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FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLET OF NORTRIPTYLINE

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ABSTRACT

The aim of the present investigation was to develop fast disintegrating tablet of Nortriptyline. Fast disintegrating tablet FDT were prepared by direct compression method. Fast disintegrating tablets containing 10 mg of Nortriptyline were manufactured using direct compression method. Experiments were evaluated for effects of formulation parameters like type & concentration of diluents, concentration of superdisintegrating agent and their interactions on Nortriptyline FDT properties, and Mannitol were used as diluents of different properties in addition to sodium starch Glycolate (SSG), and Crospovidone which was used as a natural superdisintegrant in combination with the synthetic. The obtained results revealed that disintegration time of the optimized FDT formula (12.5 sec. ± 40 sec). FDT composed of Sodium Starch Glycolate in superdisintegrants 10% level was chosen as optimized formula, as it showed the lowest disintegration time with the highest drug release up to 87.42%. These tablets provided low disintegration time and high hardness (3.6±0.15) that are acceptable for FDT.

KEYWORDS: Nortriptyline, Superdisintegrants, Sodium Starch Glycolate, Tablet.

INTRODUCTION

Tablet formulation has been conveniently and practically use for long time.[1] However, problem like swallowing the tablet, dysphasia and hand tremor make it as inconvenient dosage form. Fast disintegrating tablet is one of the dosage forms which improve the above problem.[2] Formulation and development of Nortriptyline fast disintegrating tablet offer an alternative for other dosage form of Nortriptyline (capsule). Nortriptyline is tricyclic antidepressant and used to treat mental disorder. It improved mood fillings of well-being,

relieve anxiety and tension and increases energy level. It act by inhibiting the natural chemical (Neurotransmitters) in the brain. In the present study by formulating fast disintegrating tablet an attempt was made with the aim to enhance drug release.[3] USFDA defined OD tablet as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". Effect of disintegrants at various concentrations on drug release and disintegration time was studied. The market survey revealed that there are no such types of formulation existing so it was thought to formulate fast dissolving tablet.[5] Nortriptyline is commercially available in market in many dosage forms as conventional tablets. Tablets have many advantages as: unit dosing, good stability, easy manufacturing methods, small package size and easy handling. FDTs formulations of Nortriptyline have the advantages of solid dosage forms and are useful for Anti-depressant with improved patient compliance and to help patients of all age groups who have difficulty in swallowing.

- To fulfill these medical needs, formulators have considerable efforts for developing a novel type of dosage form for oral administration known as fast disintegrating tablets.
- Reduced the side effect.
- Improve the patient compliance.
- Faster onset of action.

MATERIAL AND METHOD

The drug, excipients and chemicals / reagents used for various experiments are enlisted as follows.

Table No. 1: List of chemicals along with grades and their sources.

Sr.No.	Name	Category	Company
1	Nortriptyline	API	Pure Chem. Gujarat
2.	Microcrystalline cellulose (MCC)	Binder	Research-lab Fine chem. Industries, Mumbai.
3.	Mannitol	Diluents	S.D.Fine Ltd.Mumbai
4.	Crosprovidine	Superdisintegrant	Meher chem. Mumbai.
5.	Sodium Starch Glycolate (SSG)	Superdisintegrant	Research-lab fine chem. industries Mumbai.
6.	Magnesium Stearate	Lubricant	Research-lab fine chem. industries Mumbai.
7.	Aerosil-200	Anticaking Agent	Research-lab fine chem. industries Mumbai.
8.	Vanilla	Flavouring Agent	Meher chem., Mumbai.

Method of formulation

- Fast disintegrating tablet of Nortriptyline were prepared by direct compression method according to the formulae given in the table.
- All the ingredients were passed through 40 mesh sieve separately.
- Then the ingredients were weighed mixed in geometrical order and tablet were compressed at 6mm size to get tablet of 100 gm weight using a rotary clit 10 station compression machine.

Table no: 2 Formulation Table.

Formulation	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Nortriptyline	10	10	10	10	10	10
Microcrystalline cellulose (MCC)	28	28	28	28	28	28
Mannitol	50	47.5	45	50	47.5	45
Crospovidone	10	12.5	15	-	-	-
Sodium Starch Glycolate (SSG)	-	-	-	10	12.5	15
Magnesium Stearate	0.2	0.2	0.2	0.2	0.2	0.2
Aerosil-200	1.8	1.8	1.8	1.8	1.8	1.8
Vanilla	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total	100	100	100	100	100	100

RESULT AND DISCUSSION

Fast Disintegrating Tablet were prepared & evaluated. In present study 6 formulations with variable concentration of polymer were prepared & evaluated for physiochemical parameters, in vitro release studies.

Preparation of standard curve of Nortriptyline

Standard curve of Nortriptyline was determined by plotting absorbance V/s concentration at 239nm & it follows the Beer's law. The result were shown in table no. The R^2 is 0.996 respectively.

Table no.3: Calibration curve of Nortriptyline in Phosphate buffer pH 6.8.

Concentration	Absorbance
0	0
2	0.118
4	0.23
6	0.292
8	0.397
10	0.509
12	0.61

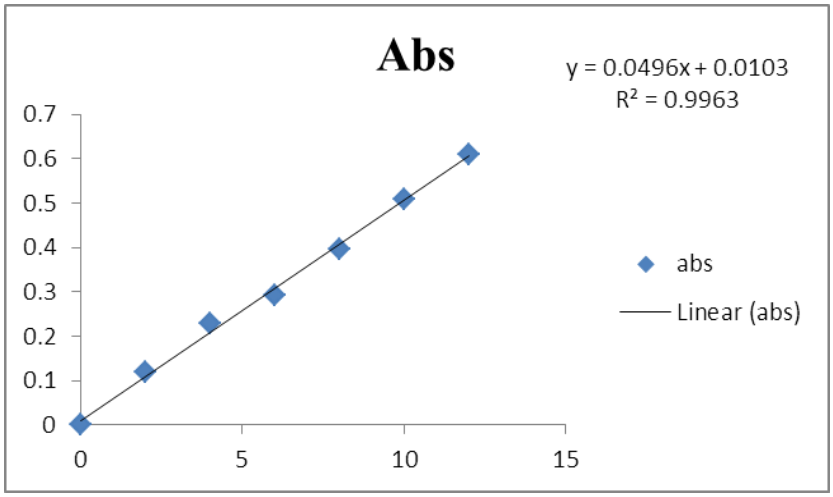

Fig.1: Calibration Curve of Nortriptyline in Phosphate buffer 6.8.

Preformulation Studies[5,6]

A. Determination of melting point

Melting point of Nortriptyline was found in the range of 214 ^{0} c, which complied with the standard, indicating purity of the drug sample.

B. Solubility

Nortriptyline is freely soluble in Phosphate Buffer pH6.8, methanol, Water etc.

C. Hardness

Tablet crushing strength is force required to break the tablets and was done by using Monsanto hardness tester. (3.2±0.40 - 3.6±0.15) Hardness was calculated in Newton's.[8]

C. Compatibility Study

Compatibility studies were performed using FTIR spectrophotometer. The FTIR spectrum of pure drug & physical mixture of drug & polymer were studied.

Precompression studies

The Nortriptyline powder were characterized with angle of repose, bulk density, tapped density, Carr's index, & Hausner's ratio. Angle of repose was less than 30^{0}c & Carr's index value were found to be less than 26 for the formulation of all batches indicating good to fair flow ability & compressibility. Hausner's ratio was less than 1.301 for all the batches indicating good flow properties.

Table no.4: Evaluation (Pre-compression) parameters of all formulation (F1-F6).

Formulation	Bulk density	Tapped density	Angle of repose	Compressibility index	Hausnar's ratio
F1	0.37±0.02	0.41±0.015	28.26±2.37	14.72±0.11	1.58±0.13
F2	0.38±0.02	0.43±0.01	27.82±1.94	11.66±0.12	1.30±0.05
F3	0.35±0.01	0.40±0.01	27.40±0.90	18.17±1.09	1.24±0.04
F4	0.37±0.01	0.44±0.01	27.92±1.97	20.51±0.86	1.17±0.05
F5	0.35±0.01	0.42±0.02	28.04±1.55	13.96±3.16	1.17±0.03
F6	0.37±0.01	0.43±0.015	27.81±1.94	12.32±0.74	1.18±0.06

Post compression studies

The result of uniformity of weight, hardness, friability, & drug content of tablet are given in the Table no.3 below. All the tablet are different batches complied with the official requirement of uniformity of weight as their weight varied between 100.3 & 101.5 mg. the hardness of tablet ranged from 3.00 to 4.3 kg/cm^2 & the friability values less than 0.90% indicating that the tablet were compact & hard. Disintegrating time ranged from 12-50sec. all the formulation satisfied the content of drug as they contained 95.30 to 99.36% of Nortriptyline & good uniformity in the drug content was observed. Thus all the physical attributes of the prepared tablets were found to practically within control.

Table no: 5 Evaluation (Post-compression) parameters of all formulation (F1-F6).

Formulation	Hardness kg/cm^2	Friability (%)	Weight variation	Content uniformity	Disintegration time (sec.)	Thickness
F1	3.5±0.35	0.85±0.13	100.3±0.5	95.23±1.09	45	2.86±0.15
F2	3.3±0.20	0.70±0.06	100.33±1.04	96.32±1.06	40	2.63±0.15
F3	3.2±0.40	0.75±0.01	100.22±0.76	99.18±0.63	37	2.80±0.10
F4	3.5±0.26	0.85±0.02	100±1.32	99.07±0.61	35	2.83±0.15
F5	3.3±0.2	0.77±0.02	100.5±0.5	99.01±0.72	32	2.60±0.2
F6	3.6±0.15	0.85±0.03	100.55±0.76	98.89±0.47	29	2.53±0.20

Disintegration time

For Fast Disintegrating tablets apply the test observes the tablets within the time limit all of the tablets have disintegrated. If 1 or 2 tablets fail to disintegrate completely repeat the test on 12 additional tablets, not less than 16 of the total of 18 tablets tested disintegrate completely. The Nortriptyline tablets were found in between the 12 sec. to 45 sec.

***In-Vitro* Drug Release Studies[7,8]**

In-Vitro drug release studies were carried out using tablet dissolution apparatus USP type III at v50 rpm. The dissolution medium consisted of 900 ml of standard buffer 6.8.themperature maintained at 37.5±1. The sample of 5 ml was withdrawn at predetermined time intervals &

an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. The samples withdrawn were filtered through Whitman filter paper & drug content in each sample was analyzed by UV- visible spectrophotometer at 239 nm.

In-vitro release of optimized formulation of Fast Dissolving tablets of Nortriptyline of formulation batch no. F-6 was found to be almost 87.42% drug releases within 30 minutes.

Table no.6: Dissolution Profiles of Formulations F1-F3.

Time	F1	F2	F3
0	0	0	0
5	5.77	9.56	11.46
10	19.05	22.85	26.64
15	36.14	36.15	39.95
20	53.25	49.46	53.27
25	66.58	64.69	68.5
30	81.82	79.93	83.74

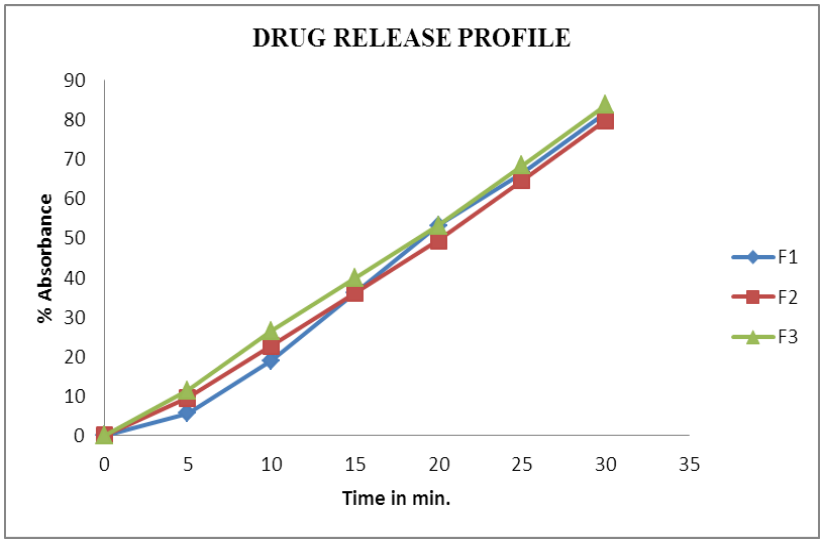

Fig. 2: % drug release for F1-F3.

Table no.7: Dissolution Profiles of Formulations F4-F6.

Time	F4	F5	F6
0	0	0	0
5	7.67	3.88	1.98
10	17.16	15.28	13.37
15	28.56	40.01	30.51
20	43.76	62.99	47.74
25	58.98	70.92	68.87
30	76.11	86.48	87.42

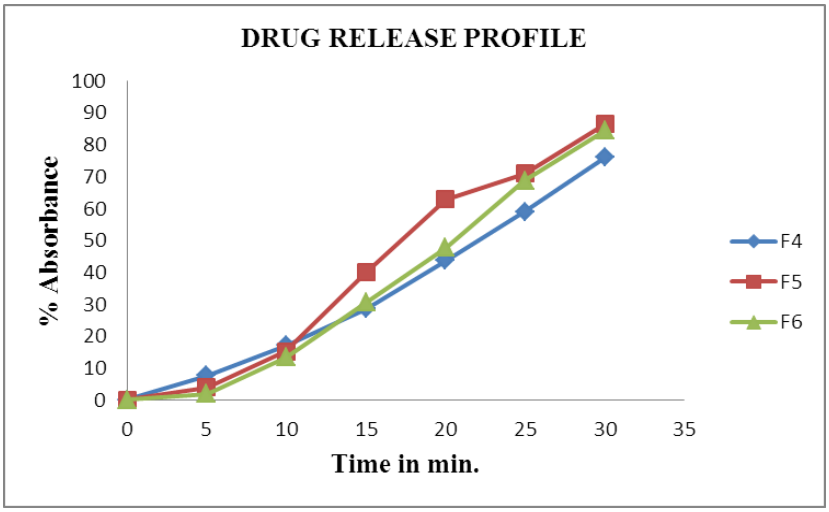

Fig.3: % drug release for F4-F6.

FT-IR RESULT

FTIR studies were conducted and the spectrum was recorded in the range of 4000-400cm-1. Significant interaction between drug and Excipients was not observed. All the spectrum i.e. drug and Excipients were concordant with that of standard IR spectra of pure drug Nortriptyline.

1) Nortriptyline

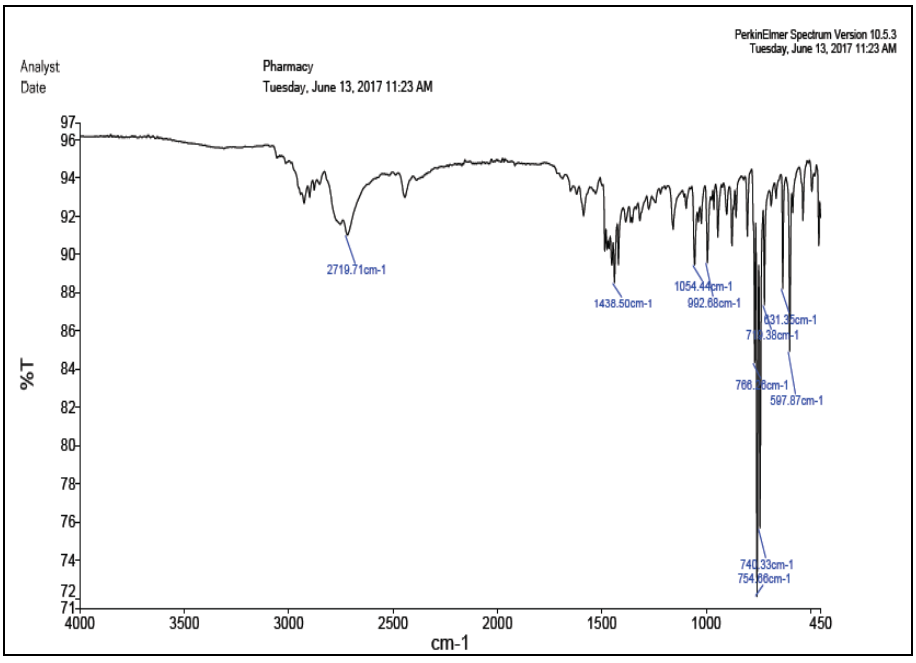

Fig. 4: FTIR of Nortriptyline.

2) Nortriptyline + Sodium Starch Glycolate

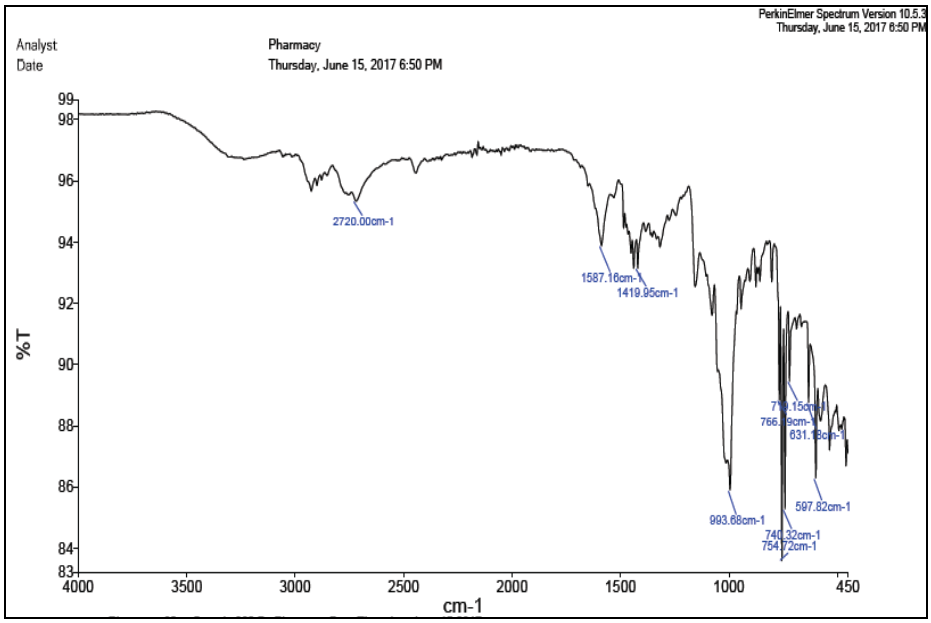

Fig.5 FTIR of Nortriptyline + Sodium Starch Glycolate.

STABILITY STUDIES

Short term stability studies were performed at a temperature of 45 ^{0} c ±1^{0}c over a period of three weeks (21days) on the promising CGPS tablet formulation F6 sufficient number of tablets (10) were packed in amber colored screw capped bottles & kept in hot air oven maintained at 45^{0}c ^{0}c.samples were taken at weekly intervals for drug content estimation. At the end of three weeks period, dissolution test & *invitro* floating studies were performed to determine the drug release profiles.

Table no.8: Accelerated Stability Study.

Sr. No.	Time (min.)	Cum. % drug released ± S.D. 1 st day	Cum. % drug released ± S.D. 21st day
1	00	00	00
2	5	36.14	38.15
3	10	46.30	50.46
4	20	60.49	58.90
5	30	76.75	74.20
6	40	83.15	82.10
7	50	97.54	96.39

CONCLUSION

Pharmaceutical companies are taking advantage of the fast dissolving tablets to extend product line and market the product first. With the rapid growth of fast dissolving tablets, it is

just the matter of time for all drugs to be produced in the fast disintegrating tablet dosage form rather than the conventional tablets.

Six batches of Fast Dissolving tablets of Nortriptyline were successfully prepared using microcrystalline cellulose, Magnesium Stearate, Mannitol, Sodium Starch Glycolate (SSG), Crosspovidone, Aerosil-200in different concentration by direct compression method.

The tablets were evaluated for Pharmacopoeial and non-Pharmacopoeial tests. Based on the results, formulation batch no. F-6 was identified as better formulation amongst all formulations developed for Fast Dissolving tablets of Nortriptyline.

In-vitro release of optimized formulation of Fast Dissolving tablets of Nortriptyline of formulation batch no. F-6 was found to be almost 87.42% drug releases within 30 minutes.

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