

Available online on 15.12.2024 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article



Research Article

Formulation, Development and Evaluation of Perampanel Oral Dispersible Tablets Utilizing Screening of Additives

Kalidas Mandal^{1*}, Dr Rakesh Kumar Jat²¹ Research Scholar, Institute of Pharmacy, S.J.J.T. University, Chudela, Jhunjhunu, Rajasthan, India² Professor & Principal, Institute of Pharmacy, S.J.J.T. University, Chudela, Jhunjhunu, Rajasthan, India

Article Info:

Abstract



Article History:

Received 20 Sep 2024
Reviewed 26 Oct 2024
Accepted 24 Nov 2024
Published 15 Dec 2024

Cite this article as:

Mandal K, Jat RK, Formulation, Development and Evaluation of Perampanel Oral Dispersible Tablets Utilizing Screening of Additives, Journal of Drug Delivery and Therapeutics. 2024; 14(12):108-116 DOI: <http://dx.doi.org/10.22270/jddt.v14i12.6871>

*Address for Correspondence:

Kalidas Mandal, Research Scholar, Institute of Pharmacy, S.J.J.T. University, Chudela, Jhunjhunu, Rajasthan, India

The mouth dissolving tablets are prepared and formulated utilizing different additives like plasticizers, polymers and other bulk forming agents. There are many different batches are manufactured and tested for their evaluation parameters like disintegration test, dissolution test, content uniformity test and weight variation tests. The many batches are tested and one of the optimized batch is selected for pharmacological action and marketing purpose. The analytical method was developed as according to calibration curve.

Oral dispersible tablets of perampanel have been prepared and formulated utilizing xanthan gum and super disintegrant sodium crosscarmillose and sodium starch glycolate with crospovidone with multi-stationary punching machine. The phosphate buffer is also utilized for maintaining buffer pH of the intestine. The natural polymers are preferred as compared to synthetic polymers. The different batches of tablets have been prepared and evaluated with official dissolution time, disintegration time, weight variation and content of uniformity tests and unofficial friability testing with Roche friabilator and hardness or tensile strength of the prepared tablets with Pfizer hardness tester.

Keywords: Perampanel, xanthan gum, crosscarmillose, crospovidone, sodium starch glycolate, mouth dissolving tablets

1. INTRODUCTION

Oral route of medicine administration is known from the long time of history for its lot of advantage compared to others. Oral route is best for tablet, capsule, syrup, solution, pellets and powders. The patient can take orally that are solid unit dosage or liquid dosage form and convenient to administer through mouth. There is no pain and easily engulf with water and other liquid but bitter tablets are some difficult to administer. The content directly goes to stomach and dissolved directly to stomach or intestine. The fast dissolving tablets are most profitable because of fast dissolution and immediately absorb from the small intestine and reaches to the site of action through systematic circulation. This is convenient and easy to transport and handle. Tablets are the most significant unit dosage form for oral route of administration. Capsules are also important for oral route of administration. The tablets and capsules can be manufactured in large numbers with big batch size in pharmaceutical industries. The packing of these tablets are easy and convenient for transport from one place to another place without any breakage or minimum

breakage and loss. These solid dosage formulations are cheap as compared to other dosage forms. The sugar coated tablets can be manufactured for children as candy like domperidone¹.

These tablets are kept under the tongue or side the cheeks and have super disintegrant to dissolve fastly like crosscarmillose, starch glycolate and other super disintegrants. The tablets are effective in case of emergency or quick action like in angina pectoris the nitroglycerin tablets are kept under the tongue and dissolved in within second and give fast relief to the patients. These tablets are effective for avoiding first pass metabolism of medicaments like propranolol and nitroglycerine "A solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly within a few seconds when placed up on tongue².

2. MATERIALS AND METHODS

2.1 Materials

Perampanel was procured as a gift sample from the Sun Pharmaceuticals Pvt Ltd, Gangtok and xanthan gum was purchased from the Himedia Laboratories Pvt. Ltd,

Mumbai. Crosscarmilose and crosspovidone was purchased from SRL chemicals Pvt. Ltd, Mumbai, S.D. Fine Chemical Ltd, Mumbai respectively. Sodium starch glycolate was purchased from Sigma Aldrich, Mumbai respectively³.

2.2 Formulation development

There are total nine formulation have been prepared from F1 to F9. The oral dispersible tablets are prepared by utilizing super disintegrant sodium starch glycolate in three bates F4 to F6 and sodium crosscarmillose in three batches F7 to F9 and crosopovidone with F1 to F3 formulations of perampanel. Microcrystalline cellulose is utilized as diluents or bulk forming agent. Talk is used as glidant in the formulation and magnesium stearate is utilized as lubricant in the pharmaceutical preparation of perampanel as anti-epileptic medicament formation. The sweetening agent is mannitols in the formulation. This function, directly compressing technique alongwith addition of super disintegrants had been accepted to preparation developing of Oral Dispersing tableting of Perampanel. Dosing of 20 milligram identified to current research. Aspartame is artificial sweetner that is made of amino acid aspartic acid and other ingredients. The allow ingredients are mixed properly and coarse powder is ready for preparation of tablet with direct compression method⁴.

Development of the formulation in the present study was mainly based on the type and concentration of superdisintegrants and the properties of the drug. The formulation design of Oral Dispersible tablets of Perampanel is shown⁵.

The main aim of the tablet manufacturing is that patients of epilepsy are psychostimulant and aggressive so these persons are unable to take medicine easily so oral dispersable tablets are very easy for administration purpose. The mouth dissolving tablets are easily dissolved in the mouth so super disintegrants are utilized for formulation of pharmaceutical oral dispersable tablet. This first super disintegration is crosopovidone, second superdisintegrant is sodium starch glycolate (SSG) and third disintegrant is sodium crosscarmilose (SCC) that are used for different batches for comparison⁶.

For direct compression micro-crystalline cellulose (avicel) is added for better compression and for increasing the flow of powder from hopper to platform and to the die the talc glidant is utilized in the formulation. The dispersible oral tablets should be sweet in taste otherwise patient will not tolerate bitter taste for this purpose mannitol sweeterner is mixed in the powder for tablet formulation. The other sweetner is aspartame that is more sweetner then dextrose. Magnesium stearate is used as lubricant for smoothening of die and punches of the tablets during compression sothat there is no adherence of powder to the punches and die of tablet machine⁷.

2.3 Manufacture of Perampanel Oral Dispersible tablets

Nine different formulations of Perampanel Oral Dispersible tablet F-1 to F-9 had been formulated along with utilizing these constituents as given above into table. Perampanel had been utilized along with SSG, Cross Povidone and Cross Carmillose Sodium to prepare these Oral Dispersible tablet dosage form. Total these constituents had been screened within sieve no sixty meshes, weighing along with mixing is done in geometric sequence. After then glidant along with lubricant (sieve no two hundred meshing) had been missed along with agitation to next five minutes. This mixture oreceived had been direct pressed utilizing eight milimeter simple spherical punching into tableting of one hundred fifty milligram. the prepared batches are tested for quality parameters⁸.

3. RESULTS AND DISCUSSION

3.1 Evaluation of Perampanel tablets.

Evaluation of compressed tablet is very essential step for the packaging of prepared tablets. There are two types of evaluation parameters in which pre compression and post compression parameters. Precompression parameters are applied on bulk powder ready for compression. In this bulk density and tapped density, hausner'ratio, angle of repose, compressibility index, Car's index⁹

In post compression parameter are thickness, hardness and frability testings as per non official pharmacopoeial test. Hardness of tablet is determined by measuring tensile strength of tablet utilizing Monsanto, Pfizer and Erwika hardness testers.

Roche friabilator is used to determine friability of tablet by revolve the tablets in Roche friabilator. The official tests in Pharmacopoea's are weight uniformity of contents, weight variation of tablets, disintegration time and dissolution time specified in the monograph. The uniformity of weight is determined by assay procedure mentioned in tablet monograph and the specifications are also mentioned in monograph as sample passes within the limits of the specification and fails if not follow the specifications mentioned in the Indian Pharmacopoeia¹⁰.

Weight variation limit is mentioned in Indian Pharmacopoeia as per the specification of tablet is 80 mg or less the limit is within variation of +10 to -10% deviation for the test sample. If the tablet is from 80 mg to 250 mg the Indian pharmacopoeia specifications are between +7.5 to -7.5% deviation. If the tablets are more than 250 mg then only +5 to -5% deviation is allowed according to Indian Pharmacopoeia

United States Pharmacopoeia as per the specification of tablet is 130 mg or less the limit is within variation of +10 to -10% deviation for the test sample. If the tablet is from 130 mg to 324 mg the Indian pharmacopoeia specifications are between +7.5 to -7.5% deviation. If the tablets are more than 324 mg then only +5 to -5% deviation is allowed according to United state Pharmacopoeia¹¹.

The disintegration time is also mentioned in the pharmacopoeia. The general tablets have disintegration

time with half an hours or 30 minutes. While coated tablets are dissolved within one hour and enteric coated tablets require 2 more hours as per specification of Pharmacopoeia. The dissolution apparatus is generally two types USP I and USP II as per basket type or paddle type. The dissolution tub is filled with simulated gastric acid and semipermeable membrane is tied upon the paddle or basket. The paddle or basket rotates as revolution per minutes according to their specification that are mentioned in pharmacopoeia.

Wtting time and drug absorption ratios are also important for study. In vitro release of drug contents are also determined in post compression parameters and dispersion time of tablet is also significant post compression parameter according to evaluation of tablets¹².

3.2 PHYSICAL PARAMETERS OF DRUG AND SUPER DISINTEGRANTS

A. Angle of repose (θ): The Angle of repose of pure drug and super disintegrants, which was found are given in **Table 1**. The value shows satisfactory flow of the powder.

B. Bulk density: The Bulk density of pure drug and super disintegrants, which was found are given in **Table 1**. The bulk densities of particulars are less than 1 gram per centimeter³ as per the readings.

C. Tapped density: The Tapped density of pure drug and super disintegrants, which was found are given in **Table 1**. The tapped densities values are between 0.5 to 1.0 as shown below.

D. Index for Carr: the value of Index to Carr of pure drug along with super disintegrants, which was found are given in **Table 1**. The values of Carr's index are between 17 to 20

E. Ratio for Hausner: Ratio for Hausner of pure drug and super disintegrants, which was found are given in **Table 1**. The hausner's ratio was found between 1.20 to 1.30. These parameters are very effective between standard parameters and are effective. These are very important parameters for preparation and formulations.

Table 1: Characteristics of medicament and polymers

Medicament with super disintegrants	Repose angle (θ)	Density of Bulk (g/cm ³)	Tape density (g/cm ³)	Index for Carr	Ratio for Hausner
Perampanel	24 ^o 62 ^l	.39	.48	18.87	1.18
S.S.G.	23 ^o 66 ^l	.38	.49	19.23	1.19
Croscarmillose	23 ^o 65 ^l	0.41	0.51	19.60	1.24
Crospovidone	21 ^o 58 ^l	0.44	0.54	18.51	1.22

PRE-COMPRESSING CHARACTERISTICS OF THE PHYSICAL MIXTURE OF PERAMPANEL ORAL DISPERSIBLE TABLETS:

A. Angle of repose (θ):

The Angle of repose of physical mixture of Perampanel tablets, which was found are given in **Table 2**. These values are between 20 to 25° angle that is good for the preparations.

B. Density of Bulk:

Density of Bulk of physical solution of Perampanel tablets, which was found are given in **Table 2**. The values of bulk densities between 0.4 to 0.8 gram per centimeter³.

C. Tappe densities:

The Tappe densities of physical solution of Perampanel tablets, which was found are given in **Table 2**. The tapped densities of these compounds have been found between 0.4 to 1.0 g per cm³.

D. Carr's index:

The Carr's index of physical mixture of Perampanel tablets, which was found are given in **Table 2**. The carr's index values are between 15 to 25 for compressibilities.

E. Ratio for Hausner:

Ratio for Hausner of physical mixture of Perampanel tablets, which was found are given in **Table 2**. Ratio for Hausner are between 1.20 to 1.50 that are optimum for the formulations and preparations of tablets as solid dosage form.

Table 2: Pre compression parameters of Perampanel Tablets Granules

Batch no of prep	Repose Angle	Density of Bulk (g/cc)	Tappe Densities (g/cc)	Ratio for Carr	Ratio for Hausner
F-1	26.43±.102	0.45 ±0.005	.56 ± .014	19.64±0.02	2.24±.001
F-2	23.11±.376	.42 ±.001	0.53 ± 0.011	20.75±.06	2.26±.001
F-3	26.31±.561	.44 ±.003	.54 ± .008	20.51±0.05	2.22±.001
F-4	24.63±.204	.45 ±.001	.53 ± .002	21.09±.07	2.17±.002
F-5	26.48±.107	.43 ±.004	.56 ± .004	23.210.07	2.30±.001
F-6	25.36±.114	.42 ±.003	.56 ± .006	25.00±0.01	1.33±.001
F7	24.31±0.221	0.46 ±0.005	0.53 ± 0.002	13.20±0.01	1.15±0.005
F8	24.19±0.472	0.45 ±0.001	0.56 ± 0.008	19.64±0.22	1.24±0.005
F9	23.66±0.508	0.42 ±0.004	0.54 ± 0.001	22.22±0.07	1.28±0.005

*Value expressed as mean ±SD, n=3

POST-COMPRESSION PARAMETER OF PERAMPANEL ORAL DISPERSIBLE TABLETS:

A. Thickness:

After the evaluation of the prepared Perampanel tablet, the result which was found is given in the **Table**. The thickness of the tablets is near 3 to 4 mm as per the results. The results were satisfactory and according to standard of the tablets. These are unofficial parameters but are very helpful for the preparation of tablets and other solid dosage forms.

B. Hardness:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 3**. The hardness of the tablets are between 2.50 to 3.0 kilogram per centimeter² as per shown in the table and are under normal standards.

C. Friability:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 3**. The friability values of the formulations are in between 0.425 to 0.500 % as per the normal standard that are determined by Roche friabilator¹³.

D. Weight Variation:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 3**. Weight variations are between 1.49 to 1.51 that are within the limit of 7.5 % for 80 to 250 mg tablets according to Indian pharmacopoeia. These parameters are evaluated separately and were found in the pharmacopoeia specifications. Thus prepared batches of tablets complies all the evaluation parameters. The other parameters are also evaluated according to specific monograph of pharmacopoeia¹⁴.

Table 3: Outcomes of hardness, thickness, variation of weight along friability of Perampanel Oral Dispersible tablets

Batch no of preparation	*Thickening In millimeter	Tensile strength (kilogn/cm ²)	Friabile test In percentage	Variation of weight
F-1	4.218 ± .23	3.21 ± .25	.523 ± .14	145.43 ± .34
F-2	4.321 ± .13	4.32 ± .23	.534 ± 0.21	231.12± .45
F-3	4.113 ± 1.10	3.42 ± .31	.603 ± .10	249.21 ± .30
F-4	4.212 ± .10	4.21 ± .42	.514 ± .11	203.47 ± .81
F-5	4.003 ± .10	4.13 ± .21	.532 ± .21	203.20 ± .41
F-6	4.378 ± .11	3.87 ± .43	.635 ± .32	150.45 ± .22
F-7	4.302 ± .13	4.21 ± .31	.687 ± .23	211.69 ± .32
F-8	4.333 ± .32	4.22 ± 0.73	.643 ± .14	204.55 ± .81
F-9	4.244 ± .34	3.34 ± .32	.546 ± .34	223.56 ± 2.00

*Data expressed as average ±Standard Deviation, n = 3

E. In-vitro dispersion Time:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 4** and **Figure 1**. The dispersion times of tablets are between 20 seconds to 60 seconds as per requirements. These are satisfactory values¹⁷.

F. Wetting time:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 4** and **Figure 1**. The wetting

dispersion time of each tablets is between 25 to 50 seconds are values are mentioned below and are satisfactory for the tablet formulations. These are internal parameters of tablet formulations¹⁵.

G. Water absorption ratio:

After the evaluation of the prepared Perampanel formulation, outcomes that had been obtained have been mentioned into **Table 4** and **Figure 1**. The water absorption ratio for tablets formulations are between 80 to 100 as the specific values are given below and are compared with graphic methods. These are significant evaluation parameters for preparations of tablets¹⁶.

Table 4: Outcomes of wetting time, water absorption ratio along with *in-vitro* dispersion time of Perampanel Oral Dispersible tablets

Batch code	In-vitro Time of Dispersion in seconds	Time of Wetting in seconds	H ₂ O absorption ratio
F-1	22 ± 2.42	27 ± 2.4895	99.06 ± 0.40
F2	36 ± 1.61	45 ± 1.4275	85.40 ± 0.81
F3	14 ± 1.00	17 ± 1.5273	109.06 ± 0.60
F4	33 ± 1.10	41 ± 1.3415	88.41 ± 0.71
F5	39 ± 1.51	48 ± 1.1185	83.70 ± 0.10
F6	19 ± 1.72	23 ± 1.5277	104.10 ± 0.16
F7	41 ± 1.52	50 ± 1.5175	81.09 ± 0.91
F8	28 ± 1.62	32 ± 1.5355	94.43 ± 0.11
F9	31 ± 1.52	37 ± 1.4147	91.54 ± 0.21

*Value expressed as mean±Standard Deviation, n=3

The all calculations have been done with SPSS softwares and minimum number of readings are 3 of triplicates as per norms. The standard deviation, mean, variance,

mode, median and coefficient of variations are calculated and plotted in the graphical representations.

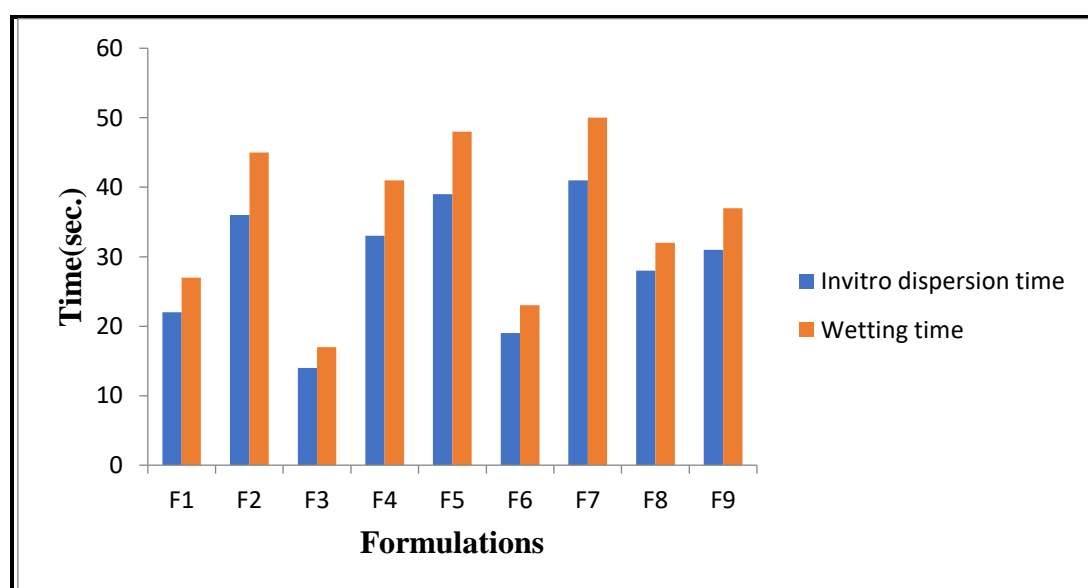


Figure 1: Comparison between wetting time along with *in-vitro* time of dispersion of Perampanel Oral Dispersible formulation

The comparison is done between time of wetting in red color along with invitro dispersion time blue color of each formulation from F1 to F9 as shown in above

graph. The water absorption ratio of prepared and formulated oral dispersible tablets are shown below in blue colors.

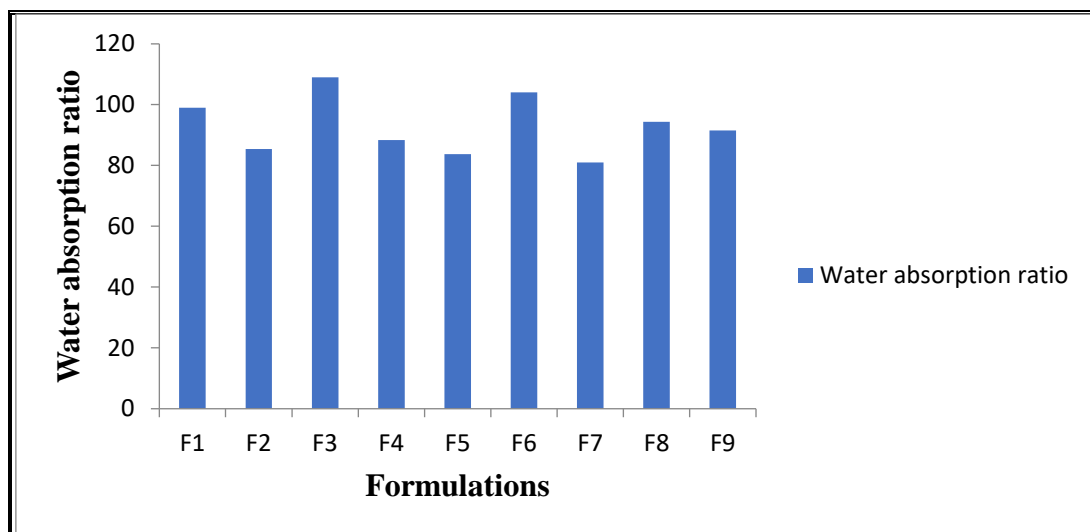


Figure 2: Water absorption ratio Perampanel Oral Dispersible tablets H. Drug Content:

After the evaluation drug content of the prepared Perampanel tablet, the result which was found has been displayed into **Table 5**.

Table 5: Data for % medicament quantity of Perampanel Oral Dispersible formulations

Formulation Code	%Drug content
F1	99.61±0.74
F2	98.73±0.38
F3	100.15±0.31
F4	98.91±0.49
F5	98.51±0.32
F6	100.02±0.45
F7	98.35±0.15
F8	99.54±0.67
F9	99.34±0.52

*Data represented average ± Standard deviation, n = 3

The table above shows percentage of drug content of medicament perampanel for evaluation of potency of the medicament. The all formulations from F1 to F9

have percentage of content between 98 to 101 percentages as the parameters mentioned in the Indian Pharmacopoeia and British Pharmacopoeia¹⁸.

I. *In-vitro* drug release profile:

After the evaluation *in-vitro* drug release profile of the prepared Perampanel tablet, the result which was found are given in the **Table 6-8** and **Figure 1-3**. The cumulative drug releases of three batches were noted and the average value of each calculated from time 1 minute to 6 minutes. At the starting the release of medicament is zero as the time passes upto one minute the medicament release reaches upto 40 to 45 percentage. Slowly slowly drug release increases and reaches upto 99 percentage within 6 minutes and the average medicament is noted down by calculating the average value of all three formulations from F1 to F3 as mentioned in the table. These values were taken and curve is drawn within percentage additive medicament along with the time period of the release of the tablets. The *in-vitro* release of the medicament is shown in the graphs given below¹⁹.

Table 6: *In vitro* release data of Perampanel Oral Dispersible tablets (F1-F3)

Sl. No.	Time (mins)	%Cumulative drug release		
		F1	F2	F3
1	0	0	0	0
2	1	45.07 ± 1.12	40.84 ± 0.87	50.70 ± 0.62
3	2	66.28 ± 0.76	50.78 ± 0.75	66.29 ± 0.38
4	3	74.87 ± 0.42	67.78 ± 0.54	88.96 ± 1.13
5	4	86.28 ± 0.33	83.41 ± 1.21	97.59 ± 0.55
6	5	96.31 ± 0.25	90.62 ± 0.84	99.05 ± 1.15

Table 7: *In vitro* delivery values of Perampanel Oral Dispersible formulations (F-4 to F-6)

Serial no	period (mins)	% Cumulative medicament delivery		
		F-4	F-5	F-6
1	0	0	0	0
2	1	45.07 ± 0.86	40.84 ± 0.38	45.07 ± 1.13
3	2	57.83 ± 0.47	59.23 ± 1.14	64.87 ± 0.32
4	3	66.40 ± 0.71	73.43 ± 0.62	80.50 ± 0.38
5	4	87.66 ± 0.39	82.03 ± 0.36	86.29 ± 0.64
6	5	92.06 ± 1.13	89.24 ± 0.69	97.73 ± 0.49

The same technique is utilized for the batches formulation F4 to F6 as shown in the table. These are very compulsory for the evaluation. The release of medicament increases cumulatively as per time period. Oral dispersible tablets of perampanel is prepared with

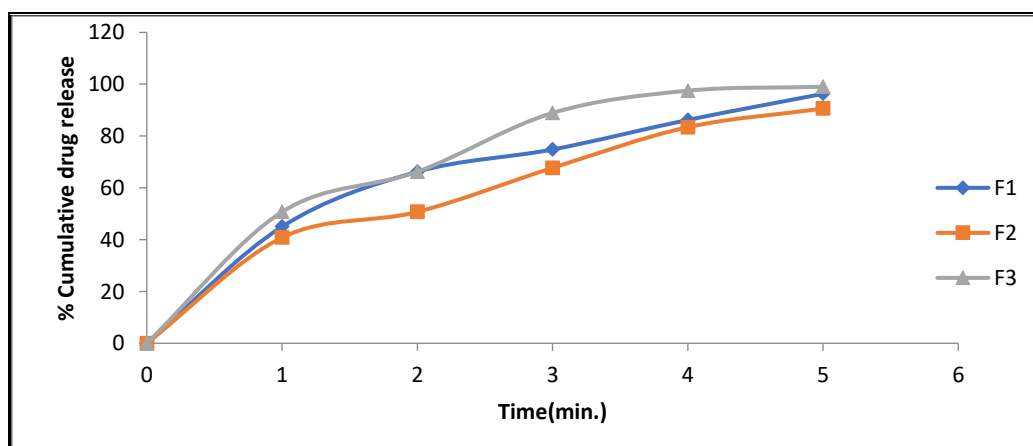
different superdisintegrants in different batches like croscopolvidone for F1 to F3 first three batches, sodium starch glycolate for next three batches F4-F6 and croscarmillose for last three batches F7-F9.

Table 8: *In vitro* delivery values of Perampanel Oral Dispersible formulations (F-7 to F-9)

Sl. No.	Time (mins)	% cumulative drug release		
		F-7	F-8	F-9
i	0.0	0.0	0.0	0.0
ii	1.1	38.02 ± 1.17	43.66 ± 0.38	43.66 ± 0.75
iii	2.1	60.63 ± 0.53	66.28 ± 0.24	67.69 ± 0.36
iv	3.1	72.02 ± 0.22	74.86 ± 0.53	80.50 ± 0.61
v	4.1	83.43 ± 1.24	86.28 ± 0.65	86.29 ± 0.46
vi	5.1	87.83 ± 0.63	94.90 ± 0.42	92.10 ± 0.23

The releasing of medicine perampanel from tablet formulation have been represented in in-vitro release pattern in the table. As the data indicates that at first

minute nearly half medicine is released and after five minutes more than 90 percent medicine is release.

**Figure 3:** *In vitro* delivery pattern of Perampanel Oral Dispersible formulations (F-1 to F-3)

The release of perampanel in-vitro pattern is shown above. There three lines have been shown for formulation F1-F3. The blue line shows F1 formulation in the graph while red line shows F2 formulation in the above figure and F3 formulation is shown in green line.

The cumulative percentage release of medicaments is represented on y-axis while times in minutes have been shown in x-axis as shown in graphical representation. There is slight variation in the release pattern of each formulation.

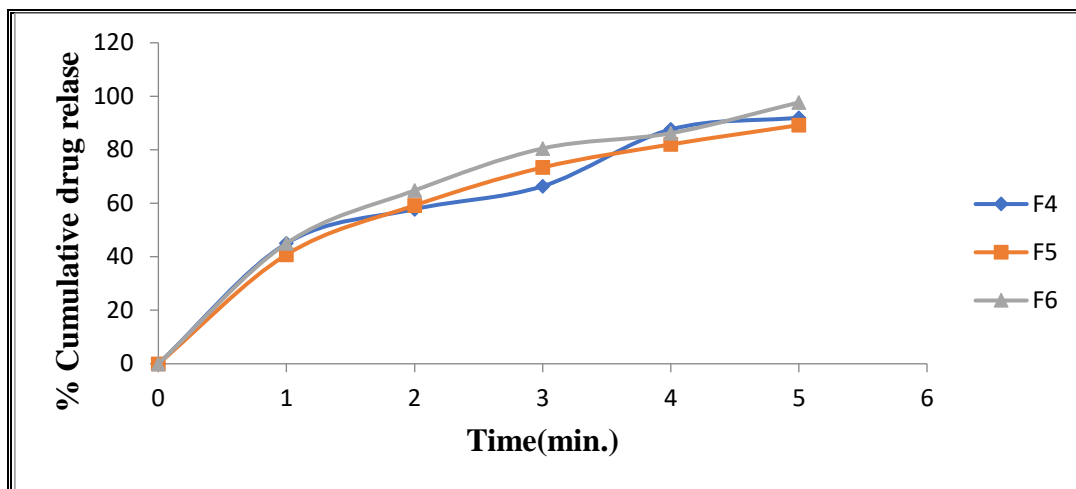


Figure 4: *In vitro* delivery pattern of Perampanel Oral Dispersible formulations (F-4 to F-6)

There three lines have been shown for formulation F4-F6. The blue line shows F4 formulation in the graph while red line shows F5 formulation in the above figure and F6 formulation is shown in green line.

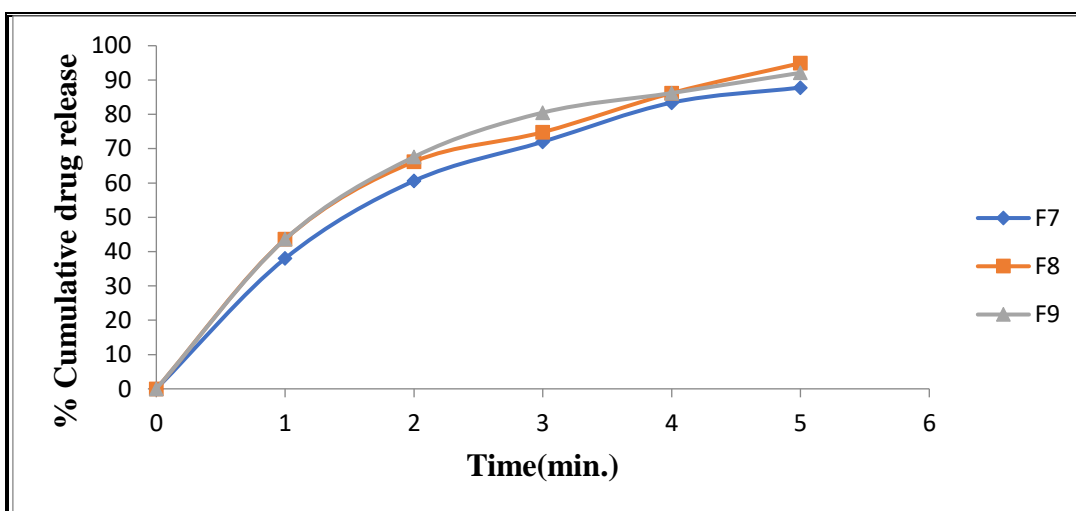


Figure 5: *In vitro* delivery pattern of Perampanel Oral Dispersible formulations (F-7 to F-9)

There three lines have been shown for formulation F7-F9. The blue line shows F7 formulation in the graph while red line shows F8 formulation in the above figure and F9 formulation is shown in green line

4. SUMMARY AND CONCLUSION

At current research, focus had been got to formulate along examine Oral Dispersible formulations of Perampanel. In general Perampanel keeping 10% peroral availability in blood due to maximum medicament is metabolized before reaching blood. These formulations are developed for avoid bypass of medicaments from liver and medicaments is quickly reach to the systemic circulation from saliva and the bioavailability of medicament is increased as compared to simple dosage forms.

Conflict of Interest: Author declares no potential conflict of interest with respect to the contents, authorship, and/or publication of this article.

Source of Support: Nil

Funding: The authors declared that this study has received no financial support.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data supporting in this paper are available on the request from corresponding author.

Ethics approval: Not applicable.

REFERENCES

- Chien Yie W Novel drug delivery systems. 2nd ed. Marcel Dekker. Drugs and pharm Sci. 2021; 50: 139-140.
- Swamivelmanickam M, Manavalan R, Valliappan K. Mouth Dissolving Tablets: An Overview. Int. J. of Pharm. Sci. and Res. 2020; 1(12): 43-55.
- Jain CP, Naruk PS. Formulation and evaluation of fast dissolving tablets of valsartan. Int J. of Pharm. & pharm Sci. 2019; 1(1): 219-226.
- Jeevan JB, Suneela G. Development of Fast Dissolving Tablets of Glibenclamide Using Crospovidone and its Kneading Mixture. Ind J. of Pharm Edu. Res. 2020; 44(4): 334-340.

5. Anjan KM, Murthy PN, Jagannath S, Sudarsan B, Sahoo SK. Formulation Design and Optimization of Mouth Dissolving Tablets of Levocetirizine Hydrochloride Using Sublimation Technique. *Ind J. of Pharm.Edu.Res.* 2019; 43(1): 39-45.
6. Seager H. Drug-delivery Products and the Zydis Fast-dissolving Dosage Form. *J. Pharm. Pharmacol.* 1997; 50: 375-382. <https://doi.org/10.1111/j.2042-7158.1998.tb06876.x> PMID:9625481
7. Kumar GA, Wadood SA, Maurya SD, Ramchand D, Interpenetrating polymeric network hydrogel for stomach-specific drug delivery of clarithromycin: Preparation and evaluation, *Asian Journal of Pharmaceutics-October-December 2010*; 179-184. <https://doi.org/10.4103/0973-8398.76738>
8. Bradoo R. Fast Dissolving Drug Delivery Systems, *JAMA India.* 2001; 4(10): 27-31.
9. Kuchekar BS, Atul, Badhan, C. Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. *Pharm Tim.* 2003; 35: 7-9.
10. Behnke K, Sogaard J, Martin S, Bauml J, Ravindran AV, Agren H, et al. Mirtazapine orally disintegrating tablet versus sertraline: A prospective onset of action study. *J Cli Psy pharmacol.* 2003; 23: 358-64. <https://doi.org/10.1097/01.jcp.0000085408.08426.05> PMID:12920411
11. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. *Cri Rev The Dru Car Sys.* 2004; 21: 433-76. <https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v21.i6.10> PMID:15658933
12. Dollo G, Chevanne F, Le CP, Chemtob C, Le VR. Bioavailability of phloroglucinol in man. *J Pharm Bel.* 1999; 54: 75-82.
13. Maurya SD, Prajapati S, Gupta A, Saxena G, Dhakar RC, Formulation Development and Evaluation of Ethosome of Stavudine, *Indian J.Pharm. Educ. Res.* 2010;44(1)
14. Maurya SD, Aggarwal S, Tilak VK, Dhakar RC, Singh A, Maurya G, Enhanced Transdermal Delivery of Indinavir Sulfate via Transfersomes, *Pharmacie Globale (IJCP)* 2010;1(06):1-7
15. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving dosage form. *US Patent.*2001; 6,207,199.
16. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. *US Patent.* 1996; 5,587,180.
17. Fitri K, Khairani TN, Sianturi KT, Leny L, Hafiz I, Anti-inflammatory Activity of Ethanol Extract of Lotus (*Nelumbo nucifera* G.) Seed Against White Male Rats Using Paw Edema Method, *Journal of Drug Delivery and Therapeutics*,2021;11(4):1-4 <https://doi.org/10.22270/jddt.v11i2-S.4622>
18. Bhaskaran S, Narmada GV. Rapid dissolving tablet A Novel dosage form *Ind Pharm.* 2002; 1: 9-12.
19. Koizumi K, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method of preparing high-porosity rapidly saliva soluble compressed tablets using mannitol with camphor: A subliming material. *Int J Pharm* 1997; 152: 127-31. [https://doi.org/10.1016/S0378-5173\(97\)04924-7](https://doi.org/10.1016/S0378-5173(97)04924-7)
20. Meyers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product there form. *PCT Patent WC 95/34293-A1*; 1995