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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF ANTIBACTERIAL AGENT

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Abstract

Norfloxacin which is an antibiotic generally used to treat upper urinary tract and genital tract infection. It is also the drug of choice in case of microbial and bacterial infection. The present goal of the investigation was to formulate and evaluate orodispersible tablets of Norfloxacin by using different superdisintegrates like sodium starch glycolate, cross carmellose sodium (CCS), crospovidone by direct compression technique. The blend was examined for angle of repose, bulk density, tapped density, total porosity, compressibility index and Hausner's ratio. The prepared tablets were evaluated for weight variation, hardness, drug content, friability, Thickness, Diameter, disintegration time, Wetting time and dissolution rate. The results revealed that the increased proportion of various superdisintegrants were associated with increase in the overall cumulative drug release rate. Release profile of F-4 having 4% CCS was found to have maximum release of 95.24 % at the end of 4 minutes. The drug release from all batches was found to be concentration dependent. It was concluded that super disintegrants addition technique is a useful method for preparing mouth dissolving tablets by direct compression method.

Introduction

The tablet is the most widely used dosage form because of its convenience in terms of self-administration,compactness, and ease in manufacturing. However, geriatric and paediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as orally disintegrating tablets (ODTs).These are novel types of tablets disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and paediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market[1,2].The basic approach used in the development of the ODTs is the use of superdisintegrants. Another approach used in developing ODTs is maximizing pore structure of the tablets. Freeze-drying [3,4] and vacuum-drying [5,6]techniques have been tried by researchers to maximize the pore structure of tablet matrix. Freeze drying is cumbersome and it yields a fragile and hygroscopicproduct. Therefore, it was decided to adopt the vacuum drying technique in the present investigation. Vacuum drying was adopted after addition of a subliming agent toincrease porosity of the tablets. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly.

Norfloxacin, l-ethyl-6-fluoro-1,4-di-hydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid, is a syntheticantibacterial fluoroquinolone[7]. Quinolones belongs to synthetic class of antimicrobial agents with potentantimicrobial activity which are effective orally and parentally for a wide variety of infectious diseases [8]. It is active on both actively dividing as well as dormantbacteria by

inhibiting bacterial DNA gyrase. It is effective in the treatment of urinary tract infections, gonococcalurethritis and infectious diarrhoea [9].

MATERIALS AND METHODS:

Materials

Norfloxacin obtained from Ankur Drugs and Pharma Limited. Microcrystaline cellulose, Sodium starch glycolate, crosspovidone were obtained as gift sample from Micro Labs (Banglore, India). Manitol from Lobachemicals (Mumbai, India). Magenisim stearate, talc and Aspartame from Arrow chemicals (Mumbai, India). All other materials used were of pharmaceutical grade.

METHOD

PREPARATION OF MIXED BLEND OFDRUG AND EXCIPIENTS

All the materials were passed through sieve no. 60. Required quantity of each ingredient was taken for each specified formulation (Mentioned in Table no.1) and all the ingredients were subjected to grinding to a required degree of fineness (except magnesium stearate and talc). The powdered blend was evaluated for flow properties as follows.

Angle of repose [10]

Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (ɵ) was calculated using the formula.

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

Bulk density [10, 11]

Bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of the blend

(M) was determined. The bulk density was calculated by using the below mentioned formula,

$$\text{Bulk density} = \frac{\text{Weight of the blend}}{\text{Volume of blend(Vb)}}$$

Tapped density [10, 12]

The measuring cylinder containing a known mass of blend was tapped for a fixed number of times. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the following formula,

$$\text{Tapped density} = \frac{\text{Weight of the blend}}{\text{Volume occupied in the cylinder(Vt)}}$$

Compressibility index [13]

The simplest way for measurement of free flow of powder is compressibility , a indication of the ease with which a material can be induced to flow is given by compressibility index (I) which is calculated as follows,

$$I = \frac{Vb - Vt}{Vb}$$

Here, Vb is bulk volume and
Vt is tapped volume.
The value between 13-19% indicates a powder with usually good flow characteristics, whereas above 21% indicate poor flowability.

Hausner's Ratio [13]

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Lower Hausner's ratio (<1.25) indicates better flow properties and higher Hausner's ratio (>1.25) indicates poor flow properties.

Compression of tablets by using direct compression technique

Finally sodium magnesium stearate and talc were added to the prepared blend. The mixed blend of drug and excipients was compressed into tablets weighing 300 mg using a flat faced punches of 8 mm diameter in a rotary tablet press(Rimek mini press- 1, Model RSB-4,Karnavati Engineering, Ahmedabad). A minimum of 50 tablets were prepared for each batch.

EVALUATION OF NORFLOXACIN MOUTH DISSOLVING TABLETS

Evaluation was done on tablets of all formulations batches considering following parameters and results were reported in Table no.3

1) Weight variation test [14]

Twenty tablets were selected randomly and average weight was determined. Then individual tablets were weighed and was compared with average weight. If

the variation is within the I.P limits, the tablets pass the weight variation test.

2) Tablet hardness [14]

The hardness of each batch of tablet was checked by using Monsanto hardness tester. The hardness was measured in terms of kg/cm2. 3 tablets were chosen randomly and tested for hardness. The average hardness of 3 determinations was recorded.

3) Wetting time [14]

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a petri dish with a 10 cm diameter. 10 ml of water was poured on the tissue paper placed in the petridish. A table is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

4) Tablet friability [14]

Five tablets were weighed and the initial weight of these tablets was recorded and placed in Roche friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator, dusted off the fines and again weighed and the weight was recorded.

Percentage friability was calculated by using the formula:

$$\frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

5) *In-Vitro* Disintegration time [14]

The test was carried out on 6 tablets using tablet disintegration tester using pH 6.8 (simulated saliva fluid) maintained at 37°±1°C as a disintegration media and the time in second taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured in seconds.

6) Thickness and Diameter [15]

The thickness and diameter of individual tablets was measured using verniercalipers, which permits accurate measurements and provides information of the variation between tablets.

7) Drug content uniformity [16]

Ten tablets were weighed and taken in mortar and crushed to make powder. A quantity of powder weighing equivalent to 25 mg of Norfloxacin was taken in 100 ml volumetric flask and 0.1 N HCl was added. Then the solution was filtered using membrane filter 0.45µm and then the solution was diluted up to 10µg and absorbance was measured at 224.2 nm. Then the amount of drug present was calculated using standard graph.

8) Dissolution studies [16]

In Vitro dissolution studies for all the prepared were carried out using USP paddle method at 100 rpm in 900 ml of 6.8 P_H phosphate buffer as dissolution media, maintained at 37 ± 0.5º. 1 ml of samples, were withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and release of the drug was determined spectrophotometrically at 274nm. An equal volume of pre warmed (37ºC) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume of the dissolution medium throughout the test. Then the cumulative percentage of drug release was calculated and represented graphically. (Figure-1).

Table- 1: Composition of mouth dissolving tablets of Norfloxacin.

	F1	F2	F3	F4	F5	F6
Norfloxacin	100	100	100	100	100	100
SSG	9	12	---	---	---	---
CCS	---	---	9	12	---	---
Crosspovidone	---	---	---	---	9	12
Aspartame	6	6	6	6	6	6
Mg.stearate	3	3	3	3	3	3
Lactose	45	45	45	45	45	45
Talc	6	6	6	6	6	6
MCC	131	128	131	128	131	128
Total weight	300	300	300	300	300	300

Table-2: **Evaluation of the Powder Blend**

	Angle of repose (θ)*	**Bulk density (g/ml)***	**Tapped density(g/ml)***	**Carr`s index (%)**	**Hausner's ratio.***
F1	28.50 ±0.462	0.4166± 0.016	0.4625± 0.019	12.5± 1.79	1.1101± 0.282
F2	22.54 ±0.137	0.4098± 0.014	0.4950± 0.017	17.21± 1.89	1.2079± 0.028
F3	27.36± 0.055	0.4201± 0.012	0.4854± 0.019	13.44± 1.91	1.1554± 0.026
F4	25.43± 0.273	0.4132± 0.006	0.4761± 0.016	13.22± 1.92	1.1522± 0.026
F5	26.65± 0.055	0.4237± 0.011	0.4901± 0.010	13.55± 1.88	1.1567±0.003
F6	28.32± 0.225	0.4310± 0.008	0.5050± 0.016	14.65± 1.95	1.1716± 0.023

* mean ± S.D., n=3 (all the values are the average of three determinations)

Table-3: Evaluation of norfloxacin mouth dissolving tablets

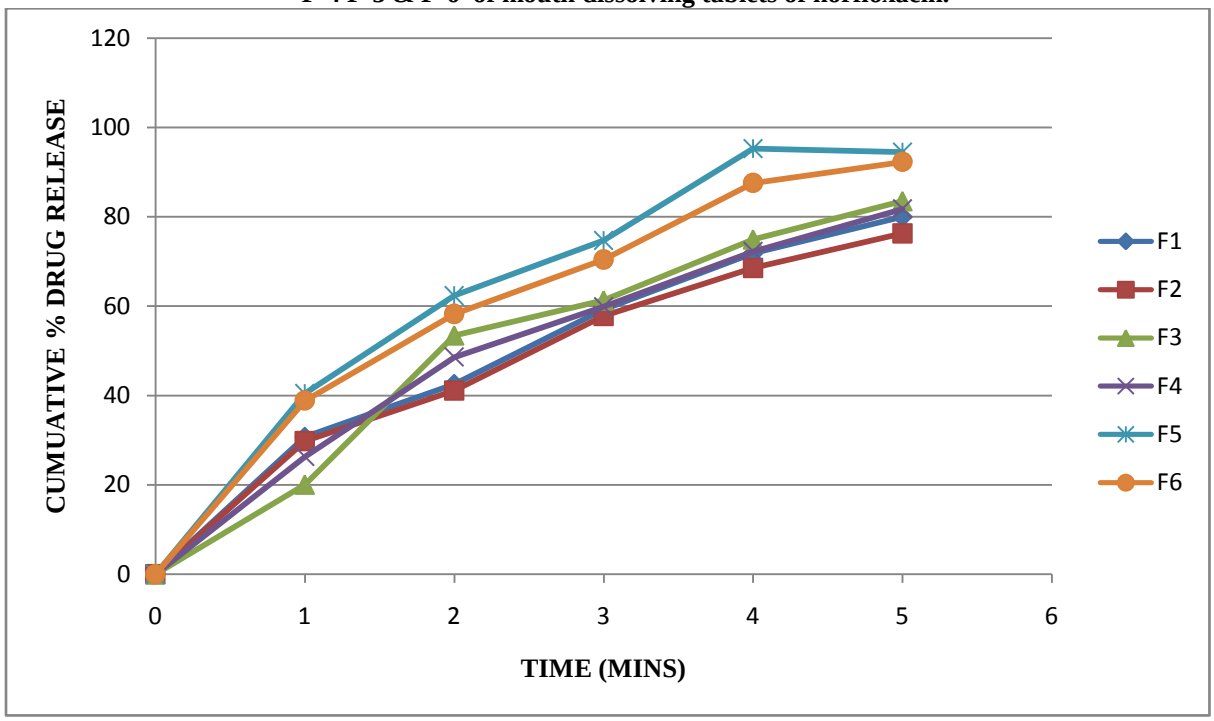
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Weight variation(%)*	301.1 ± 1.21	300.3 ± 1.02	301.5 ± 1.65	302.1 ± 1.85	301.95 ± 0.45	301.3 ± 0.76
Hardness (kg/cm^2)	3.1	3.5	3.6	3.3	3.4	3.4
Friability(%)	0.4026	0.399	0.6019	0.49	0.4995	0.4004
Wetting time (sec)*	88±1.21	54± 1.64	58 ± 1.10	67 ± 1.66	25 ± 1.60	09 ± 0.64
Disintegration time(sec)*	76± 0.51	61± 1.08	71± 1.15	99± 1.52	37± 1.00	22±1.60

* mean ± S.D., n=3 (all the values are the average of three determinations)

Table-4: In-vitro drug release of prepared norfloxacin mouth dissolving tablets.

Time in minutes	F1	F2	F3	F4	F5	F6
1	29.81	30.71	20.05	26.33	40.43	38.85
2	41.11	42.55	53.44	48.61	62.35	58.25
3	57.85	59.23	61.27	74.71	59.87	70.42
4	**68.59**	**71.83**	**74.92**	**95.24**	**72.24**	**87.57**
5	76.30	80.02	83.49	94.47	81.76	92.28

Fig. 1: Cumulative % drug Release Vs Time in min from prepared batches F-1, F-2, F3, F-4 F-5 & F-6 of mouth dissolving tablets of norfloxacin.



RESULTS AND DISCUSSION

Six formulations of Norfloxacin were prepared with combination of different concentrations of superdisintegrants like cross carmellose sodium, crospovidone, sodium starch glycolate. Foreach formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The formulated blends were evaluated and the results are shown in the table 2. The angle of repose was in the range of 22.54 ±0.137 28.50 ±0.462indicating good flow property. The bulk density and tapped density was in the range of 0.4098 ± 0.014g/ml0.4310 ± 0.008g/ml and 0.4625± 0.019g/ml0.5050 ± 0.016g/ml.The compressibility index and Hauser's ratio was in the range of 12.5 ± 1.79 % to 17.21 ± 1.89and 1.1101 ± 0.282and 1.2079 ± 0.028indicating good flow property. The powder blend was compressed using direct compression technique. The compressed tablets were evaluated for physical properties and the results are tabulated in table-3. The hardness was in the range of 3.1to 3.6kg/cm2. Uniformity of weight was found to be in the range of 300.3 ± 1.02 to 302.1 ± 1.85mg. The friability of all the formulation was within 1%, and was in the range of 0.399% to 0.6019%indicating a good mechanical resistance of tablets. The wetting time for all the formulated tablets was in the range of 09 ± 0.64 to 88±1.21 sec. The disintegration time of all the formulated tablets was found to be in the range of 22±1.60 to 99± 1.52 sec. All the formulations in-vitro drug release results were drawn in the Table no.4. The results revealed that the increase in proportion of superdisintegrants was associated with increase in the overall cumulative drug release rate. Release profile of F-4 having 4% CCS was found to have maximum release of 95.24 % at the end of 4 minutes. The drug release from all batches was found to be concentration dependent.

CONCLUSION

In the present work efforts have been made to prepare and evaluate fast dissolving tablets of norfloxacin with different concentrations of superdisintegrants sodium starch glycolate, CCS, crospovidone by direct compression technique. The results revealed that the increased proportion of various superdisintegrants were associated with increase in the overall cumulative drug release rate. Release profile of F-4 having 4% CCS was found to have maximum release of 95.24 % at the end of 4 minutes. The drug release from all batches was found to be concentration dependent. The mouth dissolving tablets (MDT) found to have excellent physical characters. The superdisintegrants were also found to be compatible with the other excipients of the formulation as well as

with drug, which is evident from the drug content values. Hence the formulation of F-4 fulfills the objective of the present study.

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