PHARMACEUTICAL EVALUATION OF DIFFERENT BRANDS OF LEVOFLOXACIN TABLETS (250MG) AVAILABLE IN LOCAL MARKET OF KARACHI (PAKISTAN)

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ABSTRACT

Purpose: Main purpose of the present study is to minimize health risk factors while maximizing the safety of the people of Karachi to maintain and improve their health. The present study is concerned to investigate and compare the physicochemical equivalence, in-vitro activity of drug against hospital isolates of bacteria and efficacy of different brands of tablets containing Levofloxacin prepared by various Pharmaceutical industries under different trade names.

Methodology: The assessment included the evaluation of physical parameters i.e. weight variation, thickness, hardness, friability, disintegration time, dissolution test as well as chemical assay. The susceptibility test of drug was also carried out using agar dilution method on standard strains of E. coli (ATCC-25922) and *Staphylococcus aureus* (ATCC - 25923) along different isolates obtained from health care setups.

Result: Weight variation of the tablets proved statistically that all of the tablets were in accordance to the required limits that is not more then ±5% deviations. Dissolution test was carried out; none had potency less than 85% within 45minutes the required specification, not less than Q+5%. Pharmaceutical assay was carried out none had potency less than the required specification (95.00% - 105.00%).Levofloxacin had MIC_{90}; 0.03μg/mL against E.coli standard and MIC_{90}; 0.12μg/mL against *Staphylococcus aureus* that are similar to previous studies. **Conclusion:** In conclusion, this study will help in the availability of economical and Quality products in the market, whether they are manufactured by local or Multinational Pharmaceutical companies – resulting in a better health care of our country. Promoting conditions that enable people to make healthy choices and providing information so that they can make appropriate decisions about their health.

Keywords: Levofloxacin; Antibacterial activity; Pharmaceutical quality; Comparative evaluation; Physiochemical property.

INTRODUCTION

The oral route is most frequently used for introducing drugs into the body, and in fact the vast majority of drug dosage forms are designed for oral ingestion, primarily for ease of administration, it should be recognized that this mode of administration may result in inefficient and erratic drug therapy. Whenever a drug is ingested orally, one would like to have that drug absorbed into the bloodstream rapidly and completely [1].

Tablets are the most frequently administered oral solid dosage form. The increase in the number of generic drug products from multiple sources has placed people involved in the delivery of health care in a position of having to select one from among several seemingly equivalent products. For instance, in 1975 approximately 9% of all prescription drugs dispensed in the United States were generic versions [2]. This figure rose to 20% in 1984 and 40% in 1991. Over 80% of the approximately 10,000 prescription drugs available in 1990 were obtained from more than one source and variable clinical responses to these dosage forms supplied by two or more drug manufacturers was documented [3]. These variable responses may be due to formulation ingredients employed, methods of handling, packaging and storage and even the rigors of in-process quality control. Thus, Michael, et al., 2003 suggested that there is need to determine their pharmaceutical and therapeutic equivalence in order to ensure interchangeability [4].

Antibiotics are among the most frequently prescribed medications in modern medicine, they cure disease by killing or inhibiting bacteria. With the increasing number of available antibiotics, prescribing these drugs has become a challenge. Levofloxacin is the optical S- (-) isomer of ofloxacin which has been developed by the Daiichi Seiyaku Pharmaceutical Co. Ltd, in Japan. Ofloxacin is a racemic mixture, but the S-isomer has antibacterial activity 32- to 128-fold more potent than the R-isomer – hence most of the antibacterial activity of ofloxacin is due to the S-isomer. Levofloxacin has been developed to take advantage of this antibacterial potency while requiring only about half the usual dose of ofloxacin to achieve similar efficacy, but potentially with an improved toxicity profile [5-9]. Levofloxacin is rapidly and essentially completely absorbed after oral administration. Therapeutically it is used for urinary tract infection, sinusitis, and chronic bronchitis.

The prime objective of the present study was to evaluate and compare the physicochemical equivalence of different tablets, of different brands that are available in local market of Karachi (Pakistan). In the present era where more than 85% of drugs can be obtained from more than one sources; for example Levofloxacin tablets that manufactured by more than 15 companies only in Karachi (Pakistan) there might be chance of presence of some superiors along with sub-standard drugs, that makes the patients conscious about the selection of safest, effective as well as economical medicine. The proposed study has been performed to provide the guideline to the physicians and pharmacists on the bases of which they can select the drugs for their patients. The physical parameters i.e. weight variation; thickness, hardness, friability, disintegration, dissolution as well as chemical assay were considered during the present study. This study was also conducted to determine the *in-vitro* activity of Levofloxacin against common and important bacterial isolates i.e *E.coli* and *S. aureus* because these Gram -ve and Gram +ve organism are present in the environment every where due to which human come in direct contact with these organism and suffering from respiratory tract, gastrointestinal tract and urinary bladder infection [10].

MATERIAL AND METHOD

Instrumentation

For the analysis of Levofloxacin content in their dosage form a Shimadzu UV-1601 spectrophotometer was utilized. Spectrophotometer system was integrated via Shimadzu model to P-III computer loaded with Shimadzu 1601 software for data acquisition and mathematical calculations. Analytical balance, Dissolution test apparatus, Disintegration test apparatus, sonicator, pH meter, autoclave, and micropipette.

Materials and reagents

Reference Levofloxacin was a kind gift sample from Aventis Pharmaceutical (Private) Limited. Six different brands of

Levofloxacin were obtained from different retail pharmacies of Karachi (Pakistan) market. Representative Gram positive (*S. aureus,* ATCC= 25923) and Gram-negative (*E.coli,* ATCC = 25922*)* standard organism obtained from Brookes Pharmaceutical (Pvt) Ltd. The bacterial isolates of these organisms obtained from Liaquat National Hospital, Karachi. Mueller Hilton broth (Merck Germany), Ethanol (Merck, Germany), hydrochloric acid, and Distilled water were prepared freshly to prepare different dilution.

Spectrophotometric condition

Base line was adjusted to zero by using blank solvent (0.1N HCl). Standard and test sample were analyzed (the result was based on three average readings).

Physiochemical parameters

Rational use of medicines requires that "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".

Drug cost and quality are the major component of the total cost of the National Health Services (NHS) which is constantly rising. As the resources of the NHS are limited, so it is the need of time to keep eye on the quality and cost of the drugs that are available in the markets. There are a number of companies that manufactures levofloxacin tablets 250mg. The label information of six different brands of tablets is presented in Table 1.

Uniformity of weight

Tablet is designed to contain a specific amount of drug in a specific amount of tablet formula. To check whether tablet contain a proper amount of drug, weight of tablet should be routinely measured.

The tablets were examined for their uniformity of weight and for tablet to tablet variations that should be within the limits of the percentage deviation allowed by USP (generally ±10% for tablets weighing 130mg or less, ±7.5%for tablet weighing more than 130mg to 324mg and ± 5%for tablet weighing more than 324mg [11].

Table 1: Label information of six different brands of levofloxacin tablets (250MG)

S.No	Product code	Manufactured by	Batch No.	Mfg. date	Exp. Date	Price/10 units Rs
1.	LEVO–1	Wilson's Pharmaceutical Islamabad	7032	March 2004	March 2007	99.00
2.	LEVO–2	Werrick Pharmaceutical Islamabad	4557	February 2004	February 2007	99.00
3.	LEVO–3	Getz Pharma Pakistan (Pvt) Limited	049-D4	April 2004	April 2007	170.00
4.	LEVO–4	S.J. & G Fazul Ellahi (Pvt) Ltd	026	May 2004	May 2006	75.00
5.	LEVO–5	Aventis Pharma (Pakistan) Limited	D002	June 2004	May 2007	417.00
6.	LEVO–6	Bosch Pharmaceutical (Pvt) Ltd.	E45156	July 2004	June 2007	143.00

Uniformity of thickness

Thickness of tablet can vary without any change in its weight because of difference in the density of the granulation and the pressure applied to the tablets as well as speed of tablet compression. The thickness variation limits allowed are ± 5% of the size of the tablet [12].

Length and diameter

BP (2002) [13] introduced a standard for tablet diameter to reduce patient confusion over generic equipments. The stated diameter can deviate by ± 5% up to 12.5 mm and by ± 3% above 15mm.

Hardness

The resistance of the tablet to chipping, abrasion, or breakage under condition of storage, transportation and handling before usage depends on its hardness [11]. The hardness of tablet depends on the weight of the material used space between the upper and lower punches at the time of compression and pressure applied during compression. In 1993, Gupta investigated that hardness also depends on the nature and quantity of excipients used during formulation [14].

Friability test for tablets

The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping.

Ten tablets were weighed and placed in the apparatus where they were 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 were weighed and the weight compared with the initial weight. The loss due to abrasion was a measure of the tablet friability. A maximum weight loss of not more than 1% of the weight of the tablets being tested (BP-2002)[12].

Disintegration

Disintegrations are required to break up tablets, capsules and granules into primary powder particles in to order to increase surface area of the drugs exposed to gastrointestinal fluids. The disintegration test was carried out by using Erweka ZT 3 Disintegrator. A 1000 ml beaker was filled with distilled water (approx. 900ml), equilibrated to 37±0.5ºC. Six tablets from each brand were subjected to the test. Time required for the last tablet to disintegrate was recorded.

Dissolution

Dissolution testing is the most important way to study, under in vitro conditions, the release of a drug from a solid dosage form and thus represents an important tool to assess factors that affect the bioavailability of a drug from a solid preparation. During dissolution test the cumulative amount of drug that passes into solution is studied as a function of time. The test thus describes the over all rate of the processes involved in release of the drug into a bioavailable form. Dissolution test was carried out by using an Erweka dissolution instrument. Paddle method (apparatus-2; USP-27) [15] was used at 50 rpm. Hydrochloric acid 0.1N (900ml) prepared as dissolution medium, was poured into the vessel and equilibrated to 37±0.5ºC. Six tablets from each brand were tested. 5ml of aliquot was withdrawn at the intervals of 15, 30 and 45min, and the volumes withdrawn, replaced with fresh dissolution medium. The sample was filtered, using Whatman filter paper and 3ml of filtrate was further diluted as working solution (16μg/ml). The absorbance was measured at 294 nm against dissolution medium.

Standard preparation

For the standard solution, 20 mg Levofloxacin was weighed and dissolved in 50ml 0.1N HCl suitably diluted to produce a 0.016mg/ml (16μg/ml) final concentration of working solution.

Content assay

Every tablet contains the amount of drug substance intended, with little variation among tablets within a batch. Analysis of drug potency in tablets not only indicating the presence of drug in dosage form but also requisite for the establishment of stability data.

Preparation of standard solution

The standard was prepared in the same concentration as for the dissolution testing**.**

Preparation of sample solution

Sample was prepared by weighing and crushing 20 tablets and transferring amount of drug substance equivalent to 20mg of standard substance of levofloxacin in 50ml of volumetric flask dissolved in 0.1N HCl. Portion of solution was filtered and the filtrate was further diluted to obtain the final working dilution of 16μg/ml.

Antibacterial activity

To evaluate the activity of an antibacterial drug product against the microorganisms and their isolates need to be tested for determining the spectrum of antimicrobial activity either by dilution or disk diffusion tests.

In the present study an economical method was performed for the determination of resistance pattern and activities of levofloxacin standard with different commercial brands (available in the local market) by using agar dilution method that was developed by Rammel kamp in 1942 [16]. The Organisms used were:

1. *E.coli* (ATCC-25922).
2. Five isolates of E.coli of different sources.
3. *S. aureus* (ATCC - 25923), and.
4. Five isolates of *S. aureus* of different sources.

Stepwise considerable points were as:

1. Preparation of the Mcfarland Standard
2. Preparation of Inoculums
3. Preparation of Antibiotic Stock Solution

Suitable ranges of antibiotic concentrations were selected for the organisms to be tested. Standard antibiotics powder (Reference levofloxacin and different brands) weighed accurately for the preparation of stock solutions by using the formula.

$$W = \frac{1000 \times V \times C}{P}$$

Where, W = Weight of antibiotic to be dissolved in volume (v).

P = Potency given by the manufacturer.

V = Volume required.

C = Final concentration of solution.

After preparing the stock solution, preparing a series of varying concentrations, usually two fold serial dilutions (0.0625, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, and 64 μg/ml), Equal volume of inoculums were added in each.

Spectrophotometric condition

Before performing the sample, adjusted the base line on zero by using blank solvent (broth dilution). The broth dilution method was used to determine the levofloxacin MICs against the pathogens.

RESULTS

In the present study, quality of the branded product Levofloxacin (250mg) tablets was evaluated through weight variation, diameter, thickness, hardness, friability disintegration time, dissolution and chemical assay. It helps to recognize the comparative difference of quality control test / parameters of levofloxacin and the effect of these differences on the release of drug from the formulation and also performed the microbial susceptibility test against *E.coli* (standard ATCC-25922 and its isolates) and *S. aureus* (standard ATCC - 25923 and its isolates).

Any changes in these characteristics may significantly affect the safety and efficacy of the product. Therefore it is very important to keep a check on each and every step during the formulation and manufacturing of a drug product. A wide range of literature [17- 24] is available regarding the comparative study of different brands of the same generic. Which indicated that the pharmaceutical equivalency of different brand is as important as the biological and clinical equivalency?

Price fluctuation

As the variation in the price has been observed from as much as 7.5 to 41.7pak rupees per unit (Fig: 1) while there was no significant variation in the quality of the tested drugs. Hence it may be suggested that the most economically available drug should be used as the pharmaceutical outcomes are promising too.
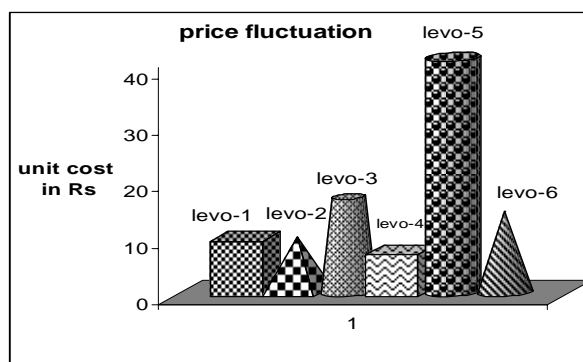

Fig. 1: Price fluctuation among different brands of levofloxacin available in local market of Karachi

Weight variation

It was found that the different brands tablets were of an average weight of 300mg to 750mg ± 5%.

Table: 2 shows weight variation and their standard deviation results were highly significant with the limits given ± 5%. The result shows

that weight uniformity can be achieved due to proper care & continuous monitoring of each batch.

Fig: 2 indicated that two brands levo-1 and levo-2 comprises on 750mg weighed that is too large as compare to levo-5, 309.50mg but the thickness was 5.73mm and 6.10mm that make it in acceptable volume range.

Table 2: Physical parameters of six different brands of levofloxacin tablets 250mg with its standard deviation

Brand name	Average weight Mg±SD	Average thickness MM±SD	Average hardness±SD
LEVO-1	752.65 ± 18.41	5.73 ± 0.11	20.36 ± 0.01
LEVO-2	766.05 ± 6.95	6.14 ± 0.07	20.43 ± 0.31
LEVO-3	399.30 ± 10.43	4.61 ± 0.12	11.76 ± 0.62
LEVO-4	362.00 ± 3.57	4.53 ± 0.08	16.34 ± 0.78
LEVO-5	309.50 ± 2.06	4.11 ± 0.03	11.52 ± 0.34
LEVO-6	405.45 ± 8.10	10.11 ± 0.02	11.22 ± 1.95

An even distribution of the force is required to reduce the weight variation problem.
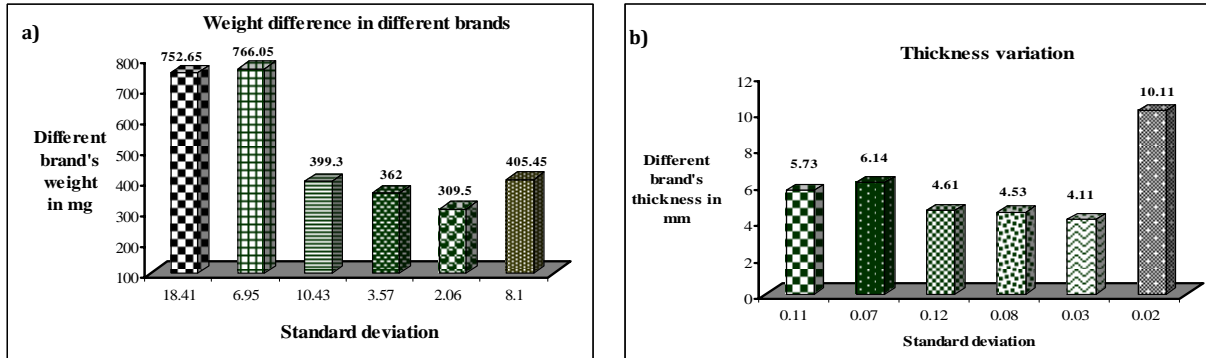

Fig. 2: A) Comparison of different brands weight variation b) thickness variation due to weight variation

The thickness of six different brands of Levofloxacin including its Mean ± Standard deviation (5%) was in accordance with B.P/U.S.P (Table 2). Levo-6 has more thickness as compare to other five brands that make it difficult for patient's points of view.

Hardness is an important parameter which helps to assess the resistance of the tablet to breakage under condition of storage, transportation and handling. Before use this parameter should be evaluated. It was found that 6 different brand of Levofloxacin tablet were in accordance with the stated B.P/U.S.P guideline (Table 2).

Disintegration

Disintegration test was conducted on the six different brands of Levofloxacin tablet 250mg. In present investigation all the six tablets of each brand disintegrated within the range of 5.84 –10.55minutes (Fig: 3).

Fig: 3 indicates that product levo-3 has shown a maximum average disintegration time about 10.55 ± 0.60 minutes and product levo-4 has shown minimum disintegration time about 5.48 ± 0.58minutes, which is best as compare to other products. The disintegration tests do serve as a component in the overall quality control of tablets manufacturing.

Dissolution

The present investigation showed that almost all the 6 brands dissolved 55% in 15minutes, 80% in 30minutes and 90% in 45minutes (Table:3) indicating that the release pattern of drugs were same either the brands manufactured by different companies by using different excipients in different ratio but on the bases of releasing factor it can be used interchangeably. The statistical evaluation (ANOVA) of dissolution test also indicated that there was no significant variation found between and within different brands of Levofloxacin tablets (Table: 4).

Chemical assay

Every unit of tablet should contain the amount of drug substance equivalent to its label amount. For the evaluation of content, assay should be performed. The results of the assay of chemical content of Levofloxacin tablets (Table 5) showed that the active content of all the brands were between 95% and 105% of the labeled amount specified for levofloxacin. The results indicated that although different manufacturer formulates the different brands by different method of formulation but all are under the BP/USP specification. The statistical evaluation (ANOVA) also indicated that there was no significant variation in content of active moiety in their dosage form (Table: 6).
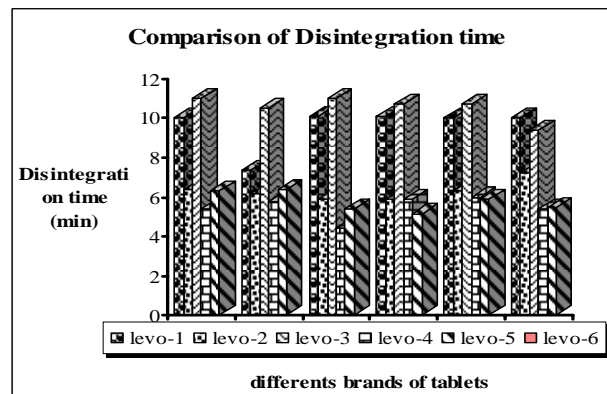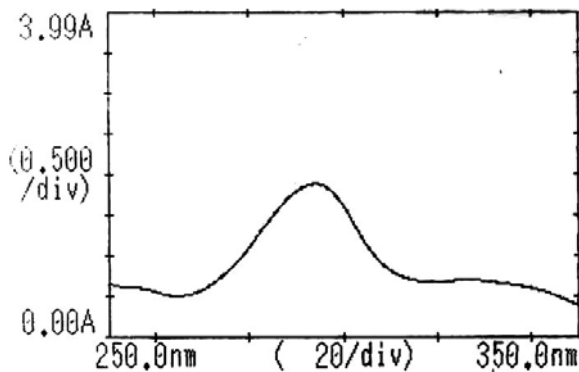

Fig. 3: Mean disintegration time for 6 different brands of levofloxacin tablets 250mg

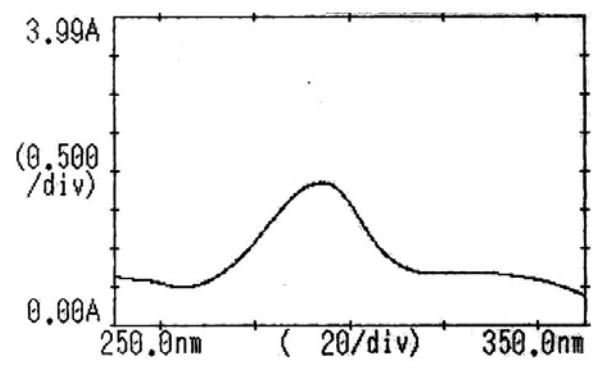**Table 3: Rate of % dissolution (mean ± sd) of the six brands of levofloxacin tablets 250mg.**

Name of brand	Average dissolution at 15min ± SD	Average dissolution at 30 Min ± SD	Average dissolution at 45 Min ± SD
LEVO-1	57.25 ± 5.48	75.78 ± 3.35	91.17 ± 3.06
LEVO-2	56.88 ± 6.17	79.32 ± 4.60	94.53 ± 1.41
LEVO-3	56.92 ± 3.62	79.07 ± 7.36	94.57 ± 3.77
LEVO-4	59.73 ± 6.17	79.00 ± 3.74	94.80 ± 4.35
LEVO-5	52.73 ± 1.51	83.55 ± 3.04	94.60 ± 3.78
LEVO-6	58.92 ±1.37	83.47 ± 6.57	94.88 ± 4.43

Table 4: Anova for extant of dissolution (%) of different brands of levo

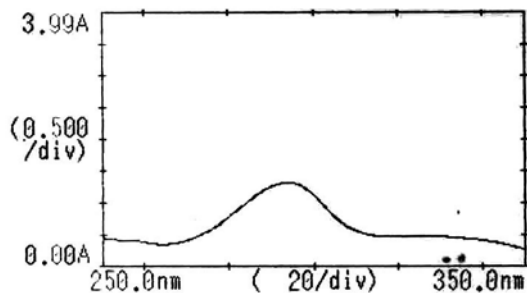| Source of Variation	SS	Df	MS	F	P-value	F crit
Between Groups	62.17916667	5	12.4358	0.95102	0.46297	2.5336
Within Groups	392.2883333	30	13.0763			
Total	454.4675	35				

a) Reference absorbance

b) Sample absorbance at 45min

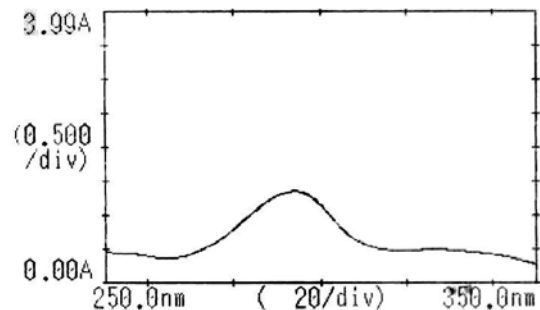**Table 5: Comparison of content assay (%) of different brands of levofloxacin**

S.No.	LEVO 1	LEVO 2	LEVO 3	LEVO 4	LEVO 5	LEVO 6
1	99.4	98.8	99.7	98.9	99.4	99
2	97.4	96.3	98.1	97.4	96.3	98.1
Mean	98.4	97.55	98.9	98.15	97.85	98.55
± SD	1.41	1.76	1.13	1.66	2.19	0.63

Table 6: Anova single factor for content assay of levofloxacin

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	2.38666667	5	0.47733	0.2248	0.9386	4.387374
Within Groups	12.74	6	2.1233			
Total	15.1267	11				

Standard Levofloxacin

Sample Levofloxacin

Antimicrobial susceptibility test

The first significant susceptibility test to be developed was the broth dilution test described by Rammel Kamp and Maxon in 1942. The broth dilution susceptibility test allows the determination of the MIC of an antimicrobial agent [16].

Resistance of common pathogens to Antimicrobial agents has emerged as one of the most important problems in the field of infectious diseases. As a matter of microbial evaluation of different brands of levofloxacin, broth micro-dilution method was employed against *E. coli* plus its isolates and *S. aureus plus* its isolates. The experiment was carried out on standardized cultures and isolates. The results were observed visually and spectrophotometrically on λ = 546nm.

The resisting pattern was assessed by their MICs (Fig: 4 and 5). The susceptibility test indicated that the MICs of standard levofloxacin against standard *E.coli* (Fig: 4) were 0.03μg/ml, as that of the reported value of *E.coli* (Drago et al., 2002; Fu et al., 1992) [25-26].

The analysis of variance Table # 7 showed that there were no significant variations found in MIC values of different brands of Levofloxacin tablets (MIC =0.05μg/ml – 1.0μg/ml) which indicated that the levofloxacin tablets are good choice of drug for *E.coli* resistance.

The Fig:5 represented the antimicrobial activity of standard levofloxacin against standard *S.aureus* (ATCC = 25923) with 5 different isolates. The susceptibility test indicated that the MICs of standard levofloxacin (MIC = 0.12μg/ml) against standard *S.aureus* were same as that of the reported value of *S.aureus* (Sariano et al., 2005) [27] which showed that levofloxacin standard as well as its different brands have a significant resistance against *S.aureus* and its isolates.
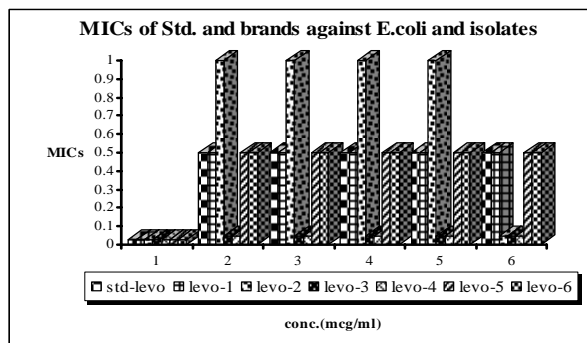

Fig. 4: Comparison of mics against e.coli among standar and different brands

Table 7: Analysis of variance (anova) for different brands of levofloxacin against e.coli

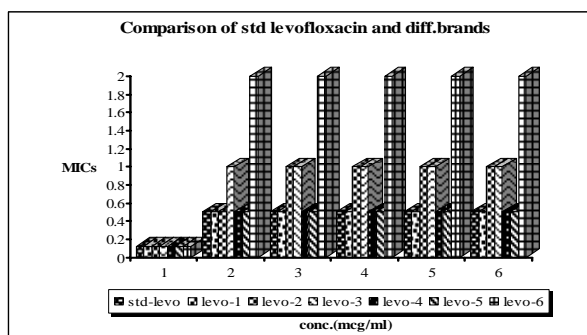| Source of variation	SS	df	MS	F	P-value	F crit
Between Groups	0.8110139	5	0.1622028	1.727348	0.1587514	2.5335538
Within Groups	2.8170833	30	0.0939028			
Total	3.6281	35				

Fig. 5: Comparison of standard and different brands of levofloxacin against *std. s.aureus* & its isolates

Table 8: Analysis of variance (anova) for different brands of levofloxacin against *s.aureus*

Source of variation	SS	df	MS	F	P-value
Between Groups	3.076619	5	0.6153238	2.3673527	0.0589224
Within Groups	9.3571429	36	0.2599206		
Total	12.433762	41			

The MIC values were also evaluated by statistical test **(ANOVA)** which concluded that no significant variation was found in different brands of levofloxacin (Table: 8)

DISCUSSION

It was evaluated by literatures (Shakoor, et al. 1997; Arya, 1997) that many drugs that are manufactured in developing countries are implicated to be substandard [28-29]. For minimizing the health risk factors and to maximizing the safety of health products and food; it is necessary to monitor all the pharmaceutical services in a regular basis that promoting the conditions and providing information on

the base of which the people become enable to make healthy choices and they can make correct decisions about their health.

Price fluctuation in societies where there is no regulatory control has been a severe problem related to the quality of the drug. Fig: 1 indicated that a significant variation in the cost of different brands of same Levofloxacin is present whereas no major variation in their quality that can help in reducing the patient's treatment cost. This would lead to more pharmaco-economic practices for the common people.

The Fig: 2 represent the variation in the weight and thickness of the tablets that generates differences in size of tablets that plays an important role in the compliance of patients. However these differences in weight of tablets have no meaning when the thickness is adjusted accordingly. The same would happen with levo-1 and levo-2 having weight 752.65 ±18.41mg and 766.05 ± 6.95mg when adjusted with the thickness of 5.73 ± 0.11mm and 6.14 ± 0.07mm that reduced the differences between the tablets of 300mg and 750mg.

Drug dissolution testing is an approach to evaluate drug release characteristics of a product (tablets/capsules) in vitro. The technique is very well established and extensively used at every stage of product manufacturing in ensuring the quality of drug products. (development, production, QC as well as for regulatory surveillance). Generally product-to-product variation occurs due to the formulation factors such as particle size, excessive amount of lubricant etc. Thus dissolution test are very effective in discriminating between and within batches of drug product (s).

A key component of the overall quality of a pharmaceutical product is control of impurities, presence of therapeutic agent that developed potency, safety and efficacy of drug. The identification and quantification of medicinal moiety is a significant challenge to the analytical chemist. Analytical science helped in the measurement of these contents.

These safety and efficacy of drug was determined by means of content assay and microbial susceptibility test. The amount of Levofloxacin in different brands that available in the local market of Karachi (Pakistan) was between 95-105% that make it sure that the amount of active ingredient in each brand complies the pharmacopeial limits. Whereas the effectiveness is conformed by its MICs (fig: 4 and 5) that was similar to that of previous reported values [25-27].

CONCLUSION

Pharmaceutical quality control and quality assurance depend on monitoring the composition and uniformity of the drug substance during processing and in the final product. Compendial tests have traditionally been used to determine identity, strength, quality, and purity. Implementation of these approaches can reduce the time and cost required for manufacturing, while improving quality control.

A number of research articles (Ashour et al., 2005; Alvarez-Lerma et al., 2004; Lichtenstein et al., 2003; Furlanut et al., 2003; Bundrick et al., 2003; Scheen,2000; Norry, 1999; North et al., 1998) [17-24] are available that indicates the physicochemical parameter's evaluation of different drugs substance are required for the achievement of a stable and effective drug product which may be pharmaceutically equivalent whether the drug is bioequivalent or not in vivo is known after the bioequivalence study but to know that if the drug is pharmaceutically equivalence initially its physicochemical parameters are needed to be found out.

Levofloxacin is one of the most promising newer quinolones that has been shown to be active against both gram positive and gram-negative organisms. The result of this parameter indicated that this test should be performed on a large number of strains for confirming the superior antibacterial activity of different brands of Levofloxacin when compared with each other

ACKNOWLEDGEMENT

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