CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.22720966

Available online at: http://www.iajps.com Research Article

FORMULATION AND IN-VITRO EVALUATION OF GASTRO-RETENTIVE DRUG DELIVERY SYSTEM FOR LEVODOPA

P. Keziakereen*[1], B.Harika[2], Md Sameena Begum[2], Ratnam Sarayu[2], Syed Misbah Hussain[2], T. Pavithra[2]

[1] Assistant professor, Department of Pharmaceutics, St. Mary's College of pharmacy, Secunderabad, Telangana.

[2]Students, Department of Pharmaceutics, St. Mary's College of Pharmacy, Secunderabad, Telangana.

Abstract:

The main purpose of the study was to develop Levodopa floating tablets via non-effervescent technique using various polymers by direct compression. Before compression, the particulate powdered mixture was evaluated for pre-compression parameters. Compatibility among the formulation components was assessed by FTIR studies. FTIR studies revealed no interaction between the drug and polymers used. The prepared Levodopa floating tablets were evaluated for post-compression parameters, swelling index, floating lag time, in vitro buoyancy studies, and in vitro drug release studies. Optimized formulation (F2) revealed that tablet was constantly floating in the stomach region, thereby indicating improved gastric retention time for more than 8 hr. Consequently, all the findings and outcomes have showed that developed Levodopa floating tablets could be effectively used for floating drug delivery system.

Keywords: *Levodopa, Natural Polymers, FTIR studies, Direct compression technique, In vitro drug release studies.*

Corresponding author:

P. Keziakereen,

Assistant Professor, St. Mary's College of Pharmacy, Hyderabad, Telangana 500025

Mobile:

Email Id:

QR CODE

Please cite this article in press ***P. Keziakereen*** *et al.,* ***Formulation And In-Vitro Evaluation Of Gastro-Retentive Drug Delivery System For Levodopa.,****. Indo Am. J. P. Sci, 2026; 13(09).*

INTRODUCTION:

Gastro retentive Drug Delivery Systems

The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with the GI mucosa, leading to higher bioavailability, and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance. Therefore, extended release DDS possessing gastric retention properties may be potentially useful. [13]

Basic gastrointestinal tract physiology

Anatomically the stomach is divided into 3 regions: fundus ,body and antrum(pylorus).The proximal part made of fundus and body acts as a reservoir for undigested material whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. During the fasting state an inter digestive series of electric events takes place, which cycle both through stomach and intestine every 2 to 3 hours .This is called interdigestive myloelectric cycle or migrating myloelectric cycle(MMC) which is further divided into following 4 phases as described by Wilson and Washington.

1. Phase I (basal phase) lasts from 40 to 60 min with rare contractions.

2. Phase II (preburst phase) lasts for 40 to 60 min with intermittent action potential and contractions .As the phase progresses the intensity and frequency also increases gradually.

3. Phase III(burst phase)lasts for 4 to 6 mins.It includes intense and regular contractions for short period. It is due this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.

4. Phase IV lasts for 0 to 5 mins and occurs between phase III and 1 & 2 consecutive cycles. Gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically 2 complications: short gastric residence time and unpredictable gastric emptying rate.

Absorption window

The G.I tract offers a varied environment capable of affecting the absorption of poorly administered drugs. Anatomical features, physiological phenomenon, and nature of gastrointestinal milieu contribute to these changes. This can lead to the variations in the intestinal permeability of drug molecules, resulting in the phenomenon of Absorption window. Where in the drug is preferentially absorbed only from a particular region of the G.I tract.

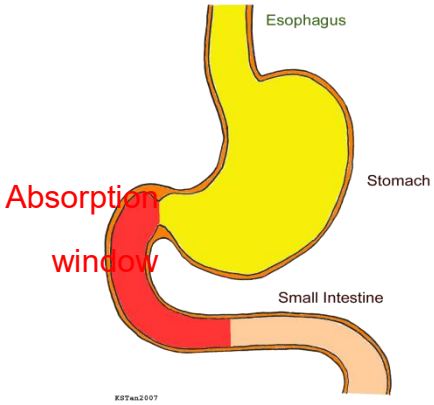

Fig-1: anatomy of stomach

MATERIALS:

Levodopa was procured from Synpharma Research Labs, Hyd, Guargum, Tragacanth, Microcrystalline cellulose, Magnesium stearate, Sodium bi carbonate and Talc were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Formulation development

METHODOLOGY:

FT-IR study

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

Table-1: Composition of levodopa floating tablets

Ingredients (mg)	F1	F2	F3	F4
Levodopa	200	200	200	200
Guargum	100	200	-	-
Tragacanth	-	-	100	200
MCC	180	80	180	80
Sodium bi carbonate	15	15	15	15
Magnesium stearate	3	3	3	3
Talc	2	2	2	2
Total wt	500	500	500	500

Preparation of Formulation:
Different tablet formulations were prepared by direct compression method. The formulations are composed of natural polymers. All powders were passed through 40-mesh sieve. The other excipients and the polymer were mixed uniformly. Drug was added to the polymers and other excipients for 20 min. The resulting mixture were mixed with magnesium Stearate and talc in polyethylene bag for 10 min. The lubricated granules were compressed using 8 mm punch (single punch tablet machine) in to tablets. Compression pressure was adjusted during tablet ting of each formula to get the tablet hardness in the range of 2.5 to 5 Kg/cm$^{2.}$ The total weight of tablet was kept at 500 mg.

Evaluation of tablets

Physical Appearance:
The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, color, presence or absence of odour, taste etc.

Size & Shape:
It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micro-meter or by another device. Tablet thickness should be controlled within a ± 5% variation of standard value.

Weight variation test:
Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two tablets should differ in their average weight by more than percentages stated in USP. No tablet must differ by more than double the relevant percentage.

Content Uniformity:
Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range.

Friability:
A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.
The percentage friability was determined by the formula:

$$\% \text{ Friability} = (W_1 - W_2) / W_1 \times 100$$

W_1 = Weight of tablets before test
W_2 = Weight of tablets after test

Floating lag time:
The time between the introduction of the tablet into the medium and its rise to upper one third of the dissolution vessel is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time. These tests are usually performed in simulated gastric fluid or

0.1NHCl maintained at 37 ^{0}C, by using USP dissolution apparatus containing 900 ml of 0.1N HCl as the dissolution medium.

Drug release studies:
The drug release from the Pirenzepine tablets was investigated in a USP-II (paddle) apparatus, 900 ml of 0.1N HCl (50 rpm, 37°C). At predetermined time intervals, 5-ml samples were withdrawn and take 1ml sample and diluted to 10 ml and then analyzed with UV spectrophotometry.

Stability studies
The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. The prepared levodopa floating tablets were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2°c for a period of 90 days.

RESULTS AND DISCUSSION:

FT-IR Spectrum of Levodopa
FT-IR Spectra of Levodopa and F2 formulation were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Levodopa and polymer. It also confirmed that the stability of drug during microencapsulation process.

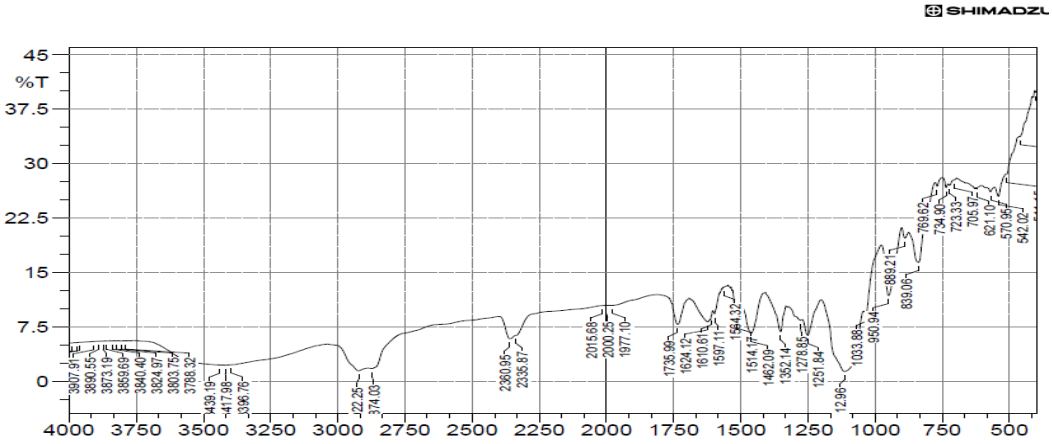

Fig-2: FT-IR Sample for Levodopa

Table-2: Characteristic Peaks and frequency of Levodopa

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3750	3824.27cm-1
2	OH Bending	3500-3000	3396.35 cm-1
3	C-H stretching	2500-2000	2335.68 cm-1
4	C-N stretching	1500-1000	1462.09 cm-1

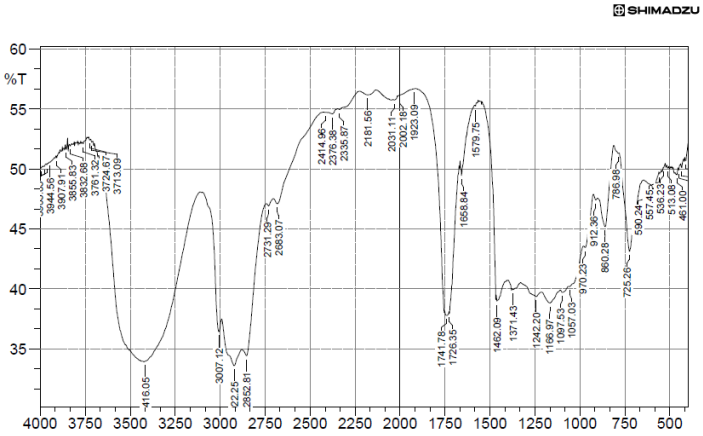

Fig-3: FT-IR Sample for physical mixture of drug and excipients

Table-3: Characteristic Peaks and frequency of physical mixture of drug and excipients

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3750	3907.91cm-1
2	OH Bending	3500-3000	3416.05 cm-1
3	C-N stretching	2500-2000	2376.38 cm-1
4	C-H stretching	1500-1000	1242.20 cm-1

The IR spectrum of drug and Drug Excipients mixture was shown in respectively. In the present study, it has been observed that there is no chemical interaction between drug and the polymers used. From the figures it was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers. This further confirms the integrity of pure drug and compatibility of them with excipients.

Evaluation of Preformulation parameters
Pre-compression Parameters
Bulk Density: The bulk density for the formulated blend was carried out for all formulation and found in the range of 0.475-0.493.

Tapped density: The tapped density for the formulated blend was carried out for all formulation and found in the range of 0.579-0.589.

Angle of repose: The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 27^0 to 30^0

Compressibility index: Compressibility index was carried out, it found between 10% to 17.47 % indicating the powder blend have the required flow property for compression.

Hauser ratio: Hauser ratio was carried out, it found between 1.20 to 1.22 indicating the powder blend have the required flow property for compression.

Table-4: Evaluation parameters of Levodopa

S. no	Bulk density	Tapped density	Compressibility index	Hausner ratio	Angle of repose (0)
F1	0.493	0.589	15.62	1.20	30^0
F2	0.479	0.580	17.47	1.21	27^0
F3	0.484	0.582	16.83	1.20	30^0
F4	0.490	0.585	16.15	1.21	29^0

Evaluation of the Prepared Tablets for Physical Parameters
All formulations were tested for Physical parameters like Hardness, thickness, Weight Variation, Friability and found to be within the Pharmacopoeial limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that all the prepared formulations were good.

Table-5: Evaluation parameters of Levodopa floating tablets

Parameter	F1	F2	F3	F4
Weight variation	499	500	500	500
Thickness (mm)	3.6	3.2	3.4	3.7
Hardness (kg/cm^2)	3.6	3.8	3.4	4.1
Friability	0.39	0.42	0.46	0.40
Content uniformity	78.42	80.12	76.98	78.12
Floating lag time (Sec)	49	45	53	50

Floating lag time

The prepared formulations were evaluated for floating lag time and buoyancy time. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). It was observed that the gas generated is trapped and protected within the matrix, formed by polymers, thus density of the tablet decreased and it becomes buoyant. The floating lag time of the optimized formulation F2 was 42 sec.

Fig-4: Floating tablet

In vitro Dissolution studies

The dissolution conditions used for studying the drug release from floating tablet of Levodopa are:

Apparatus : USP apparatus II (Paddle)
Agitation speed (rpm) : 50rpm
Medium : 0.1N HCl
Volume : 900 ml
Temperature : 37.0 ± 0.5 C
Time : 1,2,3,4,5,6,7 and 8hrs.
Wavelength : 280 nm

The samples were withdrawn at predetermined time points, and were analyzed spectrophotometrically at 280 nm.

Table-6: In vitro drug release of Levodopa floating tablets

Time	F1	F2	F3	F4
0	0	0	0	0
1	16.12	17.58	15.69	15.34
2	34.58	35.42	36.86	33.67
3	46.92	48.16	49.81	41.27
4	58.73	59.50	53.31	54.37
5	66.82	68.22	66.82	64.19
6	78.20	79.68	74.30	73.64
7	85.69	86.39	84.86	82.63
8	93.75	95.67	93.69	91.16

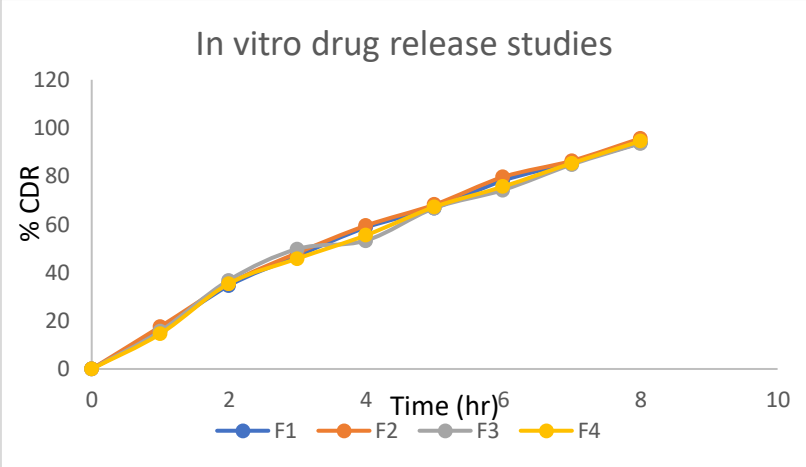

Fig-5: In vitro drug release for (F1-F4) formulations

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-4 after 90 days. Parameters quantified at various time intervals were shown. Optimized formulations F4 was selected for accelerated stability studies as per ICH guidelines. The floating tablets were observed for % cumulative drug release of the formulation was found to be decreasing.

Table-7: Stability study for optimized formulation

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-2	**25^{0}C/60%RH % Release**	95.67	94.62	93.54	92.51	**Not less than 85 %**
F-2	**30^{0}C/75% RH % Release**	95.67	94.63	93.45	92.47	**Not less than 85 %**
F-2	**40^{0}C/75% RH % Release**	95.67	94.29	93.56	92.34	**Not less than 85 %**

CONCLUSION:

The objective of the present study is to formulate a Floating tablet of Levodopa. In this present study an attempt was made to increase the GI residence time of Levodopa, as the drug is having less gastric residence time, by formulating in to Floating tablets. Systematic studies were conducted using different concentration of rate releasing different polymers for extending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, Preformulation studies to find out the micromeritic properties to assess flowability, compressibility properties and solubility studies and all the formulations gave good results for above Preformulation studies.Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, all the formulations were found within the permissible range.Finally it was concluded that:Among all the formulations (F1-F4), it was observed that formulation-2 has shown better buoyancy and dissolution profile. So Formulation-2 was found to be the best formulation among others.

REFERENCES:

1. Bagherwal A, Patidar DK, Sharma P. Formulation and evaluation of floating tablets of ciprofloxacin hydrochloride. Int J Comp Pharma 2010;1:1-4.
2. Kumar R. Development and in-vitro evaluation of sustained release floating matrix tablets of metformin hydrochloride. Int J Pharm Sci Res 2010;1:96-101.
3. Chodavarapu NP, Yendluri RB, Suryadevara H, Reddy P, Chhatoi P. Formulation and evaluation of abelmoschusesculentus mucilage based metformin hydrochloride floating matrix tablets. Int J Pharm Tech 2011;3:2725-45.
4. Kshirsagar RV, Jain V, Wattamwar S. Effect of different viscocity grade HPMC polymer on gastroretantive drug delivery of metformin hydrochloride. Int J Appl Pharm 2009; 1:44-50.
5. Chandiran IS, Kumar BP, Narayan V.

Formulation and *in-vitro* evaluation of floating drug delivery system for salbutamol sulphate. Int J Pharm Biomed Sci 2010; 1(1):12-15.
6. Hu L, Li L, Yang X, Liu W, Yang J, Jia Y, *et al.,* Floating matrix dosage form for dextromethorphan hydrobromide based on gas forming technique. *In-vitro* and *in-vivo*evalvation healthy volunteers. Eur J Pharm Sci 2011;42:99-105.
7. Raju BD, Sreenivas R, Varma MM. Formulation and evaluation of floating drug delivery system of metformin hydrochloride. J Chem Pharm Res 2010;2(2):274-78.
8. Senthilkumar SK, Jaykar B, Kavimani S. Formulation and evaluation of gastroretentive floating drug delivery system of rabeprazole sodium. Int J Biopharm 2011;2(2):57-62.
9. Mohammed MS. Formulation and *in-vitro* evaluation of sustained release intragastric tablets of propranolol hydrochloride using natural polymer. J Pharm Biomed Sci 2011;10(10):1-10.
10. Goole J, Vanderbist F, Amighi K. Development and evaluation of new multi-unit levodopa sustained-release floating dosage forms. Ind J Pharm 2007;334:35-41.
11. Sauzet C, Bruno CM, Nicolas M, Kister J, Piccerdle P, Prinderre P. An innovative floating gastro retentive dosage system. Formulation and *in-vitro* evaluation. Int J Pharm 2009;378:23-29.
12. Abrahamsson, B., Alpsten, M., Hugosson, M., Jonsson, U.E., Sundgren, M., Svenheden, A., Tölli, J., 1993. Absorption, Gastrointestinal Transit, and Tablet Erosion of Felodipine Extended-Release (ER) Tablets. Pharm. Res. 10, 709-714.
13. Agrawal, A.M., Manek, R.V., Kolling, W.M., Neau, S.H., 2003. Studies on the interaction of water with ethylcellulose: effect of polymer particle size. AAPS Pharm. Sci. Tech. 4, E60.
14. Bhongiri B, Ramachandran V, Kumar RS. Preformulation studies of S-Equol. Journal of Pharmaceutical Negative Results. 2022;13(4):1020-9.
15. Babu MK, Hasan N, Bhongiri B, Patel JR, Abirami A, Sharma S, Sarvadnya AA, Sindhu YR, ul Firdaus J. Creation and Improvement of Nanoparticulate Drug Delivery Methods for Penetration of the Blood-Brain Barrier. Journal of Neonatal Surgery. 2025;14(3).
16. Alvisi, V., Gasparetto, A., Dentale, A., Heras, H., Felletti-Spadazzi, A., D'Ambrosi, A., 1996. Bioavailability of a controlled release formulation of ursodeoxycholic acid in man. Drugs Exp. Clin. Res. 22, 29-33.
17. Amaral, M.H., Lobo, J.M., Ferreira, D.C., 2001. Effect of hydroxypropyl methylcellulose and hydrogenated castor oil on naproxen release from sustained-release tablets. AAPS Pharm. Sci. Tech. 2, E6.
18. Andrews, G.P., Laverty, T.P., Jones, D.S., 2009. Mucoadhesive polymeric platforms for controlled drug delivery. Eur. J. Pharm. Biopharm. 71, 505-518.