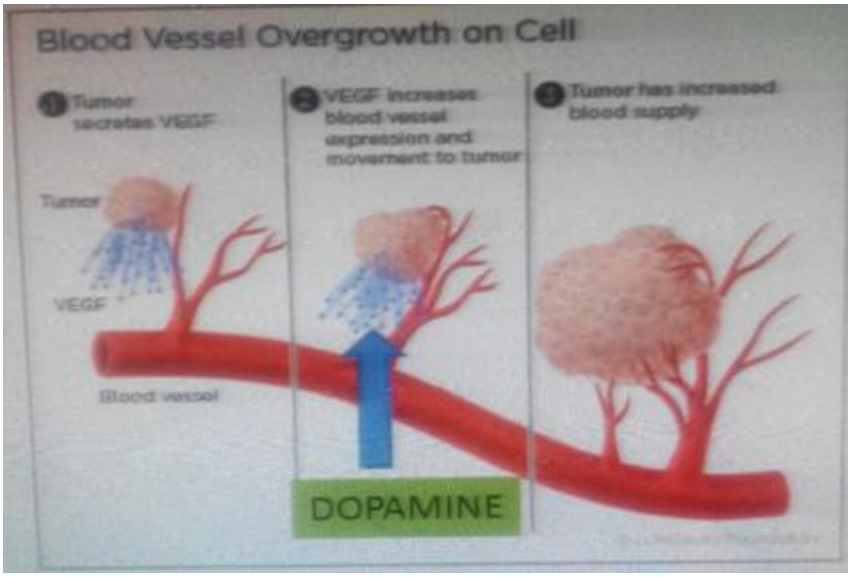

Figure 1: Mechanism of action of Dopamine

4. Standard Calibration Curve

1g extract of powdered seeds of MP is placed in 100 ml flask. Add 0.1 N HCL and make up the volume agitating for 1 hour. Filter and scan using UV Spectrophotometer. wavelength for maximum absorbance was determined, absorbance of each concentration is determined at wavelength 281nm.

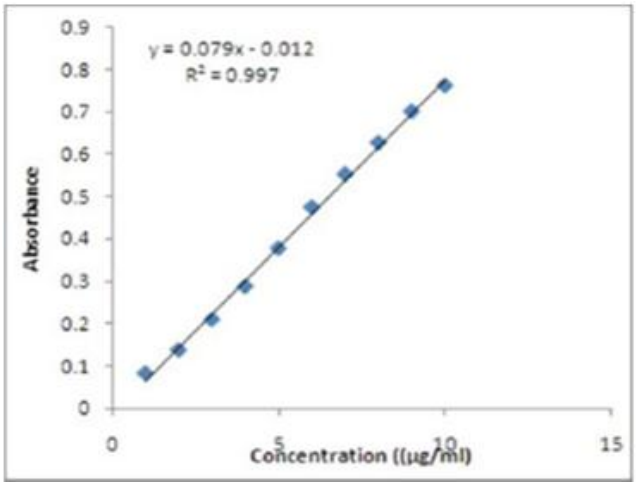

Figure 2: Standard calibration curve.

5. Experimental Methods

Preparation of Extract & Compression of granules:
Powdered seeds of Mucuna pruriens is soaked in alcohol for 24 hours and the decoction is prepared. Ethanolic extract of Mucuna pruriens seeds has been formulated into tablet dosage form by wet granulation method. The formulation includes: Mucuna pruriens (API) Lactose, Corn starch (1% or 4%w/w), PVP (1% or 4%w/w) are used as binders, MCC and Magnesium stearate were included in the formulation. The ingredients were mixed and passed through mesh sieve 12, dried in hot air oven for 12 hours at 50 ºC. The granules were compressed into tablets by single punch rotary compression machine for 30 sec and after ejection stored over silica gel for 24 hrs for hardening.

Table 1: Formulation table:

S. No	*Ingredients*	*F1(mg)*	*F2(mg)*	*F3(mg)*	*F4(mg)*
1.	Mucuna pruriens powder (API)	100	100	100	100
2.	Lactose	75	75	75	75
3	Corn starch (1%)	2	-	-	-
4.	Corn starch (4%)	-	8	-	-
5.	Pvp (binder solution)-1%	-	-	2	-
6.	Pvp (binder solution)-4%	-	-	-	8
7.	Magnesium stearate	3	3	3	3
8.	Micro crystalline cellulose	20	14	20	14
Total weight (mg)		200 mg	200 mg	200 mg	200 mg

6. Evaluation of Granules (Pre- Compression Parameters)

Bulk density and Tapped density
The bulk density of the tablet blend was determined by Bulk density apparatus. The bulk density and tapped density for the formulations prepared were found and the results are shown in the table.no-2

Carr's Index and Hausner's ratio
The results of Carr's Consolidation Index or % Compressibility Index for the formulations blend
are in the range of 22-26 and Hausner's ratio was found in the range of 1. 12 to 1.15, which shows good flow property. The results are shown in the table.no:2.

- Carr's consolidation index =Tapped density-Fluffy density/Tapped density X 100
- Hausner's ratio: Tapped density/Fluffy density

Angle of repose
It is estimated by fixed funnel method and it measures the flow ability of the granules. The angle of repose was < 25 , so the granules has excellent flow property it is shown in the table.no:2.

Table 2: Pre-compression parameter results

S. No	Bulk Density gm/Cm3	Tapped Density gm/Cm3	Carr's Index(% Compressibility)	Hausner's Ratio	Angle of Repose (Theta)
F1	0.3321	1.12	22.8035	1.1211	200.111
F2	0.3476	1.14	26.3684	1.1411	180.191
F3	0.3459	1.13	24.5929	1.1311	210.121
F4	0.3377	1.13	24.5929	1.1311	220.111

Evaluation of Tablets (Post Compression parameters)

Weight Variation test:
All the tablets passes the weight variation test , as the average % weight variation was within the pharmacopoeial limit of 10%, the results are shown in the table.no:3

Friability:
The Roche's Friability apparatus was used to determine the friability of tablets ,the values were found to be within the limit (0.1-0.2%).The friability was calculated by using this formula and the results are shown in the table.no:3.

F=W(INITIAL)-W(FINAL)/W(INITIAL) X100

Hardness test:
The tablet hardness was measured by Monsanto hardness tester, the values were in the range of 4.66 – 5.22 kg/cm2, all the formulations were in the specified limits as per pharmacopoeial standards. The results are shown in the table.no:3.

Thickness:
The tablet thickness was determined by Vernier calipers and was in the range of 1.22-1.64 mm. The results are shown in the table.no:3.

Disintegration:
The USP device to test disintegration was used and one tablet is placed in each tube and basket rack is positioned in 1 liter beaker of distilled water at 37± 2ºC, The tablets pass the test if all of them have disintegrated and the results are shown in table.no:3.

In vitro Dissolution studies:
All the Formulations were subjected to dissolution test in Electrolab Dissolution apparatus, at 50 rpm, 37 ºC± 0.5. The dissolution media i.e 900 ml of 0.1 M HCL is used and the amount of drug released was determined Spectrophotometrically at wavelength of 281 nm, the results are shown in table.no:3.

Table 3: Post compression parameter results

S. No	*Formulations*	*Weight Variation (g)*	*Friability (%)*	*Hardness (kg/cm2)*	*Thicknesss (mm)*	*Disintegration (min)*	*Dissolution (60 minutes)*
1.	F1	0.5872±0.2	0.2998	4.66	1.22	12	72%
2.	F2	0.7853±0.2	0.1178	4.73	1.26	12	75%
3.	F3	0.6525±0.2	0.1221	4.93	1.64	14	92%
4.	F4	0.8518±0.2	0.1243	5.22	1.22	15	81%

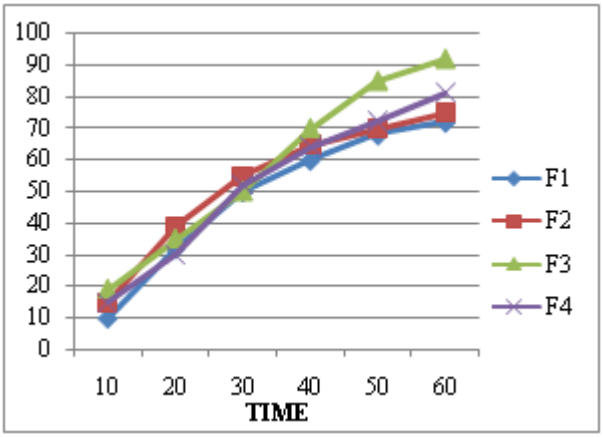

Figure 3: Dissolution Studies: X-Axis-Time, Y-Axis-%Drug release is plotted.

7. In-Vivo Studies For Anti Cancer

The tablets were prepared and evaluated for both pre-compression and post compression parameters and F3 formulation tablets were administered to mice to enhance Dopamine levels to treat cancers. The Cancers are induced in mice by Benzopyrene (BP) a potent carcinogen to induce tumors in stomach, it is given by gavage to mice, 1mg of BP in 0.1 ml of peanut oil is administered weekly twice for 4 weeks in mice. The blood is removed from Saphenous vein(tail) to check the formation of tumors. The following symptoms are noticed when tumors develops in mice:

1) Loss of Appetite and Anemia
2) Enlarged stomach
3) Enlarged lymph nodes
4) Indigestion
5) Blood in faecal matter.

The mice were divided into four groups and the Parameters tested were: 1.CBC-To Identify Anemia 2. Electrolyte levels 3. Liver function tests, it was observed that the haematology values and normal blood chemistry values increases increases in mice which indicates the formation of tumor ,.Group A(5 mice) were control animals , Group B (5 Mice) were disease induced by (BP) but no treatment, After 4 Weeks symptoms are observed in group B Mice .Group C (5 mice) were induced with cancer and treated with standard I.V dose of 25 mg/kg, Increased motor activity is observed in group C animals because of abnormal rise of Dopamine levels by I.V. Group D(5 Mice) cancer is induced but treated by test dose i.e prepared tablets of Mucuna pruriens (F3).The blood is taken from saphenous vein(tail) upto 2 ml to test the parameters to specify cancer. The cancer induced mice are treated with tablets of MP and further effects were studied, it was observed after one month, it increases dopamine levels naturally and CBC values which was

increased due to cancer reduces to normal values which is tested.

Table 4: Grouping of animals

Group A(5 Mice)	Control animals(No Disease, No Treatment)
Group B(5 Mice)	Disease Induced(No treatment)
Group C(5 Mice)	Disease Induced+ Treatment (STD I.V dose)
Group D(5 Mice)	Disease Induced+ Treatment (Test dose)

Table 5: MICE normal haemotology and blood chemistry values

Mice-normal haematology values	Hgb(g/dl) 10.2-16.6	WBC(x1000) 6-15	Platelets(x1000) 160-410	Lymph 55-95	Monocytes, basophils, Eosinophils-0.1%	Neutrophils % lymphocytes-20-70%
Normal blood chemistry values	Alb(g/dl) 2.5-3	ALK P(u/l) 35-96	ALT(u/l) 17.7	BILI(mg/dl) 0-0.9	Creatinine(mg/dl)0.2-0.9	Glucose(g/dl) 62-175

8. Results & Discussions

The induction of tumors were confirmed by the abnormal results of haematological levels and altered liver function test levels.

Table 6: In-Vivo Studies

Group A	Healthy mice
Group B	Symptoms of tumors
Group C	Symptoms of increase in body weight(decrease urine output),Pain and swelling at site injected by needle, increased motor activity.
Group D	No side effects , normal haematological levels and normal liver functions.

Table 7: Mice- Abnormal haemotology and blood chemistry values after inducing cancer.

Mice-normal haematology values	Hgb(g/dl) 26.5-32.1	WBC(x1000) 30-35	Platelets(x1000) 200-650	Lymph 70-120	Monocytes, basophils, Eosinophils-1%	Neutrophils % lymphocytes80-90%
Normal blood chemistry values	Alb(g/dl) 5-7	ALK P(u/l) 50-110	ALT(u/l) 25.6	BILI(mg/dl) 1-3%	Creatinine(mg/dl)3-5	Glucose(g/dl) 100-250

9. Conclusions

The study shows inexpensive drug like Dopamine have role of anti angiogenic agent for treating cancers and by using very economical tablets prepared from Mucuna Pruriens Dopamine levels are enhanced without toxicities. The side effects associated with STD I.V dose are not observed when treated with Test dose.

References

[1] Sarkar C et al.Dopamine increases the efficacy of anticancer drug in breast cancer & colon cancer preclinical models.Pubmed .2008 April 15;14(8).
[2] Stephen O Majekodunmi et al.Formulation of Mucuna Pruriens seed extracts as tablets and in vitro evaluation of anti diabetic properties of tablets.Journal of Pharmaceutics & drug delivery research 2014.
[3] R. Katzenschlager et al. Mucuna Pruriens in parkinson's disease: A double blind clinical and pharmacological study, J Neurosurg Psychiatry 2004;75:1672-1677 doi:10.1136/jnnp.2003.028761, jan 2004 .
[4] Manyam B. Paralysis agitans and levodopa in "Ayurveda": ancient Indian medical treatise Mov Disord 1990;5:47-8.
[5] Vadya AB, Rajgopalan TS, Mankodi NA, et al. Treatment of parkinson's disease with the cowhage plant- Mucuna pruriens(BAK), Neurol India 1978;36:171-6.
[6] Tripathi YB, Upadhyay AK. Effect of the alcohol extract of the seeds of Mucuna pruriens on free radicals and oxidative stress in albino rats. Phytother Res 2002;16:534-8.
[7] Kempster PA, Bogetic Z, Secombe JW, et al.Motor effects of broad beans (Vicia fava) in Parkinson's disease: single dose studies. Asia Pac J Clin Nutr 1993;2:85-9 .
[8] Melvin E, Daxenbichler CH, Etten V, et al. L-dopa recovery from mucuna seed. J Agric Food Chem 1972;20:1046-8.
[9] Miller ER. Dihydroxyphenylalanine, a constituent of the velvet bean. J Biol Chem 1920;44:481-6.
[10] Damodaran M, Ramaswamy R.Isolation of L-dopa from the seeds of mucuna pruriens.Biochem J1937;31:2149-451.
[11] Lieu CA et al, The Antiparkinsonian and Antidyskinetic Mechanisms of Mucuna pruriens in the MPTP-Treated Nonhuman Primate,2012;2012:840247. Epub 2012 Sep 10.