Research Article CODEN: IJPRNK ISSN: 2277-8713
Kalyan Chakravarthi T, IJPRBS, 2015; Volume 4(6): 238-258 IJPRBS

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

FORMULATION AND EVALUATION OF LEVOFLOXACIN IMMEDIATE RELEASE TABLETS

KALYAN CHAKRAVARTHI T, SIVARAM PRASAD AKURATHI, RAM BHRAMHA REDDY

Department of Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Kantepudi, Sattenapalli, Andhra Pradesh, India.

Accepted Date: 19/12/2015; Published Date: 27/12/2015

Abstract: The objective of the present study to design and to develop a stable immediate release oral solid dosage form for levofloxacin (250mg) of film coated tablets with an aim to improve the bioavailability of the drug. Levofloxacin is an antibacterial agent. Then prepared tablets were evaluated for in-vitro drug release. In the present study Crospovidone is used as disintegrate, HPMC as a binder. Different Formulation were made with different concentrations. Finally film coated tablet for optimized formulation that is F4 is obtained. From above all trials and observations we conclude that batch no F-4 is showing result within limits. It gives for all required parameters for core tablet. Finally packed in HDPE Containers for stability studies were conducted at 40^{o}C/ 75%RH, evaluated for some parameters after 3 months and the formulation is stable for all evaluation parameters.

Keywords: Levofloxacin, Immediate Release Tablets, Crospovidone, Dissolution studies, Stability studies.

PAPER-QR CODE

Corresponding Author: MR. KALYAN CHAKRAVARTHI T

Access Online On:

www.ijprbs.com

How to Cite This Article:

Kalyan Chakravarthi T, IJPRBS, 2015; Volume 4(6): 238-258

INTRODUCTION

1.1. ORAL DRUG DELIVERY

Oral drug delivery is the most widely utilized route of administration among all the routes of administration that has been explored for the systematic delivery of drug through different pharmaceutical dosage forms. The oral route of drug administration is the most important method of drugs for systemic affects. It can be said that at least 90% of all drugs used to produce systemic effect by are administered orally. They present wide range of comforts to manufacturer as well as the patient.[2] A drug delivery system (DDS) is defined as a formulation or a device that enables the introduction of a therapeutic substance into the body and improves its efficacy and safety by controlling the rate, time, and site of release of drugs in the body. The goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration. Oral route of drug administration is most appealing route for delivery of drugs for various dosage forms [1-4].

1.2. Immediate release drug delivery system

The term immediate release'' pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation and / or the absorption of drug, is neither intentionally non apreciably, retarded by galenic manipulations. In the present study, immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluents or carriers does not prolong, to an appreciable extent, the rate of drug release or absorption. The term excludes formulations which are adapted to provide for controlled, prolonged, sustained, modified, extended or delayed release of drugs.

The term ''release'' includes the presentation of drug from the formulation to the gastrointestinal tract, to body tissues and/ or in to systemic circulation. For gastrointestinal tract release, the release is under pH conditions such as 1 to 3. In an aspects of the invention a formulation as described here with a compound of formula, or an acid addition salt thereof, release drug under pH conditions such as pH 1 to 3, especially at or about pH=1. Formulations of the invention may release at least 70% of active ingredient within 4 hours, preferably 2 hours, most preferably 1.5 hours, especially within hour (within 30minutes) of administration whether this be oral or parenteral. [5-8]

Immediate release drug delivery system is also conventional type of drug delivery system as it is defined as – Immediate release tablets are designed to disintegrate and release their medicaments with no special rate controlling features such as special coatings and other techniques [8-10].

1.3. Advantages of immediate release drug delivery systems:

- Release the drug immediately.
- More flexibility for adjusting the dose.
- It can be prepared with minimum dose of drug.
- There is no dose dumping problem.
- Immediate release drug delivery systems used in both initial stage and final stage of disease.
- At the particular site of action, the drug is released from the system.

2. MATERIALS AND METHODS

2.1. MATERIALS USED

Materials	Functional category
Levofloxacin	Anti-bacterial
Microcrystalline cellulose (P^H 101 and 102)	Diluent
Crosspovidone	Disintegrant
Hydroxy propyl methyl cellulose 5cps	Binder
Magnesium stearate	Lubricant
Opadry brown 03f86991	Coating aid

2.2. METHODS USED

2.2.1. PREFORMULATION STUDIES

Preformulation studies are performed to investigate the physical and chemical properties of a drug substance alone and also when combined with other substances such as excipients. It is the first step in the rational development of dosage forms.

Objective and Scope

The objective of performing Preformulation testing is to generate information that will be helpful in developing a stable and bioavailable dosage form when combined with excipients. The use of Preformulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product and at same time provides the basis for optimization of the drug product quality.

Organoleptic properties

The colour, odour and taste of the drug were recorded using descriptive terminology.

Angle of Repose:

The flow property was determined by measuring the Angle of Repose. It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal plane. Such measurements give at least a qualitative assessment of the internal cohesive and frictional effects under low levels of external loading, as might apply in powder mixing, or in tablet die or capsule shell filling operations. [11]

$\tan \Phi = 2h / D$

where, h = height of the heap

D = diameter of the horizontal plane

Bulk density:

Bulk density is ratio of given mass of powder and its bulk volume. Bulk density was determined by measuring the volume of known mass of powder sample that has been passed through the screen in to graduated cylinder or through volume measuring apparatus in to cup. [12]

Bulk density $(\rho_b) = M / V_b$

Where, M= mass of the powder;

V_b= bulk volume of the powder.

Tapped density:

A known quantity of powder was transferred to a graduated cylinder and volume V_0 was noted. The cylinder fixed to a density determination apparatus, tapped for 500 times then reading was observed. The density is achieved by mechanically tapped by a measuring cylinder containing the powder sample. After observing the initial volume, the cylinder is mechanically tapped and volume reading were taken until little further volume changes is observed. [13]

Tapped density = M / V_r

Where, M = mass of the powder,

V_r= final tapping volume of the powder

Compressibility Index and Hausner Ratio:

While there are some variations in the method of determining the compressibility index and Hausner ratio, the basic procedure is to measure the unsettled apparent volume ($\mathbf{V_O}$), and the final tapped volume, ($\mathbf{V_f}$) of the powder after tapping the material until no further volume changes occur. [14-16]

The compressibility index and the Hausner ratio are calculated as follows:

Compressibility index = $100 \times V_o\text{-}V_f / V_o$

Hausner ratio = Vo/Vf

Where, **Vo** = apparent volume

$\mathbf{V_f}$ = final tapped volume

Alternatively, the Compressibility index and Hausner ratio may be calculated using measured values of Bulk density and Tapped density as follows:

Compressibility index = 100 × Tapped density / Bulk density

Hausner ratio = Tapped density / Bulk density

Table-1: Flow properties and corresponding Angle of repose, Compressibility index and Hausner ratio

S. No	Flow properties	Angle of repose (Φ)	Compressibility Index (%)	Hausner ratio
1	Excellent	25-30	<10	1.00-1.11
2	Good	31-35	11-15	1.12-1.18
3	Fair	36-40	16-20	1.19-1.25
4	Passable	41-45	21-25	1.26-1.34
5	Poor	46-55	26-31	1.35-1.45
6	Very poor	56-65	32-37	1.46-1.59
7	Very very poor	> 66	>38	>1.6

Drug-Excipient Compatibility studies:

Drug is in intimate contact with one or more excipients in all the dosage forms. Later it could affect the stability of drug. Knowledge of drug-excipients interaction is useful in selecting an appropriate excipient.

Drug and excipients are stored at 550^{0}C for 14 days, 400^{0}C at RH 75% for 14 days, 28days. After 14, 28 days they are subjected for analysis of description, assay, LOD, purity

Solubility studies:

Solubility can be determined by adding the solute in small incremental amount to fixed volume of the solvents. After each addition, the system is vigorously shaken and examined visually for any un dissolved solute particles. Solubility of acid base drug is pH dependent. It is determined over the pH range 1-8. Then the assay is carried out by using following formula by U.V or HPLC method.

% solubility = sample absorbance /standard absorbance × dilution factor x 100

2.2.2. COMPARATOR PRODUCT CHARACTERISATION

The Innovator product **TAVANIC** tablets 250mg (Levofloxacin hemihydrate) manufactured by **Sanofi-Aventis, Russia** were studied for physicochemical properties. The results are tabulated below.

Table 2: Comparator Product Characterisation

S.NO	TAVANIC (Excipients in tablet core)	MSN (Excipients in tablet core)
1	Crosspovidone	Crosspovidone
2	Hydroxy propyl methyl cellulose	Hydroxy propyl methyl cellulose
3	Microcrystalline cellulose	Microcrystalline cellulose
4	Sodium stearylfumerate	-
5	-	Magnesium stearate
	Excipients in tablet coating	**Excipients in tablet coating**
6	Hydroxy propyl methyl cellulose	Hydroxy propyl methyl cellulose
7	Titanium dioxide E 171	Titanium dioxide E 171
8	Talc	Talc
10	-	Triacetin

11	Macrogol	Macrogol
12	Yellow ferric oxide E 172	Yellow ferric oxide E 172

2.2.3. EVALUATION OF TABLETS:

1. Physical Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

2. Size & Shape:

It can be dimensionally described & controlled. The thickness of a tablet is only variable. Tablet thickness can be measured by micro-meter or by other device. Tablet thickness should be controlled within a ± 5% variation of the standard value.

3. Weight Variation Test:

Twenty tablets were weighed individually and the average weight was calculated. The individual tablet weights are then compared to the average weight. Not more than two tablets should differ in their average weight by more than percentages stated in USP. No tablet must differ by more than double the relevant percentage. [17]

Table 3: Limits for Tablet Weight variation test:

Average weight of tablet (mg)	% Difference allowed
130 or less	10 %
From 130 to 324	7.5 %
> 324	5 %

4. Content Uniformity:

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. Due to increased awareness of physiological availability, the content uniformity test has been included in the monographs of all coated and uncoated tablets and all capsules intended for oral

administration where the range of size of the dosage form available include 50mg or smaller sizes. [18]

Method:

Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labelled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labelled content. If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range.

5. Thickness and diameter:

The thickness and diameter of 10 tablets were recorded during the process of compression using Vernier calipers.

6. Hardness:

Hardness, which is now more appropriately called **Crushing strength** determinations are made during tablet production and are used to determine the need for pressure adjustment on compression machine.

If the tablet is too hard, it may not disintegrate in the required period of time to meet the dissolution specifications; if it is too soft, it may not be able to withstand the handling during subsequent processing such as coating or packaging and shipping operations.

The force required to break the tablet is measured in kilograms. The small and portable hardness tester measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet. [19]

7. Friability:

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. It is usually measured by the use of the Roche friabilator. [20]

Method:

A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is

expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked.

The percentage friability was determined by the formula:

% Friability = $(W_1-W_2) / W_1 X 100$

W_1 = Weight of tablets before test

W_2 = Weight of tablets after test

8. Disintegration Test:

For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the first important step toward this condition is usually the break-up of the tablet, a process known as disintegration.

The disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. Generally, the test is useful as a quality assurance tool for conventional dosage forms. [21]

Method:

The U.S.P. device to test disintegration uses 6 glass tubes. Long, open at the top and 10 mesh screen at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2^0 C such that the tablet remains 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. If one or two tablets fail to disintegrate, the test is repeated using 12 tablets.

Disintegration time specifications:

- Uncoated tablet: NMT 30 minutes
- Coated tablet: NMT1 hours

9. Dissolution:

Dissolution is the process by which a solid solute enters a solution. In the pharmaceutical industry, it may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition. [22-25]

Dissolution is considered one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability.

In-vitro drug release of the samples is carried out in **USP-Type II** Dissolution Apparatus (**Paddle type**) and Quantitative determination by **UV-Spectroscopic method**.

Stability studies:

The purpose of stability testing is to provide evidence of the quality of the drug substance or drug product, and how it varies with time under the influence of a variety of environmental conditions (heat, light, humidity, air etc). The final formulation was packed in suitable packing like blister and strip packs and then they will be kept at different temperature, humidity conditions and the samples will be analyzed for their chemical and physical properties. The formulation is subjected to Short term testing at 40±2°C and 70±5 % RH for 3 months. [23]

Table 4: Composition of Immediate release Levofloxacin hemihydrate 250 mg tablets

	Ingredients	F2 (mg)	F1 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)
1	**Levoxacin hemihydrate**	259.05	259.05	259.05	**259.05**	259.05	259.05	259.05	259.05
2	**Microcrystalline cellulose P^H 101**	57.35	57.35	52.35	**52.35**	62.35	62.35	57.35	57.35
3	**HPMC-5CPS (binder)**	15.00	15.00	20.00	**15.00**	10.00	10.00	15.00	15.00
4	**Crosspovidone (disintegrant)**	15.00	10.00	15.00	**15.00**	15.00	10.00	–	7.5
5	**Magnesium stearate**	3.6	3.6	3.6	**3.6**	3.6	3.6	3.6	3.6
6	**Crospovidone**	-	5.00	-	**5.00**	-	5.00	15.00	7.5
7	**Purified Water**	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
8	**Opadry red premix**	10.00	10.00	10.00	**10.00**	10.00	10.00	10.00	10.00
	Total	360	360	360	**360**	360	360	360	360

3. RESULTS AND DISCUSSION

Analysis of innovator product:

1. **Description:**

Tablet was yellow colored caplet shaped film-coated with plane surface on both sides with 15.0mm length and 6.5mm width.

2. **Average weight:**

Average weight of tablet was found to be 360.0mg

3. **Thickness:**

Average thickness was found to be 4.00± 0.3mm

4. **Hardness:**

Hardness was found to be 6.5-7.5kp

5. **Friability:**

Friability was found to be0.5 %

6. **Uniformity of weight:**

Randomly tablet weights were taken and found to be

Table 5: Results for uniformity of weight of innovator product

s.no	Weight(mg)	s.no	Weight
1)	355.6	6)	360.4
2)	363.5	7)	360.2
3)	360.8	8)	359.8
4)	362.1	9)	356.6
5)	361.0	10)	359.8

7. **Disintegration time:**

Average disintegration time was found to be 5 ±0.35minutes.

***In vitro* dissolution studies:**

Table 6: Results for *in-vitro* drug release of innovator product

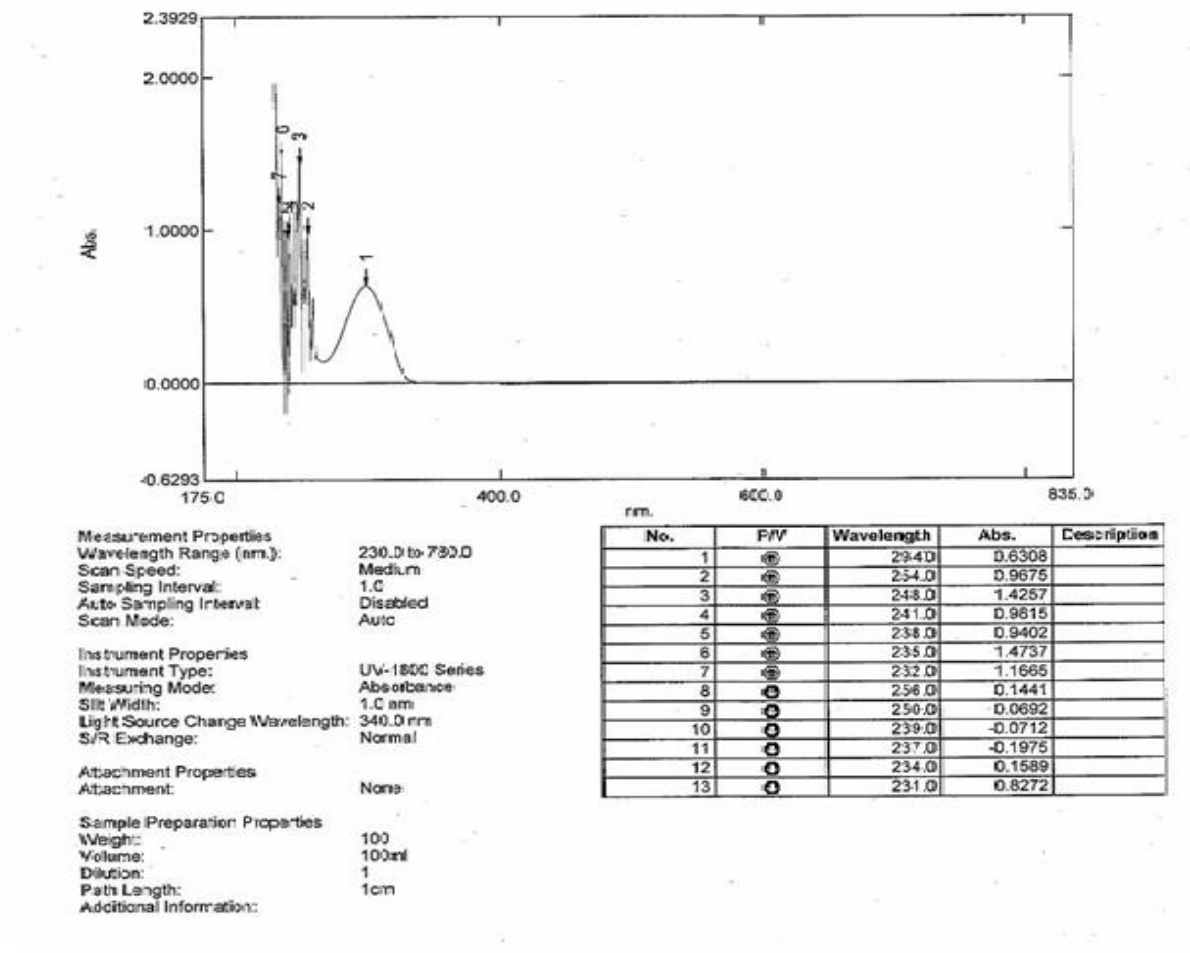
	10min	20min	30min	45min
Average	44.1±0.18	88.5±0.25	101.3±0.28	101.4±0.35

Results for Pre-formulation studies of Levofloxacin hemihydrate:

Table 7: Results for pre formulation studies of Levofloxacin hemihydrate

Sr. No.	Test	Test Procedure / Methods
1.	Appearance	Almost white to yellow crystalline powder.
2.	Solubility	Soluble in chloroform, slightly soluble in methanol and water.
4.	Identification	a) Melting point-218.0 b) UV absorbance maximum- 293 c) IR absorption spectrum of sample should be concordant with the Levofloxacin hemihydrate reference standard.
5.	Bulk density	0.537gm/ml
7.	Loss on Drying (in vaccum)	3.4 %w/w
9.	Assay	=99.9%

Report for λ_{max}:



No.	P/V	Wavelength	Abs.	Description
1		294.0	0.6308	
2		254.0	0.9675	
3		248.0	1.4257	
4		241.0	0.9815	
5		238.0	0.9402	
6		235.0	1.4737	
7		232.0	1.1665	
8		256.0	0.1441	
9		250.0	0.0692	
10		239.0	-0.0712	
11		237.0	-0.1975	
12		234.0	0.1589	
13		231.0	0.8272	

Results for evaluated lubricated blend ready for compression:

Table 8: Results for evaluated blend

S.NO	B.D	T.D	C.I	H.R	Angle of repose(θ)
F 1	0.545	0.664	17.92	1.219	27.30
F 2	0.535	0.701	23.3	1.30	27.74
F 3	0.533	0.652	18.21	1.22	28.60
F 4	0.441	0.571	22.94	1.29	29.52
F 5	0.492	0.614	19.86	1.2479	29.65
F 6	0.4255	0.555	23.33	1.304	28.40
F 7	0.537	0.622	19.0	1.234	28.35
F 8	0.533	0.652	18.21	1.22	29.65
Reproducibility batch's :					
R-1	0.4255	0.555	23.33	1.304	29.52

R-2	0.492	0.614	19.86	1.2479	29.88
R-3	0.441	0.571	22.94	1.29	28.65

Table 9: Results for weight variation

S.NO	Limit **(342.0-378.0mg)**
F 1	355.9±0.28
F 2	362.9±0.24
F 3	363±0.21
F 4	358.9±0.29
F 5	365.1±0.20
F 6	362.8±0.27
F 7	355.6±0.18
F 8	363.1±0.39
R-1	360.4±0.26
R-2	357.2±0.19
R-3	363±0.21

Table 10: Results for Average weight, Thickness, Hardness, Friability, D.T.

Formulation	Average weight (mg)	Thickness (range in mm)	Hardness (Range in kp)	Friability (%)	D.T (minutes)
Limits	352.8-367.2 mg	4.00 ±0 .3 mm	6.5–7.5 kp	NMT 1%	NMT 30min
F 1	359.45	4.09	7.1	0.17	5’50”
F 2	360.01	4.07	6.7	0.11	4’20”
F 3	361.05	4.18	7.4	0.15	7’30”
F 4	361.45	4.12	6.9	0.13	5’00”
F 5	362.6	4.19	6.6	0.15	3’30”
F 6	359.45	4.19	6.9	0.24	4’45”
F 7	358.15	4.08	7.0	0.24	6’45”
F 8	359.78	4.22	6.7	0.17	5’15”
R-1	359.2	4.16	7.1	0.22	5’00”
R-2	361.1	4.18	6.9	0.23	5’20”
R-3	360.02	4.08	6.9	0.22	5’45”

Fig. No.1: Comparative graphical representation of friability of 9 trails

Fig. No. 2. Comparative graphical representation of DT of 9 trails

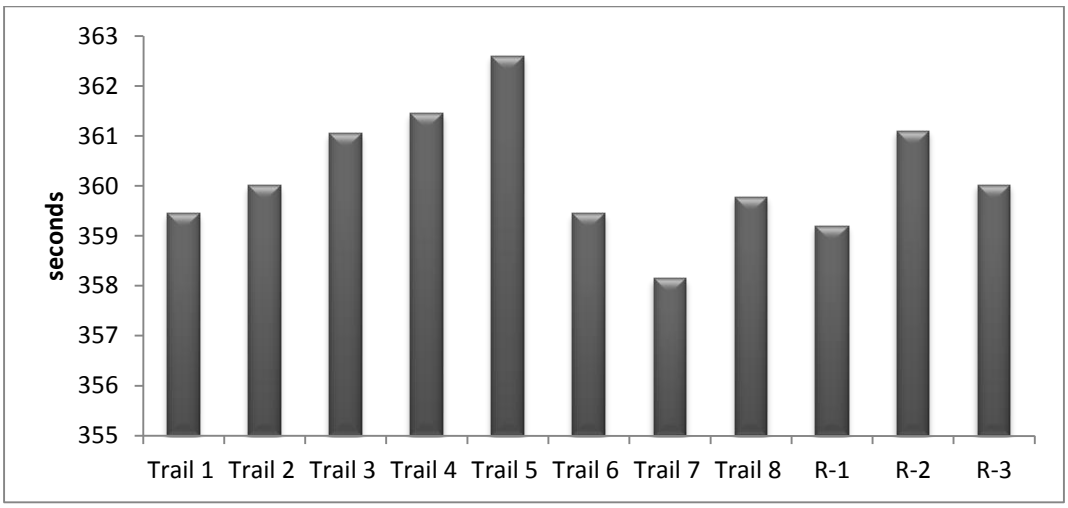
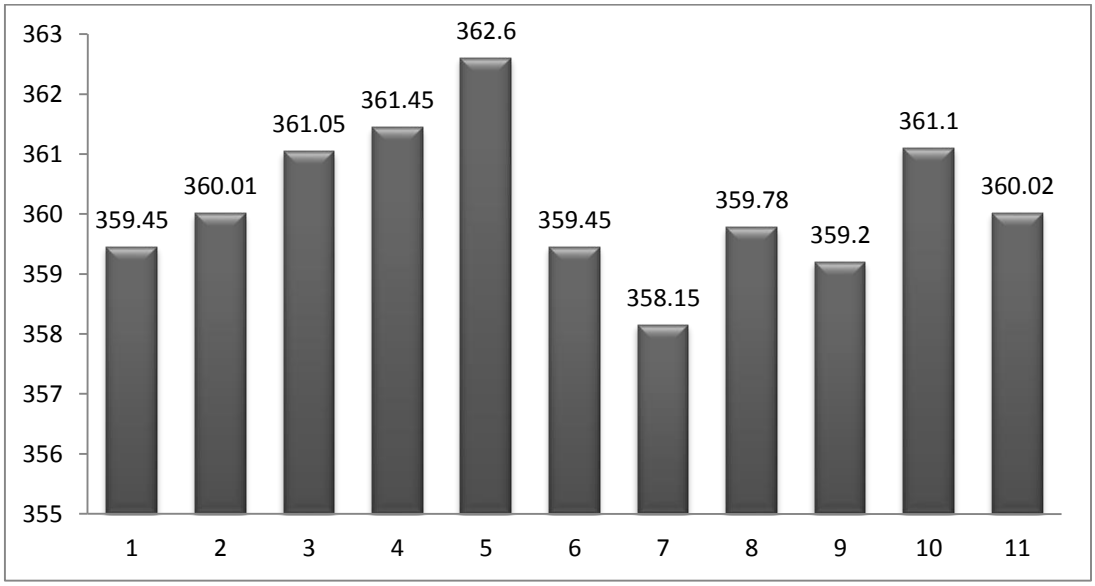


Fig. No.3: Comparative graphical representation of average weight of 9 trails



***In vitro* Drug Release Studies:**

In vitro drug release of the samples was carried out by using **USP Type II Dissolution Apparatus (paddle type).** The dissolution medium,**900 ml 0.1N Hcl**, was placed into dissolution flask, maintaining a temperature of **37±0.5^{0}C** and rpm of **100**.The apparatus was allowed to run for 1hour. Samples measuring 2 ml were withdrawn at 10min, 20min, 30min, 45 mins, using 2 ml pipette. The fresh dissolution medium (37^{0}C) was replaced every time with the same quantity (2 ml) of dissolution medium. Collected samples were suitably diluted with 0.1N Hcl and analysed at **294 nm** using **0.1N Hcl as blank**. The percentage drug release was calculated.

Table 11: Percentage Drug Release in 0.1N Hcl

Trail's	% Drug release in 0.1N Hcl, 900ml, Basket, 100 RPM			
	10min	20min	30min	45 min
F 1	41.2	75.5	90.2	99.6
F 2	45.6	80.1	98.2	101.2
F 3	38.6	69.5	82.4	98.2
F 4	**46.5**	**80.6**	**98.9**	**100.6**
F 5	53.8	79.9	99.6	100.1
F 6	50.4	78.6	94.6	99.6
F 7	40.8	75.8	98.6	100.6
F 8	46.6	81.0	94.8	99.9
Innovator	44	88.5	101.3	101.4
R-1	46.5	80.6	98.9	100.3
R-2	46.5	80.6	98.9	100.6
R-3	46.5	79.9	98.4	100.2

Dissolution Studies

The dissolution rate studies were performed to evaluate the dissolution character of immediate release Levofloxacin tablets. The dissolution study of all formulations showed the percentage drug release and were found to be F1-99.6%, F2-101.1%, F3-98.2%, F4-100.6%, F5-100.1%, F6-99.6%, F7-100.6%, F8-99.9% in 45min period. Among all the formulations, F4 values were found very near to that of Innovator (Tavanic) drug, when compared to other trial batches. Hence F4 is considered to be the best formulation based on its release characteristics.

Fig No:4. Dissolution Profile of Different Formulations (F1-F5)

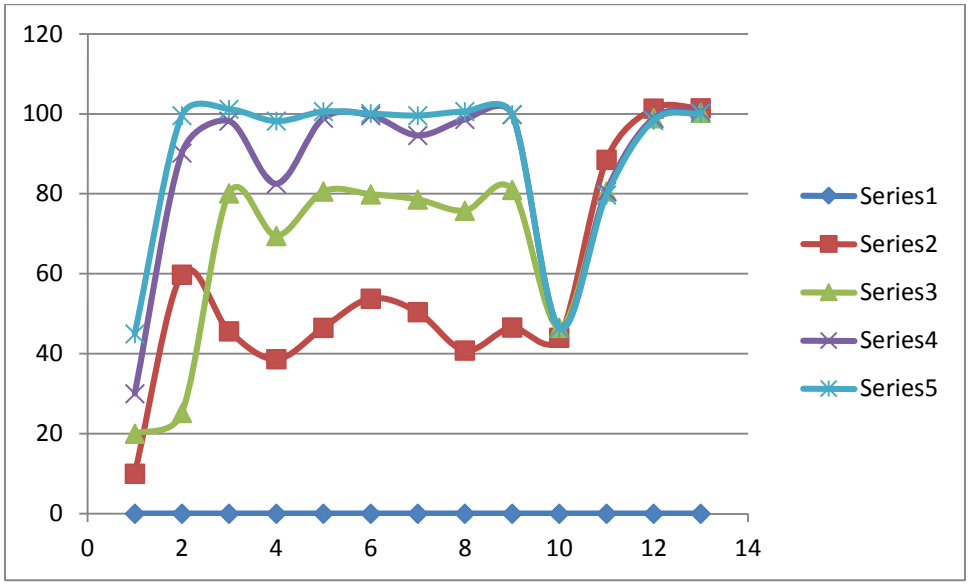
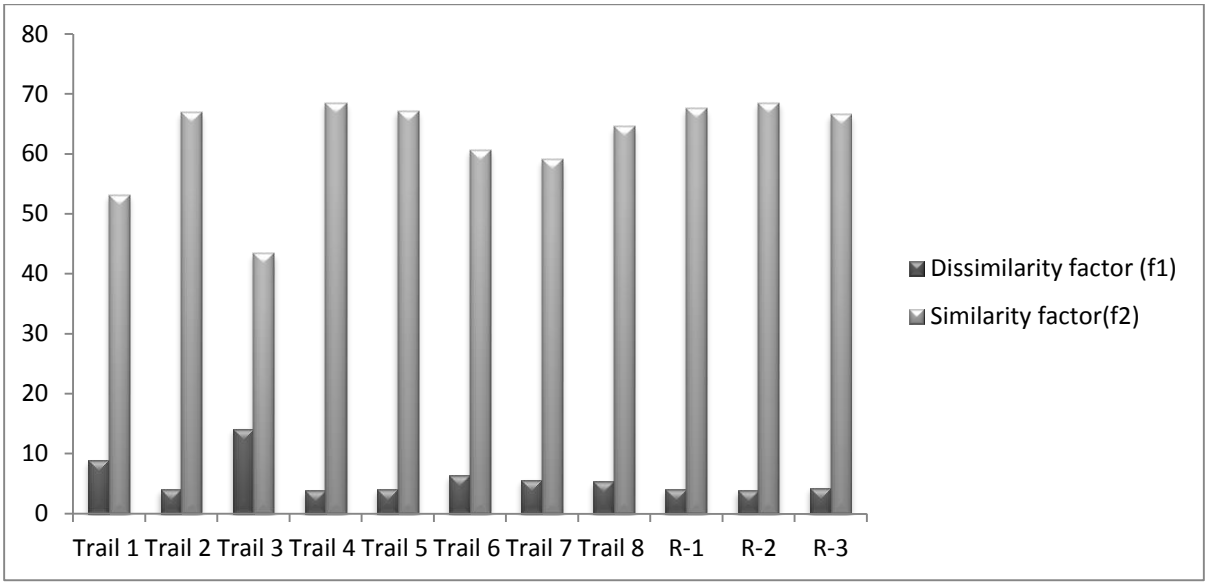


Table 12: Results for Dissimilarity (*f1*) and similarity (*f2*) factors

Formulation	Dissimilarity factor (*f1*)	Similarity factor(*f2*)
F 1	8.89	53.14
F 2	4.02	66.92
F 3	14.11	43.43
F 4	3.81	68.50
F 5	3.98	67.13
F 6	6.32	60.64
F 7	5.56	59.09
F 8	5.32	64.55
R-1	4.05	67.51
R-2	3.81	68.50
R-3	4.22	66.56

FigNo.5: Comparative representation of *f1* and *f2* values of 9 Formulation



4. SUMMARY AND CONCLUSION

Formulation **1** to **8** was prepared by the method of wet granulation with varying concentrations of disintegrate, binders.

Formulation **1** all physical parameters of the tablet found satisfactory, hardness was found to near to the upper limit and similarity factor (53.14) was near to limit NMT 50, initially release was slow compared to innovator.

Formulation **2** all physical parameters found satisfactory a small portion of disintegrate was added to the extra granular portion, there was a slight increase in the initial release of drug and similarity factor was found to be increased.

Formulation **3, 4, 5:** These 3 formulations were done with varying concentrations of binder. In formulation 3 binder concentration was slightly increased and was not found satisfactory in terms of DT (>7 min), similarity factor (43.43) which was not in the limit

In formulation **4** all the parameters were found to be good, similarity factor was also with in the limit (68.5)

In formulation **5** was also found to good in all aspects and hardness was found to in lower limit.

Formulation **6** in this formulation concentration of binder and disintegrate was slightly decreased and was found to be good in all aspects.

Formulations **7, 8:** In this formulations varying amount of disintegrate was added in intra and extra granular portion and found to be satisfactory and similarity factors was found to be 59.09, 64.55 for formulation 7 & 8 respectively.

Among all the design formulations F-4 is showing optimized (acceptable) results with in USP limits &same like that of innovator. Similarity and dissimilarity study the obtained results matched with innovator. There is no undesirable change is found in accelerated stability condition for 1&3 months in optimized formulated batch.

From above all trials and observations we conclude that batch no F-4 is showing result within limits.

5. REFERENCES

1. http://www.drugbank.ca/drugs/ketoralac.

2. *Hand book of excipients*; 2006: 5: 132-135, 211-213, 430-433,731-733, 800-801.

3. http://www.drugs.com/cdi/levofloxacin .html#MIOX7WDxw8ws6Qiy.99

4. http://en.wikipedia.org/wiki/levofloxacin.

5. Brahmankar, sunil jaiswal, Biopharmaceutics and pharmacokinetics a treatise:25.

6. Modern Pharmaceutics, Gilbert S. Banker Christophel T. Rhodes, 2nd edition,1990.

7. Modern Pharmaceutics, Gilbert S. Banker Christophel T. Rhodes, 2nd edition,1990.

8. Leon Lachmann, Herbert A, Liberman, Joseph L. King, The theory and practice of Industrial pharmacy 293-303.

9. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 8th edition 227-260.

10. Aulton's Pharmaceutics, The design and Manufacture of Medicines, Biopharmaceutics and Pharmacokinetics, A Treatise, 2nd edition valabh Prakashan 315-384.

11. Debjit Bhowmik, Chiranjib. B, krishnakanth, Pankaj, R. Margret Chandira.

12. Fast Dissolving Tablet: An Overview, Journal of Chemical and Pharmaceutical Research, 2009, 1(1): 163-177.

13. Dali SHUKLA, Subhashis, CHAKRABORTY, Sanjay SINGH, Brameshwar Mishra Mouth Dissolving Tablets II: An Overview of Evaluation Techniques www.scipharm.at.

14. SusijitSahoo, B. Mishra, P.IK. Biswal, Omprakash Panda, Santosh Kumar Mahapatra, Goutam Kumar Jana, Fast Dissolving Tablet: As a Potential Drug Delivery System, Drug Invention Today 2010, (2), 130-133.

15. Gupta, AK Mishra, V Gupta, P Bansal, R. Singh, AK Singh, REVIEW ARTICLE, Recent Trends of Fast Dissolving Tablet: An Overview of Formulation Technology, International Journal of Pharmaceutical & Biological Archives 2010: 1(1): 1-10.

16. Reddy L.H et al., "Fast Dissolving Drug Delivery Systems: A Review of the Literature, IJPS July 2002: 331-336.

17. Margert Chandira. R Jayakar. B, Pasupathi, A. Chakrabarty, B.L Maruya. P, Design Development and Evaluation of Immediate Release Atorvastatin and Sustained Release Gliclazide Tablets Journal of Pharmacy Research, Vol 2, No 6 (2009).

18. Vaishali Kilor, Nidhi Sapkal, Jasmine Awari, Bharti Shewale, Development and Characterization of Enteric-Coated Immediate-Release Pellets of Aceclofenac by Extrusion/Spheronization Technique Using Carrageenan as a Pelletizing Agent, AAPS Pharm Sci Tech Vol11, No 1 Mar 2010, doi: 10.1208/s12249-0109389-9, Pages 336-343.

19. Marc Hochberg, Jay L. Goldstein, John G. Fort, Mark Sostek, John Plachetka, A Novel Single Tablet Formulation that Delivers Immediate- Release Omeprazole of Followed by Enteric* Coated Naproxen significantly reduces the incidence of Gastric ulcers compared with EC. Naproxen alone: Results of Prospective, Randamized, Double blinded 6-month study including patients with OA and RA EULAR 2008 Paris, France 11-14 June 2008.

20. http://www.pozen.com/product/posters/EULAR%AZ44531_hochberg.pdf

21. B. G. Shiyani, R. B. Dholakiyal, B. V. Akbari, D. J. Lodhiyal, G. K. Ramani, Development and Evaluation of Novel Immediate Release Tablets of Metoclopramide HCl by direct compression using treated gellan gum as disintegration-accelerating agent. Journal of Pharmacy Research, 2009 2(9),1460-1464.

22. Pharmaceutical evaluation of different brands of levofloxacin tablets (250 mg) available in local market of Karachi (Pakistan) Raheelabano, Shahnazgauhar, Syed baqirshyumnaqvi and Shoukat mahmood, Baqai Institute of Pharmaceutical Sciences, Baqai Medical University, Karachi, Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi *Received: 04 July 2010, Revised and Accepted: 31 July 2010.*

23. Sekar V, Chellan VR, Immediate Release tablets of Telmisartan using super disintegrate-formulation, evaluation and stability studies. Chem Pharm Bull (Tokoyo), 2008 Apr; 56(4): 575-577.

24. Brahmaiah. B, Prasannakumar Desu, Ch. Dileep, Sreekanth Nama, Formulation and evaluation of extended release mucoadhesive microspheres of simvastatin, International journal of Pharmaceutical and Biomedical Research, 2013, 4(1), 57-64.

25. Brahmaiah Bonthagarala, Nama Sreekanth, Leela Madhuri Pola, Enhancement of Dissolution Rate of Ciprofloxacin by using Various Solid Dispersion Technique, International Journal of Pharmaceutical Sciences and Research, IJPSR, 2013; Vol. 4(11): 4376-4383.