IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Formulation and Evaluation of Solid Dispersion Incorporated Fast Disintegrating Tablet Of Antiemetic Drug

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Abstract

In the present work, the aim is to successfully formulate solid dispersion and incorporated it into a fast disintegrating tablet of aprepitant. Firstly increases the solubility of poorly water-soluble aprepitant by solid dispersion and then it is formulated into FDTs with improved patient compliance and convenience. Solid dispersions are prepared by the fusion method and solvent evaporation method. The formulation F9 is selected for best formulation because it shows the % yield 95%, drug content, dissolution 94%. after then selected batch F9 is formulated into FDTs results are disintegration time 12 seconds, dissolution drug release 99 % of this formulation respectively.

Keywords: Solubility, Solid dispersion, Fast disintegrating tablet, Aprepitant.

INTRODUCTION

Nausea is an unpleasant sensory and emotional experience accompanied by an autonomic driven physiological change of pallor and upper GI track hypersecretion [1]. A current oral formulation of aprepitant is indicated for the administration of multiple doses, which was due to the half-life of approximately 9-13 h with a time to peak plasmas level of 4 h [2].

Approximately 40% of patients who receive chemotherapy have experienced nausea and vomiting [3, 4]. Control of nausea and vomiting following chemotherapy and surgery has been improved in recent years due to the advancement of novel, effective, and better-tolerated antiemetic therapies [5-7].

Solubility is a significant physicochemical factor affecting the absorption of a drug and its therapeutic effectiveness. The rate and extent of dissolution of the drug from any solid dosage form determine the rate and extent of absorption of the drug. In the case of poorly water-soluble drugs, dissolution is the rate-limiting step in the process of drug absorption [8]. Solid dispersion (SD) is the method that involves the dispersion of one or more active ingredients in an inert carrier or matrix in solid-state prepared by melting, dissolution insolvent, or melting-solvent method. Conventional oral drug delivery systems, including solutions, suspension, tablets, and capsules are difficult to administer to patients with dysphagia. Swallowing problems can also appear often in specific populations, including pediatric, elderly, nauseated patients, and developmentally disabled patients. In addition to these difficulties, convenience is also a notable concern associated with oral antiemetics like the patients taking tablet formulations to require water to ease swallowing, which is not always available [10]. Fast disintegrating tablets (FDTs) have been designed to allow a solid dose to be rapidly dissolved in the oral cavity without the need for water [11-12]. Several approaches have been used to formulate FDTs like freeze-drying, tablet molding, sublimation, direct compression, etc. Out of these direct compression has become the most popular used technique. [13-14].

MATERIALS :

Aprepitant, Sodium Starch glycolate, Polyethylene glycol 6000, Poloxamers 188, Microcrystalline cellulose, Magnesium Stearate, Mannitol, Sodium saccharin, Talc, Croscarmellose Sodium. All reagents used were of analytical grade and parched from LOBA Chemie Pvt. Ltd.

METHODS:

Fusion Method and Solvent Evaporation Method.

1. **PREPARATION OF SOLID DISPERSION:**

   Solid dispersions of Aprepitant were prepared by the fusion method and solvent evaporation method. For the optimization of solid dispersion with drug and Polymer ratio, with the different polymers in the ratio of 1:1, 1.3, and 1:5 three polymers were taken for screening of polymer for solid dispersion. They were PEG 6000, Poloxamers, and sodium starch glycolate.F1-F3 Batch was prepared with the Fusion method and the F4-F9 Batches were Prepared with solvent evaporation method.[15]

2. FORMULATION OPTIMIZATION OF SOLID DISPERSION

S.NO.	Formulation No.	Drug [mg]	PEG 6000 [mg]	Poloxamers 188 [mg]	Sodium Starch glycolate [mg]
1.	F1	10	10	-	-
2.	F2	10	30	-	-
3.	F3	10	50	-	-
4.	F4	10	-	10	-
5.	F5	10	-	30	-
6.	F6	10	-	50	-
7.	F7	10	-	-	10
8.	F8	10	-	-	30
9.	F9	10	-	-	50

Table No.01 Formulation optimization of Solid dispersion

Fusion Method.

Weight accurately 10 mg polymer and placed it into a china dish and heat it on a water bath with continuous stirring until the polymer is dissolved. Add 10 mg Aprepitant (drug) in dissolved polymer solution with continuous stirring to form a homogenous mixer. After complete mixing of drug and polymer rapidly transfer into the ice bath to solidified with vigorous stirring. Then, the final solid mass is crushed, pulverized, and sieved. Different optimized combinations of solid dispersion with different polymers were prepared and evaluated for different evaluation parameters.[16]

Solvent Evaporation Method

Weight accurately 10mg of polymer and 10mg aprepitant (drug) placed into china dish. Add a sufficient volume of methanol to dissolve completely with continuous stirring. Allow mixture to evaporate completely on a water bath at 45^0c with continuous stirring to obtain dry mass. The dried mass was pulverized and passed through 44 mesh sizes. Different optimized combinations of solid dispersion with different polymers were prepared and evaluated for different evaluation parameters.[17]

3.CHARACTERIZATION OF SOLID DISPERSION

1.**Determination Of Percent Drug Content.**

Determination Percent drug content, accurately weighed solid dispersion equivalent to 10 mg of Aprepitant was transferred to100 ml of volumetric flask and diluted to 100 ml with methanol and sonicated for 30 min for complete solubilization of the drug. The solution was filtered through a 0.45 µ filter and measured at 245nm in a double beam UV spectrophotometer (UV 1800, Shimadzu, Kyoto, Japan). The concentration of Aprepitant was determined using the calibration curve of the drug in methanol.[18,19]

2. Solubility Studies

Saturation solubility studies were conducted as per the method described by Higuchi. The saturation solubility was performed by adding an excess amount of solid dispersion in 10 ml 6.8 PH phosphate buffer in a glass vial. Mixed vigorously for 30 mins and shaken mechanically for 72 h at 37°C ± 0.5°C. then vials are centrifuged for 10 mins at 2500 RPM. The saturated solutions were filtered through a 0.45-µm membrane filter. And filtrates were suitably diluted, analyzed using Shimadzu UV-1800, (UV-1800 Shimadzu, Kyoto, Japan) UV-1800 spectrophotometer at 206 nm.

3.Percentage Yield

Thoroughly dried solid dispersion was collected and weighed accurately. The percentage yield was then calculated using formulae given below

$$\text{Percentage yield} = \frac{\text{Mass of Solid dispersion obtained}}{\text{Total weight of drug and polymer}} \times 100$$

4. In Vitro Dissolution Studies

The dissolution study was carried out using a USP apparatus type-II. The dissolution medium was 900 ml 6.8 pH phosphate buffer kept at 37±1ºC. The basket was rotated at 50 rpm. Samples of 5 ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 206 nm using Shimadzu-1800 UV-visible spectrophotometer. The samples withdrawn were replaced by fresh buffer solutions. The dissolution study was continued for the next 2 h.[20,21]

5. Dsc Analysis Differential Scanning Colorimetry (Dsc) Analysis

The thermal properties of the pure drug and sodium starch glycolate mixtures were evaluated using a differential scanning calorimeter. The analysis was performed with a heating range of 48-50ºC and a rate of 10 $^{o}C\ min^{-1}$ in an inert nitrogen atmosphere.[22]

4.FORMULATION FAST DISINTEGRATING TABLET WITH OPTIMIZED SOLID DISPERSION.

S.NO	Ingredients	B1	B2	B3
1.	Optimized solid dispersion(F9)	240	240	240
2.	Croscarmellose sodium	10	20	30
3.	Microcrystalline cellulose	60	50	40
4.	Mannitol	33	33	33
5.	Talc	5	5	5
6.	Magnesium stearate	10	10	10
7.	Sodium saccharin	2	2	2
	Total	360 mg	360 mg	360 mg

Table No.02 Formulation Fast Disintegrating Tablet

5.PREPARATION OF FAST DISINTEGRATING TABLET:

1.All the ingredients were passed through an 80# sieve.

2.Solid dispersion (45 mg is equivalent to 10 mg Aprepitant) was mixed with super disintegrant Croscarmellose sodium, mannitol, and directly compressible microcrystalline cellulose as diluents and other excipients such as magnesium stearate and talc, Sodium saccharin.

3.The powder blend was directly compressed using flat punches on a double rotary tablet compression machine.[23]

6.EVALUATION OF TABLET

1. PRE-COMPRESSION STUDIES

1) Angle Of Repose

The angle of repose is defining as the maximum angle possible between the surface of the pile of the horizontal plate and powder. For determining the angle of repose of powder a funnel was kept on a stand in a vertical position and about 10 gm of the drug was filled in that funnel. Then the powder was release on the paper to form a conical heap. Then that heap was measured in different directions like height was measured by the scale. And the angle of repose was calculated by using the following formulae

$$\theta = \tan^{-1}(h/r)$$

θ = Angle of the repose

h = Height of the heap

r = Radius of the heap

2) Bulk Density

It is obtained by measuring the volume of a mass of powder that passed through the screen. The ratio of the mass of powder to the volume of bulk. Bulk density mostly depends on the shape if the shape of the powder is spherical bulk density is increase. The powder sample equivalent to the 10 gm is weighed then that powder was filled in a 50ml of cylinder. And then the powder will be leveled and that volume was noted.[25]

$$\rho i = m / Vi$$

ρi=Bulk density

m=mass of the blend

Vi = untapped volume

3). Tapped Density

It is the ratio of a mass of the powder which was occupied the volume after it has been tapped for a defined period.

$$\rho t = m/Vt$$

ρt = Tapped density

m = mass of the blend

Vt = tapped volume

4). Powder Compressibility

The compressibility index measures the propensity of a powder to be compressed. As such, they are measuring the relative importance of inter particulate interactions. In a free-flowing powder, such interactions generally less, and tapped densities will be closer in value. And for the poorer flowing materials, there are frequently greater and larger inter particulate interactions and a greater difference between tapped and bulk density will be observed. These differences are reflected in the compressibility index calculated by the formula. One of the important measures that can be obtained from bulk and tapped density determinations is the percent compressibility or Carr's index (I), which is determined by the following equation.[26]

$$I = \frac{\text{Tapped density - Tapped density}}{\text{Bulk density}} \times 100$$

5). Hausner's Ratio

Hausner ratio is related to interparticle friction and, as such used to predict powder flow properties. The compressibility index [Carr's index (%)] is an indication of changes that occur in the packing arrangement while tapping the powder and is a direct measure of the propensity of a powder to consolidate when undergoing vibration, shipping, and handling. The table shows that the compressibility index was the highest for all the polymers which had poor, flow properties since higher values tend to indicate poor flowability of powders. As

per Table, higher values for Hausner ratio and angle of repose indicate poor flow properties of the polymers. This data suggests the need for granulation.[27]

$$\text{Hausner's ration} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

7.POST COMPRESSION STUDIES

The prepared tablet of Aprepitant was evaluated on the various parameters according to the Indian Pharmacopeia e.g. appearance, dimensions (diameter and thickness), weight variation, hardness, friability, assay, and drug content.

1. Weight Variation

Randomly selected 20 tablets will be weighed individually and calculate average weight will be calculated. The individual weight is compared with the average weight. And the difference in weight variation should be within the standard limits according to the USP and IP. And the percent in deviation was calculated by formulating.[28]

$$\textbf{\% Weight Variation Difference} = \frac{\text{Individual Weight - Average Weight}}{\text{The Average Weight Of}} \times 100$$

Table No.03:- Allowed Percentage Deviation In Weight Variation

The Average Weight Of The Tablet (According To IP)	Allowed Percentage Deviation (%)	Average Weight Of The Tablet (According To USP)
80 mg or less	10	130mg or less
More than 80 mg but less than 250 mg	7.5	130mg to 324
250 mg or more	5	More than 324

2.Friability Test

This test is used for the determination of the physical strength of the tablets and mainly applies to the compressed tablet. De dust the 10 tablets and weigh accurately the required number of tablets. Keep the tablets in the friability and rotate them 100 times. Then after that remove the tablets. Remove its dust and then weigh them accurately.

$$\frac{\%\ F = I - F}{I} \times 100$$

I=initial weight

F=final weight

3.Hardness

Tablet hardness has been defined as the force required breaking a tablet in a diametric compression test. Several devices are used to test tablet hardness: the Monsanto tester, the strong- cobb tester, the Pfizer tester, the Erweka tester, and the Schleuniger tester Pfizer tester operates on the same mechanical principle as a pair of pliers. As the plier handles are squeezed, the tablet is compressed between a holding anvil, and a piston connected to a direct force reading gauge. The dial indicator remains at the reading where the tablet breaks and is returned to zero by depressing a reset button.[28]

4. Drug Content Uniformity

Ten tablets will be finely powdered and an amount equivalent to 100 mg of powder will be accurately weighed and transferred to a 100 ml volumetric flask, then 100 ml of methanol will be added. The filtrate is further diluted with phosphate buffer 6.8 pH. Then analyzed with UV visible spectrophotometrically. Drug content was calculated using a standard curve generated using various concentrations of Aprepitant in phosphate buffer (pH6.8).

5.Dissolution Test

In vitro dissolution study is performed by using USP Type I Apparatus (Basket type). The tablet is kept in 900 ml of dissolution fluid is generally gastric fluid for first 2 hr and intestinal fluid(for subsequent fluid) with a stirrer rotating at a specified r.p.m and maintaining the temperature at 37 ± 0.5 °C of dissolution media. 5 ml of samples withdrawn at different time intervals were replaced with fresh medium and analyzed in UV Visible spectrophotometer for estimation of absorbance taking a suitable blank solution. Finally, the drug release rate is calculated using a suitable equation.[29]

8. RESULT AND DISCUSSION

8.1 PREFORMULATION STUDIES: -

1 Physical Appearance

Table No.04 Physical Appearance of Drug

S. No.	Properties	Observation
1.	Color	White Powder
2.	State	Solid
3.	Odor	Odorless

2. Identification Of Drug:

2.1. By UV Spectroscopy by UV spectroscopy at 200-400nm**.**

Table No. 05 Observation Table Of UV Spectroscopy In 6.8 PH Buffer Solution

S. No	Conc.(µg/ml)	Absorbance(nm)
1	0	0
2	1	0.198±0.1
3	2	0.398±0.3
4	3	0.594±0.1
5	4	0.793±0.2
6	5	0.963±0.5

2.2 Spectroscopy Studies: Drug Excipient Compatibility Studies By FTIR Spectroscopy

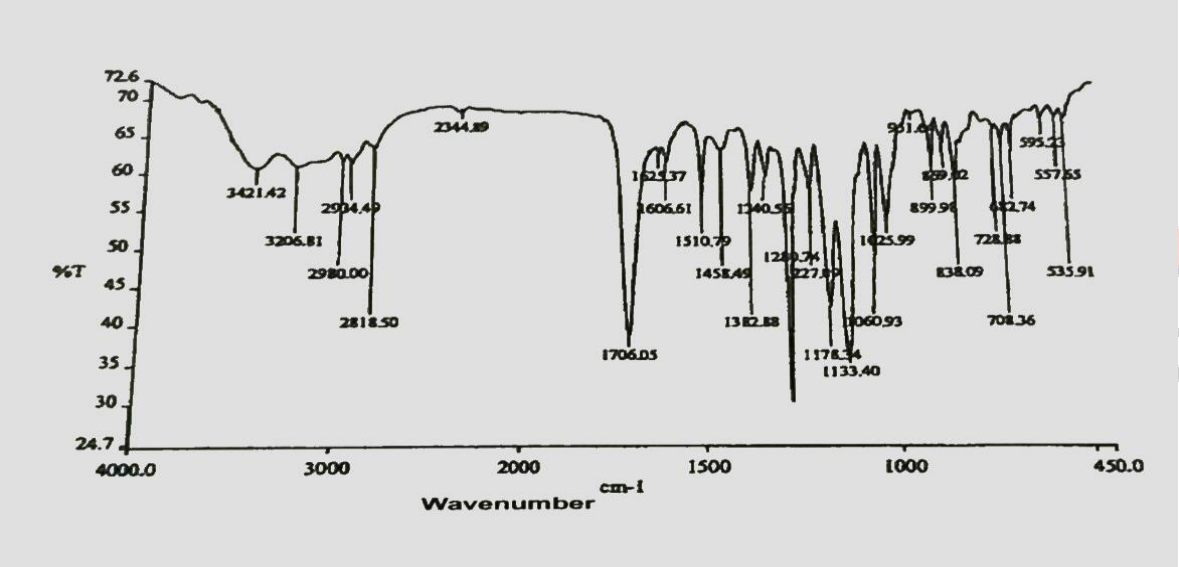


Figure No 01 :IR Spectra of Aprepitant

Melting Point Determination: - By using Electronic Melting Point Apparatus. The melting point of Aprepitant is = 225 ºC

Table No.06 Observation Table of Melting Point

S. No.	Initial MP (ºC)	Final MP (ºC)
1.	190	225±0.25
2.	196	255±0.21
3.	190	225±0.25

4 Solubility Studies in Different Solvents- The various solvents are used for solubility studies of Aprepitant by test tube method**.**

Table No.07 Observation Table of Solubility

S. No.	Solvents	Results
1.	0.1 N HCL	Soluble
2.	6.8 pH Buffer	Soluble
3.	Methanol	Freely Soluble
4.	Ethanol	Sparingly Soluble
5.	Acetonitrile	Slightly soluble
6.	water	Practically insoluble

5.Partition Coefficient: -

A partition coefficient (P) or distribution coefficient (D) is the proportion of concentration of a a compound in a combination of two immiscible phases at equilibrium.

By the separating funnel method using determine the partition coefficient of the drug. (n Octanol: water)

(KD)A = [A]org/ [A]aq

Log pKa = 9.5

6. HPLC

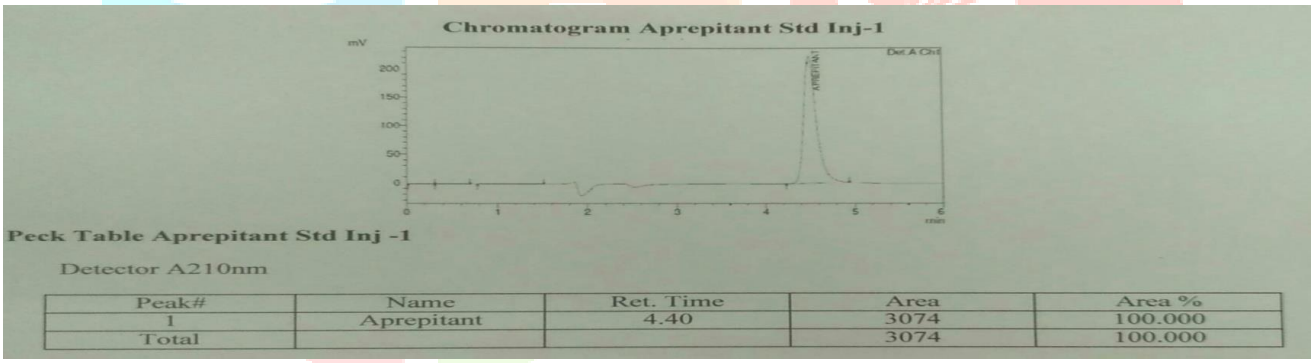


Figure No 02: Aprepitant Standard Sample Peak of HPLC chromatograph

EVALUATION OF SOLID DISPERSION

1. Drug Content

S.NO.	Formulation NO	Drug Content (%)
1.	F1	95.84±0.45
2.	F2	96.61±0.23
3.	F3	97.33±0.74
4.	F4	92.67±0.26
5.	F5	94.12±0.36
6.	F6	97.97±0.28
7.	F7	96.25±0.56
8.	F8	97.66±0.85
9.	F9	98.36±0.29

Table No.17 Observation Of Drug Content

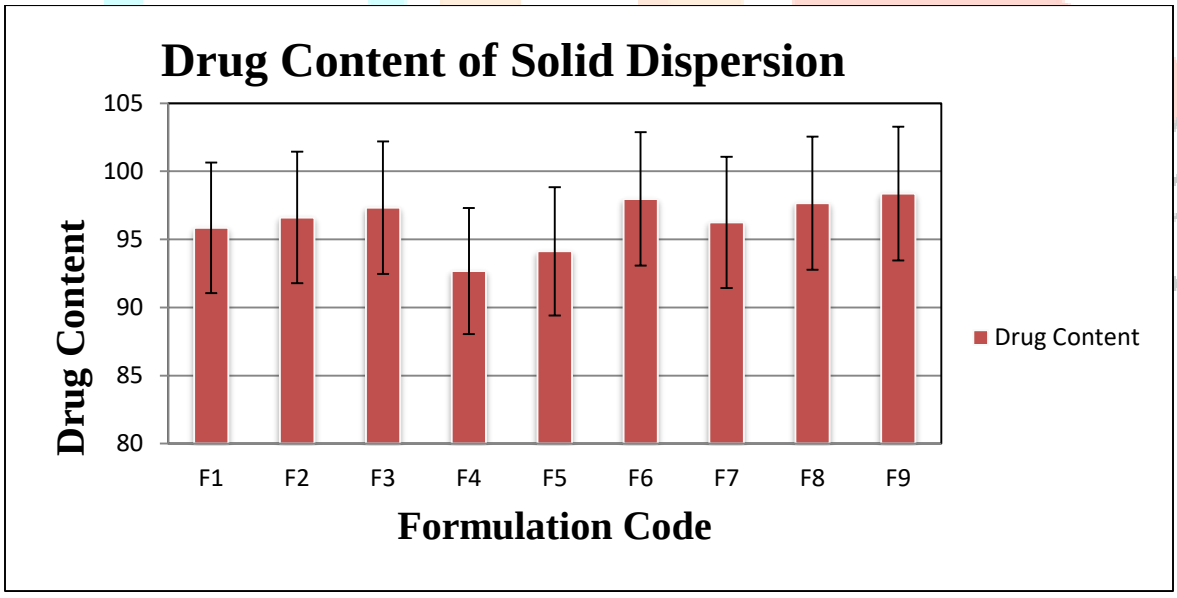


Figure No.03 Graph Of Drug Content

2. Solubility Studies

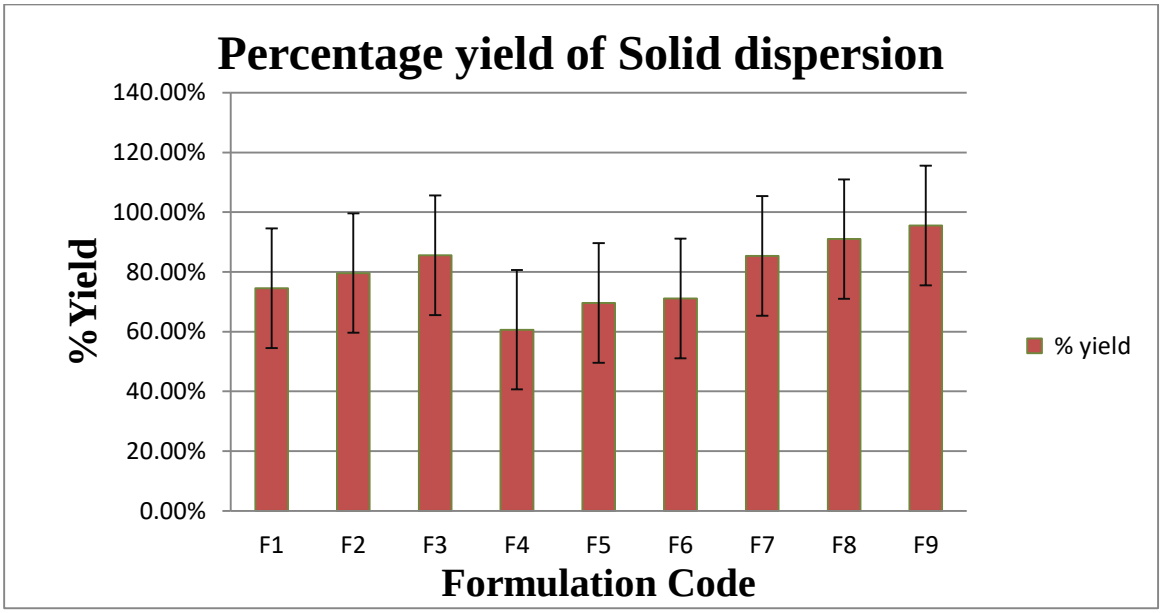
S.NO.	Formulation Batch	Saturation Solubility (Mg/Ml)
1.	F1	0.231±0.013
2.	F2	0.423±0.025
3.	F3	0.943±0.028
4.	F4	0.540±0.012
5.	F5	0.678±0.048
6.	F6	1.516±0.052
7.	F7	0.112±0.026
8.	F8	0.567±0.015
9.	F9	1.603±0.010

Table No. 08 Observation of Saturation solubility studies

3. Percentage Yield

S.NO.	Formulation NO.	Percentage yield (%)
1.	F1	74.55±0.52
2.	F2	79.61±0.20
3.	F3	85.55±0.45
4.	F4	60.66±0.32
5.	F5	69.61±0.48
6.	F6	71.11±0.85
7.	F7	85.33±0.53
8.	F8	90.99±0.10
9.	F9	95.51±0.50

Table No.09 Observation Of Percentage Yield

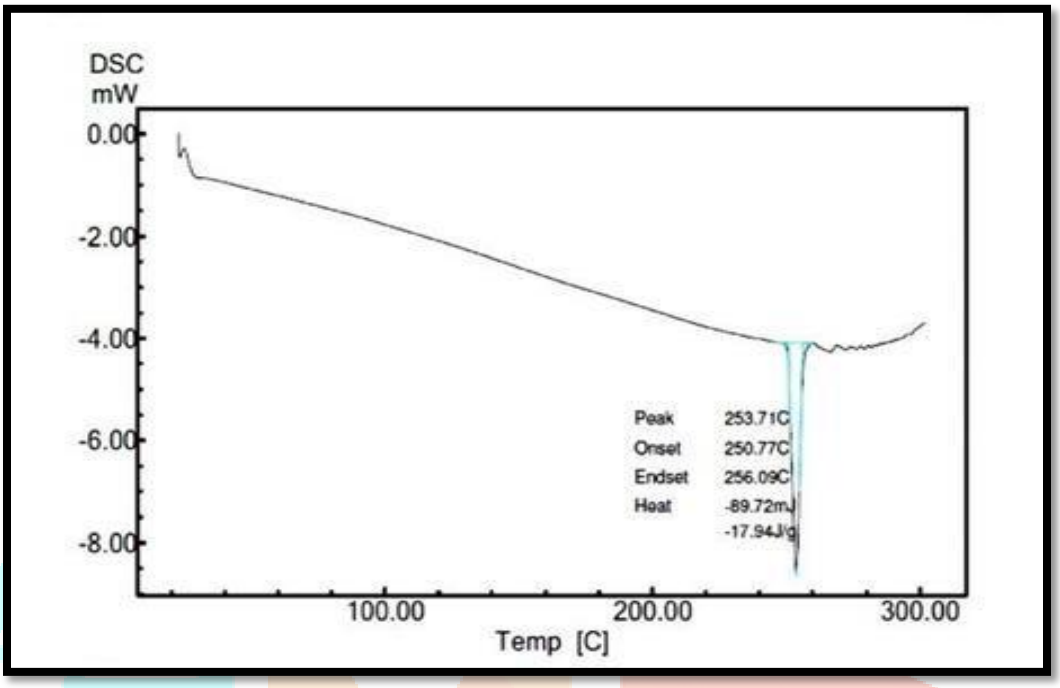


4. Dissolution Studies

S. NO	Formulations	%Drug released at 15 mins	%Drug released at 30 mins	%Drug Released at 60 mins	Zero-order rate constant	The first-order rate constant K(min-1)	Peppas Model Constant	Higuchi Model Constant
1.	F1	66.1±0.2	85.4±0.10	96.5±0.15	0.7299	0.9908	0.9465	0.9427
2.	F2	69.1±0.3	92.8±0.11	100±0.45	0.7276	0.995	0.8674	0.9204
3.	F3	67.5±0.1	85.2±0.45	97.7±0.62	0.7402	0.9861	0.9034	0.9407
4.	F4	71.2±0.25	93.6±0.15	100.3±0.32	0.7082	0.9902	0.8253	0.9081
5.	F5	80.9±0.21	95±0.28	100.6±0.78	0.6093	0.9942	0.8389	0.8662
6.	F6	78.2±0.32	93.5±0.51	97.2±0.52	0.6055	0.9912	0.8727	0.8667
7.	F7	87.1±0.33	98.5±0.45	99.9±0.32	0.4809	0.9938	0.8894	0.776
8.	F8	87.4±0.42	95.2±0.56	97.8±0.20	0.4831	0.9367	0.7771	0.7751
9.	F9	74±0.50	89.6±0.22	94.1±0.27	0.6391	0.9775	0.7811	0.8665

Table No.10 Observation Of Dissolution Studies

5. Differential Scanning Colorimetry Studies.



EVALUATION of FAST DISINTEGRATING TABLET

1.PRE COMPRESSION EVALUATION

Formulations	Angle of repose (θ)	Bulk density (gr/ml)	Tapped density (gr/ml)	Hausner's ratio	Carr's index (%)
B1	32.61	0.488	0.640	1.33	24.99
B2	33.03	0.515	0.644	1.24	19.99
B3	32.00	0.549	0.640	1.16	14.29

Table No.11 Observation Table Of Pre Compression Evaluation Of Tablet

2.POST COMPRESSION EVALUATION

Formulations	Weight Variation (mg)	Hardness (kg /cm^2)	Friability (%)	Disintegration time (sec)	Wetting time (sec)	Water Absorption Ratio (%)	Drug content
B1	356.10 ± 1.0	3.2 ± 0.2	0.88±0.010	25 ± 1	30 ± 0.1	55.10 ± 1.6	99.42 ±1.02
B2	352.68 ± 1.0	3.2 ± 0.2	0.79±0.020	13 ± 1	25 ± 0.1	60.61 ± 7.2	99 ± 0.25
B3	355 ± 1.1	3.1 ± 0.2	0.53±0.015	12 ± 5	15 ± 0.3	64.10 ± 4.2	100.45 ± 0.70

Table No.12 Observation Table Of Post Compression Evaluation Of Tablet

Dissolution Studies

Time (min)	B1	B2	B3
0	0	0	0
5	58.5 ± 0.87	42.16 ± 0.46	58.4 ± 0.33
10	78.3 ± 0.78	56.83 ± 0.57	75.6 ± 0.47
15	80.33 ± 0.87	65.5 ± 0.87	81.56 ± 0.89
20	84 ± 0.98	88.6 ± 0.76	78.5 ± 0.89
25	88.77 ± 1.1	90.66 ± 0.9	92.66 ± 0.83
30	91.77 ± 0.9	96.4 ± 1.1	99.10 ± 0.67

Table No.13 Observation Table Of Dissolution Studies

Summary and conclusion

- Increased the solubility of the drug by using the solid dispersion technique.
- Successfully formulated solid dispersion of Aprepitant with sodium starch glycolate having 94% drug released and 98 % drug content.
- After a selection of optimized solid dispersion incorporated into Fast disintegrating tablet by using direct compression method.
- Increased the disintegration time of table in 12 seconds tablet get disintegrated, % drug release is 99.10%.

REFERENCES

1.Rao B Chandrasekhara, 2020, Dissolution enhancement of poorly soluble drug aprepitant by hot-melt extrusion method using hydrophilic polymer: A solid dispersion technique, Research journal of pharmaceutical, biological and chemical sciences, page no 1469-1485.

2. Singh & Sarangi, 2020, Solid dispersion a novel approach for enhancement of bioavailability of poorly soluble drugs in oral drug delivery system, Global journal of pharmacy & pharmaceutical science, vol 3, Issue 2, Page no.01-10.

3.Comoglu & Ozyilmaz, 2019, Orally disintegrating tablets novel dosage froms for pediatric use, Pharmaceutical development and technology, vol 24, no7, page no 902-914.

4. Barmpalexis Panagiotis, 2019, Development of a new aprepitant liquisolid formulation with the aid of artificial neural networks and genetic programming, AAPS pharma SciTech, vol 10, page no -893.

5. Spiegel DR, Pattison A, Lyons A, Ansari U, Mccroskey AL, Luehrs E, *et al*. The role and treatment implications of peripheral and central processing of pain, pruritus, and nausea in heightened somatic awareness: a review. Innov Clin Neurosci 2017;14:11–20.

6.Merck and Co. Inc. EMEND® (aprepitant) capsules. US FDA Label, Whitehouse Station, NJ; 2003.

7.Warr DG MD. Chemotherapy-and cancer-related nausea and vomiting. Curr Oncol 2008;15:S4–9.

8.Yogesh S. Thorat, et. al, 2017, solubility enhancement conventional and novel approaches pharmaceutics science and research, project impact factor, vol 15, page no 725-735.

9.Poovi Ganesan, et. al. -2015 Developed methods for characterization and solubility, Asian journal of pharmaceutics science vol10, issue 5, page no.433-441.

10.Jain N K, the textbook of Pharmaceutical product development published by CBS publishers and distributors Pvt. Ltd., New Delhi, first edition, 2006. Page no.335.

11.Tripathi K.D., the textbook of essential of medical pharmacology, published by Jaypee b Brothers Medical Publishers, New Delhi, India, 14th edition, 2010.

12.Kommuru, T. R., et. al,2001 Self-emulsifying drug delivery system of coenzyme Q10: Formulation development and bioavailability assessment. Int. J. Pharm. vol 212, page no233- 246.

13.Stephenson J, Davies A. An assessment of etiology-based guidelines for the management of nausea and vomiting in patients with advanced cancer. Support Care Cancer 2006;14:348–53.

14.Hickok JT, Roscoe JA, Morrow GR, Bole CW, Zhao H, Hoelzer KL, *et al.* 5-Hydroxytryptamine-receptor antagonists versus prochlorperazine for control of delayed nausea caused by doxorubicin: a URCC CCOP randomised controlled trial. Lancet Oncol 2005;6:765–72.

15.Hickok JT, Morrow GW, Roscoe JA. Prevalence and severity of acute and delayed NV association with 3 highly emetogenic chemotherapies. Supportive Care Cancer 2001;9:289.

16.Hofman M, Morrow GR, Roscoe JA. Cancer patient's expectations of experiencing treatment-related side effects. Cancer 2004;101:851–7.

17. Aulton ME (1998) Pharmaceutics: The science of dosage form design(10th edn). Edinburgh: Churchill Livingstone, pp 63-64.

18.Costa P, Sarmento B, Vasconcelos T,2009 Solid dispersions as a strategy to improve oral bioavailability of poorly water soluble drugs. Drug Discov Today 12(23-24): 1068-1075.

19. Arunachalam M, Karthikeyan M, 2010 Solid dispersions A review Current Pharm Res 1(1): 82-90.

20. Mooter GV,2012 The use of amorphous solid dispersions: A formulation strategy to overcome poor solubility and dissolution rate. Drug Discov Today 9(2): 9-85.

21.Karavas E, Georgarakis E, Sigalas MP, Avgoustakis K, Bikiaris D,2007)Investigation of the release mechanism of a sparingly water-soluble drug from solid dispersions in hydrophilic carriers based on the physical state of drug, particle size distribution, and drug–polymer interactions. Eur J Pharm Biopharm 66(3): 334-347.

22.Kapoor B, Kaur R, Kaur S,2012 Solid Dispersion An Evolutionary Approach for Solubility Enhancement of Poorly Water-Soluble Drugs. Int J Rec Adv Pharm Res 2(2): 1-16.

23.Mura P, Fauccia MT, 2001 The influence of polyvinylpyrrolidone on naproxen complexation with hydroxypropyl-b-cyclodextrin. Eur J Pharm Sci 13(2): 187-194.

24.Giri TK, Alexandra, Tripathi DK, 2010, Physicochemical Classification and Formulation Development Of Solid Dispersion Of Poorly Water-Soluble Drugs: An Updated Review, Int.J.PharmBio. Arch. 1(4):309-324.

25.Sekiguchi K, Obi N, 1961, Studies on Absorption of Eutectic Mixture. I. A comparison of the behavior of a eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man, Chem. Pharm. Bull. 9:866-872.

26. Mogal SA, Gurjar PN, Yamgar DS, KamodAC,2012, Solid dispersion technique for improving solubility of some poorly soluble Drugs. 4(5): 1574-1586.

27.Patidar K, Kshirsagar Md, Saini V, Joshi Pb, Soni M; 2011, Solid Dispersion Technology: A Boon for Poor Water-Soluble Drugs, Ind.J.Novel drug del. 3(2): 83-90.

28.Sayyad A, Sawant SD.2010, Techniques of solubility enhancement of poorly soluble drug with special emphasis on solid dispersion, Journal of pharmacy research. 3: 2494- 2501.

29.S.S.Biradar, S.T.Bhagavati and I. J. Kuppasad, 2006, Fast Dissolving Drug Delivery Systems: A Brief Overview, Internet J. Pharmacology, 4(2).

30.Kuccherkar B.S., BadhanA.C., Mahajan H.S.,2003Mouth dissolving tablets: A novel drug delivery system, PhrmaTimes, 35, 3-10.

31.Kaushik D, Dureja H., Saini T. R.,2004, Mouth Dissolving Tablets: A review, Indian Drugs, 41(4), 187-193.

32.Amin A. F., Shah T. J., Bhadani M. N., Patel M. M.,2005 Emerging trends in orally disintegrating tablets, www.pharminfo.net.

33.Renon J.P. and Corveleyn S., Freeze-dried rapidly disintegrating tablets, US Patent No. 6,010,719, 2000.

34. Papageorgiou, G.Z.; Bikiaris, D.; Karavas, E.; Politis, S.; Docoslis, A.; Park, Y.; Stergiou, A.; Georgarakis,2006, Effect of physical state and particle size distribution on dissolution enhancement of nimodipine/PEGsoliddispersions prepared by melt mixing and solvent evaporation. AAPS J. 8, E623–E631.

35. Vithani, K.; Maniruzzaman, M.; Slipper, I.J.; Mostafa, S.; Miolane, C.; Cuppok, Y.; Marchand, D.; Douroumis,2013, Sustained release solid lipid matrices processed by hot-melt extrusion(HME).Colloids Surf. B biointerfaces 110, 403–410

36. Janssens, S.; de Armas, H.N.; Roberts, C.J.; Van den Mooter, G., 2008, Characterization of ternary solid dispersions of itraconazole, PEG 6000, and HPMC 2910 E5. J. Pharm. Sci 8, 97, 2110–2120.

37.. Meng, F.; Gala, U.; Chauhan, H, 2015, Classification of solid dispersions: Correlation to (i) stability and solubility(ii) preparation and characterization techniques. Drug Dev. Ind. Pharm, 41, 1401–1415.

38. Prasad, D.; Chauhan, H.; Atef, E, 2014, Amorphous stabilization and dissolution enhancement of amorphous ternary solid dispersions: Combination of polymers showing drug-polymer interaction for synergistic effects. J. Pharm. Sci.103, 3511–3523.

39. Fousteris, E.; Tarantini, P.A.; Karavas, E.; Bikiaris, D. 2013, Poly(vinyl pyrrolidone)–poloxamer-188 solid dispersions prepared by hot-melt extrusion. J. Therm. Anal. Calorim. 113, 1037–1047

40. Wu, D.; Paul, D.J.; Zhao, X.G.; Douglas, S.D.; Barrett, J.S.2009, A sensitive and rapid chromatography-tandem mass spectrometry method for the quantification of the novel neurokinin-1receptor antagonist aprepitant in rhesus macaque plasma, and cerebral spinal fluid, and human plasma with application in translational NeuroAIDs research. Eur. J. Pharm. Biopharm. 49,739–745.

41. Navari, R.M.; Reinhardt, R.R.; Gralla, R.J.; Kris, M.G.; Hesketh, P.J.; Khojasteh, A.; Grote, T.H.; Pendergrass, K.; Grunberg, S.M.; Carides, A.D.; et al. 1999, Reduction of cisplatin-indued emesis by a selective neurokinin-1-receptor antagonist. N. Engl. J. Med.340, 190–195.

42. Maulvi, F.A.; Dalwadi, S.J.; Thakkar, V.T.; Soni, T.G.; Gohel, M.C.; Gandhi, T.R. 2017, Improvementof dissolution rate of aceclofenac by solid dispersion technique. Powder Technol. 207, 47–54.

43. Frizon, F.; Eloy, J.O.; Donaduzzi, C.M.; Mitsui, M.L.; Marchetti, J.M.2013, Dissolution rate enhancement of loratadine in polyvinylpyrrolidone K-30 solid dispersions by solvent methods. Powder Technol. 235, 532–539

44. Soumya M, Babu MM, Aparna K, Himabindu P.2012, A review on fast-dissolving drug delivery systems-a pioneering drug delivery technology. Indian J Nov Drug Deliv 4:252-63.

45. Mahtre SS, Khanekar PV, Momin MM.2009, Rapid dissolve oral dosage forms A detailed review. J Glob Pharm Technol.10:1-14.

46. Patel HA, Patel JK, Patel KN, Patel RR.2010 Studies on formulation and in vitro evaluation of fast dissolving tablet of domperidone.Int J Pharm Sci 2:470-6.