



To Formulation and Evaluation of Oral Drug Delivery of Entacapone Tablet Used for Treatment of Parkinson's Disease.

Mahesh Ashok Kardule , Prof. Pranjal D. Lohakane, Dr.Megha T. Salve

Shivajirao Pawar College of Pharmacy, Pachegaon Tal- Newasa Dist-Ahilyanagar – 413725

ABSTRACT

Tolcapone trilayer matrix tablets featuring mucoadhesive properties were created through direct compression technique, incorporating a central active layer made up of different viscosity grades of HPMC, ethyl cellulose, and Na CMC as release retardants. Barrier layers were created using Eudragit L100-55, guar gum, ethyl cellulose, magnesium stearate, talc, and DCP. The trilayer matrix tablets were assessed for their physicochemical properties, in vitro drug performance, compatibility between the drug and excipients, mucoadhesive characteristics, release kinetics, and in vivo bioavailability. According to the assessment criteria, the drug dissolution characteristics and release order kinetics, formulation HF16 was determined to be the optimized formulation exhibiting mucoadhesive properties. The created drug delivery system achieved drug release rates sustained for 24 hours. The release pattern of the optimized formulation (HF16) was characterized by zero-order kinetics and aligned best with the Higuchi model. FT-IR and DSC analyses confirmed that no chemical interaction occurred between the drug and the excipients utilized in the formulation .

Keywords: Parkinson's disease, Entacapone, Oral drug delivery Nanotechnology, Sustained release tablets

INTRODUCTION

➤ Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative condition of the extra pyramidal nervous system that impacts mobility and regulation of the skeletal muscular system. Key traits of Parkinson's disease include resting tremors, stiffness, and slow movement. Recent research suggests that signs of Parkinson's disease are linked to a decrease in the neurotransmitter dopamine (Harrison 2015).

Certain neurons in the human brain generate dopamine. These neurons gather in a specific region of the brain known as the substantia nigra. Dopamine is a substance that transmits signals between the substantia nigra and different areas of the brain to regulate bodily movements. Dopamine assists humans in achieving fluid, coordinated muscle movements. When around 60 to 80% of the cells that produce dopamine are harmed and fail to generate sufficient dopamine, the motor symptoms associated with Parkinson's disease emerge (Albin 2006). This process of damage to brain cells is referred to as neurodegeneration. The brain of an individual gradually ceases to generate dopamine. As dopamine levels decrease, an individual finds it increasingly challenging to manage their movements, bodily functions, and emotions. Parkinson's disease is not a life-threatening condition. Nonetheless, the complications arising from the illness are severe. Occasionally, it is hereditary, yet the majority of instances do not appear to be familial (National Parkinson's Foundation 2008).

Symptoms of Parkinson's disease start slowly, typically beginning on one side of the body but eventually impacting both sides. Typical symptoms include

- Shaking of hands, arms, legs, jaw, and face
- Rigidity of the arms, legs, and container
- Lack of speed in movement
- Weak coordination and teamwork

As symptoms escalate, individuals with the issue might find it difficult to walk, speak, or perform basic activities. They might also experience issues similar to depression, sleep disturbances, or difficulties with smelling, swallowing, or speaking. There is no laboratory test for PD, making it challenging to diagnose. Doctors utilize a medical history and a neurological assessment to identify it (Goldenberg 2008).

• Medications for Managing Parkinson's Disease

Several details are provided for the management of Parkinson's condition. Due to the variety of symptoms present in individuals with Parkinson's disease, the selection of medication greatly differs among them. Croakers suggest various specifics for the signs of Parkinson's illness. Levodopa, carbidopa, and entacapone are among the most highly recommended medications for treating PD.

• Generic medications

A generic drug is a medication that is the same as or bioequivalent to a branded drug in terms of capsule form, safety, strength, method of delivery, quality, performance traits, and intended purpose. Though generic drugs are chemically the same as their branded equivalents, they are typically offered at significant discounts from the branded price. It is consistent in dosing, safety, potency, quality, its mechanism of action, administration method, and intended use (Ahire et al, 2013).

When new medications are initially created, they are protected by drug patents. Most drug patents are safeguarded for 20 years. A general medicine can only be retailed after the brandname medicine's patent has expired, which may take up to 20 times after the patent holder's medicine is first filed with the U.S. Food and Drug Administration. Generics are less precious also because the medicine manufacturer does n't have to duplicate the original clinical trials for effectiveness and safety, which lowers the cost to bring the medicine to request. still, general medicine makers must show that their product performs in the same way as the brand- name medicine. When patents or other ages of exclusivity expire, other manufacturers can submit an abbreviated new medicine operation (ANDA) to the USFDA for blessing to request a general interpretation of the brand- name medicine (https://www.drugs.com/generic_drugs.html). In order to prove sameness of the general medicines with inventor product, a series of tests are to be carried out in logical lab. Most important of all those tests are assay, dissolution and contamination profile.

Materials and Methods

Entacapone, HPMC K 4M, HPMC K 15 M, Xanthan gum, Ethyl Cellulose, Sodium carboxyl methyl cellulose, Magnesium stearate, Dibasic calcium phosphate

• Preparation of standard graph.

A stock arrangement of 100mcg/mL was set up by accurately weighed 10mg of API was dissolved in phosphate buffers of pH 5.5 and 7.4 for Entacapone and Tolcapone respectively. From the stock solution, the solutions of concentrations (2µg/mL to 20µg/mL) were prepared and the absorbance was determined by UV spectrophotometer at 377 nm (Entacapone) and 257 nm (Tolcapone). Utilizing the square estimation of relationship coefficient (r²), the Linearity of standard curve can be evaluated. The r² value is calculated from least-square linear regression analysis.

• Formulation of Enatacapone Tablet

Table: Composition of Enatacapone Tablet

INGREDIENTS (mg)	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)
Entacapone	200	200	200	200	200	200	200	200	200	200
HPMC K 4M	50	55	60	---	---	----	25	30	----	----
HPMC K 15M	---	----	----	50	55	60	45	40	----	----
HPMC K 100M	---	---	---	----	---	----	----	----	40	45
Ethyl cellulose	22	30	32	22	30	32	15	15	40	35
Xanthan gum	20	22	25	20	22	25	30	32	15	17.5
Sodium carboxy methyl cellulose	25	15	10	25	15	10	15	15	27	21.5
Dibasic calcium phosphate	27	22	17	27	22	17	14	12	22	24
Magnesium stearate	3	3	3	3	3	3	3	3	3	3

• Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) studies were done utilizing DSC 60, having TA60 software, Shimadzu, Japan. Samples were accurately weighed and warmed in sealed aluminium pans at a rate of 10°C/ min somewhere around 25 and 350°C temperature range under nitrogen climate.

- **Evaluation of post compression parameters**

- **Physical appearance**

The general appearance of tablets, its visual character and general polish is vital for purchaser acknowledgment. The control of general appearance of tablet includes estimation of number of parcels, for illustration, tablet size, shape, shading, nearness or nonappearance of scent, taste, face composition and thickness of any ID marks.

- **Bulk viscosity**

Viscosity is the rate of weight of a substance to its unit volume. Whereas Bulk viscosity is the rate of mass of the substance to its bulk volume and units for bulk viscosity are gm/ cm³. Properties of greasepaint patches like their shape, size distribution, adherence to one another greatly affect bulk viscosity. Bulk viscosity plays a major part in design of holders employed for shipping maquillages, their storehouse, to decide size of the holders and size of coalescing outfit. A dry cylinder of 100 ml capacity is taken and about 10 gm settled greasepaint composites were placed into it without compacting.

- **Weight variation**

Twenty aimlessly taken tablets were counted together and the average weight was determined. Each tablet was also counted collectively and divagation from average weight was calculated.

- **Hardness test**

This is the force needed to break a tablet in a contrary contraction. Hardness of ten aimlessly picked tablets was bent by Stock's Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the creek in the barrel fracture.

- **Friability**

Take a sample of 6.5 g of tablets for tablet weight is equal to or lower than 650 mg or take 10 tablets weight for tablet weight is further than 650 mg. The Friabilator was operated for 4 min at a speed of 25 rpm. The tablets were removed from the Friabilator, de-dusted and revisited. The percent loss in weight due to bruise and impact was calculated as,

$$\text{Friability} = (\text{Loss in weight} / \text{original weight}) \times 100.$$

- **Tablet size and Thickness:**

Control of physical confines of the tablets similar as size and consistence is essential for consumer acceptance and tablet- tablet uniformity. The periphery size and punch size of tablets depends on the bones and punches named for making the tablets. The consistence of tablet is measured by Vernier Calipers scale.

- **Drug content / Assay**

20 tablets were directly counted collectively and pulverized. 200 mg of original greasepaint was dissolved in phosphate buffer pH 5.5. Final volume was made up to 100 ml with phosphate buffer pH 5.5 and filtered. Absorbance of this result was determined in a UV spectrophotometer at 377 nm. quantum of Entacapone in tablets was calculated by using retrogression equation.

- **Angle of repose**

Angle of repose has been employed to characterize the inflow parcels of solids. It's a characteristic affiliated to inter particulate bruise or attrition to movement between patches. This is the maximum angle possible between face of pile of greasepaint or grains and the vertical aeroplane

$$\tan \square = h / r$$

$$\square = \tan^{-1} h / r$$

Where $\square$ = angle of repose, h = height of heap, r = radius of base of heap circle.

A funnel was fine-tuned at a height approximately 2-4 cm over the platform. The coalescence or powder was gradually passed along the wall of funnel, till the tip of powder cone so composed just physically contacted the tip of funnel stem. Angle of repose was then determined by quantifying the height of the cone of powder and radius of the circular base of powder heap.

Result and Discussion

- **Standard curve of Entacapone**

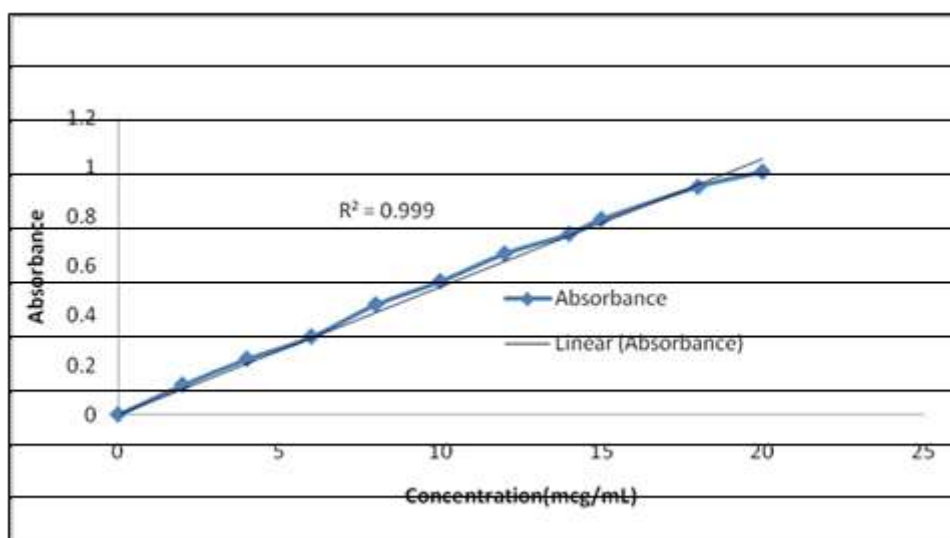


Figure: Standard graph of Entacapone in phosphate buffer, pH 5.5 at 377nm

- Differential scanning calorimetry (DSC studies)

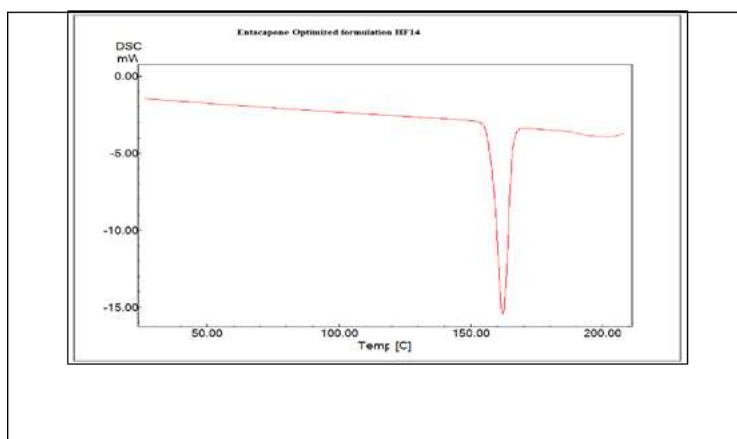


Figure: DSC thermograms of Entacapone pure drug

- Micromeritic Studies

Powder properties	F1	F2	F3	F4	F5	F6
Bulk density (g/cc)	0.556±0.02	0.536±0.08	0.500±0.02	0.517±0.09	0.484±0.06	0.469±0.08
Tapped density(g/cc)	0.625±0.08	0.577±0.03	0.556±0.08	0.577±0.01	0.517±0.03	0.536±0.12
Angle of repose (°)	31.42±0.42	30.85±0.52	32.18±0.42	29.45±0.48	28.62±0.85	31.06±0.17
Carr's index	11.11±0.89	7.14±0.62	10.00±0.51	10.34±0.86	6.45±0.15	12.50±0.50
Hausner's ratio	1.13±0.08	1.05±0.06	1.11±0.06	1.12±0.05	1.07±0.03	1.14±0.04

Table: Powder flow properties of Entacapone

- Physical and chemical evaluation of Entacapone tablets.

Table: Physical and chemical evaluation of Entacapone tablets.

TESTS	AF14	BF14	CF14	DF14	EF14	FF14	GF14
Color	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow
shape	Round	Round	Round	Round	Round	Round	Round
Hardness(Kg/Cm ²)	7	6	6	7	6	7	6
Thickness (mm)	4.86±0.2	4.82±0.2	4.86±0.2	4.81±0.2	4.88±0.2	4.91±0.2	4.85±0.2
Weight variation (mg)	596±20	599±20	595±20	594±20	597±20	595±20	596±20
Friability(%)	0.15	0.28	0.26	0.30	0.35	0.18	0.23
Assay (%)	97.5	96.8	96.2	98.0	95.7	97.4	96
Swelling Index (%)	134.68	142.52	159.64	167.53	179.12	186.43	206.21
In vitro residence time, n=3	7 hr 30 min	8 hr 30 min	8 hr 15 min	7 hr 15 min	8 hr 45 min	9 hr 30 min	Above 12 hrs

CONCLUSION

Grounded on assessment of colourful parameters, in vitro medicine dissolution profile and medicine kinetics, HF14 was set up to be optimize expression. FT- IR & DSC studies revealed that there was no commerce between the medicine and polymers used in the phrasings. The medicine release from HF14 was set up to fit Zero order of attention independent and stylish fitted to Higuchie model attesting to be prolixit supported medium. It was inferred that trilayerentacapone and tolcapone matrix tablets were effectively arranged by direct contraction system with mucoadhesive property exercising different polymers combination with patient compliance and viscosity by lessening the cure rush in complete administration of parkinson's illness.

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