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Formulation and Evaluation of Sustained Release Tablet of Levofloxacin

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ABSTRACT
The objective of present work was to formulate and evaluate sustained release tablets of levofloxacin for treating microbial infection effectively. Levofloxacin is the active component of the racemate ofloxacin, and used for treating a variety of clinical conditions such as lower respiratory tract infection, acute sinusitis, uncomplicated skin and soft-tissue infections and complicated urinary tract infection. Different formulation (F1-F6) was prepared by wet granulation method using various release rate controlling hydrophilic polymers ethyl cellulose and HPMC with different amount. The formulation (F1-F6) was evaluated for hardness, weight variation, friability and drug content uniformity. The in vitro release of drug from the formulations was studied, and it was found that the prepared tablets were able to sustain the release of the drug. For conclusion, the developed formulations may reduce the dosing intervals, reduce the dose related side effects and increase the drug's efficacy for treating infections.

I. INTRODUCTION

Tablets are solid dosage form each containing a unit dose of one or more medicament. Pharmaceutical tablets are solid, flat or biconvex discs, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents[1-2.] Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical product of different dosage form. For many decades, treatment of acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patient using various pharmaceutical dosage forms including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols, and injectables as a drug carrier. Drug administered by variety of routes but oral administration is adopted ware ever possible. Oral drug delivery is considered the holy grail of drug delivery because convenience results in high patients' compliance. Oral route is the most commonly employed route. all though different route of administration is used for the delivery of drugs, oral route remains the preferred more. It is safest, easiest, and most economical route of drug administration. Amongst drugs that are administered orally solid oral dosage forms i.e., tablets and capsules, represent the preferred class of product. Out of the two oral solid dosage forms, the tablets have number of advantages like temper proof, low, cost and speed of manufacturing (direct compression), ease of administration, patient compliance, and flexibility in formulation etc.

II. MATERIALS &METHODS

Table: 1 List of Material

MATERIAL	NAME OF SUPPLIER
Levofloxacin	Gift sample of IPCA Ratlam

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Ethyl cellulose	Oxford Laboratory, Mumbai.
HPMC	Oxford Laboratory, Mumbai.
HPC	Oxford Laboratory, Mumbai.
Microcrystalline cellulose (MCC)	SU lab baroda
Talc	Oxford Laboratory, Mumbai.
Mg stearate	Central Drug house, New Delhi
Isopropyl alcohol	Oxford Laboratory, Mumbai.
HCL	Oxford Laboratory, Mumbai.
NaOH	RanbaxyFine chemical Ltd. (new Delhi).
Potassium dihydrogen phosphate	Ranbaxy Fine chemical Ltd. (new Delhi).

Table: 2 List of Equipment

EQUIPMENTS	**MANUFACTURED BY**
Digital Weighing balance	DJ Series Shinko Dolphin
Digital Bulk density Apparatus	Jyoti scientific Ind. Gwalior (M.P)

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UV-VIS Spectrophotometer	UV- 1800, Shimadzu Japan
Dissolution apparatus	Jyoti scientific Ind. Gwalior (M.P.)
Fournier- transform	Bunker
Melting point apparatus	Jyoti scientific Ind. Gwalior (M.P.)
Friabilator	Jyoti scientific Ind. Gwalior (M.P.)
Table machine	Rimek macinary
Hardness tester	Monsato

EXPERIMENTAL WORK

1.1. PERFORMULATION STUDY

❖ **Organoleptic characteristics**

- **Colou**r- A small quantity of levofloxacin powder was taken on butter paper and viewed in well-illuminated place.
- **Odour**- Very less quantity of levofloxacin was used to get the odour.

❖ **Melting point determination**

The melting point was determined by the capillary method using digital melting point apparatus. The capillary tube was filled by the pressing the open end gently into pure drug sample and packed by tapping the bottom of the capillary on a hard surface so that the drug pack down into the bottom of the tube. When the drug was packed into the bottom of the tube, the tube was placed into the slot of the apparatus, the apparatus was started and the temperature was noted at which the drug melting.

❖ **Determination of wavelength of maximum absorbance** (λmax): -

50mg of drug was weighed accurately and transferred to 100ml of volumetric flask. Then 0.1N HCL. Was added to dissolve the frug completely. The volume was made up to 100 ml with 0.1N HCL.

❖ **FT-IR Determination: -**

The Ft-IR Analysis of the levofloxacin was carried out for qualitative compound identification. The FT-IR spectra for pure drug were carrier out by KBr disc method, the spectrum was recorded in the range of 4000 cm^{-1} and 400 cm^{-1}.

❖ **SOLUBILITY**

Determination of Solubility of Drug by visual observation. A fixed amount of drug was taken and the distilled water was added and observe the solubility visually. The same procedure was followed for glacial acetic acid, dichloromethane, methanol, phosphate buffer and 0.1N HCL.

❖ **PARTITION COEFICIANT**

Partition coefficient determination of Levofloxacin was done by simple shaking flask method. The 50g of drug was dissolved in 50ml of distilled wate and 50ml of n-octanol inspirating funnel. Shake well the flask then stand for phase separation. After that the

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two phases was separated out and measure the concentration of drug in water and n-octanol.

$P_{o/w} = C_{oil}/C_{water}$

1.2. EVALUATION OF PRECOMPRESSION PARAMETERS

❖ **Angle of Repose**

The angle of repose was determined by fixed funnel method. A funnel was kept vertically in a stand at specific height above a paper on a horizontal surface. The funnel bottom was closed and granules was filled in funnel.

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

Table: 3 RELATIONSHIPS BETWEEN ANGLE OF REPOSE AND FLOW PROPERTIES

ANGLE OF REPOSE (DEGREES).	FLOW
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

1.3 EVALUATION OF TABLETS

❖ **Hardness:**

The term hardness indicates the ability of a tablet to a withstand shocks while handling. Its generally expressed in Kg/cm or in Newton (N).

Tablet hardness was determined by using a Tablet Monsanto Hardness Tester.

❖ **Weight variation test:**

To study weight variation, 20 tablets of each formulation were collected randomly during compression and weighed using an electronic balance to obtain average weight of each tablet. Also, the individual tablet was weighted.

Limit: weight of all individual tablets should be in the limit of average wt. ±5%.

❖ **Friability;**

The test was carried out by using Roche Friabilator. Ten tablets were taken and carefully dedusted prior to testing. The drum was allowed to rotate 100 times, and that the tablets were removed.

Removed loose dust form tablets as before, and weighed accurately.

PARAMETER	TEXTING CONTENT		
	After 1 month	After 2 months	After 3 months
Hardness	5.2±0.1	5.1+0.1	5.0+0.1

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Friability (%)	0.74+0.02	0.74+0.03	0.73+0.03
Weight varration (%)	0.73+0.05	0.73+0.03	0.73+0.04
Drug content	99.24%	99.18%	98.89%

❖ **In -Vitro dissolution studies**

In – Vitro drug release study of tablets was performed in USP dissolution apparatus type 2(paddle). The dissolution test was performed using 900ml of 0.1 n HCL, at 37± 0.5ºC with 50rpm for first 2hr then after dissolution media using phosphate buffer pH 6.8. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus and volume equipment to the amount of sample withdrawn was replaced with fresh dissolution medium.

❖ **IN-VITRO DRUG RELEAFE KINETIC STUDIES**

Kinetic mode had described drug dissolution from solid dosage from where the dissolved amount of drug is a function of test time. In order to study the exact mechanism of drug release from the tablets. Drugs release data was analysed according to zero order, first order, Higuchi square root. Korsmeyer- peppas model. The regression coefficient R^2 value nearer to 1 indicated the model fitting of the release mechanism.

III. RESULT ANDDISCUSSION

Best formulation (F6) was selected among the prepared formulation and used for the stability study. The below table depicts that there is no significant changes were found in the hardness, friability, weight variation, when the tablets were investigated at 40ºC/75% RH for 3 months. Only drug content was found to be decrease.

IV. CONCLUSION

The conclusion drawn from the present investigation were given below:

Suitable analytical method based on UV-Visible spectrophotometer was developed for levofloxacin max of 290 nm (0.1 N HCL) and (pH 6.8 buffer) was identified. All the excipients used did not interfere with the estimation levofloxacin at analytical wave length 290nm (0.1 N HCL) and (pH 6.8 buffer) procedure to manufacture sustained release tablets were established. Sustained release tablets of levofloxacin were successfully prepared using ethyl cellulose, HPMC and HPC as excipients and by wet granulation method. The tablets evaluated for pharmacopoeia and non-pharmacopeial (industry specified) tastes. Based on the results, formulation F1 – F6 was prepared amongst this formulation F6 was better release. The prepare sustained release tablet formulation was found to exhibit satisfactory physiochemical characteristics and release kinetic study of optimised formulation showered that the drug release from sustained release tablet of levofloxacin followed zero ordered release kinetics. The sustained release tablets were successfully developed.

Further studies are needed to investigate these formulations for its performance in vivo and its bioequivalence with the available commercial product.

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