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Pharmaceutical Sciences **Research Article……!!!**

DESIGN AND*IN-VITRO* EVALUATION OF FAST DISSOLVING TABLETS OF NORFLOXCIN

K.S. SRILATHA,[1*]PYNSKHEMLIN SYIEMLIEH[1],NIVIN V S[1]and KAVITHA S.K[2]

[1].Department of Pharmaceutics, RR college of Pharmacy Bangalore 560090.

[2.]Department of Pharmacology, RR college of Pharmacy Bangalore 560090

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FOR CORRESPONDENCE:

K.S. SRILATHA *

ADDRESS:

Department of Pharmaceutics, RR college of Pharmacy Bangalore 560090.

ABSTRACT

The objective of the study was to formulate and evaluate fast dissolving tablets of Norfloxacin.It is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a type IItopoisomerase, and topoisomerase IV enzymes necessary to separate bacterial DNA,there byinhibiting cell division. Norfloxacin does not bind to DNA gyrase but doesbind to the substrate DNA. Studysuggests that Cytotoxicity offluoroquinolones is likely a 2-step process involving (1) conversion of thetopoisomerase-quinolone-DNA complex to an irreversible form and (2) generation ofa double-strand break by denaturation of the topoisomerase. Present study demonstrates the formulation of fast dissolving tablets of Norfloxacin with various Superdisintegrants like crospovidone,croscarmellose sodium and sodium starch glycolate .To improve its bioavailability and to provide immediate drug release thereby improving the patient compliance.Norfloxacin showed maximum absorbance at273.8nm so absorbance was measured at the same wavelength and found to obey Beer lamberts law in the concentration range of 10-40 mcg/ml. In the pre formulation study of IR spectra of pure drug with the different Superdisintegrants showed no interaction6 formulation of Norfloxacin fast dissolving tablets were prepared and they were examined for physical properties and appearance like hardness, thickness, weight variation,thickness,hardness, friability uniformity of drug content and*in-vitro* drug release studies. All the parameters were within the limits.

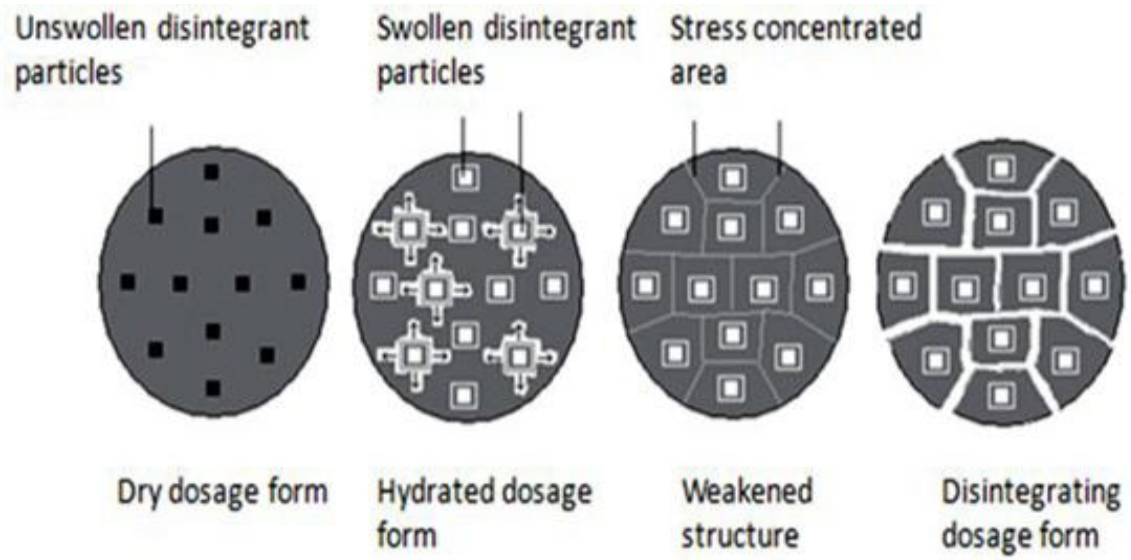
INTRODUCTION:

Solid oral delivery systems do not require sterile conditions and therefore, less expensive to manufacture. A vast variety of pharmaceutical research is directed at developing new dosage forms for oral administration. Most of these efforts have focused on either formulating novel drug delivery systems or increasing the patient compliance.Tablets that rapidly dissolve upon contact with saliva in the buccal cavity could present a solution to those problems, so there is an increased interest in fast dissolving dosage forms for buccal, sublingual and oral administration.The targetpopulation for these fast-dissolving dosage form have generally been paediatric, geriatric and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling or who have little or no access to water are good candidates for fast dissolving drug delivery system. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Oro dispersible tablets, rapimelts, porous tablets, quick dissolving tablets etc.

Superdisintegrants

Disintegrating agents are the substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They enhance moisture penetration and dispersion of the tablet matrix. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces to act under compression to form the tablet. Recently new materials termed as “superdisintegrants” have been developed to improve the disintegrationprocesses. Superdisintegrants are another version of super-absorbing materials with swelling properties as required. These materials swell quickly and are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Superdisintegrants are generally used at a low quantity in the solid dosage form, typically 1 - 10 % by weight relative to the total weight of the dosage unit. Generally, one gram of superdisintegrant absorbs 10-40 g of water or aqueous medium. After absorption, swelling pressure and isotropic swelling of the superdisintegrant particles create stress concentrated areas where a gradient of mechanical properties will exist due to which whole structure will break apart.

Figure 1: Superdisintegrants breaking the tablet structure



MATERIALS AND METHODS

Norfloxacin and Microcrystalline cellulose were obtained fromKAPL Bangalore.All other chemicals were obtained from laboratory grade.

PREPARATION OF FAST DISSOLVING TABLETS OF NORFLOXCIN

Accurately weighed quantities of Superdisintegrants and MCC were taken in a mortar and mixed geometrically, to this required quantity of Norfloxacinwas added and mixed slightly with pestle. Accurately weighed quantity of Mannitol was added and mixed in a mortar and pestle. The powder was passed through sieve no 40 and mixed with the drug blend which is also passed through sieve no 40. The whole mixture was collected in a plastic bag and mixed for 3 minutes. To this Magnesium stearate and talc was added and mixed for 5 minutes. The mixture equivalent to 402mg was compressed into tablets

Table 1: Composition of fast dissolving tablets of Norfloxacin

Ingredients	Formulations					
(weight in mg)	F1	F2	F3	F4	F5	F6
Norfloxacin	300	300	300	300	300	300
Crospovidone	30	20	-	-	-	-
Croscarmellose sodium	-	-	30	20	-	-
Sodium starch glycolate	-	-	-	-	30	20
MCC	30	30	30	30	30	30
Mannitol	40	50	40	50	40	50
Talc	1	1	1	1	1	1
Magnesium Stearate	1	1	1	1	1	1

Figure 2: Fast dissolving tablets of Norfloxacin

Standard graph of Norfloxacinin Phosphate buffer 6.8 pH

A stock solution of 1mg/ml of Norfloxacin was prepared by dissolving 10 mg ofdrug with100 ml ofPhosphate buffer 6.8 pH. The stock solution was serially dilutedto get solutionin the range of 10-50µg/ml and λ max of the solution was found outby scanning from 200-400 nm. The λ max was found to be 273.8 nm.

DRUG-EXCIPIENT COMPATIBILITY STUDIES

Fourier Transform Infrared (FTIR) Spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR spectrophotometer (Perkin Elmer). Pure drug, individual polymers and optimised formulations were subjected to FTIR

study. About 2–3 mg of sample was mixed with dried potassium bromide of equal weight and compressed to form a KBr disk. The samples were scanned from 400 to 4000 cm^{-1}.

Pre-compression parameters

Angle of Repose: The angle of repose is the constant, three-dimension angle (relative to horizontal base) assumed by a cone like pile of material formed by any of several different methods. When the angle of repose exceeds 50degrees, the flow is rarely accepted for manufacturing purpose.

Bulk Density: The bulk density was determined by transferring the accurately weighed sample of powder to the graduate cylinder. The initial volume and weight was noted. Ratio of weight of the sample was calculated by using the following formula.

Bulk Density =Mass /Bulk volume.

Tapped Density: Weighed powder sample was transferring to a graduated cylinder and was placed on the tap density apparatus, was operated for fixed number of taps(100).The tapped density was determined by the following formula.

Tapped Density =Mass/Tapped volume.

Percentagecompressibility: Based on the apparent bulk density and tapped density,the percentage compressibility of the bulk drug was determined by the following formula

% Compressibility=Tapped density-Bulk density×100/ Tapped density.

Hauser's Ratio: It is measured by the tapped density to bulk density.

Hauser's Ratio= Tapped density/Bulk density

POST COMPRESSION PARAMETERS

Tablet thickness:

Randomly 5 tablets were taken from each formulation trial batch and their thickness was determined by using screw gauge.

Weight variation test:

20 tablets were randomly selected from each formulation trial batch and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight.

Measurement of tablet hardness:

Hardness of 10 tablets was found using Monsanto hardness tester, mean and standard deviation were computed and reported. It is expressed in kg/cm^2.

Friability:

10 tablets were weighed and placed in Roche friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. The Friabilator was operated at 25 rpm

for 4 mins. After 100 revolutions, tablets are removed, deducted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

***In vitro* Drug Release Studies**

The *in vitro* drug release study was performed for the single and multiple-unit tablets using USP Type II dissolution apparatus using900ml of phosphate buffer 50 rpm37±0.5ºCsampling volume 5ml was withdrawn at predetermined time intervals samples (5 ml) were collected and replenished with same volume of fresh media. The drug content in the samples was estimated using UV-spectrophotometer at273.8 nm.

Water absorption ratio

A piece of tissue paper fouled twice was placed in petri plate containing 6 ml of water .A tablet was placed on it and the time required for complete wetting was measured .The wetted tablet was weighed.Water absorption ratio was measured R was determined using following formula.

R=100(Wa-Wb)/Wb

Wb-Weight of tablets before absorption

Wa-Weight of tablets after absorption

RESULTS AND DISCUSSION

CALIBRATION CURVES OF NORFLOXACIN.

Preparation of Norfloxacin standard stock solution (100 µg/ml) pH 6.8phosphate buffer.

Standard stock solution of norfloxacin was prepared by dissolving accurately weighed10 mg of Norfloxacin in little quantity of 1% v/v acetic acid in a 100 ml volumetric flask. The volume was then made up to 100 ml using pH 6.6 phosphate buffer to obtained the solution of 100 µg/ml.

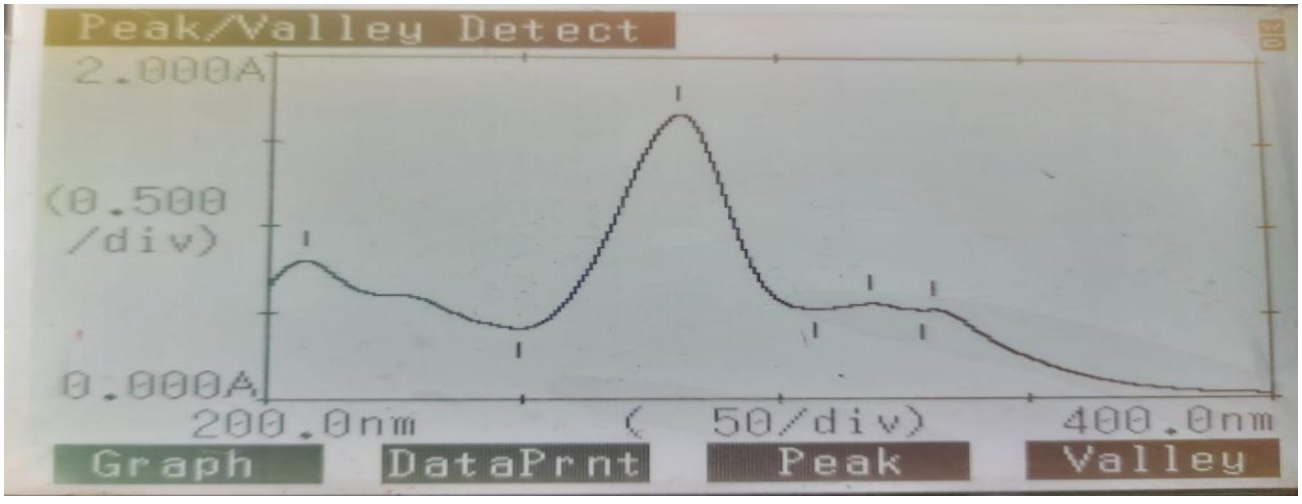


Figure 3:λ max of Norfloxacin inphosphate buffer 6.8 pH.

DRUG-EXCIPIENT COMPATIBILITY STUDIES

Fourier Transform Infrared (FTIR) Spectroscopy

Potential chemical interaction between drug and polymer may change the therapeutic efficacy of the drug. To investigate the possibility of chemical interaction between drug and polymer FTIR spectra of pure Norfloxacinand Superdisintegrants used in formulations were analysed over the range 400–4000 cm^{-1}.

Figure 4:FTIR spectra of pure drug

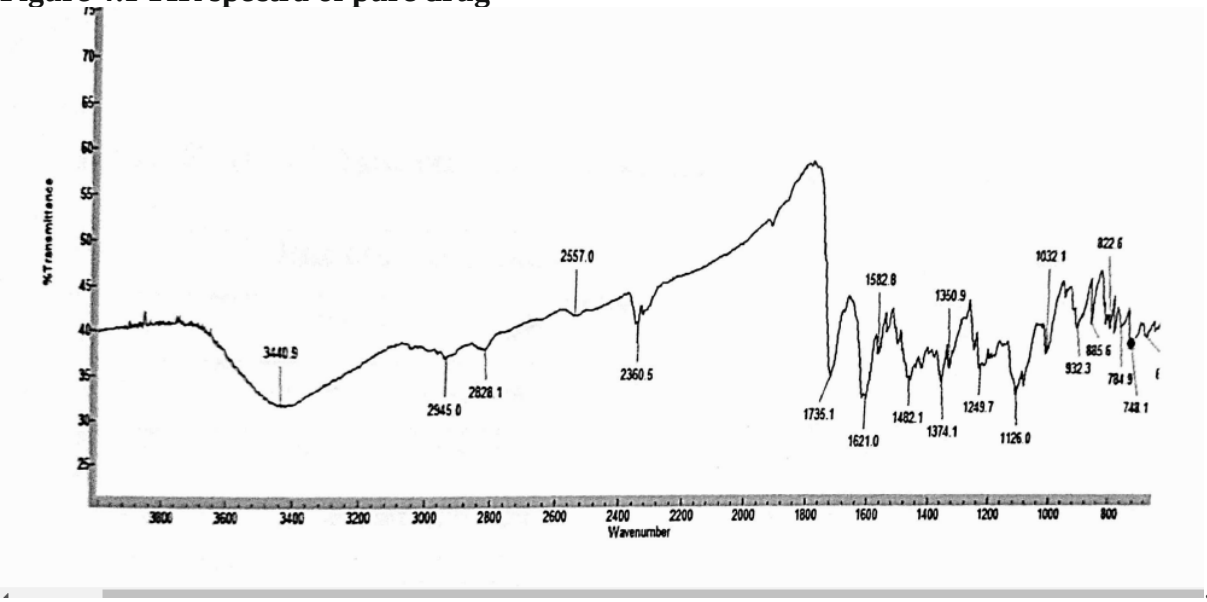


Figure 5:FTIR spectra of pure drug and Superdisintegrants used in formulations.

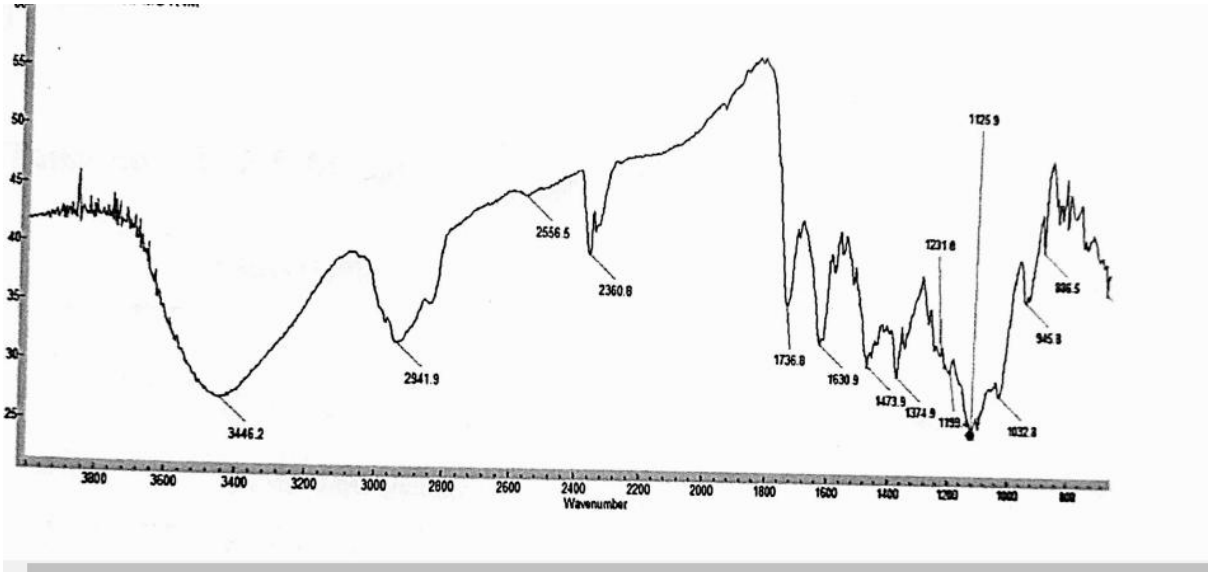


Table 2: Micrometric properties.

Formulation code	Angleofrepose (°)± SD	Bulk density(gm/ml) ± SD	Tappeddensity(gm/ml) ± SD	Carr'sIndex(%) ± SD	Hausner's ratio ± SD
F1	36.68 ± 0.05	3.70±0.01	4.86±0.01	23.86±0.16	1.31±0.03
F2	31.42±0.04	4.05±0.03	4.52±0.04	10.39± 0.25	1.11±0.05
F3	32.89±0.05	3.34±0.01	4.34±0.04	20.96±1.9	1.26±0.02
F4	34.56±0.06	3.70±0.02	5.01±0.06	26.14±0.53	1.35±0.004
F5	35.04±0.04	3.74±0.03	4.57±0.04	18.16±0.18	1.22±0.01
F6	33.22±0.13	3.34±0.04	4.82±0.04	30.70± 0.24	1.44±0.05

Table 3:Physical parameters of Norfloxacin fast dissolving tablets.

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
F1	**400.38±3.84**	**3.5±0.3**	**4.84±0.05**	**1.7**	**98.23**
F2	**401.52±2.87**	**5.2±0.5**	**4.76±0.06**	**0.64**	**99.65**
F3	**399.23±2.73**	**7.1±0.4**	**4.86±0.03**	**0.71**	**99.12**
F4	**402.6±2.13**	**7.2±0.5**	**4.76±0.04**	**0.64**	**98.44**
F5	**400.19±3.48**	**5±0.2**	**4.63±0.06**	**0.64**	**99.23**
F6	**401.71±2.3**	**6.1±0.4**	**4.65 ±0.06**	**0.64**	**98.63**

Table 4:Water absorption ratio of Norfloxacin fast dissolving tablets

Formulation code	Disintegration time (sec)	Water absorption ratio	Wetting time (sec)
F1	**39.23±0.13**	**87.89±0.14**	**17±0.99**
F2	**20±0.23**	**47.19±0.22**	**11±0.54**
F3	**38.34±0.23**	**69.40±0.49**	**14±0.16**
F4	**35.66±0.34**	**59.49±0.33**	**25±0.55**
F5	**39.32±0.78**	**62.51±0.23**	**27±0.67**
F6	**37.89±0.46**	**60.40±0.42**	**29±0.59**

Figure6:Water absorption ratio of Norfloxacin fast dissolving tablets.

Figure7:Water absorption ratio of Norfloxacin fast dissolving tablets after complete wetting.

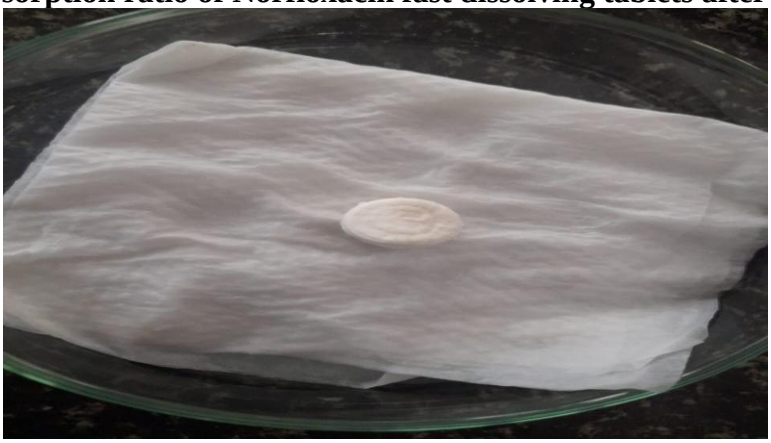


Table 5:Cumulative drug release of Norfloxacin fast dissolving tablets.

Time (min)	F1	F2	F3	F4	F5	F6
5	8.12	9.4	7.10	7.22	8.243	7.145
10	20.7	23.4	19.72	20.76	22.89	23.78
15	41.82	44.8	39.82	39.45	38.98	35.99
20	54.31	64.2	44.34	47.38	45.37	46.77
25	68.61	78.5	55.77	56.79	57.78	58.75
30	82.22	85.2	62.22	64.23	68.44	73.44
45	85.61	88.6	76.72	75.74	76.88	74.89
60	87.23	99.2	77.45	78.47	79.55	76.55

Conclusion

Fast dissolving tablets of Norfloxacin were successfully prepared with different super disinterdents by simple direct compression method. FTIR studies showed no incompatibility between drug, superdisintergents and various excipients used in the formulations. Formulated tablets gave satisfactory results for various evaluation parameters like tablet dimensions, hardness, weight variation, friability, content uniformity angle of repose, bulk density, Carr's index, Hausner's ratio and post compression

parameters like hardness, thickness, friability, weight variation, werrin time water absorption ratio, drug content, *in-vitro* disintegration time and *in-vitro* dissolution studies.

The observations have shown that all the FDT formulations were accepted with reasonable limits of standards required for fast dissolving tablets. The study reveals that the formulations prepared by Crospovindone was best than Croscarmellose and Sodium starch glycolate. Formulations prepared by Crospovindone F2 was the best formulation. The study revealed that superdisintegrants used were effecrive in low concentration level.

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