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# Formulation and Evaluation of Orally Disintegrating Taste masked Gemifloxacin Mesylate Tablet

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## ABSTRACT

Gemifloxacin is a broad spectrum antibacterial agent active against gram positive and gram negative organism. It is very bitter in taste. In the present work an attempt has been made to develop orally disintegrating taste masked tablet of Gemifloxacin using ion exchangeresins (Amberlite IRP 88) as a taste masking agent. Different drug: resin ratios were tried to prepare taste maskedcomplex. FT-IR spectroscopy and differential scanning calorimetry were used to investigate the physical characteristics of the complex. Tablets were prepared by direct compression technique using two super disintegrants viz.cross povidone and sodium starch glycolate. Tablets of all batches were tested for various evaluation parameters. Tablets formulated with10% Crosspovidone (GRT05) showed lowest wetting time (16 sec). The % cumulative release of drug from tablet (GRT05) was found to be more than 99% within 40mins. It was thus possible to formulate Orally disintegrating tablets of Gemifloxacin using simple and cost effective, Ion Exchange Resin Complexation technique.

**Keywords:** Gemifloxacin Mesylate, Ion Exchange Resin, Drug Resin Complex (DRC), super disintegrant.

## INTRODUCTION

One of the attractive methods for oral drug delivery systems preferably is the use of ion exchange resins as carrier.[1] Taste masking technologies rely on preventing interaction between the drug molecule and the oral mucosal surface. By creating a physical barrier around each particle, drug substance can be prevented from going into solution and interacting directly withtaste receptors. When an ionisable drug reacts with a suitable ion exchange resin the drug: resin complex formed is known as a drug resinate. Because the drug resinate is insoluble it has virtually no taste, so that even very bitter drugs lose their taste when converted into a drug resinate. With the correct- selection of the ion exchange resin, the drug resinate can be made sufficiently stable that it does not break down in the mouth so that the patient does not taste the drug when it is swallowed. However, when the drug resinate comes into contact with the gastrointestinal fluids, usually the acid of the stomach, the complex is broken down quickly and completely. The drug is released from the Resinates, directly into solution and then absorbed in the usual way. The resin passes through the GI tract without being absorbed.[2]

Gemifloxacin Mesylate is chemically 7-[(4Z)-3-(aminomethyl)-4-(methoxyimino) pyrrolidin-1-yl]-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid.[3] It has an in vitro activity against a broad spectrum of gram positive and gram negative and anaerobic

bacteria.[4] Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques.[5] Among those, taste masking by use of ion exchange resin is most commonly used commercially.[6] Most of the bitter drugs have nitrogen atom and amine as a functional group, which is the cause of their obnoxious taste. If the nitrogen atom and functional groups are blocked by complex formation the bitterness of the drug reduces drastically. Ion exchange blocks the functional group responsible for causing the bitter taste by forming complex with drug and it not allow the drug to release in the saliva. Thus the resin reduces the drug and taste buds interaction.[7]In present study an attempt has been made to prepare taste masked complex of Gemifloxacin with ion exchange resins and complex was further formulated into the rapid disintegrating tablet by direct compression method using, cross povidone and Sodium Starch Glycolate as the super disintegrants.

## MATERIALS AND METHODS

### Materials

Gemifloxacin Mesylate was obtained as a gift sample from Cipla private Laboratories Ltd.
Ion exchange resins obtained fromIon Exchange India Limited as a gift sample.

### Preparation of standard curve of Gemifloxacin Mesylate

100 mg of Gemifloxacin Mesylate was dissolved in 0.1 N HCl in 100 ml of volumetric flask and the solution was made upto volume with 0.1 N HCl.

The standard solution of Gemifloxacin Mesylate was subsequently diluted with 0.1 N HCl to obtain a series of dilutions containing 1, 2, 3, 4 and 5 µg of Gemifloxacin Mesylate in 1 ml solution. The absorbance of these solutions was measured at 267 nm using UV-VIS spectrophotometer (ELICO, Model SL 1500) against blank.

### Preparation of drug-resin complex

Drug resin complexes (DRC) were prepared by using batch process. Accurately weighed amount of Amberlite IRP 88 dispersed in a beaker containing deionized water and allowed to swell for 30 minutes. Swelled resin slurry was filtered on what man filter paper. Then it was washed with deionized water and then activated with 1 N HCl. The acid activated resin was rewashed with water until neutral pH was reached. Drug resin complex (DRC) was prepared, by placing acid activated resin in a beaker containing deionized water. Accurately weighed amount of Gemifloxacin Mesylate was added slowly to the resin slurry and stirred for 3hours in magnetic stirrer. During stirring, pH of the drug resin slurry was measured frequently and adjusts to 6.5 by using 0.1 M KOH. After three hours of stirring, the DRC was separated from dispersion by filtration and washed with deionized water. DRC was dried at 55°C until it was dry. The dried mass was powdered and sieved through 60-mesh sieve. Complex was evaluated for drug loading efficiency.

### Optimization:[8,9]

### Effect of drug-resin ratio on complex formation

Ratio of the resin to drug can greatly impact the complex formation and ultimately affects the taste masking ability. It was necessary to find out the optimum drug to resin ratio. In each case drug resin complexes (DRC) of Gemifloxacin Mesylate and Amberlite IRP 88 were prepared in 1:1, 1:2 and 1:3 ratios. The taste masking ability and drug loading efficiency were estimated.

### Drug loading efficiency for DRC

DRC equivalent to 100 mg of Gemifloxacin Mesylate was weighed accurately and was transferred into 100 ml of volumetric flask. 100 ml of 0.1 N HCl was added to this volumetric flask and was stirred continuously for 1 hour on a magnetic stirrer. After stirring, this solution was filtered through whattman filter paper. Filtered sample solution was suitably diluted with 0.1 N HCl and the amount of drug dissolved were determined by UV spectrophotometer, by measuring the absorbance of the sample at 267 nm.

### Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) thermo grams of the Gemifloxacin, Amberlite IRP 88and drug resin complexes were recorded on NETZSCH DSC 204 (Germany). Samples (2-7 mg) were sealed into aluminum pans and scanned at a heating rate of 10°C/min over a temperature range of 20-360°C under a nitrogen gas stream.

### Fourier Transform Infrared (FT-IR) Studies

FT-IR spectra of Gemifloxacin, Amberlite IRP 88and drug resin complexes were recorded in the range of 400 to 4,000 cm−1 using a Brukeralpa FTIR spectrophotometer (Bruker, Germany) by the KBr disc method.

### Formulation of tablets

Gemifloxacin Mesylate orally disintegrating tablets were prepared by direct compression method using DRC (1:3) and the superdisintegrants in different quantity. According to the formula given in Table 1, all the ingredients were passed through 40-mesh sieve separately and collected. The DRC (ratio 1:3) containing amount equivalent to 100 mg of Gemifloxacin Mesylate was mixed with the other excipients and compressed into tablets, after lubrication with magnesium stearate, and talc by using 16 station rotary tablet compression machine equipped with 10 mm flat faced punches. The tablet weight was adjusted to 600 mg.

**Table 1: Formulation of ODTs of Gemifloxacin- Amberlite IRP 88 complex**

| Ingredients mg/tab | Formulation | | | | |
|---|---|---|---|---|---|
| | GRT01 (mg) | GRT02 (mg) | GRT03 (mg) | GRT04 (mg) | GRT05 (mg) |
| DRC | 422 | 422 | 422 | 422 | 422 |
| Mannitol | 57 | 57 | 45 | 49 | 41 |

| | | | | | |
|---|---|---|---|---|---|
| Povidone | 36 | 36 | 36 | 36 | 36 |
| Sodium starch glycolate | 44 | --- | 28 | --- | --- |
| Crospovidone | --- | 44 | 28 | 52 | 60 |
| Aspartame | 24 | 24 | 24 | 24 | 24 |
| Menthol | 5 | 5 | 5 | 5 | 5 |
| Talc | 6 | 6 | 6 | 6 | 6 |
| Magnesium stearate | 6 | 6 | 6 | 6 | 6 |
| **Total weight (mg)** | **600** | **600** | **600** | **600** | **600** |

### Evaluations of powder blend[10'11]

Powder blend was evaluated for Angle of Repose, bulk density, tapped density and Hausner's ratio.

### Evaluation parameters of the tablet Physical characterization[12,13]

- **Hardness**

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester. It is expressed in kg/cm$^2$. Five tablets were randomly picked and hardness of the tablet was determined.

- **Weight variation test**

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. Twenty tablets were randomly selected and accurately weighed, in grams on an analytical balance

- **Friability Test**

According to the BP specifications 10 tablets were randomly selected and placed in the drum of a tablet friability test apparatus (Electrolab, India). The drum was adjusted to rotate 100 times in 4 min. the tablets were removed, dedusted and accurately weighed. The percent weight loss was calculated.

- **Wetting time**

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

- **Water absorption ratio**

Water absorption ratio, R was determined using following equation.

$$R = (Wa - Wb/Wa) \times 100$$

Where, Wa = Weight of tablet after water absorption
Wb = Weight of tablet before water absorption.

- **Disintegration Time**

The test is carried out on the 6 tablets using the apparatus specified in IP distilled water at $37^0$ C ± $2^0$C was used as a disintegration media and the time in second taken for complete disinigration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

- **In vitro dissolution studies**

In vitro dissolution studies for fabricated Fast Dissolving tablet is carried out by using USP XXIV paddle method at 50 rpm in 900 ml of Sorenson's buffer pH 6.8 as dissolution media, maintained at 37±0.5$^0$C. 10 ml aliquots was withdrawn at the specified time intervals, filtered and assayed spectrophotometrically. An equal volume of fresh medium, which was prewarmed at $37^0$C is replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies are performed in triplicate.

## RESULTS AND DISCUSSION

### Standard Graph of Gemifloxacin Mesylate

**Table 2: Standard graph of Gemifloxacin in 0.1N HCl**

| Concentration (µg/ml) | Absorbance |
|---|---|
| 1 | 0.141 |
| 2 | 0.272 |
| 3 | 0.386 |
| 4 | 0.527 |
| 5 | 0.648 |

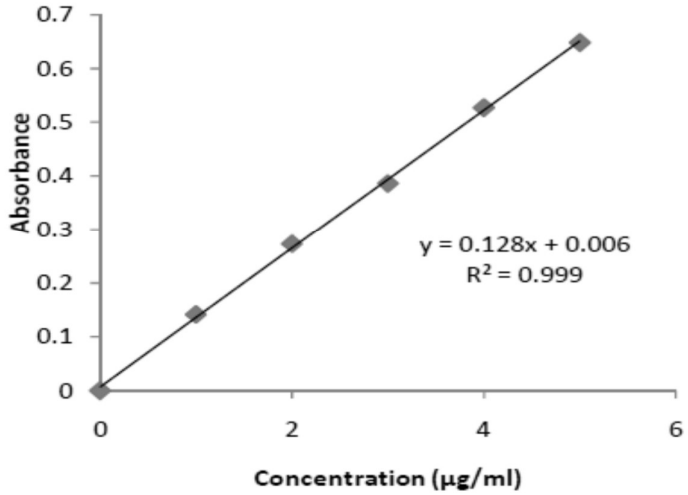


**Fig. 1: Calibration curve of Gemifloxacin in 0.1 N HCl**

## Evaluation of Gemifloxacin- Amberlite IRP 88 Complex

### A) Effect of drug-resin ratio on complex formation

**Table 3: Effect of Drug Resin Ratio on complex formation**

| Drug –Resin Ratio | Time (hrs) | Percent Gemifloxacin Loading |
|---|---|---|
| 1:1 | 3 | 68.02 |
| 1:2 | | 85.26 |
| 1:3 | | 94.75 |

### B) Differential Scanning Calorimetry

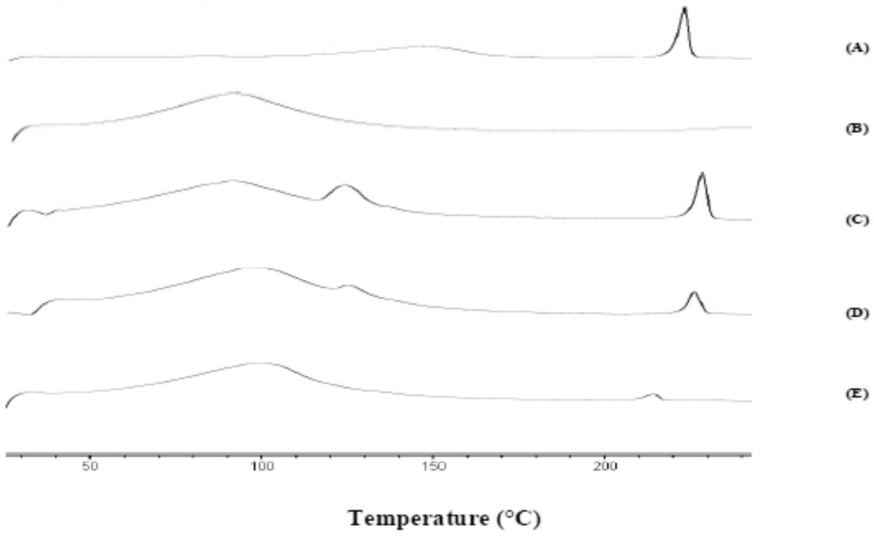


**Fig. 2: DSC Thermograms of (A) Gemifloxacin (B) Amberlite IRP 88 (C) G-IRP 88 (1:1) (D) G-IRP 88 (1:2) (E) G-IRP 88 (1:3)**

## C) Fourier Transform Infrared (FT-IR) Studies

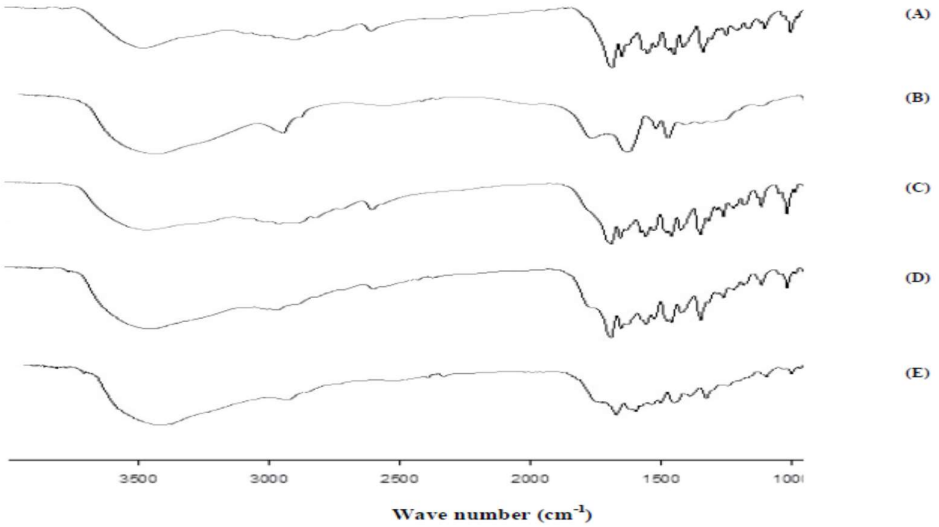


**Fig. 3: FTIR Spectras of (A) Gemifloxacin (B) Amberlite IRP 88(C) G-IRP 88 (1:1) (D) G-IRP 88 (1:2) (E) G-IRP 88 (1:3)**

## D) Drug loading efficiency for DRC

**Table 4: Drug loading efficiency for DRC**

| Drug –Resin Ratio | Time (hrs) | Percent Gemifloxacin Loading |
|---|---|---|
| 1:3 | 3 | 94.75 |

## Precompression parameters of granules

**Table 5: Evaluation of precompression parameters of granules (Drug + IRP 88)**

| Formulation | Angle of repose (θ) | Bulk density (gm/cm$^3$) | Tapped density (gm/cm$^3$) | Compressibility index (%) | Hausner's ratio |
|---|---|---|---|---|---|
| GRT01 | 28.2 | 0.82 | 0.92 | 12.20 | 1.12 |
| GRT02 | 27.8 | 0.81 | 0.91 | 12.35 | 1.12 |
| GRT03 | 27.4 | 0.82 | 0.92 | 12.20 | 1.12 |
| GRT04 | 28.7 | 0.81 | 0.91 | 12.35 | 1.12 |
| GRT05 | 28.3 | 0.82 | 0.91 | 10.98 | 1.11 |

## Post-compression parameters of Gemifloxacin ODTs

**Table 6: Evaluation of Post-compression parameters of Tablets (Drug + IRP 88)**

| Formulation | Thickness (mm) | Hardness (Kg/cm$^2$) | Friability (%) | Weight Variation (mg) | Drug content (%) | Disintegration Time (sec) | Wetting time (sec) | Water Absortion ratio |
|---|---|---|---|---|---|---|---|---|
| GRT01 | 4.59 | 3.9 | 0.19 | 1.5 | 98.25 | 64 | 54 | 0.39 |
| GRT02 | 4.60 | 4.2 | 0.21 | 1.4 | 98.35 | 68 | 60 | 0.38 |
| GRT03 | 4.59 | 4.1 | 0.17 | 1.6 | 98.37 | 39 | 32 | 0.40 |
| GRT04 | 4.60 | 4.1 | 0.20 | 1.3 | 98.43 | 27 | 22 | 0.41 |
| GRT05 | 4.60 | 4.2 | 0.18 | 1.3 | 98.47 | 18 | 16 | 0.42 |

**Table 7: *In vitro* dissolution studies of Gemifloxacin ODTs (Drug + IRP 88)**

| Time (min) | Cumulative % of drug release | | | | |
|---|---|---|---|---|---|
| | GRT01 | GRT02 | GRT03 | GRT04 | GRT05 |
| 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 58.78 | 63.67 | 67.33 | 69.05 | 70.12 |
| 10 | 64.73 | 67.20 | 72.34 | 75.01 | 78.48 |
| 15 | 68.05 | 72.13 | 78.10 | 81.12 | 84.09 |
| 20 | 74.19 | 77.71 | 83.06 | 87.35 | 89.37 |
| 25 | 78.10 | 83.04 | 88.08 | 90.44 | 93.07 |
| 30 | 81.83 | 87.15 | 90.03 | 94.91 | 97.71 |
| 40 | 86.63 | 91.44 | 94.05 | 98.85 | 99.01 |
| 50 | 90.04 | 94.44 | 98.25 | --- | --- |
| 60 | 93.05 | 98.52 | --- | --- | --- |

The percentage drug content of all the tablets was found to be between 98.25 and 98.47 %, which was within the acceptable limits. The results of in vitro disintegration of all the tablets were found to be within the prescribed limits and satisfying the criteria of fast dissolving tablets. The lowest wetting time (16 sec) was obtained with formulation GRT05. Among all the formulations GRT05 which contain 10% of Crosspovidone gave the highest dissolution (99.01 %) at the end of 40 minutes.

## CONCLUSION

Gemifloxacin Mesylate is a broad spectrum antibiotics, active against both Gram- positive and Gram negative bacteria. This drug is highly bitter in taste. The present investigation was undertaken with an overall objective of studying the drug resin complexation (DRC) to mask the bitter taste of the drug. The resin, namely, Amberlite IRP 88 (weak acid cation exchanger) was selected for the study of feasibility of employing drug resin complexation for masking the bitter taste of drug. The main objectives of this research project were to study the drug resin of these drug resin complexes.

From the present study, it is concluded that the Amberlite IRP 88 can be used for taste masking and for formulating fast release products.

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