RESEARCH ARTICLE

Formulation Optimization and Evaluation of Orally Disintegrating Tablets of Moxifloxacin

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ABSTRACT

Oral administration of a pharmacologically active agent is the common and most preferred route among patients suffering from different types of illness. In the market, different type of oral dosage form is available among them tablet is the most favorite and demanded formulation. Further, the tablets, which are easy to use and swallow, are the ideal dosage form like orally disintegrating tablets (ODT's). The main advantage of this type of formulation is that they can give easily to old aged and under-aged patients.

In this research work, ODT's formulation was manufactured, which get easily disintegrates and gives no bitter taste in the buccal cavity during administration. To achieve this task, moxifloxacin was complexed with suitable ion exchange resins (IER) like Kyron T314. In this course of action, multiple trials were performed using variable percentages or ratio of moxifloxacin and Kyron T 314. The resulting complex powder was characterized by different parameters like IR spectroscopy and differential scanning calorimetry (DSC).

Along with the other excipients, drug resin complex (DRC) was used to manufacture the tablets. In this process, two super disintegrants viz. cross povidone and Ac di sol were used, and tablets were prepared by direct compression methodology.

The finished product parameters of the tablet were estimated using the different available analytical methodologies.

In this research work, it was concluded that the minimum time (19 seconds) for the wetting of tablets was observed when the quantity of crospovidone used was around 10% (MIT05). Additionally, this formulation gives maximum drug release (84.48%) after 120 minutes.

Therefore, by using a suitable IER, taste-masked ODT's of moxifloxacin can be prepared. This method is more efficient and effective in the development of such type of formulations.

Keywords: Drug resin complex, Ion exchange resin, Moxifloxacin, Orally disintegrating tablet.

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INTRODUCTION

Different categories of patients according to their age, physical abilities or mental conditions, face problems in acceptance of oral solid dosage forms like tablets or capsules. In these circumstances, it becomes quite compulsory to present a dosage form with good acceptability among such patients. Therefore, formulations in the form of the chewable, oral solid dosage form or the form of liquid come as a better solution to overcome such types of conditions. Before presenting such type of formulation for the patients' formulator has to face a major problem related to the bitter or undesirable taste of the drug. Because during the administration of these types of formulations, taste buds primarily come in contact with the drug. This becomes more challenging when the drug is to be given to a child. Therefore, it was needed to hinder the undesirable taste of the active agents in the formulations to enhance their palatability.[1]

Among the available methods for subsiding the taste of the drug, one of the most suitable and efficient is the resinification of the drug. In this technique, a suitable ion exchange resin (IER) is selected according to the properties and chemical structure of the drug. In the media, IER made a complex with the active pharmaceutical igredients (API) and subsides its physical properties. IER forms a coating or a layer around the

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drug and prevents it from contacting the taste buds. When the complex passed through the acidic media in the stomach, this complex got broken down due to lower pH. As a result, the drug gets free from the complex and gets absorbed as per its mechanism of action. Un-complexed resin remains unabsorbed and removed from the body in the usual way.[2]

Moxifloxacin is chemically 1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]nonan-8-yl]-6-fluoro-8-methoxy-4-oxoquinoline-3-carboxylic acid.[3]

Moxifloxacin shows bactericidal activity against the broad spectrum of anaerobic bacteria.[4] This drug acts against both gram-positive and negative bacteria. The taste of the drug is obnoxious. Therefore, taste masking of the drug is the primary requirement before formulating this drug. Chemically, one of the prime reasons for the bitterness in a drug is the presence of nitrogen molecules and the amine groups in their molecular structure. So, the feel of a drug can be surpassed if, by any means or a technique, exposure of these groups to the oral cavity can be blocked.[5,6]

One of the most advance and advantageous techniques for achieving this task is the resinification of the drug. Moxifloxacin drug also has amine groups in its structure, giving it an obnoxious feeling in the buccal cavity. In the resinification process, ion exchange resin prevents the exposure of these groups by chemically reacting with the drug and diminishes the drug's release in the buccal cavity. As a result, the API molecule does not come in contact with the tongue.[7]

MATERIALS AND METHODS

Materials

A sample quantity of moxifloxacin was received from M/s Sun Pharma. A sample quantity of resins was received from Corel Pharma Limited.

Standard curve of Moxifloxacin

A solution of 100 mg moxifloxacin was prepared by solubilizing the drug in 0.1 N HCl in 100 mL of a volumetric flask and made up the volume with 0.1 N HCl.

Further dilution samples of moxifloxacin were made using 0.1 N HCl in the series of 2, 4, 6, 8 and 10 µg/mL of moxifloxacin (Table 2).

The solution was evaluated by UV-spectrophotometric method at the λ of 294 nm (Figure 1).

Drug-resin Complex Powder

Each batch for the complexation of drug and resin was manufactured separately. Kyron T314 was used for the complexing with the moxifloxacin drug. Initially, Kyron T314 was suspended in the purified water for swelling and stirred for 45 minutes. After that, purified water was decanted, and the swelled Kyron T314 has washed again with purified water. This resin was further activated by using 1N HCl. This resin was further rewashed with purified water to get a neutral pH.

This activated resin was transferred to a beaker having purified water for the complexation process. Thereafter, the drug moxifloxacin was added gradually in the beaker containing resin under stirring. The mixture was stirred for about 2 hours. During the mixing process, the pH of the mixture was checked at regular time intervals and adjusted to around pH 6.5 by adding 0.1M KOH solution. After mixing time, DRC was removed from the mixture by decantation and filtration method. DRC was further washed with purified water and dried at 65°C. This dried mass was further converted into the granular form by sizing it through a suitable sieve.

Characterization of Complex[8,9]

Impact of Drug-resin Percentage on a Complex Mixture

The proportion of the drug and resin in a mixture significantly affects the formation of a complex. Therefore, its becomes an important parameter to quantify the proportion between a drug and resin in a complex. In the present work moxifloxacin and Kyron T314 were mixed in the proportion of 1:1, 1:2 and 1:3. In the mixture loaded % the quantity of the drug was estimated (Table 3).

Drug Loading Efficiency for DRC

DRC with a quantity of 100 mg of moxifloxacin was transferred in a beaker. In the beaker, 100 mL of 0.1 N HCl was added and

Table 1: Formulation of ODTs of Moxifloxacin- Kyron T314 complex

Constituents	*Batch No.*				
	MIT01	*MIT02*	*MIT03*	*MIT04*	*MIT05*
	mg/tablet	*mg/tablet*	*mg/tablet*	*mg/tablet*	*mg/tablet*
Complex powder	481	481	481	481	481
Pearlitol 200 SD	84	84	69	74	65
PVP K-30	42	42	42	42	42
Ac di sol	51	---	33	---	---
Crospovidone	---	51	33	61	70
Xylitol	28	28	28	28	28
Talcum powder	7	7	7	7	7
Calcium stearate	7	7	7	7	7
Avg. weight (mg)	700	700	700	700	700

mixed continuously for 2 hours. After mixing, this solution was taken out from the mixture. This solution was further diluted with 0.1 N HCl and the quantity of moxifloxacin solubilized was quantified by the UV method, at the λ_{max} of 294 nm (Table 4).

Differential Scanning Calorimetry (DSC)

DSC of the moxifloxacin and Kyron T314 and their complexes was measured using DSC equipment (Figure 2). Samples quantity not more than 10 mg, were transferred into pierced Al. pans and evaluated in the range of 20–360°C, at 10°C/min under the flow of N_2 gas.

International Relations (IR) Studies

IR spectra of the moxifloxacin and Kyron T314 and their mixture were measured in the range of 400 to 4,000 cm^{-1} using IR equipment and KBr pellets (Figure 3).

Formulation of Tablets

Tablets of the moxifloxacin were manufactured by using a direct compression process (Table 1). In the process, DRC (1:3) was used along with the variable amount of super disintegrants. The material was dispensed as per the composition mentioned in Table 1. Initially, all materials of the composition were passed individually using a suitable sieve (#30 SS) sieve and transferred in a polybag. All materials in the polybag were mixed together properly and then lubricated using magnesium stearate and other ingredients. The blend was mixed for 15 minutes. Finally, the blend was compressed at 8 st. compression machine using 11 mm plain, biconvex punches. The tablets were compressed at the avg. weight of 700 mg.

Evaluations of Final Blend[10,11]

The final blend or granules was analyzed by the different parameters of powder like its density (bulk and tapped), HR, and angle of repose (AR) (Table 5).

Characterization of Tablets[12,13] (Table 6)

Hardness

The capability of bearing mechanical shocks indicates the strength or hardness of a dosage form. It was analyzed by using the Harness tester (M/s Electrolab). The hardness unit was Kp. it was determined to take 10 tablets from the bulk in a random manner.

Weight Variation Test

This test gives information about the tablet weight range and ensures that the tablets were compressed in the specified range. It was determined to take 20 tablets from the bulk in a random manner.

Friability Test

This test also helps in the determination of the capability of the tablets to bear mechanical shocks. As per the pharmacopoeial requirement, tablets quantity equivalent to 6.5 g taken and transferred in the friabilator. The test was operated for four minutes at 25 rpm speed. After completion of the test, tablets were taken out, dedusted and weighed. Loss in the weight of the tablet was quantified in the form of a percentage.

Wetting Time

In this test time taken by the water to completely wet the tablet is measured. In this technique, Tablet was placed on tissue paper, which is already soaked with the solution of pH 6.8 buffer. Time taken by the water to completely wet the tablet was noted. The test was performed three times.

Disintegration Time (DT)

This parameter gives an idea about how much time is needed for a tablet to completely disintegrate in the media.

In this test, tablets were transferred into the tubes of DT testing equipment. The test was operated in the purified water maintaining the temperature at 37 ± 2°C. Time is taken to completely disintegrate the tablet was noted.

In-vitro Dissolution Studies

This test indicates the *in-vivo* behavior of the tablet dosage form. The test was performed in the USP - 2 methods at 100

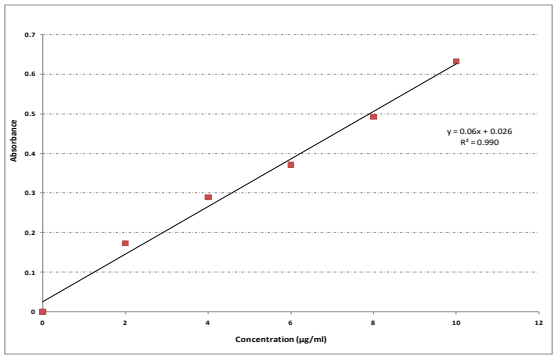

Figure 1: Standard curve of moxifloxacin in 0.1 N HCl

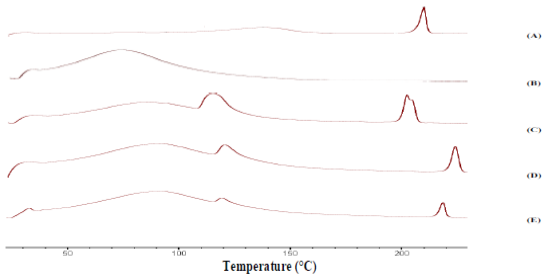

Figure 2: DSC of (a) Moxifloxacin (b) Kyron T314 (c) M- Kyron T314 (1:1) (d) M- Kyron T314 (1:2) (e) M- Kyron T314 (1:3)

Table 2: Standard graph of Moxifloxacin in 0.1N HCl

Concentration (µg/mL)	*Abso.*
2	0.173
4	0.289
6	0.371
8	0.492
10	0.632

rpm in 900 mL pH 6.8 buffer. The tablets were transferred to the basket of dissolution testing equipment. After a fixed time, interval aliquots were withdrawn from the media and drug content was determined spectrophotometrically after proper dilution (Table 7).

RESULTS AND DISCUSSION

Standard Curve of Moxifloxacin

Standard Curve of Moxifloxacin in 0.1 N HCl follows the Beer Lambert's Law. From the given equation we can calculate the drug concentration of a drug solution by using its absorbance.

Table 3: Impact of drug-resin percentage on a complex mixture

Proportion of Drug-resin	*Time (hours)*	*Loaded% qty. of Gemifloxacin*
1:1		54.81
1:2	2	69.78
1:3		84.32

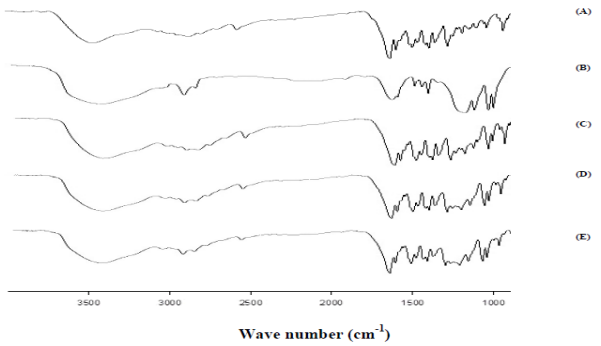

Figure 3: IR Spectra of (A) Moxifloxacin (B) Kyron T314 (C) M-Kyron T314 (1:1) (D) M- Kyron T314 (1:2) (E) M- Kyron T314 (1:3).

Table 4: Drug loading efficiency for DRC

Proportion of Drug –Resin	*Time (hrs)*	*Loaded percentage moxifloxacin*
1:3	1	84.32

Table 5: Results of powder blend (Drug + T314)

Batch No.	*Angle of repose (θ)*	*Initial density (gm/cm^3)*	*Tapped density (gm/cm^3)*	*index of Compressibility (CI) (%)*	*HR*
MIT01	27.9	0.78	0.91	14.29	1.17
MIT02	28.1	0.81	0.91	10.99	1.12
MIT03	28.2	0.83	0.93	10.75	1.12
MIT04	29.1	0.81	0.94	13.83	1.16
MIT05	29.2	0.82	0.92	10.87	1.12

Table 6: Finished product results of Moxifloxacin Tablets (Drug + T314)

Batch No.	*Thickness (mm)*	*Hardness (Kp)*	*Friability (%w/w)*	*Weight Variation (mg)*	*Assay (%)*	*DT (sec)*	*Wetting time (sec)*
MIT01	5.26	3.9	0.17	1.6	87.23	78	65
MIT02	5.28	3.8	0.16	1.4	85.02	81	64
MIT03	5.21	4.1	0.21	1.2	86.08	39	29
MIT04	5.23	3.9	0.17	1.3	84.95	29	27
MIT05	5.26	3.8	0.19	1.3	87.38	19	17

Table 7: Percentage drug release of Moxifloxacin ODTs (Drug + T314)

Time (min)	*Batch No.*				
	MIT01	*MIT02*	*MIT03*	*MIT04*	*MIT05*
5	31.11	34.91	39.31	40.58	42.55
10	35.21	42.13	44.11	45.12	46.51
15	37.98	49.11	50.07	53.41	54.27
20	42.55	54.73	55.32	55.98	57.92
25	48.13	56.51	59.13	62.06	62.31
30	53.12	58.98	61.89	64.38	65.83
45	58.11	64.58	67.28	69.82	70.31
60	64.53	70.08	72.48	73.21	75.26
90	70.83	75.71	78.55	80.21	81.18
120	78.13	80.32	82.41	84.11	84.59

Assay of tablets was observed between 84.95 and 87.38%. Among all the formulations, MIT05 was observed to be the most efficient, having a very low wetting time (17 sec). Additionally, the disintegration time of the tablet was well within the specified limit. Drug dissolution was observed 84.59% after the time of 120 minutes.

Evaluation of Moxifloxacin- Kyron T314 Complex

In this process we had evaluated the drug loaded quantity in the complex prepared in the different ratio.

Impact of Drug-resin Percentage on a Complex Mixture

From the different proportion of the Drug and Resin complex it was found that as the ratio of Resin increases the drug loading efficiency increases.

Differential Scanning Calorimetry

As per the DSC graphs of Drug, Resin and their complex it was found that there is no change in the melting point in the Drug Resin complex which indicates the compatibility between Drug and Resin.

Infrared (IR) Studies

IR Spectrum of Drug, Resin and their complex is overlapping on one another which indicates the compatibility between Drug and Resin.

Drug Loading Efficiency for DRC

As per the observed results in the Ratio of 1:3 Drug and Resin gives maximum drug loading i.e. 84.32%

Results of Powder Blend

Powder blend results of different batches shows that powder blend of all batches have good flowability as well as compressibility.

Finished Product Results of Moxifloxacin Tablets

Physical parameter result of all batches were found satisfactory and as per the pharmacopoeial requirement.

CONCLUSION

Moxifloxacin is an antibiotic have a therapeutic effect covering the broad range of gram-positive and negative bacteria. Moxifloxacin gives a sense of bitterness when comes into contact with the buccal cavity. Therefore, in this study, it was tried to surpass the taste of moxifloxacin by the technique of resinification. Here, Kyron T314 resin was used for the complexing with the drug due to its feasibility with the moxifloxacin. From this research work, it can be concluded that the Kyron T314 can be utilized to develop fast-release drug products.

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