

FORMULATION OF CONTROLLED RELEASE OF LOXACIN TABLETS USING NATURAL POLYMERS

S. R. SENTHIL KUMAR^{1*}, V. GANESAN²

¹Department of Pharmaceutics, S.B. College of Pharmacy, Annaikuttam, Sivakasi 626130, Tami Nadu, India, ²Department of Pharmaceutics, The Erode College of Pharmacy, Veppampalyam, Erode- 638112, Tamil Nadu, India. Email: srsmpfarm@gmail.com

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ABSTRACT

Objective: Ofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class considered to be a second generation fluoroquinolone. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram positive and Gram negative bacteria. The aim of the present study is to control the release Ofloxacin by formulating a tablet using the natural polymer likes Aloes powder and neem resin (powder).

Methods: Tablets were formulated by direct compression technique. The fabricated tablets were evaluated for various pre compressional parameters like angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio and post compressional parameters like average weight, hardness, friability, assay, disintegration time and dissolution studies.

Results: In our present study, the effect of Aloes powder and neem resin (powder) with Ofloxacin is studied. The pre-compression and post compression parameters were found to be satisfactory. The results proved that at higher proportion of neem resin (powder) ratio, the drug release was prolonged than the lower proportion.

Conclusion: The results of the present study showed that ofloxacin may be formulated as controlled release tablets by using the natural polymers aloes and neem resins.

Keywords: Ofloxacin, Antibiotics, Pre compression, Post compression, Aloes, Neem Resin.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body and then maintain the desired drug concentration [1]. Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form [2]. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process [3].

Ofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class considered to be a second-generation fluoroquinolone. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram negative bacteria [4, 5]. Ofloxacin is chemically known as (RS)-7-fluoro-2-methyl-6-(4-methylpiperazin-1-yl)-10-oxo-4-oxa-1-azatricyclo [7.3.1.0^{1,5}]-trideca-5(13),6,8,11-tetraene-11-carboxylic acid.

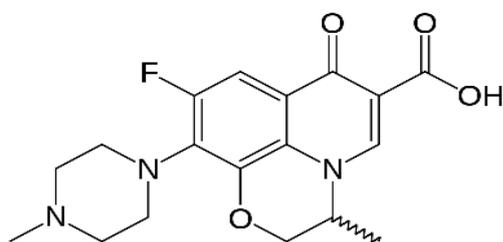


Fig. 1: It shows chemical structure of Ofloxacin

The fluoroquinolones interfere with DNA replication by inhibiting an enzyme complex called DNA gyrase. In particular, some congeners of this drug family display high activity not only against bacterial topoisomerases, but also against eukaryotic topoisomerases and are toxic to cultured mammalian cells and in vivo tumor models [6]. The bioavailability of Ofloxacin in the tablet forms is approximately 98% after oral administration reaching the maximum serum concentrations within one to two hours. Between 65% and 80% of an administered oral dose of Ofloxacin is excreted unchanged via the kidneys within 48 hours of dosing [7].

Both synthetic and natural polymers have been investigated extensively in designing bioadhesive controlled drug delivery systems. Various natural polymers have been investigated for their applications as pharmaceutical excipients [8, 9]. Natural materials are preferred in the field of drug delivery because they are readily available, cost-effective, eco-friendly, capable of multitude of chemical modifications, potentially degradable and compatible due to their natural origin [10]. Many researchers have explored the usefulness of plant-based materials for their application in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven [11-13]. These polymers are useful as tablet binders, disintegrants, emulsifiers, suspending agents, gelling agents, stabilizing agents, thickening agents and sustaining agents in tablets [14].

In controlled release formulation, various studies have been carried out to provide the action of anti-bacterial drugs. The suitability of various anti-bacterial drugs such as Ofloxacin has been studied for their controlled release drug delivery system by using natural gums. Various new approaches have been used in the formulation to increase controlled action throughout GI tract. In pharmaceutical formulation, polymers used as the sustained agents, they have the property to increasing the controlled action for long periods in the therapeutic range. The main objective is to formulate an oral solid dosage form of ofloxacin tablets which is considered to be a stable with robust quality along with reduced cost.

MATERIALS AND METHODS

Ofloxacin (Suchem bulk drug manufacturer, Ahmedabad) was received as a gift sample. Aloes powder, Neem Resin Powder Dabur India Limited, India, Lactose (Paxmy speciality chemicals, Chennai), Talc (Merck Limited, Mumbai), Magnesium stearate (Loba chemical pvt ltd Mumbai), Potassium dihydrogen phosphate (S.D fine chem. Pvt limited) and Sodium hydroxide (Reachem laboratory, Chennai) were commercially procured and used for this study.

Formulation of tablets

The Ofloxacin Controlled Release tablets were prepared by direct compression method employing various excipients as mentioned in

Table 1. Ofloxacin, aloes powder and neem resin were passed through 40 # mesh and mixed well for 10 minutes. Lactose was added to the drug and polymer mixture after passing through 40 # mesh and blended thoroughly for 5 minutes. The blend was lubricated with Magnesium stearate and Talc after passing through 60 # mesh.

Measurement of Flow Properties

Flow properties of the dispersion granules were determined by measuring the Carr's compressibility index (CI). Bulk density was calculated by measuring the volume of 5g of granules in a 50 ml measuring cylinder. The cylinder was tapped 100 times manually through a fixed height of 10 cm from the surface, till there was no further reduction in volume of the granules. Tapped density was calculated using the volume obtained after tapping. Carr's compressibility index values were determined by the following formula.

$$\text{Compressibility Index} = \frac{[\text{Tapped Density} - \text{Bulk Density}]}{\text{Tapped Density}} \times 100$$

Optimized dispersion granules were also characterized for angle of repose; it was determined by allowing the dispersion granules to flow through a glass funnel of internal diameter 10 mm on the horizontal surface. The height (h) of the heap formed was measured, and the radius (r) of the cone base was also determined. The angle of repose was calculated from the following formula

$$\tan \theta = h/r$$

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

The tablets were compressed using prepared granules with the help of the compression machine and evaluated for post compression parameters.

Table 1: It shows the formulation composition of Ofloxacin Controlled Release tablets

S. No.	Ingredients	Quantity per tablet (mg)					
		F1	F2	F3	F4	F5	F6
1	Ofloxacin	200	200	200	200	200	200
2	Aloes Powder	10	10	10	10	10	10
3	Neem Resin	-	5	10	20	30	40
4	Lactose	174	169	164	154	144	134
5	Talc	8	8	8	8	8	8
6	Magnesium Stearate	8	8	8	8	8	8
Total		400	400	400	400	400	400

Evaluation of tablets

Various standards have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. The following standards or quality control tests were carried out on compressed tablets. The formulated tablets were evaluated for the following physicochemical parameters [19 – 21].

Physical tests for the prepared tablets

Ten tablets from each formulation were taken for measurement of average weight. Hardness of the ofloxacin tablets was evaluated by using hardness tester (Pfizer) and mass determination was performed for twenty Bulk density tablets from each batch and uniformity of weights were calculated. Friability of the ofloxacin tablets was determined by first weighing 10 tablets after dedusting and placing in a friability tester (Roche friabilator, Pharmalabs, Ahmedabad, India), which was rotated for 4 min at 25 rpm. After dedusting, the total remaining weight of the tablets was recorded and the percent friability was calculated. The drug content of the prepared tablets of each batch was determined in triplicate [20-23].

Dissolution rate studies

Dissolution is the process by which a solid solute enters a solution. In vitro drug release of the samples was carried out using USP – type I dissolution apparatus [paddle type]. The dissolution medium used was 900 ml of buffer with pH – 7.4 were placed into the dissolution flask maintaining the temperature of 37± 0.5° C. One Ofloxacin tablet was placed in each flask of dissolution apparatus. The apparatus was allowed to run for 10hrs.

The sample measuring 10 ml was withdrawn after every 30 minutes interval up to 8 hrs using 10 ml pipette. The fresh dissolution medium [37°C] was replaced every time with the same quantity of the sample. Collected samples were suitability diluted with pH 7.4 and analyzed in UV double beam spectrophotometer at 294 nm using pH 7.4 as blank. The % drug release was calculated [24].

RESULTS AND DISCUSSION

Evaluation of Ofloxacin Powder: Bulk Density for Ofloxacin blend was found to be in the range of 0.372 to 0.384. Tapped density

for granules were found to be between 0.436 and 0.442. Compressibility index and Hausner's ratio were obtained in the range of 13.20 to 14.47 and 1.14 to 1.6 respectively.

Angle of repose was observed in the range of 32.06' to 34.20' (Table 4). The result indicates that the granules of all formulations have good flow properties.

Post-compression parameters

Prepared blends were compressed and these compressed tablets were evaluated for Uniformity of weight, friability, hardness and drug content.

The Uniformity of weight of tablets was found to be in the range of 398.8– 402.0. The percentage friability of all batches ranged from 0.500 to 0.5%W/W.

The hardness of the tablet ranged from 5.72 – 6.36 kg/cm² respectively (Table 5). The result showed that the percentage of Ofloxacin was ranging from 94.88 to 97.98 % in all the formulations.

Dissolution Rate Studies

In vitro dissolution studies were performed at 37± 0.5°C for 8 hours at 50 rpm by using 7.4 phosphate buffer as a dissolution medium. The dissolution rate studies were performed to evaluate the dissolution character of ofloxacin from controlled release tablet with different ratios of neem resin.

The percentage drug release for all the formulations were evaluated for 8 hours with various ratio of the neem resin was found to be 99.5 % for F-1formulations, 78.55 % for F-2 formulations, 72.27 % for F-3 formulations, 61.36 % for F-4 formulations, 56.25 % for F-5 formulations and 53.05 % for F-6 formulations at 390min.

The result showed that there was a decrease in the drug release with the increase in the ratio of neem resin (powder). From the result it was found that the dissolution rate of ofloxacin from controlled release tablets was significantly decreased than that of prepared without polymer. Polymer ratio played a major role in drug release.

The results proved that at higher proportion of neem resin (powder) ratio, the drug release was prolonged than the lower proportion. The results are shown in table 6 and figure 2.

Table 4: It shows Pre-compression Parameters of Ofloxacin Powder

S. No.	Formulations	Parameters				
		Bulk Density	Tapped Density	Compressibility Index	Hausner's Ratio	Angle of Repose
1	F-1	0.374 ± 0.0055	0.438 ± 0.0084	14.13 ± 0.0034	1.16 ± 0.0122	33.90 ± 0.5048
2	F-2	0.376 ± 0.0055	0.436 ± 0.0114	14.05 ± 0.8537	1.16 ± 0.0122	33.71 ± 0.09789
3	F-3	0.384 ± 0.0055	0.438 ± 0.0084	13.202 ± 2.3148	1.14 ± 0.095	33.86 ± 0.4807
4	F-4	0.378 ± 0.0084	0.422 ± 0.0084	14.47 ± 1.1712	1.16 ± 0.0125	34.37 ± 0.4807
5	F-5	0.372 ± 0.0045	0.438 ± 0.0084	13.66 ± 1.3814	1.15 ± 0.0182	32.06 ± 0.7446
6	F-6	0.380 ± 0.0071	0.440 ± 0.100	13.61 ± 1.4069	1.14 ± 0.0114	34.20 ± 1.9658

Table 5: It shows Evaluation of Post-Compression parameters of Ofloxacin tablets

S. No.	Formulations	Parameters			
		Hardness (Kg / Cm ²)	Uniformity of Weight	Friability (%)	Drug Content (%)
1	F-1	6.20 ± 0.27	399.60 ± 1.14	0.508 ± 0.50	97.98 ± 0.94
2	F-2	6.36 ± 0.37	401.00 ± 1.22	0.500 ± 0.03	95.94 ± 1.73
3	F-3	6.20 ± 0.27	398.80 ± 0.83	0.540 ± 0.04	94.88 ± 2.13
4	F-4	5.72 ± 0.67	400.20 ± 1.48	0.581 ± 0.02	97.74 ± 1.29
5	F-5	6.28 ± 0.65	399.40 ± 1.14	0.522 ± 0.02	96.98 ± 1.04
6	F-6	6.10 ± 0.17	402.00 ± 0.70	0.520 ± 0.02	97.46 ± 1.04

Table 6: It shows Comparative dissolution profile for the formulations F-1 to F-6

Time (min)	F-1	F-2	F-3	F-4	F-5	F-6
30	15.20	9.27	9.14	7.64	6.07	5.32
60	23.93	16.09	13.57	11.25	9.20	8.32
90	32.80	22.16	19.64	17.59	15.20	11.25
120	39.95	29.32	26.52	22.23	19.98	16.02
150	46.64	33.14	30.89	27.61	23.05	20.73
180	52.57	36.48	34.70	31.64	26.32	24.07
210	60.75	42.20	38.80	35.32	31.57	27.48
240	66.07	47.18	43.02	37.64	33.61	29.11
270	71.73	52.23	45.75	40.30	36.68	32.18
300	80.52	56.73	50.18	43.91	38.52	36.82
330	87.34	60.75	53.66	47.05	40.84	38.11
360	94.84	62.73	57.20	50.45	43.57	41.45
390	99.95	69.55	61.98	52.23	45.68	43.50
420	-	70.84	65.59	54.41	48.82	47.73
450	-	74.52	68.18	57.07	52.09	49.09
480	-	78.55	72.27	61.36	56.25	53.05

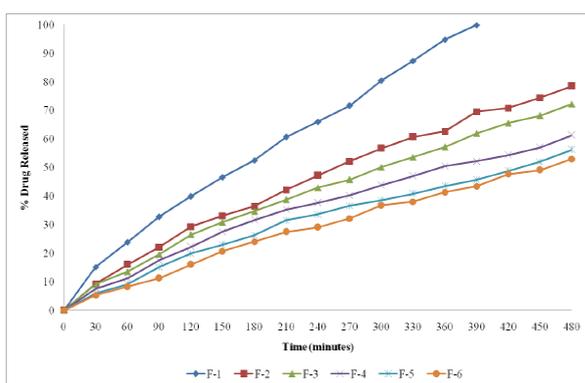


Fig. 2: It shows Comparative dissolution profile of formulation F-1 to F-6

CONCLUSION

The present study shows the effect of natural polymers on the formulation and development of ofloxacin controlled release tablets. The natural polymers used exhibited a good binding capacity, the mechanical properties of tablets were assessed using the crushing strength and friability of tablets. Drug release properties of the tablets were assessed using disintegration time and dissolution time as assessment

parameters. It may be concluded that ofloxacin may be formulated as controlled release tablets by using the natural polymers aloe and neem resins. Compatibility study showed that there were no physicochemical changes in the drug-excipients mixture. The drug release from tablets decreased with increase in polymer concentration. The increased concentration of gum showed retardation in drug release from tablet. Abundant availability, economical feasibility, commercial suitability and reliability make the gum as an alternative for the existing toxic, synthetic and ineffective excipients.

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