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FORMULATION DEVELOPMENT AND IN-VITRO EVALUATION OF OPICAPONE ORAL FAST DISINTEGRATING TABLETS

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ABSTRACT

Aim: The goal of this research is to develop Opicapone oral disintegrating tablets. This is an oral COMT inhibitor for the treatment of pakinson's disease symptoms that are 'wearing off.' **Purpose:** A fast-dissolving Opicapone pill dissolves quickly in saliva, and the medicine is also available in solution or suspension form for instant absorption and activity. **Materials and methods:** Opicapone is the subject of the current study. Orally disintegrating tablets were made utilising a direct compression process with different superdisintegrant concentrations of Lycoat, Crosspovidone, and SSG (sodium starch glycolate).. **Results and Discussion:** The precompression and postcompression parameters of the formulations were assessed. We found no interactions between the pure drug (Opicapone) and the optimised formulation (Opicapone + excipients) in the drug excipient compatibility studies, indicating that there are no physical changes. The IP restrictions for post compression and post compression Parameters were verified to be met. **Conclusion:** The tablet with the highest concentration of Crosspovidone releases 98.13 percent of the medication within 20 minutes and follows first order kinetics. Overall, the results showed that the formulation F8 containing Crosspovidone was superior and more capable of meeting the needs of the orally disintegrating tablet.

Keywords: Orally disintegrating tablet, Opicapone, Crosspovidone, Lycoat, Sodium starch glycolate, superdisintegrant

1. INTRODUCTION

Because of its convenience of self-administration, compactness, and ease of manufacture, the oral route of administration is the most frequently adopted **[1-2]**. However, the most obvious disadvantage of commonly used oral dosage forms such as tablets and capsules is difficulty swallowing, which leads to patient noncompliance, especially in paediatric and geriatric patients **[1]**, but it also applies to people who are sick in bed and active working patients who are busy or travelling, especially those who do not have access to water **[2]**. The demand for fast dissolving tablets (FDTs) has skyrocketed in the last decade, owing to their major impact on patient compliance. A considerable segment of the population, particularly those who have difficulties swallowing, prefers fast dissolving tablets. Dysphagia **[3]** (difficulty swallowing) has been observed to be widespread in all age categories, but especially in children and the elderly, as well as institutionalised patients, psychiatric patients, and individuals with nausea, vomiting, and motion sickness problems **[1]**. Bitter medications are more acceptable to many groups of people when FDTs have a pleasant taste and flavour. The benefits of both dry and liquid formulations are combined in this dose form. Some innovative FDT technologies provide high drug loading, have a pleasant mouth feel, and leave minimum residue in the mouth following oral administration. FDTs have been studied for their potential to improve bioavailability of poorly soluble medications by changing the drug's solubility profile and hepatic metabolism pharmaceuticals. Orodispersible tablets, quick dissolving tablets, oral dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts are all names for fast dissolving tablets. The United States Pharmacopoeia (USP) approved these dose forms as FDTs, despite all of the aforementioned terms. The word orodispersible tablet **[5]** was recently coined by the European Pharmacopoeia to describe tablets that scatter quickly and within 3 minutes in the mouth before ingesting **[4]**. FDT is defined by the US Food and Drug Administration (FDA) as "a solid dosage form containing a medical drug or active ingredient that disintegrates fast when placed on the tongue, usually within seconds." The time it takes for FDTs to disintegrate varies from a few seconds to nearly a minute.

1.1 Opicapone (API):

Opicapone is a strong, reversible, and peripherally acting third generation medicinal agent that is the first and only licenced catechol-o-methyltransferase

(COMT) inhibitor for the treatment of Parkinson's disease. Opicapone 50 mg was shown to be very helpful and well tolerated in Parkinson's disease patients who experienced changes in their capacity to move, sometimes known as "on-off" times. When the Parkinson's medication (levodopa and dopamine agonists) starts to work. It has a poor bioavailability and a half-life of roughly 1-2 hours, hence it requires a rapid release tablet formulation to achieve immediate therapeutic activity. A simple strategy to formulating instant release tablets is one of the several techniques that use super disintegrants. FDT can alleviate this issue by increasing bioavailability and releasing the medication immediately.

1.2 Super Disintegrants

A disintegrant is an excipient that is added to a tablet or capsule formulation to help break apart the compacted mass when it is placed in a fluid environment.

Advantages:

1. It works in low concentrations.
2. Compressibility and flowability are less affected.
3. Some super disintegrants are more effective intragranularly.

- Sodium Starch Glycolate (SSG) is utilised in concentrations ranging from 2 to 8%, with 4% being the best. Swelling that is both rapid and extensive, with little gelling. Water wicking and microcrystalline cellulose (Avicel, celex) in a concentration of 2-15 percent of tablet weight **[6]**.
- Cross-linked Povidone (crospovidone) was utilised at a concentration of 2–5% of the tablet's weight. Water wicking, swelling, and probably some deformation recovery. Completely insoluble in water. In water, it quickly disperses and swells, but it does not gel, even after extended exposure. When compared to other disintegrants, it has a high rate of edoema. Other disintegrants have a lower surface area to volume ratio.
- Insoluble in water hydroxyl propyl cellulose with low substituents. In water, it expands quickly. Swelling is more noticeable in grades LH-11 and LH-21. Certain grades can also have some binding capabilities while still being able to disintegrate. 1–5% is the recommended concentration.

2. MATERIALS AND METHODS

Materials: Opicapone (active pharmaceutical ingredient), Lycoat, crosspovidone, sodium starch glycolate (SSG), Aspartate, Lactose, Talc, and Magnesium stearate were all employed in this study. Analytical grade pharmaceutical components and excipients were employed throughout.

2.1 Method:

Opicapone oro-dispersible tablets **[7]** were made by direct compression using the equations listed in **Table 1**.

Separately, all of the ingredients were sieved using # 60 mesh sieves. The medication and lactose were combined by adding a tiny amount of each at a time and blending until a homogenous combination was obtained, which was then set aside. The remaining materials were then combined in a geometrical arrangement and passed through a coarse filter (#44 mesh) before being compacted using a hydraulic press. The machine's compression force was adjusted to achieve a hardness of 3-4 kg/cm^2 for all batches. For all of the formulations F1 through F12 in **Table 1**, the weight of the tablets was kept constant **[8]**.

2.2 Opicapone oro-dispersible tablet formulation:

The drug Opicapone 50mg, various concentrations of super disintegrants such as Sodium starch glycolate (SSG), Crosspovidone, lycoat, and other additives lactose, magnesium stearate, and talc were used for glident, lubrication, and aspartame was used as a sweetening agent were used in the formulations of Opicapone FDT tablets (F1-F12), as shown in **Table 1 [9]**.

Table 1: Composition of Opicapone FDT Tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Opicapone	50	50	50	50	50	50	50	50	50	50	50	50
SSG (sodium starch glycolate)	3	6	9	12	-	-	-	-	-	-	-	-
crosspovidone	-	-	-	-	3	6	9	12	-	-	-	-
Lycoat	-	-	-	-	-	-	-	-	3	6	9	12
Aspartame	2	2	2	2	2	2	2	2	2	2	2	2
Lactose	64	61	58	55	64	61	58	55	64	61	58	55
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3	3	3	3
Total (mg)	150	150	150	150	150	150	150	150	150	150	150	150

3. RESULTS AND DISCUSSION

3.1 Solubility studies:

Solubility of Opicapone was carried out at temp 25^0C using 0.1Normal HCL, 6.8 P^H buffer, 7.4 P^H buffer and purified waters showed in **Table 2** .

From the above conducted solubility studies in various buffers we can say 6.8pH phosphate buffer solution has more solubility when compared to other buffer solutions showed in **Graph 1**.

3.2 Calibration Curve of Opicapone in 6.8 P^H Phosphate Buffer

In this standard calibration determination, The drug Opicapone was diluted in various concentrations of 0, 2, 4,6,8,10,12 μg/ml and absorbance values were observed through UV spectrum showed in Table no 3, The λmax of Opicapone was found to be 275nm and R^2 value was found to be 0.999

showed in **Graph 2**.

3.3 Compatibility of drugs and excipients

The drug Opicapone and excipient compatibility was established by comparing the FT-IR spectra of the pure drug with that of the excipients used in the FDT formulations of Opicapone **(Figure 1 and Figure 2) [10]**.

We found no interactions between the pure drug (Opicapone) and the optimised formulation (Opicapone + excipients) in the drug excipient compatibility testing, indicating that there are no physical changes observed in **Figure 2**.

3.4 Characterization of Blend

The angle of repose of the various formulations was 29.42, indicating that the material had good flow characteristics. As a result, the free-flowing nature of mixes was confirmed. The blend's bulk density ranged from 0.61g/cm^3 to 0.68g/cm^3. The tapped density ranged from 0.70g/cm^3 to 0.77g/cm^3. These figures show that the blends have good flow characteristics. Carr's index ranged from 10.81 to 15.78 for all formulations, and Hausner's ratio ranged from 1.12-1.18, indicating that the blends have good flow character **[12]**.

3.5 Characterization of Tablets

3.5.1 Post compression parameters

The official assessment parameters of weight variation, hardness, friability, tablet thickness, and drug content were characterized for all batches (F1-F12) of tablet formulations, and the findings are displayed in **Table 5 [13]**.

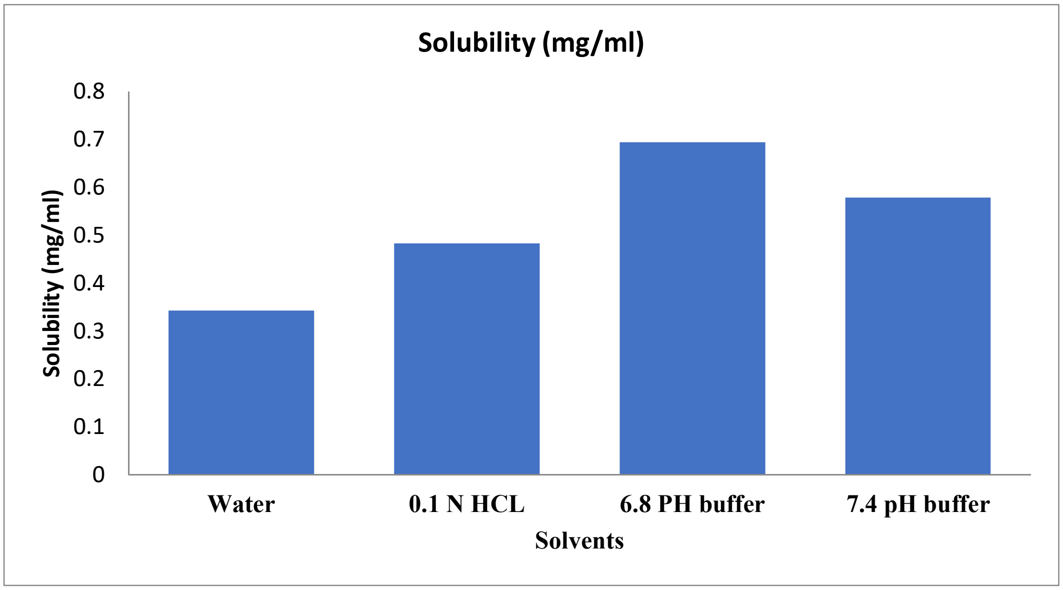
The tablet's hardness was adequate and consistent from batch to batch, ranging from 3.2 to 3.8 kg/cm^2. The weight variation test was passed for all formulations since the percent weight variation was within the pharmacopoeia standards for tablet weight. Friability values of less than 1% were recorded in all F1–F12 formulations and were deemed satisfactory, indicating that all formulations are mechanically stable. All of the formulations' disintegration times were determined to be within IP limits, and the drug content values of formulations F1–F12 were found to be in the range of 82.24–98.12 percent, which was well within IP limits **[14]**.

3.6 Dissolution investigations in vitro

The prepared tablets were subjected to dissolution studies in order to know the amount drug release.

Table 2: Opicapone solubility experiments in various solvents

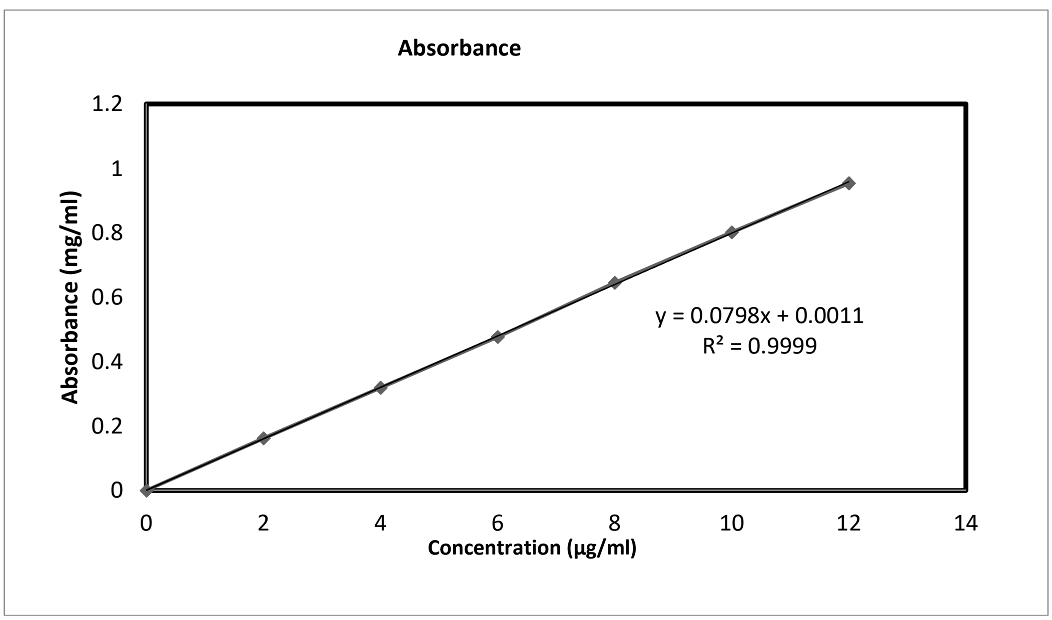
Medium	Solubility (mg/ml)
Water	0.342
0.1 N HCL	0.483
6.8 P^H buffer	0.694
7.4pH buffer	0.578



Graph 1: Opicapone solubility in various solvents

Table 3: Standard Calibration values of Opicapone in 6.8 P^H buffer

Concentration(µg/ml)	Absorbance
0	0
2	0.162
4	0.319
6	0.477
8	0.645
10	0.802
12	0.954



Graph 2: Standard graph of Opicapone

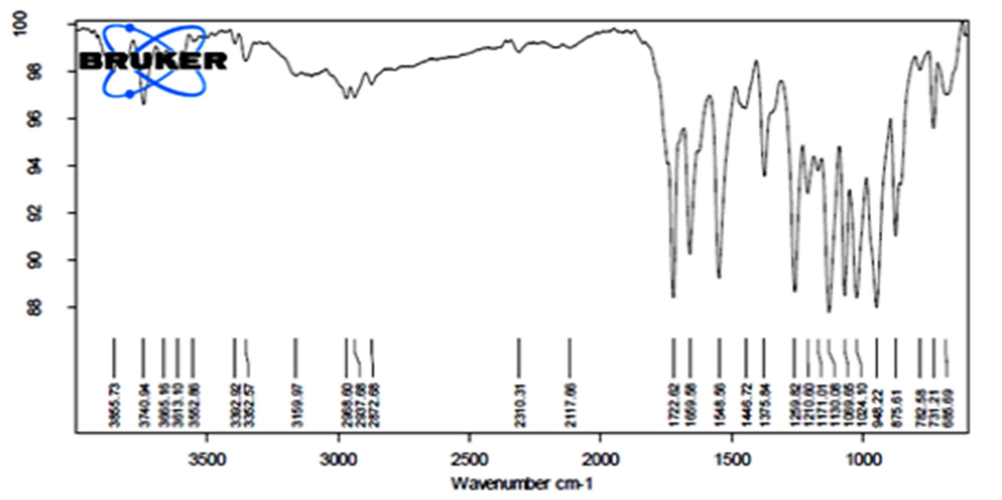


Figure 1: FT-IR spectrum of Opicapone

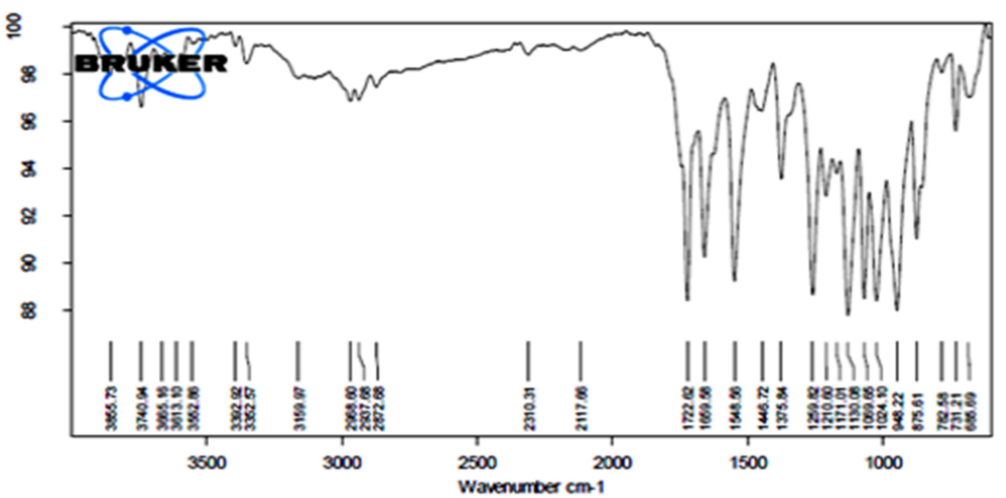


Figure 2: FT-IR spectrum of Opicapone and excipients.

Table 4: Pre compression parameters

Formulation Code	Derived properties		Flow properties		
	Bulk density	Tapped density	Angle of repose	Carr's index	Hausner's ratio
F1	0.63	0.72	26.46	11.27	1.12
F2	0.62	0.73	27.65	14.61	1.14
F3	0.65	0.71	25.84	12.37	1.17
F4	0.64	0.70	28.12	13.41	1.14
F5	0.67	0.75	29.42	10.81	1.15
F6	0.61	0.74	27.52	13.58	1.12
F7	0.63	0.72	25.14	14.63	1.14
F8	0.65	0.77	27.43	12.72	1.18
F9	0.63	0.75	25.75	13.28	1.16
F10	0.68	0.72	29.25	15.78	1.14
F11	0.65	0.71	26.34	12.81	1.17
F12	0.66	0.73	28.27	14.97	1.15

Table 5: Characteristics of Opicapone Oral Disintegrating Tablets

Formulation code	Weight variation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegrating time(sec)	%Drug content
F1	149.2	3.3	3.4	0.48	61.18	96.96
F2	148.3	3.4	4.1	0.42	50.16	94.65
F3	151.4	3.2	3.6	0.59	45.36	98.122
F4	148.6	3.5	3.3	0.55	49.08	87.02
F5	151.2	3.7	3.7	0.59	46.29	94.71
F6	150.5	3.4	4.2	0.38	39.12	97.16
F7	148.3	3.6	4.0	0.54	61.49	82.24
F8	149.3	3.8	3.5	0.29	58.42	84.18
F9	150.2	3.4	3.8	0.45	52.50	92.06
F10	148.3	3.7	4.1	0.42	75.16	86.68
F11	149.5	3.5	3.9	0.49	69.29	85.29
F12	151.8	3.3	3.2	0.58	57.12	94.64

Table 6: % Cumulative drug release of Opicapone formulations F1-F12

Time (Min)/Code	0	5	10	15	20	25	30
F1	0	18.98	29.05	38.53	48.47	59.04	70.15
F2	0	27.46	38.24	48.02	57.72	68.08	78.57
F3	0	38.21	45.81	54.98	65.15	75.02	84.96
F4	0	43.9	56.13	65.47	75.01	86.03	95.96
F5	0	31.41	42.98	53.01	62.64	71.97	82.19
F6	0	35.05	46.78	57.05	66.53	75.93	86.74
F7	0	48.61	62.72	73.63	84.45	95.45	
F8	0	59.64	75.42	86.71	98.13		
F9	0	28.45	39.78	49.43	58.91	69.43	80.42
F10	0	35.85	47.05	56.41	65.94	76.76	87.49
F11	0	45.18	58.17	67.91	77.66	89.02	99.53
F12	0	52.48	66.05	75.15	85.79	97.42	

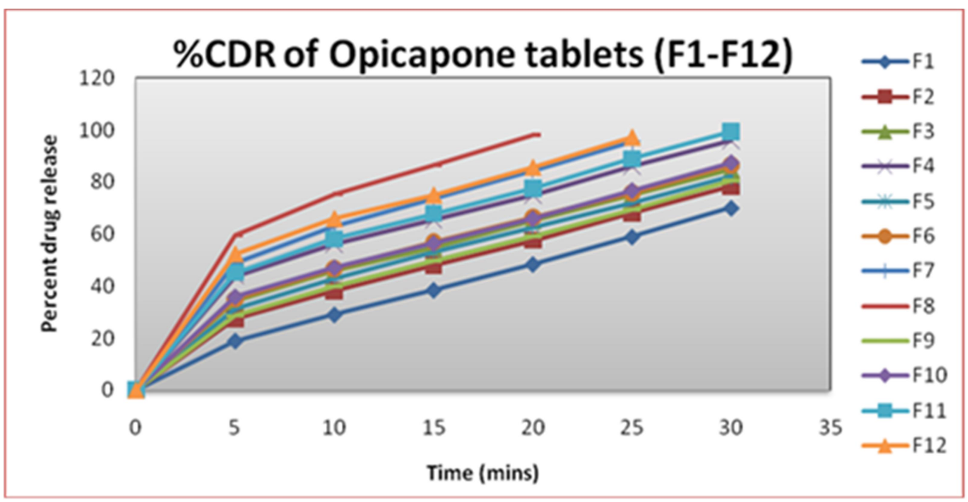


Figure 5: % Drug release of Opicapone tablets (F1-F12)

DISCUSSION

In vitro drug release tests revealed that formulations incorporating SSG (F1-F4) as a superdisintegrant in doses of (3, 6, 9, 12mg). At the end of 30 minutes, F1, F2, F3, and F4 indicate 70.15 percent, 78.57 percent, 84.96 percent, and 95.96 percent drug release. In contrast, formulations include Crosspovidone (F5-F8) as a super disintegrant in concentrations of (3, 6, 9, 12mg). At the end of 30 minutes, F5 and F6 demonstrate 82.19 percent and 86.74 percent drug release, respectively. F7 formulation shows 95.45 percent drug release after 25 minutes, while F8 formulation shows 98.13 percent drug release after 20 minutes. While the formulations containing Lycoat (F9-F11) as a super disintegrant in concentrations of (3, 6, 9, 12mg) show 80.42 percent, 87.49 percent, and 99.53 percent, respectively, the formulations containing Lycoat (F9-F11) as a super disintegrant in concentrations of (3, 6, 9, 12mg) show 80.42 percent, 87.49 percent, and 99.53 percent, respectively. F12, on the other hand, showed 97.42 percent drug release after 25 minutes. The drug release in natural super disintegrants was not found to be satisfactory when comparing the dissolving profiles of formulations F1-F12 including synthetic and natural super disintegrants in concentrations of 3, 6, 9, 12 mg in a 150mg tablet containing 50 mg of Opicapone. Synthetic super disintegrants such as lycoat and Crosspovidone, on the other hand, exhibit acceptable drug release after 30 minutes. F8, which contains 12mg Crosspovidone, has the highest drug release rate of all the formulations at 98.13 percent after 20 minutes. As a result, the F8 formulation was chosen as the best. For the F8 formulation, more kinetics was measured **[15]**.

3.7 Studies on drug release kinetics:

Zero order release of kinetics

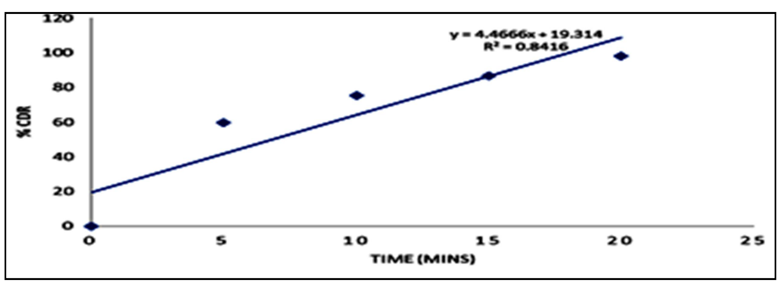


Figure 9: Zero order plot of Opicapone F8 Formulation

First order release of kinetics

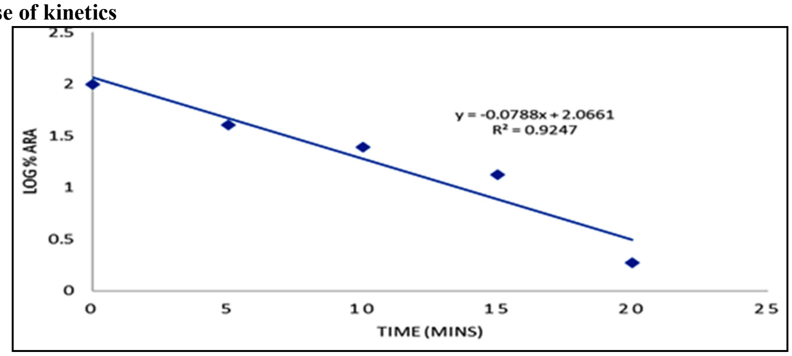


Figure 10: First order plot of Opicapone F8 Formulation (Time Vs Log% ARA

Table 5: order of kinetic values of Formulation F8

Order of kinetics	Zero order	First order
Regression values	0.842	0.925

Mathematical model equations such as zero order and first order techniques were used to describe drug release from oral disintegrating tablets. The improved formulation F8 was found to follow First order drug release based on the regression data.

4. CONCLUSION

The goal of this study is to find the optimal diluent-disintegrant combination for making Fast dissolving Opicapone tablets that dissolve in seconds in the oral cavity, reducing the time it takes for pharmacological activity to begin.

As disintegrants, Lycoat, Cross povidone, and SSG were used. Magnesium stearate and talc were utilised as lubricant and glidant in all of the formulations. The findings of the drug-excipient compatibility experiments demonstrated that the pure drug and excipients had no chemical interaction. Because of its economic effectiveness and reduced number of manufacturing processes, the direct compression method was used to create the tablets. The bulk density, tapped density, Carr's index, and angle of repose were all determined prior to compression. All of the formulations had good flow characteristics. The hardness, thickness, friability, and weight fluctuation, disintegration time, disintegration time in the oral cavity, and Invitro release parameters were all tested after compression and determined to be within IP limits. All of the tablets had a percentage drug content of between 82.24 and 98.16 percent Opicapone, which was within permissible limits. F8 has the highest medication release rate of all the formulations at 98.13 percent after 20 minutes. When compared to previous formulations, F8 contains 12 mg of Crosspovidone, which results in a higher percent drug release. As a result, F8 was chosen as the best formulation. The improved formulation F8 follows first order drug release, according to the drug release kinetics.

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6. REFERENCES

[1] Sastry SV, Nyshdham JR, Fix JA. Recent technological advances in oral drug delivery: A review.

Pharmaceutical Science and Technology Today. 2000; 3:138-45.

[2] Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50(4):375-82

[3] Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. Critical Review in Therapeutic Drug Carrier System. 2004; 21:433-76.

[4] V. Metker, A. Kumar, N. Pathak, K. Padhee, and S. Sahoo, "Formulation and evaluation of orodispersible tablets of lornoxicam," International Journal of Drug Development and Research, vol. 3, no. 1, pp. 281–285, 2011.

[5] A. Arya, S. Sharma, J. Kumar, A. Chandra, and P. Jaiswal, "Formulation and evaluation of mouth dissolving tablets of ranitidine HCL," International Journal of Pharm Tech Research, vol. 2, no. 2, pp. 1574–1577, 2010.

[6] R. B. Parmar, A. H. Baria, H. M. Tank, and S. D. Faldu, "Formulation and evaluation of domperidone fast dissolving tablets," International Journal of PharmTech Research, vol. 1, no. 3, pp. 483–487, 2009.

[7] B. Senthilnathan and A. Rupenagunta, "Formulation development and evaluation of venlafaxine hydrochloride orodispersible tablets," International Journal of Pharmaceutical Sciences and Research, vol. 2, no. 4, pp. 913–921, 2011.

[8] Pinumalla Kavya Sree, Srinivas Martha, Sharma JVC. Formulation and evaluation of oral fast disintegrating tablets of Delafloxacin. International Journal of Pharmacy and Biological Sciences. 2019; 9(3):1035-1044.

[9] P. B. Anjankumar, M. Nazmuddin, U. Kulkarni, and R. C. Hariprasanna, "Formulation and evaluation of lornoxicam fast dissolving tablet," International Research Journal of Pharmacy, 2011: 2 (4); 130–133.

[10] Vaneetha G, Srinivas Martha, Nagaraju Potnuri. Design and solubility enhancement of empagliflozin immediate release tablets by using solid dispersion method. International Journal of Pharmacy and Pharmaceutical Research. 2017:10(2);163-179

[11] Yang S, Fu Y, Jeong SH, Park K. Application of poly (acrylicacid) superporous hydrogel microparticles as asuperdisintegrant in fast disintegrating tablets. Journal of Pharmacology 2004; 56:429-36.

[12] Srinivas Martha, Kumara Swamy Linga,sreeja, Formulation and In Vitro Evaluation of Oral Disintegrating Tablets of Benralizumab, Intenational

Journal of Pharma sciences 2018:8(6); 2025-2028.

[13] Ozeki T, Yasuzawa Y, Katsuyama H, Takshima Y, Kasai T, Eguchi T. Design of rapidly disintegrating oral tablets using acid-treated yeast cell wall: A technical note. AAPS Pharm Sci Tech 2003;4.

[14] Bhagwati ST, Hiremath SN, Sreenivas SA. Comparative evaluation of disintigrants by formulating cefixime dispersible tablets. Indian J Pharm Edu Res 2005; 39(4): 194- 7.

[15] Raghavendra Rao NG, Patel T, Gandhi S. Development and evaluation of Carbamazepine fast dissolving tablets prepared with a complex by direct compression technique. Asian J Pharm 2009; 97-103.