



A Review on Quality Control Analysis and Assessment of Different Market Brands of Ciprofloxacin.

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ABSTRACT :

Ciprofloxacin is a widely used fluoroquinolone antibiotic that is effective against a variety of bacterial infections. It belongs to the quinolone family, which has activity against both gram-negative and gram-positive bacteria. Ciprofloxacin is among the most popular antibiotics on the market. This article provides an overview of the drug's history, pharmacokinetics, mechanism of action, available dosage forms, costs, ongoing research, applications, and methods for estimating its concentration. It also discusses potential drug interactions, adverse reactions, and available patents. Quality control tests have been conducted on brands of ciprofloxacin 500 mg tablets to assess their bioequivalence through tests such as weight uniformity, hardness, friability, assay, disintegration, and dissolution. Ciprofloxacin has high bioavailability.

Keywords : Ciprofloxacin, Methods, Derivatives, Leading brands.

Introduction :

Ciprofloxacin is classified under the category of fluoroquinolones. The introduction of the initial fluorinated quinolone, norfloxacin, paved the way for the creation of other members within this classification, including ciprofloxacin. Ciprofloxacin boasts a broad range of clinical applications, a superior safety profile, and notable in vitro efficacy against resistant pathogenic organisms when compared to alternative classes of antibiotics.

In many developing countries, generic drugs are supplied to the healthcare system to improve drug accessibility and distribution. Despite the benefits, this endeavor faces several challenges, with the circulation of substandard medications being a major issue.

The process of drug surveillance involves collecting comprehensive data about a product after it has been authorized for marketing and made available to the public. This data, obtained through various procedures, can then be used to set standards. Ensuring enhancements in product quality is vital in order to meet regulatory requirements. Regulatory authorities heavily depend on limited information from clinical trials and literature to make decisions regarding the approval of medications. Therefore, closely monitoring the therapeutic effectiveness and quality of approved medicines is of utmost importance, particularly due to their widespread usage among the population.

Regulatory authorities base their decisions on a restricted amount of data gathered from clinical trials and various sources of literature when approving medicines. It is essential to rigorously monitor the efficacy and quality of approved medications, particularly due to their extensive utilization within the population.

The significance of medication in enhancing patient contentment and decreasing mortality cannot be emphasized enough, as inadequate medications present safety hazards and can result in increased treatment costs.

Therefore, it is of utmost importance to consistently carry out drug testing in laboratories in order to protect the welfare of the overall population, especially in developing countries. The World Health Organization has already implemented regulations regarding the requirements, quality assurance, and approval process of generic drugs.

Generic medications are required to adhere to the effectiveness, safety, and quality criteria established by the original drug manufacturer. The existence of substandard drugs in circulation is attributed to insufficient quality control measures and the regulatory bodies' lack of oversight.

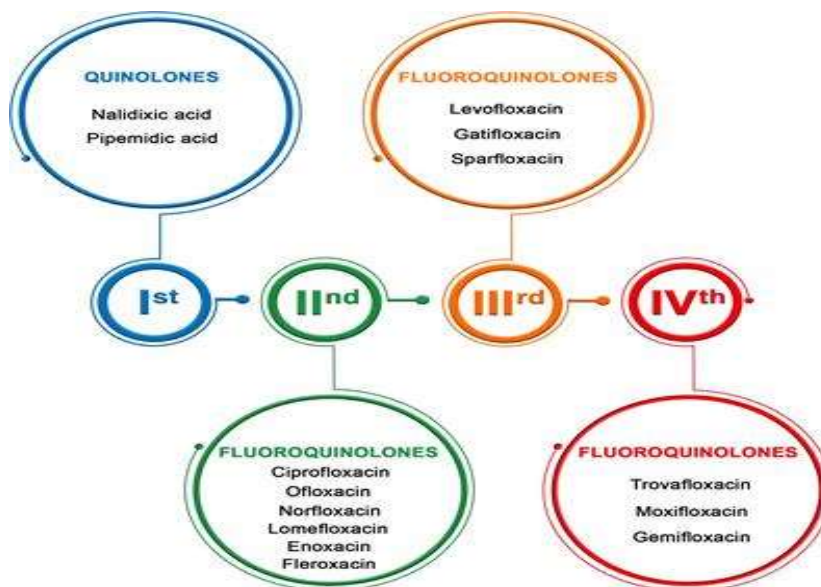
The degradation of the active ingredient in a medication can be caused by multiple factors, including storage conditions like humidity and temperature, as well as inadequate quality checks during the production phase.

Ciprofloxacin is a type of antibiotic that is commonly used to treat bacterial infections. It works by inhibiting the action of bacterial enzymes, thereby reducing the growth of microorganisms and ultimately killing the bacteria. This medication is specifically used to treat infections in various parts of the body, including the urinary tract, tonsils, sinuses, nose, throat, female genital organs, skin, soft tissues, and lungs (such as pneumonia). In order to ensure

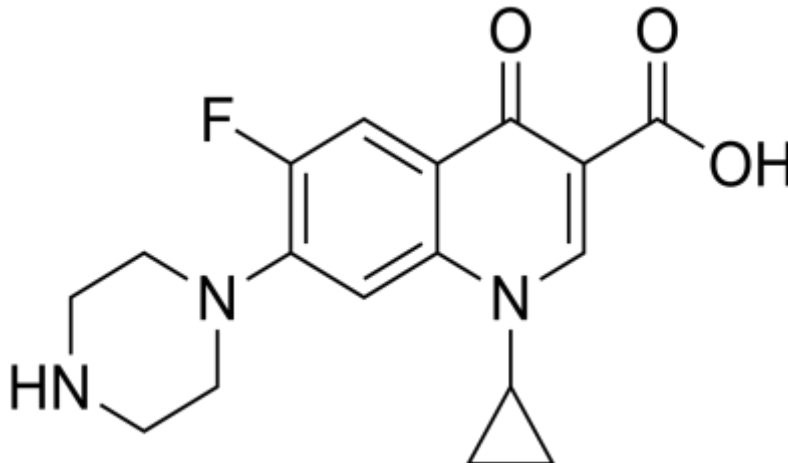
the quality and effectiveness of Ciprofloxacin available in the market, a comprehensive review was conducted to evaluate different brands of this medication.

Ciprofloxacin is solely accessible through a prescription. It is provided in various forms including tablets, liquid for oral consumption, ear drops, and eye drops. Injections are also an option, typically administered in a hospital setting. Additionally, Ciprofloxacin ear drops may be combined with other medications like fluocinolone (Cetraxal Plus) or dexamethasone.

Ciprofloxacin tablets and liquid are exclusively prescribed in cases where alternative antibiotics are not appropriate, due to the potential for severe and prolonged adverse reactions. The components encompassed by Ciprofloxacin include:



Structure Of Ciprofloxacin :



Background :

Ciprofloxacin, a member of the fluoroquinolones group, was discovered by Bayer in Germany in 1981. The Food and Drug Administration (FDA) approved this drug in 1987, marking it as the first oral broad-spectrum antibiotic accessible in the United States. It is recognized as one of the essential medicines by the World Health Organization (WHO) and is commonly utilized in the primary healthcare system. Ciprofloxacin is offered as a generic medication and is reasonably priced. Generic drugs are required to adhere to the same quality standards as the original drug, ensuring chemical and biopharmaceutical equivalence.

It is guaranteed that factors like potency, cleanliness, consistency of ingredients, disintegration time (DT), and rate of dissolution remain consistent. The utilization of generic medications not only aids in lowering healthcare expenses but also gives rise to apprehensions regarding their quality, especially in impoverished, developing, and industrialized nations.

There are many cases related to subpar and counterfeit medications. Subpar drugs do not meet the necessary scientific standards in terms of their composition and ingredients, making them ineffective and potentially dangerous for patients. On the other hand, counterfeit drugs may have the correct ingredients but are packaged in a deceptive manner, contain incorrect ingredients, lack active ingredients, or have insufficient amounts of active ingredients. It is widely accepted that counterfeit drugs pose a greater risk to health compared to substandard drugs. Both substandard and counterfeit drugs have a significant impact on morbidity, mortality, and the erosion of public trust in pharmaceuticals and healthcare systems.

According to the World Health Organization (WHO), approximately 10% of the global pharmaceuticals market consists of counterfeit drugs. However, this percentage significantly increases to 25% in developing nations, and in certain countries, it may even exceed 50%. The Food and Drug Administration (FDA) states that up to 25% of medications consumed in impoverished countries are either substandard or counterfeit. China and India are widely recognized as the primary sources of counterfeit drugs and the active ingredients used for counterfeiting on a worldwide scale. Numerous research studies have uncovered that counterfeit pharmaceuticals originating from China were discovered in 42 countries, while those from India were identified in 33 countries.

A study conducted by Almuzaini et al. uncovered the widespread presence of substandard or counterfeit medicines in multiple countries. The research findings indicated that the prevalence of such medicines varied between 12.2% and 44.5% in Lao PDR, Tanzania, Cambodia, and Uganda. Similarly, in Indonesia, Nigeria, and Cameroon, the prevalence ranged from 18% to 48%. Moreover, in Myanmar, Cambodia, Lao PDR, Ghana, Kenya, Tanzania, Uganda, Madagascar, Mali, Mozambique, and Zimbabwe, the prevalence was found to be between 11% and 44%. Tragically, in 2009, Bangladesh witnessed a devastating incident where 25 children lost their lives due to the consumption of paracetamol syrup contaminated with poisonous diethylene glycol.

It should be emphasized that substandard and counterfeit medications pose a significant issue not only in impoverished and developing nations but also in developed countries, where their prevalence is quite evident. For instance, between 2007 and 2008, 149 Americans tragically lost their lives as a result of consuming contaminated blood thinner, heparin, which had been legally imported into the country. In 2012, tainted steroids caused the deaths of 11 individuals and sickness in another 100 people in the United States. Furthermore, it was discovered that vials of the cancer drug, avastin, were devoid of any active ingredients. A study carried out by the World Health Organization found that 28% of antibiotics and 20-90% of antimalarial drugs failed to meet quality standards.

Pharmaceuticals are required to adhere to precise standards to qualify as a top-notch medication. The fundamental factors for evaluating the excellence of any medication in its prescribed form consist of safety, strength, efficiency, durability, patient satisfaction, and adherence to regulations. To guarantee the safety and efficacy of pharmaceuticals, it is essential for the quality of medications to stay uniform and replicable across different batches. Manufacturers of drugs have the responsibility to perform tests on their products during and post-production, at different time points during the product's lifespan.

Pharmaceuticals need to meet specific criteria to be classified as high-quality drugs. The primary standards for evaluating the quality of any drug in its dosage form include safety, potency, effectiveness, stability, patient satisfaction, and compliance with regulations. To ensure the safety and efficacy of pharmaceutical products, it is vital for the quality of pharmaceuticals to remain consistent and reproducible from one batch to another. Drug manufacturers are required to conduct tests on their products during and after the manufacturing process, at various intervals throughout the product's shelf-life.

The World Health Organization (WHO) supports the utilization of generic medications as a means to decrease healthcare expenses. However, it is crucial to have substantial evidence to justify the replacement of one brand with another.

The evaluation of bioequivalence trials comparing generic drugs with the original product is a major obstacle and plays a vital role in securing approval for generic marketing. Several researches have shown that transitioning from branded to generic medication can alter the pharmacokinetics/pharmacodynamics profile, leading to inadequate drug levels, treatment failure, or adverse effects. Hence, it is essential to conduct bioequivalence trials for generic drugs to detect any notable variations in the speed and amount at which the active ingredients are released at the drug's site of action, in controlled circumstances and through a well-structured study. Dissolution testing acts as a tool to pinpoint potential bioavailability concerns.

Drug products that are biopharmaceutically and chemically equivalent should demonstrate identical characteristics such as quality, strength, purity, content uniformity, disintegration, and dissolution rates. In vitro quality control (QC) of pharmaceutical products involves a standardized series of examinations carried out during production through in-process quality control tests, as well as after production through finished product quality control tests, following the guidelines provided by official pharmacopoeias and regulatory agencies. The implementation of QC tests is vital in guaranteeing the safety, effectiveness, potency, and stability of pharmaceuticals, thereby preventing any potential confusion.

The prevalence of substandard and counterfeit medications is significantly higher in impoverished and developing countries. With ciprofloxacin being a widely used antibiotic in Bangladesh, the objective of this study was to assess the quality and legitimacy of the drug in the area. The effectiveness of different leading brands of 500 mg ciprofloxacin hydrochloride tablet formulations currently available in the Indian market was evaluated.

Ciprofloxacin Derivative :

It has been proven that the active DNA-gyrase binding site is the 3-oxo-4-carboxylic acid core, and when the carboxylic acid group is replaced, the overall anti-bacterial activity is reduced [21,22]. The ciprofloxacin hybrids with 4-thiazolidinones replacing the carboxylic acid of ciprofloxacin showed weak anti-bacterial activity, confirming that modifying the carboxylic acid at the C-3 position leads to a loss of activity [23,24]. Notably, it was observed that...

(1) Ciprofloxacin-azine hybrids :

The antibacterial activity of a macromolecule 10 (Fig. 3) consisting of 1,3,5-triazine dendrimer with eight molecules of ciprofloxacin drug attached as a surface moiety was studied against Gram-positive (*S. aureus* and *B. subtilis*) and Gram-negative bacteria (*E. coli*, *P. aeruginosa*, and *P. mirabilis*) [38]. The research revealed that the balance between hydrophobic and hydrophilic properties per repeat unit of the dendrimer significantly impacts antibacterial effectiveness. This was demonstrated by hybrid 10 (MIC: 0.716–1.213 µg/mL) showing a 3–5 fold increase in activity.

(2) Ciprofloxacin-azole hybrids:

Zhang et al. conducted an evaluation of fluoroquinolone hybrids derived from 2-hydroxy-3-(nitroimidazolyl)propyl, which included the ciprofloxacin conjugate 12 (Fig. 4). The antibacterial activity of these hybrids was tested against representative Gram-positive and Gram-negative organisms, such as MSSA, MRSA, MSSE, and MRSE. Hybrid 12 exhibited promising potency against all tested Gram-positive strains and Gram-negative *E. coli*, with MIC values ranging from 2 to 32 µg/mL. However, it was found to be less active compared to the reference gatifloxacin.

(3) Ciprofloxacin-azolidinone hybrids:

The benzothiazolyl-4-thiazolidinone hybrids containing fluoroquinolone (ciprofloxacin or norfloxacin) at the C-7 position exhibited significant efficacy against both Gram-positive and two Gram-negative strains. The majority of these hybrids demonstrated MIC values ranging from 2.0–16.0 µg/mL. The structure-activity relationship (SAR) analysis indicated that, in general, the ciprofloxacin hybrids 24 displayed higher activity against Gram-negative bacteria compared to the corresponding norfloxacin analogs. However, their effectiveness against Gram-positive pathogens was not specified.

(4) Ciprofloxacin-quinolone hybrids:

In contrast to the monomeric compounds, the dimmeric compounds frequently displayed distinct properties. It is therefore logical to assess the antibacterial effectiveness of dimmeric fluoroquinolones.

A range of fluoroquinolone dimers, consisting of either the same fluoroquinolone core or two different fluoroquinolones connected by different linkers at the C-7 position, were examined for their antibacterial activities against a selection of clinically significant pathogens, including those resistant to drugs.

(5) Ciprofloxacin-bisphosphonate hybrids:

Bisphosphonates have been recognized for their ability to strongly bind metal ions, making them ideal for conjugation with ciprofloxacin. This conjugation can result in hybrids that possess an enhanced capacity to bind the enzyme site.

In their research, Buxton and Hartmann et al. discovered that hybrid 27 (depicted in Figure 7), which combines ciprofloxacin with bisphosphonates, maintained the *in vitro* antibacterial activity of ciprofloxacin. Interestingly, this hybrid exhibited greater activity than its ethyl ester counterpart, albeit at a slightly lower level [80,81]. Furthermore, in an *in vivo* test using a rat fracture model of osteomyelitis, hybrid 27 also...

(6) Ciprofloxacin-coumarin/ flavonoid/ lactone hybrids:

Coumarin derivatives demonstrate a wide range of pharmacological properties including anti-cancer, anti-malarial, anti-TB, and anti-bacterial activities. These effects are attributed to their capacity to engage in noncovalent interactions with different active sites within organisms. Some coumarin derivatives, like novobiocin and clorobiocin, are recognized for their antibacterial properties, as they can hinder the ATPase activity of DNA gyrase by vying with ATP for binding to the B subunit of the enzyme.

(7) Ciprofloxacin-fur(ox)an/thiophene/isatin hybrids:

Various ciprofloxacin hybrids containing furan and thiophene were assessed for their antibacterial properties. The structure-activity relationship of the furan and thiophene components had a notable impact on the effectiveness, with thiophene showing the highest contribution followed by furan and furoxan. Substituting carbonyl (Y = O) with (alkyl)oximes was found to decrease the activity. In general, most hybrids exhibited lower potency compared to ciprofloxacin against Gram-positive and Gram-negative bacteria.

(8) Ciprofloxacin-macrocyle hybrids:

Macrocyclic drugs like erythromycin are highly significant antibiotics that are extensively utilized for treating different bacterial infections [105, 106, 107]. It is evident that combining ciprofloxacin with macrocycles can potentially produce more potent candidates with dual action mechanisms [108, 109].

A collection of innovative 8a-aza-8a-homoerythromycin-4''-(3-substituted-amino)propionates, including the hybrid of 8a-aza-8a-homoerythromycin and ciprofloxacin.

(9) Ciprofloxacin-pyrimidine/pyrimidone hybrids:

It has been proven that 6-anilinoouracils can specifically target DNA polymerase III during replication. As a result, the 6-anilinoouracil-ciprofloxacin hybrids 38a,b (shown in Figure 11) may possess dual action mechanisms [113,114]. Initial findings suggest that both hybrids exhibit high activity against *B. subtilis* DNA polymerase III (Ki: 0.024 and 0.019 μM) and also demonstrate excellent efficacy against a range of pathogens, including drug-resistant bacteria, with MIC values ranging from 0.313 to 2.5 $\mu\text{g/mL}$.

Ciprofloxacin-sugar hybrids: Sugars have been shown to possess a wide range of biological activities and have garnered significant interest in the development of new drugs [116,117]. Therefore, the combination of sugars with ciprofloxacin may yield more potent candidates.

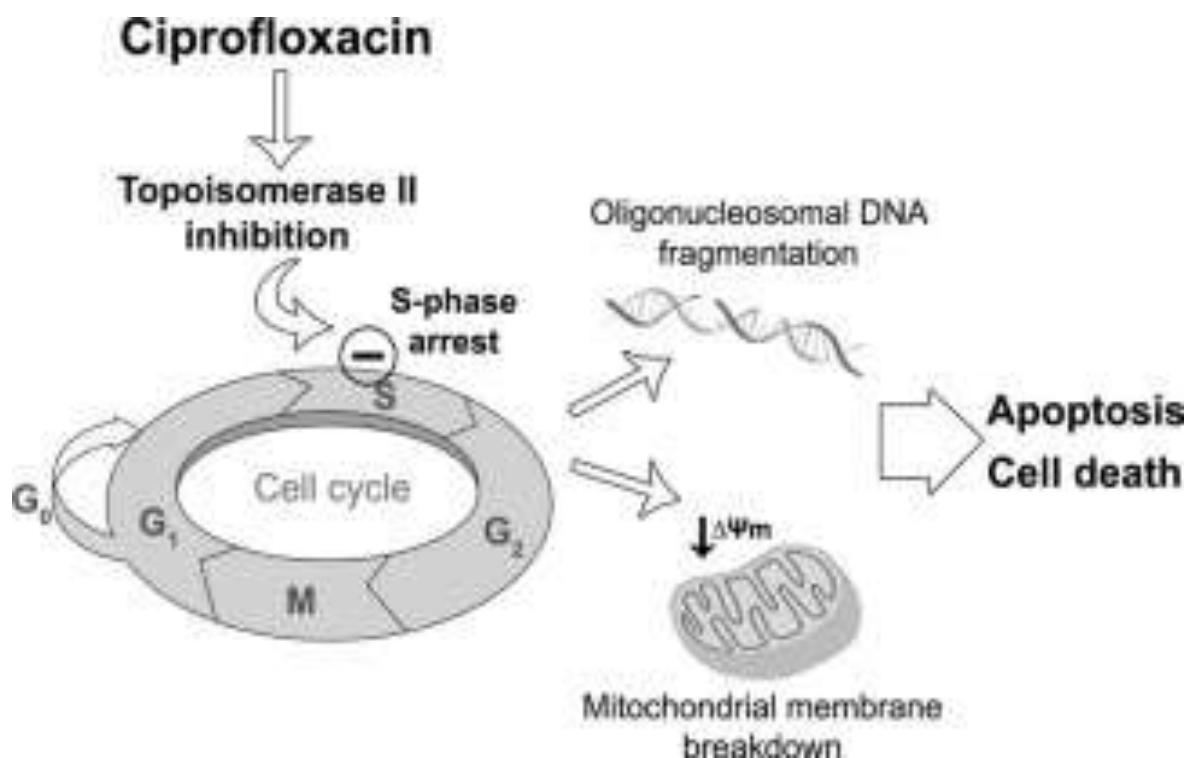
Jung et al. synthesized eight novel fluoroquinolone glycosides, six of which were ciprofloxacin hybrids. All of these hybrids were assessed for their antimicrobial susceptibility [118]. The structure-activity relationship (SAR) analysis revealed that the hybrids lacking a linker between the glycoside and ciprofloxacin exhibited...

(10) Miscellaneous ciprofloxacin hybrids:

Routledge et al. [124,125] conducted a study where they synthesized and assessed the antimicrobial properties of various citric acid-ciprofloxacin conjugates against a range of clinically significant bacteria. Despite the presence of two regioisomeric citrate-functionalized ciprofloxacin hybrids 42a,b (Fig. 13) that maintained activity against susceptible strains, all hybrids showed no activity against ciprofloxacin resistant bacteria. This indicates that these hybrids may operate through a similar mechanism of action.

Mechanism of action:

Ciprofloxacin, belonging to the fluoroquinolone class, is a wide-ranging antibiotic that targets both Gram-positive and numerous Gram-negative bacteria. Its mechanism of action involves the inhibition of type II topoisomerase (DNA gyrase) and topoisomerase, which are essential for the separation of bacterial DNA and ultimately halting cell division. Consequently, the enzyme inhibition leads to bacterial DNA fragmentation.



Pharmacokinetic data:

Bioavailability : 70%.

Protein binding. : 30%.

Metabolism. : Liver

Elimination half-life :3.5 hours.

Excretion. : Kidney.

Pharmacokinetic:

Ciprofloxacin is available in various forms for systemic administration, including immediate-release tablets, extended-release tablets, an oral suspension, and a solution for intravenous use. When given intravenously as an infusion lasting one hour, ciprofloxacin quickly spreads throughout the body, with some tissues containing higher levels than the serum. However, its penetration into the central nervous system is limited, as the levels in the cerebrospinal fluid are typically less than 10% of the peak serum concentrations. The serum half-life of ciprofloxacin is approximately 4-6 hours, and around 50-70% of the administered dose is eliminated unchanged in the urine. About 10% of the dose is excreted as metabolites in the urine. Complete urinary excretion occurs within 24 hours after administration. It is important to adjust the dosage in elderly individuals and those with kidney problems.

Ciprofloxacin exhibits low binding to serum proteins, ranging from 20% to 40%. As an inhibitor of cytochrome P450 1A2, a drug-metabolizing enzyme, it has the potential to cause significant drug interactions with medications metabolized by this enzyme. When taken orally, approximately 70% of Ciprofloxacin is available for absorption.

The prolonged release tablets enable once-daily dosing by gradually releasing the medication in the digestive system. These tablets consist of 35% of the total dose in an immediate-release format and 65% in a slow-release matrix. The highest levels of the drug in the bloodstream are reached within 1 to 4 hours after taking the tablets. In comparison to the immediate-release tablets of 250 mg and 500 mg, the XR tablets of 500 mg and 1000 mg offer higher maximum serum concentrations (C_{max}), while the 24-hour area under the curve (AUC) remains the same.

Ciprofloxacin immediate-release tablets consist of ciprofloxacin in the form of the hydrochloride salt, while the XR tablets contain a combination of the hydrochloride salt and the free base.

Pharmacokinetic aspects:

Pharmacokinetic characteristics, namely absorption, distribution, metabolism, and elimination of ciprofloxacin, are described below.

Absorption:

Ciprofloxacin is readily absorbed, although complete absorption is generally not attained following oral administration. The oral bioavailability of ciprofloxacin typically ranges from 70-80%, with minimal loss due to first-pass metabolism. Studies have demonstrated that administering a 400mg ciprofloxacin intravenous infusion over a 60-minute period every 12 hours yields an area under the serum concentration-time curve (AUC) equivalent to that of a 500mg oral dose given every 12 hours. To achieve therapeutic concentrations in brain tissue, a dose higher than 200mg intravenously is required, as indicated by a brain tissue concentration of 0.87 ± 0.08 mg/kg with a single 200mg intravenous dose. Numerous studies have provided detailed information on the pharmacokinetics of ciprofloxacin in cerebrospinal fluid (CSF).

The penetration showed superiority when compared to the corresponding serum levels, although the actual concentration in the cerebrospinal fluid was sometimes considered inadequate. The steady level of ciprofloxacin in the cerebrospinal fluid suggests a slow passage through the blood-brain barrier. Although food interactions can postpone the achievement of peak plasma concentration (t_{max}) and consequently influence the concentration-time profile, this does not significantly alter the drug's availability.

Distribution:

Ciprofloxacin shows superior tissue distribution in comparison to many other medications within its category because of its low affinity for plasma proteins. It displays remarkable penetration into various fluids and tissues in the body, except for the central nervous system (CNS), after being taken orally.

The drug concentration in the urine surpasses the minimum inhibitory concentration, which primarily makes it suitable for the treatment of urinary tract infections. There is only a minimal amount of ciprofloxacin that passes from the mother to the fetus, indicating a limited transfer of fluoroquinolones through the human placenta. The presence of ciprofloxacin at the intended site in the interstitial space is crucial for the effectiveness of antimicrobial therapy and the clinical outcome of an infection. Research indicates that concentrations in the interstitial fluid space at the target sites and AUCs were significantly lower than those in plasma for dosages of 400 and 500mg.

Metabolism and elimination:

Ciprofloxacin demonstrates notable variances in its metabolism and elimination mechanisms, wherein the liver and renal excretion play pivotal roles. The primary metabolic pathway involves deactivation via glucuronide conjugation at the 3-carboxylic group, while the piperazine ring undergoes facile metabolism, resulting in diminished antimicrobial efficacy. The elimination of ciprofloxacin occurs through [Specify the elimination pathway].

Material And Methods:

(1) Weight variation and disintegration test :

(2) Hardness Test/Crushing Strength

(3) Chemical Assay of Ciprofloxacin Tablets:

(4) In Vitro Dissolution Study:

(1)Weight variation and

disintegration test :

The weight of twenty tablets from each brand was individually measured, and the average weight of each tablet was calculated. The maximum and minimum values for the weight were then recorded. The data was assessed using the weight variation test limits established by the USP. The disintegration test for the film-coated tablets was carried out following USP specifications, with a constant frequency of 32 c.p.m (within the speed limit of 29-32 c.p.m as per USP specification) at a temperature of 37 C° (within the temperature limit of 35 C° - 39 C° as per USP specifications).

There are two steps that can be taken using two different media.

(1) Water:

(2) 0.1 N HCL:

(1)Water:

The tablets were initially submerged in water for a period of five minutes prior to disintegration, with the purpose of dissolving the film coating of the tablets.

(2) 0.1 N HCL:

The coating of the tablet was dissolved, following which it was placed into the disintegration apparatus with 0.1 N HCl as the disintegration medium. Six tablets from every Ciprofloxacin brand were chosen, and the average disintegration time (in minutes) was calculated. If the test did not pass for these first six tablets, a second round was carried out with twelve tablets from each brand, split into two sets of six tablets each. The results obtained were assessed based on the USP tolerance standards.

(2) Hardness Test/Crushing Strength:

Twenty tablets from each brand were selected at random to undergo a hardness test. The range of crushing strength was measured, with the breaking force recorded in Newtons and later converted to Kg/cm². Following that, the results were evaluated against the tolerance limits set by the USP.

(3) Chemical Assay of Ciprofloxacin Tablets:

The UV-Visible spectrophotometer was employed to analyze the active ingredients in the film-coated tablets of Ciprofloxacin HCl. The chemical analyses were performed three times, and the results are presented as the mean of three measurements.

(4) In Vitro Dissolution Study:

Dissolution of tablets of Ciprofloxacin were carried in the following two Medias.

1. Distilled Water

2. 0.1 N HCl Solution.

(1) Distilled Water:

In order to evaluate the quality of tablets for my project, dissolution tests were carried out using 0.1 N HCl as the dissolution medium. This was conducted to analyze the effects of storage conditions in tropical climates.

Calibration curve for Ciprofloxacin HCl in Distilled water:

Forty milligrams of Ciprofloxacin HCl powder of high quality were accurately weighed using a digital electronic balance and subsequently transferred into 100 ml volumetric flasks. The powder was dissolved in a small quantity of distilled water and subjected to sonication for 20 minutes to achieve a transparent stock solution. This solution was then diluted by the addition of distilled water until the desired volume in the flask was reached.

The stock solution of Ciprofloxacin was prepared by dissolving it in water to achieve a concentration of 0.4 mg/ml. Different volumes of this stock solution were then measured and transferred into 100 ml flasks. To obtain Ciprofloxacin HCl solutions with concentrations of 0.008, 0.01, 0.012, 0.014, 0.016, 0.018, and 0.02 mg/ml, each volume of the stock solution was diluted with distilled water to a total volume of 100 ml.

To analyze these solutions, a UV-Visible Spectrophotometer was used at a wavelength of 276nm, with distilled water as the blank solution. Three readings were taken for each dilution, and the average of these readings was calculated for the corresponding concentration.

By plotting the absorbance values against the concentrations, a calibration curve was generated. The equation of the curve was determined to be $y=87.597x-0.0079$, with a coefficient of variation (R²) of 0.9999 (n=7).

Calibration curve for Ciprofloxacin HCl in 0.1 N HCl :

A calibration curve was constructed for Ciprofloxacin HCl in 0.1 N HCl solutions using the same method described earlier for the calibration curve in Distilled Water, except that 0.1N HCl was used as the solvent. The obtained equation was $y= 122.49 \times +0.0004$, with a coefficient of determination (R²) of 0.9997. The concentrations of unknown Ciprofloxacin HCl were calculated using the regression equation.

$Y=MC+B$

Where Y= absorbance of solution containing Ciprofloxacin HCl at λ max 276nm.

M= Slope of Ciprofloxacin HCl Standard curve of Known concentrations.

C= concentration to Calculate

B= Intercept of curve

After rearranging the above equation we got:

$$C = (Y - B) / M$$

Dissolution tests for Ciprofloxacin HCl were carried out using the USP paddle method (Apparatus II) at a speed of 50rpm. Each vessel contained a dissolution medium volume of 900 ml, maintained at a temperature of 37.0 ± 0.5 °C. 5ml aliquots of the dissolution medium were withdrawn at 5, 15, 30, 45, and 60-minute intervals. Manual withdrawal using a 5ml syringe was conducted from each vessel of the dissolution apparatus. Subsequent to each sampling, an equivalent volume of dissolution medium was added to each vessel as a replacement solution.

The dissolution samples were diluted with the dissolution medium (1:50) in order to obtain absorbance within the linear range of the Lambert-Beer Law. Afterwards, a UV-Visible spectrophotometer was used to analyze them at λ max 276nm. After calculating the dissolution profiles for the finished pharmaceutical products of Ciprofloxacin in the dissolution media (D/W and 0.1 N HCl), a comparison was also made between the two.

Various Brands Of Ciprofloxacin In India

The Following are brands of Ciprofloxacin:

- (1)BACTOQUIN-(Otsira) India
- (2)BIOCIP- (Biochem, India)
- (3)BIOCIP-TZ (Biochem, India)
- (4)CIFRAN- (Ranbaxy , India)
- (5)CIPLOX -(Cipla, India)
- (6) CIPLOX D -(cipla, India)
- (7)CIPLOX TZ-(cipla ,India)
- (8)CIPROBID-(Cadila,India)
- (9)CEPROB-CENT- (centaur, India)
- (10)IFICIPRO (FM)-(Unique, India).
- (11)NEOCIP(Cipla, India).
- (12)OCIMIX-(panacea, India).
- (13) PROCIP-(Ipca, India).
- (14) STROX- (Dabur , India).

(1)BACTOQUIN-(Otsira) India:

Bactocin Tablet, containing ciprofloxacin as its active ingredient, is an antibiotic used to treat various bacterial infections like pneumonia, sinus infection, skin infections, ear infections, nose infections, stomach infections, urinary tract infections, and more. It works by inhibiting enzymes crucial for DNA replication and repair, ultimately killing the bacteria causing the infection. It is important to follow the doctor's instructions regarding the dosage and duration of Bactocin Tablet, whether taken with or without food. It is crucial not to use Bactocin Tablet or any other antibiotics if unsure whether the infection is bacterial, as unnecessary use can render antibiotics ineffective for future treatments. Abruptly stopping the medication may result in a relapse or the infection returning.

Mode of Action of Bactocin 500 MG:

Ciprofloxacin in Bactocin Tablet blocks the action of an enzyme essential for DNA synthesis in bacteria, inhibiting its growth, multiplication and repair.

Uses of Bactocin 500 MG:

Bactocin Tablet is indicated for the management of bacterial infections affecting various parts of the body such as the respiratory tract, ear, lung, stomach, intestine, skin, soft tissue, bone, joint, urinary tract, as well as sexually transmitted diseases like gonorrhoea. Additionally, it is prescribed for infections resulting from specific surgical procedures and septicemia in individuals with compromised immune systems.

Side Effects -

Headache

Dizziness

Nausea

Vomiting

Stomach ache

Diarrhoea

Joint pain

Interactions of Bactoquin 500 MG

Interactions with other medicines:

Certain medications can alter the functioning of Bactoquin Tablet, while others may diminish the efficacy of concurrently administered medications.

Please ensure to disclose to the doctor all medications, supplements, or herbal remedies you are currently using or considering taking to prevent any potential interactions. Additionally, inform the doctor if you have an upcoming surgery or vaccination planned. Exercise caution if you are taking medications for the treatment of irregular heart rhythm, mental health issues, gout, acid reflux, muscle spasms, seizures, rheumatoid arthritis, Parkinson's disease, erectile dysfunction, sleep disorders, skin conditions, or blood thinners.

Bactoquin Tablet should be consumed either 2 hours prior to or 6 hours after ingesting dietary supplements containing zinc, iron, aluminum or magnesium-based antacids,

medications for kidney issues like sevelamer and lanthanum carbonate, as well as ulcer treatment drugs such as sucralfate. It is important to note that Bactoquin Tablet can boost the blood sugar-lowering effects of anti-diabetic medications, therefore, it should be used with care.

Interactions with food items:

Taking Bactoquin Tablet alongside dietary supplements or mineral-fortified drinks such as milk, yoghurt, or calcium-fortified orange juice is not recommended as it could potentially hinder the absorption of the medication.

Infection Treated with Ciprofloxacin:

**Reference**

1. Dax SL. Antibacterial Chemotherapeutic Agents. London: Blackie Academic & Professional, 1997:298–345.
2. Lee C, Ronald AR. Norfloxacin: its potential in clinical practice. Am J Med 1987;82:27–34.
3. Patrick GL. An Introduction to Medicinal Chemistry. Oxford: Oxford University Press, 2003:379–435.

4. Buck ML. Ciprofloxacin use in children: a review of recent findings. *Pediatr Pharm* 1998;4:12–18.
5. Pandey SN. *A Text Book of Medicinal Chemistry (Synthetic and Biochemical Approach)*. Bhelapur: Mahavir Press, 2003:547–85.
6. Torriero AAJ, Ruiz-Diaz JJJ, Salinas E, Marchevsky EJ, Sanz MI, Raba J. Enzymatic rotating biosensor for ciprofloxacin determination. *Talanta* 2006;69:691–9.
7. Guneyssel O, Onur O, Erdede M, Dehizbasi A. Trimetoprim/sulfamethoxazole resistance in urinary tract infections. *J Emerg Med* 2009;36:338–41.
8. Karachalios GN, Zografos G, Patrikakos V, Nassopoulou D, Kehagioglou K. Biliary tract infections treated with ciprofloxacin. *Infection* 2005;21:262–4.
9. Abraham DJ. *Burger's Medicinal Chemistry Drug Discovery*. Hoboken, NJ: John Wiley & Sons, 2003:582–7.
10. Appelbaum PC, Hunter PA. The fluoroquinolone antibacterials: past, present and future perspectives. *Int J Antimicrob Agents* 2000;16:5–15.
11. De Almeida MV, Saraiva MF, De Souza MVN, Da Costa CF, Vincente FRC, Lourenco MCS. Synthesis and antitubercular activity of lipophilic moxifloxacin and gatifloxacin derivatives. *Bioorg Med Chem Lett* 2007;17:5661–4.
12. Cooper JG, Harboe K, Frost SK, Skadberg O. Ciprofloxacin interacts with thyroid replacement therapy. *BMJ* 2005;330:1002.
13. Ciprofloxacin. <http://en.wikipedia.org/w/index.php?title=Ciprofloxacin&oldid=287777716>. Accessed 6 May 2009.
14. Cipro. Bayer response 12 Feb 2009. <http://www.fda.gov/cder/foi/label/2009/019537s69,19847s43,19857s50,20780s27lbl.pdf>. Accessed 6 May 2009.
15. Anquetin G, Greiner J, Mahmoud N, Santillana HM, Gozalbes R, Farhati K, et al. Design, synthesis and activity against *Toxoplasma gondii*, *Plasmodium* spp., and *Mycobacterium tuberculosis* of new 6-fluoroquinolones. *Eur J Med Chem* 2006;41:1478–93.
16. Farhi D, Dupin N. The rise of fluoroquinolone-resistant *Neisseria gonorrhoeae*. *Swiss Med Wkly* 2008;138:223–4.
17. Brunner M, Langer O, Dobrozemsky G, Muller U, Zeitlinger M, Mitterhauser M, et al. [18F] Ciprofloxacin, a new positron emission tomography tracer for noninvasive assessment of the tissue distribution and pharmacokinetics of ciprofloxacin in humans. *Antimicrob Agents Chemother* 2004;48:3850–7.
18. Kubin R. Safety and efficacy of ciprofloxacin in paediatric patients—review. *Infection* 1993;21:413–21.
19. Wimer SM, Schoonover L, Garrison MW. Levofloxacin: a therapeutic review. *Clin Ther* 1998;20:1049–68.
20. Antonio DD, Piccolomini R, Iacone A, Fioritoni G, Parruti G, Betti S, et al. Comparison of ciprofloxacin, ofloxacin and pefloxacin for the prevention of the bacterial infection in neutropenic patients with haematological malignancies. *J Antimicrob Chemother* 1994;33:837–44.
21. Yamane N, Jones RN, Frei R, Hoban DJ, Pignatari AC, Marco F. Levofloxacin in vitro activity: results from an international comparative study with ofloxacin and ciprofloxacin. *J Chemother* 1994;6:83–91.
22. Joseph E, Dohar MD, Wall M, Peter S, Roland PS, Dupre SJ, et al. Topical ciprofloxacin/dexamethasone found superior to oral amoxicillin/ clavulanic acid in acute otitis media with otorrhea. *Otolaryngol Head Neck Surg* 2005;133:127.
23. Brunner H, Zeiler HJ. Oral ciprofloxacin treatment for salmonella typhimurium infection of normal and immunocompromised mice. *Antimicrob Agents Chemother* 1988;32:57–62.
24. Herold C, Ocker M, Ganslmayer M, Gerauer H, Hahn EG, Schuppan D. Ciprofloxacin induces apoptosis and inhibits proliferation of human colorectal carcinoma cells. *Br J Cancer* 2002;86:443–8.
25. Aranha O, Wood DP, Sarkar FH. Ciprofloxacin mediated cell growth inhibition, S/G2-M cell cycle arrest, and apoptosis in a human transitional cell carcinoma of the bladder cell line. *Clin Cancer Res* 2000;6:891–900.
26. Aranha O, Grignon R, Fernandes N, McDonnell TJ, Wood DP, Sarkar FH. Suppression of human prostate cancer cell growth by ciprofloxacin is associated with cell cycle arrest and apoptosis. *Int J Oncol* 2003;22:787–94.
27. Pinto AC, Moreira JN, Simoes S. Ciprofloxacin sensitizes hormone- refractory prostate cancer cell lines to doxorubicin and docetaxel treatment on a schedule-dependent manner. *Cancer Chemother Pharmacol* 2009;64:445–54.
28. Bourikas LA, Kolios G, Valatas V, Notas G, Drygiannakis I, Pelagiadis I, et al. Ciprofloxacin decreases survival in HT-29 cells via the induction of TGF-beta1 secretion and enhances the anti-proliferative effect of 5-fluorouracil. *Br J Pharmacol* 2009;157:362–70.
29. Ibukun EA, Eytayo OA, Nwaka DUC, Aminat OA, Aderemi TA, Oludare FA, et al. Emergence of cross-resistance to fluoroquinolones in Gram-negative isolates from cancer infections in a tertiary hospital in Nigeria. *J Am Sci* 2008;4:14–20.
30. Dekker AW, Rosenberg AM, Verhoef J. Infection prophylaxis in acute leukaemia: a comparison of ciprofloxacin with trimethoprim–sulfamethoxazole and colistin. *Anna Intern Med* 1987;106:7–11.

31. Haron E, Rolston KVI, Cunningham C, Holmes F, Umsawasdi T, Bodey GP. Oral ciprofloxacin therapy for infections in cancer patients. *J Antimicrob Chemother* 1989;24:955–62.
32. Balkhy HH, Memish ZA, Shibl A, Elbasher A, Osoba A. In vitro activity of quinolones against *S. pneumoniae*, *H. influenzae* and *M. catarrhalis* in Saudi Arabia. *East Mediterr Health J* 2005;11:36–44.
33. Aydemir S, Tunger A, Cilli F. In vitro activity of fluoroquinolones against common respiratory pathogens. *West Indian Med J* 2006;55:9–12.
34. Cassell GH, Mekalanos J. Development of antimicrobial agent in the era of new and reemerging infectious diseases and increasing antibiotic resistance. *JAMA* 2001;285:601–5.
35. Rubin J, Walker RD, Blickenstaff K, Jones SB, Zhao S. Antimicrobial resistance and genetic characterization of fluoroquinolone resistance of *Pseudomonas aeruginosa* isolated from canine infections. *Vet Microbiol* 2008;131:164–72.
36. Cozzarelli NR. DNA gyrase and the supercoiling of DNA. *Science* 1980;207:953–60.
37. Schmidt FJ, Hofmann B, Hansen B, Scheuring S, Luckefahr M, Klootwijk M, et al. Relationship between ciprofloxacin, ofloxacin, levofloxacin, sparfloxacin and moxifloxacin (BAY 12-8039) MICs and mutations in *grlA*, *grlB*, *gyrA* and *gyrB* in 116 unrelated clinical isolates of *Staphylococcus aureus*. *J Antimicrob Chemother* 1998;41:481–4.
38. Walters JD, Zhang F, Nakkula RJ. Mechanism of fluoroquinolone transport by human neutrophils. *Antimicrob Agents Chemother* 1999;43:2710–15.
39. Shaharyar M, Ashraf Ali EM, Abdullah MM. Synthesis and antiproliferative activity 1-[(sub)]-6-fluoro-3-[(sub)]-1,3,4-oxadiazol-2-yl-7-piperazino-1,4-dihydro-4-quinolone derivatives. *Med Chem Res* 2007;16:292–9.
40. Vila J, Sanchez-Céspedes J, Sierra JM, Piqueras M, Nicolas E, Freixas J, et al. Antibacterial evaluation of a collection of norfloxacin and ciprofloxacin derivatives against multidrug-resistant bacteria. *Int J Antimicrob Agents* 2006;28:19–24.
41. Emmerson, A. M., & Jones, A. M. The quinolones: decades of development and use. *Journal of Antimicrobial Chemotherapy*, 2003;51(suppl 1), 13–20.
42. Asif, M., Siddiqui, A. A., & Husain, A. Quinolone derivatives as antitubercular drugs. *Medicinal Chemistry Research*, 2013;22(3), 1029–1042.
43. Herrlin, K., Segerdahl, M., Gustafsson, L. L., & Kalso, E. Methadone, ciprofloxacin, and adverse drug reactions. *The Lancet*, 2000;356(9247), 2069–2070.
44. Johnson, J. L., Hadad, D. J., Boom, W. H., Daley, C. L., Peloquin, C. A., Eisenach, K. D., ... & Dietze, R. Early and extended early bactericidal activity of levofloxacin, gatifloxacin and moxifloxacin in pulmonary tuberculosis. *The International Journal of Tuberculosis and Lung Disease*, 2006;10(6), 605–612.
45. Si, Z., Wang, L., Hu, J., & Jiang, W. Enhanced luminescence of terbium - 1 - cyclopropyl - 6 fluoro-1, 4-dihydro - 4 - oxo - 7 - (1 - piperazinyl) - 3-quinolinecarboxylic acid with lanthanum and its application. *Microchemical journal*, 2001;70(1), 19–24.
46. Hossen, S. M., Islam, M. S., Masumder, K. U., Hossain, M. S., Chowdhury, A., Deb, A. K., & Shobuj, S. M. In-vitro interactions of Ciprofloxacin Hydrochloride with different essential mineral salts and its influence on antimicrobial activity (MIC) of Ciprofloxacin Hydrochloride. *International Journal of Pharmaceutical and Life Sciences*, 2012;1(3).
47. Jiménez-Garrido, N., Perello, L., Ortiz, R., Alzuet, G., Gonzalez-Alvarez, M., Canton, E., ... & Perez-Priede, M. Antibacterial studies, DNA oxidative cleavage, and crystal structures of Cu (II) and Co (II) complexes with two quinolone family members, ciprofloxacin and enoxacin. *Journal of inorganic biochemistry*, 2005;99(3), 677–689.
48. Lister, P. D., & Sanders, C. C. Pharmacodynamics of trovafloxacin, ofloxacin, and ciprofloxacin against *Streptococcus pneumoniae* in an in vitro pharmacokinetic model. *Antimicrobial agents and chemotherapy*, 1999;43(5), 1118–1123.
49. Alan, C., Koçoglu, H., Ersay, A. R., Ertung, Y., & Kurt, H. A. Unexpected severe hepatotoxicity of ciprofloxacin: two case reports. *Drug and chemical toxicology*, 2011;34(2), 189–191.
50. Rodvold, K. A., & Piscitelli, S. C. New oral macrolide and fluoroquinolone antibiotics: an overview of pharmacokinetics, interactions, and safety. *Clinical infectious diseases*, 1993; 17(Supplement 1), S192–S199.
51. Wallace, R. J., Brown, B. A., & Onyi, G. O. Skin, soft tissue, and bone infections due to *Mycobacterium chelonae*: importance of prior corticosteroid therapy, frequency of disseminated infections, and resistance to oral antimicrobials other than clarithromycin. *Journal of Infectious Diseases*, 1992;166(2), 405–412.
52. Yalvac, I. S., Basci, N. E., Bozkurt, A., & Duman, S. Penetration of topically applied ciprofloxacin and ofloxacin into the aqueous humor and vitreous. *Journal of Cataract & Refractive Surgery*, 2003;29(3), 487–491.
53. Navalón, A., Ballesteros, O., Blanc, R., & Vilchez, J. L. Determination of ciprofloxacin in human urine and serum samples by solid-phase spectrophotometry. *Talanta*, 2000;52(5), 845–852.

54. Granfors, M. T., Backman, J. T., Neuvonen, M., & Neuvonen, P. J. Ciprofloxacin greatly increases concentrations and cytotensive effect of tizanidine by inhibiting its cytochrome P450 1A2-mediated presystemic metabolism*. *Clinical Pharmacology & Therapeutics*, 2004;76(6), 598-606.
55. Schaeffer, A. J. The expanding role of fluoroquinolones. *The American journal of medicine*, 2002;113(1), 45-54.
56. Matera, M. G. Pharmacologic characteristics of prulifloxacin. *Pulmonary pharmacology & therapeutics*, 2006;19, 20-29.
57. Zhang, L., Reynolds, K. S., Zhao, P., & Huang, S. M. Drug interactions evaluation: an integrated part of risk assessment of therapeutics. *Toxicology and applied pharmacology*, 2010;243(2), 134-145.
58. Hawkey, P. M. Mechanisms of quinolone action and microbial response. *Journal of Antimicrobial Chemotherapy*, 2003;51(suppl 1), 29-35.
59. Paterson, D. L., Mulazimoglu, L., Casellas, J. M., Ko, W. C., Goossens, H., Von Gottberg, A., ... & Victor, L. Y. Epidemiology of ciprofloxacin resistance and its relationship to extended-spectrum β -lactamase production in *Klebsiella pneumoniae* isolates causing bacteremia. *Clinical infectious diseases*, 2000;30(3), 473-478.
60. Kümmerer, K. Antibiotics in the aquatic environment—a review—part I. *Chemosphere*, 2009;75(4), 417-434.
61. Ruiz, J. Mechanisms of resistance to quinolones: target alterations, decreased accumulation and DNA gyrase protection. *Journal of Antimicrobial Chemotherapy*, 2003;51(5), 1109-1117.
62. Schaeffer, A. J. The expanding role of fluoroquinolones. *The American journal of medicine*, 2002;113(1), 45-54.
63. Halling-Sørensen, B., Lützhøft, H. C. H., Andersen, H. R., & Ingerslev, F. Environmental risk assessment of antibiotics: comparison of mecillinam, trimethoprim and ciprofloxacin. *Journal of antimicrobial chemotherapy*, 2000;46(suppl 1), 53-58.
64. Petrilli, A. S., Dantas, L. S., Campos, M. C., Tanaka, C., Ginani, V. C., & Seber, A. Oral ciprofloxacin vs. intravenous ceftriaxone administered in an outpatient setting for fever and neutropenia in low-risk pediatric oncology patients: Randomized prospective trial. *Medical and pediatric oncology*, 2000;34(2), 87-91.
65. Arslan, H., Azap, Ö. K., Ergönül, Ö., & Timurkaynak, L. F. Risk factors for ciprofloxacin resistance among *Escherichia coli* strains isolated from community-acquired urinary tract infections in Turkey. *Journal of Antimicrobial Chemotherapy*, 2005;56(5), 914-918.
66. Heystek, M., & Ross, J. D. C. A randomized double-blind comparison of moxifloxacin and doxycycline/metronidazole/ciprofloxacin in the treatment of acute, uncomplicated pelvic inflammatory disease. *International journal of STD & AIDS*, 2009;20(10), 690-695.
67. Mishra, S. K., & Agrawal, D. *A Concise Manual of Pathogenic Microbiology*. John Wiley & Sons 2012.
68. Nili, H., & Asasi, K. Natural cases and an experimental study of H9N2 avian influenza in commercial broiler chickens of Iran. *Avian Pathology*, 2002;31(3), 247-252.
69. Kariyawasam, S., Wilkie, B. N., & Gyles, C. L. Resistance of broiler chickens to *Escherichia coli* respiratory tract infection induced by passively transferred egg-yolk antibodies. *Veterinary microbiology*, 2004;98(3), 273-284.
70. Posyniak, A., Zmudzki, J., & Niedzielska, J. Liquid chromatography analysis of enrofloxacin and ciprofloxacin in chicken blood spotted on filter-paper disks. *Journal of Chromatography B*, 2002;780(2), 309-314.71.