JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue

JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)

An International Scholarly Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND EVALUATION OF PHENYTOIN SODIUM FAST DISSOLVING TABLRTS BY DITRCT COMPRESSION METHOD USING VARIOUS SUPERDISINTEGRANTS

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ABSTRACT:

The objective of the present study was to develop Phenytoin sodium Fast dissolving tablets to improve the versatility, patient counselling and accurate dosing. The FDT's are prepared by direct compression method using different concentrations of superdisintegrants. A combination of Crosspovidone & Cross carmellose sodium is used as superdisintegrants. The prepared tablets are evaluated for pre-compression & Post compression parameters. A total of nine formulations are prepared with varied concentrations of superdisintegrants and they are compared with marketed product Dilantin tablets and the results showed that formulation F_5 was found to be the best among the all 9 Phenytoin sodium FDT's as it exhibited faster disintegration time when compared to other formulations & showed a drug release of 99.25% drug release at the end of 60mins.

INTRODUCTION:

Oral administration is the most popular route about 50-60% of total dosage forms are administered due to ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates) and most importantly patient compliance. Solid oral delivery systems do not require sterile conditions and are therefore less expensive to manufacture. One important drawback of solid dosage forms is the difficulty in swallowing (dysplasia) or chewing in some patients particularly pediatric and geriatric patients. The problem of swallowing is common phenomenon in geriatric patient due to fear of choking. Hand tremors, dysphasia in children's due to underdeveloped muscular and nervous systems, in schizophrenic patients resulting in poor compliance with oral tablet drug therapy

which leads to reduced overall therapy effectiveness. Difficulties in swallowing of tablet and capsule also occur when water is not available, in diarrhea, coughing during the common cold, allergic condition and bronchial infection.

MATERIALS AND INSTRUMENTS

MATERIAL USED

S.No	Material name	Mfg./suppliers details
1	Phenytoin Sodium	Gift sample (Dr.Reddy's Laboratories, hyd.)
2	Di calcium phosphate	Nice chemical[p] LTD, Kerala
3	Croscarmellose sodium	Yarrow chem [p], Mumbai
4	Crospovidone	Yarrow chem [p], Mumbai
5	Magnesium stearate	Indian research [p], Chennai
6	Talc	Nice chemical[p] LTD, Kerala
7	Potassium Di hydrogen ortho phosphate	Finar Limited, Gujarat
8	Sodium Hydroxide	Dr.Reddy's Laboratories, hyd.

INSTRUMENTS USED

S.No	Equipment name	Mfg./suppliers details
1	Digital balance	Infra instruments PVT.LTD Chennai.
2	UV-Visible spectrophotiometer	Analytical Technologies.LTD
3	Hot air oven	Infra instruments PVT.LTD Chennai.
4	Tapped density apparatus (USP)	Kshitif innovation, kacha bazaar, ambala.
5	Rotary compression machine	Cemach ahmadabad.india
6	Friabilator	Kshitif innovation, kacha bazaar, ambala.

7	Hardness tester	Kshitif innovation, kacha bazaar, ambala.
8	Disintegration appraratus	Kshitif innovation, kacha bazaar, ambala.
9	Dissolution apparatus	Labindia
10	Digital PH meter	Infra instruments PVT.LTD Chennai.
11	Vernier calipers	Infra instruments PVT.LTD Chennai.
12	Water bath shaker	SG Scientific LTD gujarat.

METHODOLOGY &PREFORMULATION STUDIES

METHODOLOGY STUDIES

PREFORMULATION STUDIES

Evaluation of the lubricated blend:

The lubricated blend is evaluated for physicochemical characteristics like angle of repose (flow properties), bulk density, tapped density, compressibility index, hausner ratio and the data is shown as given in the Table No.:13.The detail procedure of the test as given as below.

Angle of repose:

Flow properties of powders are important in the manufacture of tablets. Because non-uniform flow will result in variation in weight of the tablets, which in turn affects the dose of the drug per tablet. It also creates problem of hardness during compression of tablets. It was measured by the fixed funnel method using the procedure as follows:

A glass funnel was selected to with a stem of 15-30 mm and fixed to the funnel stand, graph paper was placed on table. Granules were allowed to flow to form a heap. The circumference of the heap was marked and measured the height of the pile using two rulers. The height was measured and noted it as (h).The area (πr^2) was determined, radius(r)was calculated and substituted in the formula to obtain the angle of repose ($\theta=\tan^{-1} h/r$). Repeated the experiment twice more and calculated average angle of repose

Bulk density:

Weigh accurately 1.5 g of lubricated blend, which was previously passed through 20# sieve and transferred in 100 ml graduated cylinder, Carefully level the powder without

compacting, and read the unsettled apparent volume (VO) Calculate the apparent bulk density in gm/ml by the following equation.

Bulk density=Weigh of powder/ Bulk volume

Tapped density:

Weigh accurately 1.5 g of drug, which was previously passed through 20# sieve and transferred 100 ml graduated cylinder.Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop

under its own weight using mechanically tapped density tester the provides a food drop of 14±2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped measure the tap volume (V2) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped value volume (V2) to the nearest graduated units. If the difference between the two volumes is less than 2% the final the volume (V2) calculate the tapped bulk density in gm/ml by the following equation

Tipped density=Weigh of powder/Tapped volume.

Carr's index:

Compressibility index of the powder bland was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down.

The formula for Carr's index is as below equation:

Can's index (%) = [(TD-BD) ×100] /TD

Hausner's Ratio:

Hausner's Ratio is a number that is correlated to theFlowability of a powder. The formula for Hausner's ration is as below equation.

Hausner's Ratio=TD/BD.

The tables were evaluated for the following parameters:

- General appearance
  - Colour
  - Odour
  - Shape
- Thickness
- Diameter
- Hardness test
- Weight variation test
- Friability
- In vitro disintegration time
- Wetting Time
- In vitro dissolution studies
- Drug content uniformity
- Assay
- Comparative studies of the final formulation with marked formulation

Evaluation of tablets:

General appearance:

Five tablets from all batches were randomly selected and organoleptic properties such as colour, odour and shape were evaluated .

Thickness:

The thickness of five tablets for all batches was measured using vernier calipers .The diameter was also determined by using vernier calipers.

Hardness test:

Hardness of for five tablets for all the batches was tested using "Monsanto" Hardness tester. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet and a zero reading is taken .The upper plunger is then forced against a spring by turning a thread bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force, which is a measure of hardness..

Weight variation test:

Weighed 20 tablets selected at random and calculated the average weight. Then percentage deviation from the average was calculated. Acceding to IP standards, not more that two of the individual weight deviate from the average weight by more than the percentage shown in the below table, and none deviates by more than twice that percentage.

IP standards of percentage of weight variation:

Average weight of tablet	% deviation
80 mg or less	10
More than 60 mg but less than 250 mg	7.5
250 mg or more	5

Since, the tablets made have the average weight in the range of 200 mg, the limit of % deviation to be taken as ±5.

Friability test:

The Roche friabilator was used for this test, This device subjects as number of tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm by dropping the tablets from a distance of six inches with each revolution Normally, a pre weighed 10 tablets are placed in the friabilator which is operated for 100 revolutions. The tablets are then dusted and reweighed.

Standards:

Compressed tablets that lose less than 1.0% of their weight are generally considered acceptable.

In vitro disintegration test:

This test is performed to ensure disintegration of tablets in water. Disintegration time is considered to be one of the important criteria in selecting the best formulation. To achieve correlation between disintegration time in vitro and in vivo (in oral cavity) several methods were proposed, developed and followed at their convenience. One of the simple methods followed is described below. One tablet is introduced to one tube of disintegration apparatus IP. The assembly is suspended in the beaker containing 900 ml Phosphate buffet P^H 6.8 and the apparatus is operated until the tablet disintegrated.

Standards:

The tablets must disintegrate less than 60 seconds when examined by the disintegration test for tablets.

Wetting time: To measure Wetting time of the Tablet, a piece of Tissue paper folded twice was placed in a small petri dish (Internal Diameter is= 65 cm) containing 5 ml of Distilled water. A Tablet placed on the paper, and the time for complete wetting of the tablet was measured in seconds.

Assay:

The assay of the proposed method was ascertained by performing assay of the standard drug with reference to the sample drug.10 tablets of marketed sample were taken and crushed, average weight is recorded. Equivalent weight to average weight is weighed and taken in to 100ml volumetric flask small quantity of P^H 6.8 phosphate buffer is taken and sonicated for 30 minutes. After sonication filter it and the volume is adjusted with 6.8 phosphate buffer to 100ml. The concentration was diluted to 10mcg/ml and the absorbance was observed at 220 nm and the % purity of the drug was calculated using the formula.

$$\% \text{ purity} = \frac{\text{test absorbance}}{\text{standard abssorbance}} \times \text{Dilution factor} \times \text{Label claim}$$

Standards:

Assay for Phenytoin Sodium Orally disintegrating tablets should be not less than 90% and not more than 110% of the standard amount of Phenytoin Sodium. **Drug content uniformity:**

Five tablets of various formulations were weighed individually and powdered. The power equivalent to average weight of tablet was weighed and drug was extracted in phosphate buffer PH 6.8, the drug content was determined measuring the absorbance at 220 nm using a UV- visible spectrophotometer (Analytical).

Standards:

Phenytoin Sodium table contains not less than115% of the stated amount of Phenytoin Sodium.

In vitro dissolution studies:

Dissolution study was conducted to determine the drug release from the table using USP apparatus type-II (paddle type,50 rpm). A 10 ml sample was withdrawn at 5 minutes time intervals and replace by an equal volume of prewarmed phosphate buffer PH6.8,.samples withdrawn were filtered through whatmann filter paper(0.45 micron). The amount of phenytoin sodium released was analysed at 220 nm using a UV double-beam spectrophotometer.

RESULTS AND DISCUSSION:

Standard graph for phenytoin sodium:

Preparation of standard stock solution:

Standard stock solution of Phenytoin sodium was prepared by dissolving accurately weighed 100 mg of Phenytoin sodium in the lade quantity of phosphate buffer pH 6.8 in 100 ml volumetric flask. Volume was made up with phosphate buffer pH 6.8 up to the mark in order to get standard stock solution containing drug 1000 µg/ ml.

Spectrophotometric scanning of Phenytoin sodium:

From the stock solution, ultraviolet scan was taken between the wave lengths: 200-400 mm (Figure No. 6) which gave s highest peak at 220 nm and the same was selected for Phenytoin sodium estimation.

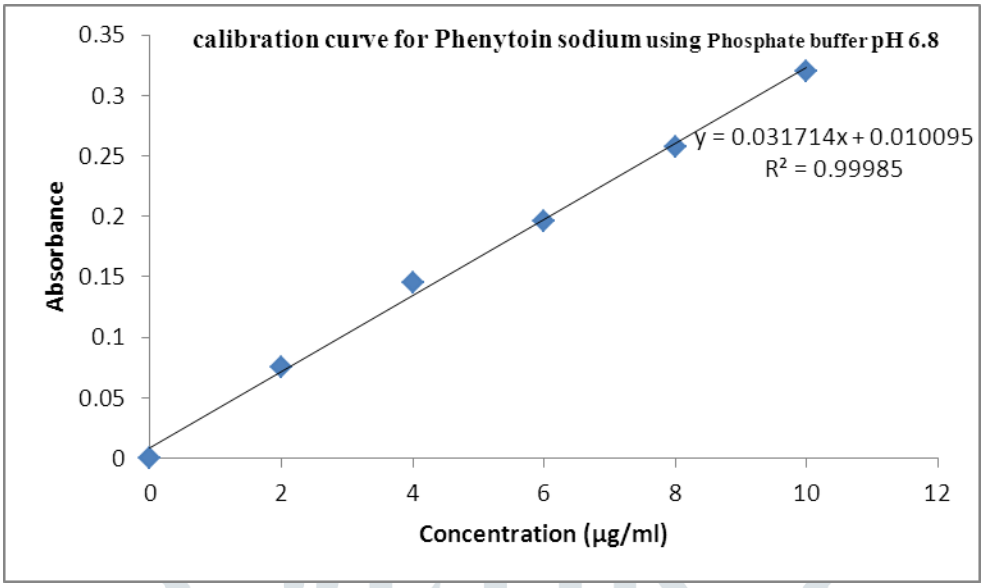
Preparation of standard plot of phenytoin sodium:

From the standard stock solution (1000µg/ml) series of dilutions were made to get 2,4,6,8 & 10 µg/ml solution using Phosphate buffer pH 6.8 and corresponding absorbance was measured at 220 nm in a UV-Visible spectrophotometer and the absorbance values are listed as shown in Table No: 11. A standard graph was drawn taking Concentrating on X-axis and Absorbance on Y-axis .

CONSTRUCTION OF STANDARD CURVE FOR PHENYTOIN SODIUM:

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.079
3	4	0.148
4	6	0.199
5	8	0.262
6	10	0.324

STANDARD CURVE FOR PHENYTOIN SODIUM:



COMPOSITON OF DIFFERENT FORMULATIONS:

NameofIngredients	QuantityofIngredientspereach Tablet(mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Phenytoinsodium	100	100	100	100	100	100	100	100	100
DiCalciumPhosphate	46	52.25	58.5	52.25	58.5	64.75	58.5	64.75	71
Crospovidone	25	25	25	18.75	18.75	18.75	12.5	12.5	12.5
Croscarmellosesodium	25	18.75	12.5	25	18.75	12.5	25	18.75	12.5
MagnesiumStearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
TotalWeight	200	200	200	200	200	200	200	200	200

PRECOMPRESSION PARAMETES:

Parameter batch no	Angle of repose (Ɵ in °)	Bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausners ratio
F_1	27.522	0.560	0.678	17.42	1.110
F_2	27.361	0.714	0.372	17.79	1.121
F_3	26.98	0.716	0.871	17.82	1.116
F_4	27.74	0.45	0.597	24.64	1.227
F_5	27.57	0.64	0.792	23.61	1.203
F_6	27.154	0.605	0.790	23.42	1.205
F_7	27.08	0.432	0.586	23.28	1.256
F_8	26.95	0.586	0.780	21.87	1.231
F^9	26.54	0.587	0.780	21.74	1.228

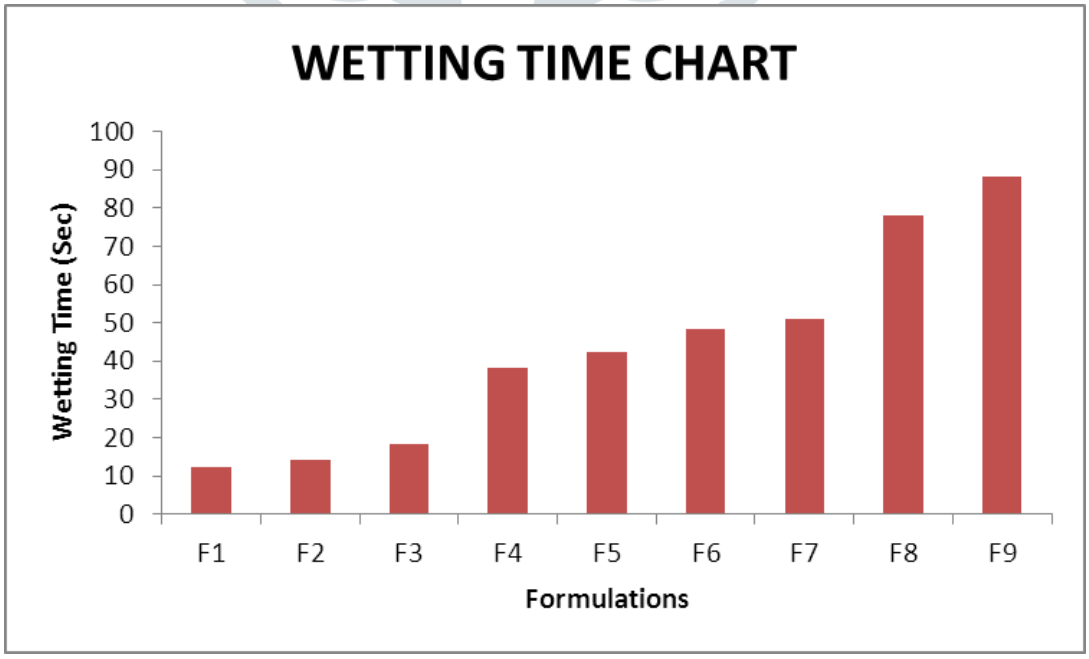
POSTCOMPRESSION PARAMETERS:

S.No	Formulation Code	Hardness(kg/cm^2)	Thickness(mm)	Friability(%)	WeightV ariation	DrugCo ntent(%)	Wetting Time(sec)	Disintegration Time(sec)
1	**F_1**	**3.12±0.12**	**3.41±0.8**	**0.58±0.2**	**200.69±0.9**	**99.45±1.1**	**12.18±1.3**	**9.13±0.5**
2	**F_2**	**3.21±0.15**	**3.45±0.7**	**0.64±0.3**	**201.46±1.9**	**99.28±0.7**	**14.09±1.3**	**9.32±0.6**
3	**F_3**	**3.21±0.11**	**3.62±0.5**	**0.62±0.1**	**200.67±1.1**	**99.41±0.5**	**18.10±1.7**	**10.30±0.7**
4	**F_4**	**3.21±0.14**	**3.53±0.6**	**0.62±0.19**	**200.55±2.2**	**99.53±0.4**	**38.23±1.5**	**12.5±0.9**
5	**F_5**	**3.15±0.16**	**3.55±0.4**	**0.52±0.30**	**201.48±1.1**	**99.39±0.6**	**42.31±1.1**	**12.8±0.8**
6	**F_6**	**3.53±.10**	**3.70±0.2**	**0.65±0.04**	**201.04±2.0**	**99.92±0.4**	**48.2±1.2**	**13.21±0.7**
7	**F_7**	**3.34±0.15**	**3.55±0.6**	**0.61±0.3**	**200.48±1.4**	**99.23±1.0**	**51.16±1.5**	**28.18±1.2**
8	**F_8**	**3.32±0.12**	**3.66±0.4**	**0.57±0.4**	**199.68±0.3**	**99.51±0.8**	**78.11±1.9**	**42.39±0.5**
9	**F_9**	**3.27±0.13**	**3.75±0.1**	**0.62±0.4**	**200.45±0.9**	**99.49±0.9**	**88.04±1.2**	**53.20±2.2**

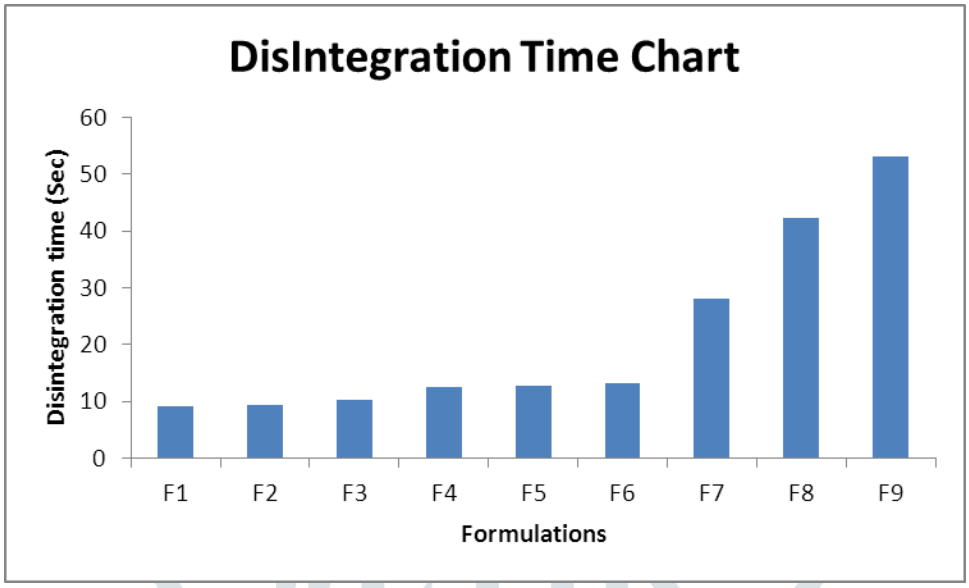
INVITRO-DISSOLUTION STUDIES:

S.No	Time(min)	*IN-VITRO*DISSOLUTIONPROFILE %CDR								
		F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
1	0	0	0	0	0	0	0	0	0	0
2	5	51.20	47.31	43.52	47.21	43.59	39.5	45.25	40.55	39.28
3	10	81.32	77.13	74.64	79.5	75.52	72.5	77.53	72.64	71.50
4	15	88.51	86.25	82.55	86.31	84.68	80.5	85.64	83.18	80.65
5	20	94.53	91.53	89.58	95.54	92.55	90.5	91.5	89.27	89.45
6	30	96.21	96.59	94.52	97.5	97.28	95.12	95.5	95.11	93.24
7	45	97.98	97.25	97.02	97.68	98.18	97.5	96.29	96.08	94.92
8	60	98.99	97.50	97.03	97.85	99.25	97.55	97.28	97.15	95.34

WETTING CHART:



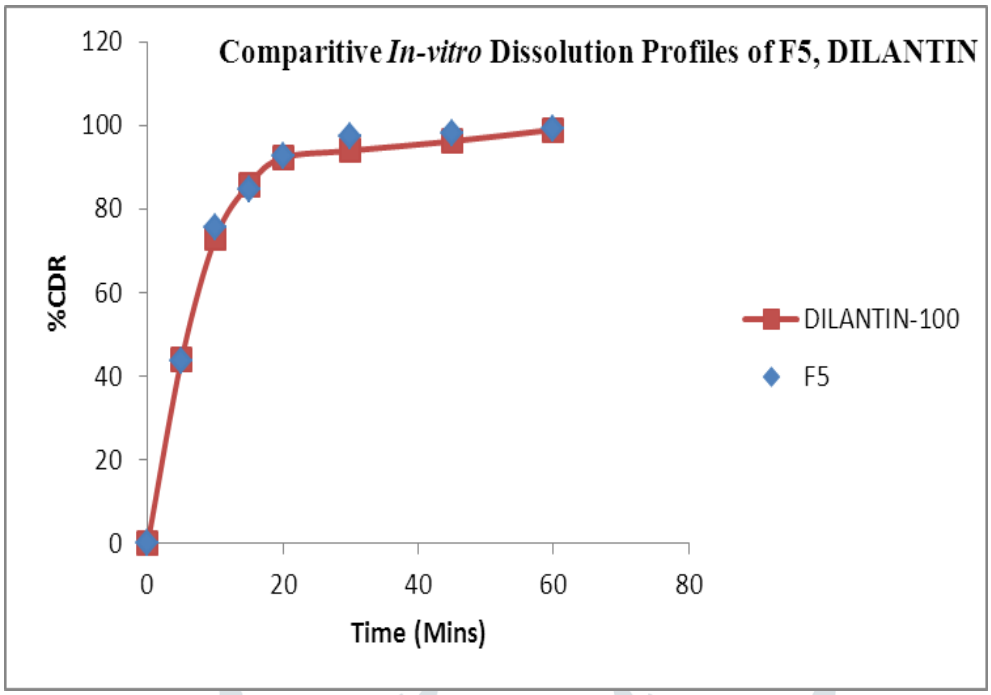
DISITEGRATION TIME CHART:



COMPARISION OF DISOLUTION PROFILE OF FORMULATION F5 WITH DILANTIN:

S.No	Time(min)	F_5	DILANTIN-100
1	0	0	0
2	5	43.59	43.89
3	10	75.52	72.91
4	15	84.68	85.89
5	20	92.55	92.23
6	30	97.28	93.95
7	45	98.18	96.21
8	60	99.25	98.98

COMPARITIVE IN-VITRO DISSOLUTION PROFILES OF F5, DILANTIN



CONCLUSION:

Hence, we may conclude that, Super disintegrant like Crospovidone effectively reduces disintegration time less than 10 seconds. Thus, we are able to achieve our objective of preparing fast dissolving tablets of phenytoin sodium with minimum excipients and simple method of manufacturing. Formulation F_5 was found to be the best among the all 9 Phenytoin sodium FDT's as it exhibited faster disintegration time when compared to other formulations & showed a drug release of 99.25% drug release at the end of 60mins.

REFERRENCES:

1. Alpesh R. Patel. Dharmendra S, Prajapati. Jignyasha A., Raval, fast dissolving films (fdfs) as a newer venture in fast dissolving dosage forms, International Journal of Drug Development & Research, 2(2), 232-246, 2010.
2. Dixit RP.; Puthli SP. Oral strip technology: Overview and future potential. J. Control Release 139(2), 94-10, 2009,
3. Suresh Bandari; Rajender kumar Mittapalli; Ramesh Ganna;MadhusudanRao Y. Orol dispersible tablets: An overview. Asian J Pharm. 2(1), 2-11, 2008.
4. Parakh S.R, Gothoskar A.V: A review of mouth dissolving tablet technologiesPharm. Tech, 27(11) ;92-98, 2003
5. Guidance for Industry Orally Disintegrating Tablets published by centre for drug evolution and research, accessed at http://www.fda gov/eder/ guidance/ index.htm
6. Rakesh Pahwa, Mora Piplani, Prabodh C. Sharma, Dhirender Kaushik and SanjuNanda. Orally Disintegrating Tablets-Friendly to Pediatrics and Geriatries Archivesof Applied Science Research: 2(2), 35-48, 2010.

7. Tejvir Kaur, Bhawandeep Gill, Sandeep Kumar, and G.D. Guptha Mouth DissolvingTablets: A Novel Approach to Drug Delivery, Vol-3, issue 1, 2011.
8. A Guptha, AK Mishra, V Guptha, P Bansal, R Singh, AK Singh. Recent Trends of Fast Dissolving Tablet-An Overview of Formulation Technology. International Journal of Pharmaceutical & Biological Archieves: 1(1), 1-10, 2010.
9. Debjit Bhowmik, Chiranjib.B. Krishnakanth, Pankaj, R Margret Chandira. Fast Dissolving Tablets: An Overiew. Journal of Chemical and Pharmacetical Research: 1(1), 163-177, 2009.
10. William R.P. Fister, Tapash K Ghosh Orally disintegrating tablets. PharmaceuticalTechnology (Product. Technologies and Development issues in Oct 2005).
11. Manoj Ashok Wagh Kothwade Parag Dilip, Kishor Sahebrao Salunkhe, Nayana Vijay Chavan, Vandana Radheshyam Daga. Techniques used in orally disintegrating drug delivery system International Journal of Drug Delivery: 2, 98-107, 2010.
12. Rosic Mc Laughlin, Susan Banbury, and Kieran Crowley. Supplement to Pharmaceutcial technology; Orally Disintegrating Tablets - The Effect of Recent FDA Guidance on ODT Technologies and Applications. 2009.
13. Debjith Bhowmik, Chiranjib, Jyoti Jaiswal, Vinod Dubey, Margret Chanits. Fast Dissolving Tablets. A review on revolution of novel drug delivery system and new market opportunities. Der Pharmacia Lettre: 1 (2), 262-276, 2009.
14. Honey Goel. Parshuram Rai, Vikas Rana, and Ashok k. Trwary Orally Disintegrating Systems: Innovations in Formulation and Technology. Recent Patents on drug delivery & formulation: 2, 258-274, 2008.
15. Bupendra G Prajapathi and Nayan Ratnakar. A Review on Recent patents on Fast Dissolving Drug Delivery System. International Journal of PharmTech. Research 1(3), 790-798, 2009).
16. Dobetti L: Fast-Melting Tablets Developments and Technologies. Pharm. TechnolDrug delivery supplement, 44-50, 2001.
17. Yarwood R: Zydis- A novel, Fast Dissolving Dosage Form Man. Chem.,61:36-37, 1990.
18. Kuldeepak Sharma, William R. Pfister, and Tapash K Ghosh ,Drug Delivery to the Oral cavity Quick-Dispersing Oral Drug Delivery Systems, 261-289, 2005.
19. R. Margret Chandra, B.S. Venkateshwarlu, M. V. Kumudhavalli, Debjit Bhowmik, Dr. B. Jayakar. Formulation and Evaluation of the Fast Dissolving Tablets of Aceclofenac. The Pharma Review 164-167, 2008.
20. Suhas M. Kakade, Vinodh S. Mannur, Ketan B. Ramani, Ayaz A. Dhada, Chirag V. Naval, Avinash Bhagwat Formulation and Evaluation of Mouth dissolving tablets of Zolpidem Tartarate by direct compression techniques, Int. J Res Pharm. Sci, Vol-1, Issue-3, 2010, pp:290-295.