Pro Index | Journal of Science in Medicine and Life
Volume: 2 Issue: 9 Year: 2024
ISSN: 2992-9202 | http://journals.proindex.uz

Estimation of Residues of Tetracycline and Ciprofloxacin in Hospital Wastewater

Hamad Hussein Hamad

Abstract: The research included estimating the residues of the antibiotics tetracycline and ciprofloxacin in the wastewater of some hospitals. Samples were taken, one sample from each hospital, and these antibiotics were extracted using solid phase extraction methods and then determined using high-performance liquid chromatography technology, with a fluorescence detector, Em = 420, Ex = 310, a C18 column, 25 cm, 4.6 mm, and a mobile phase, Methanol: Dw70:30, for tetracycline, and for ciprofloxacin, a C18 column, 25 cm, 4.6 mm. and 3.5µm with a wavelength of 278nm and a mobile phase of phosphoric acid, acetonitrile and methanol in ratios of 40:40:20, respectively.It was noted that there are significant concentrations of the studied antibiotics, with tetracycline concentrations ranging from 201.1 - 142.5 ppm and ciprofloxacin concentrations from 156.98 - 78.99 ppm. Therefore, it is necessary to monitor these concentrations leaking into the water as long as they affect the environment and human and animal health.

Introduction

Tetracycline (TCN) is considered one of the most important antibiotics given to treat many infections caused by different types of infectious bacteria. It is an odorless yellow crystalline powder with the partial formula C22H24N2O8 Its chemical composition is expressed as follows:

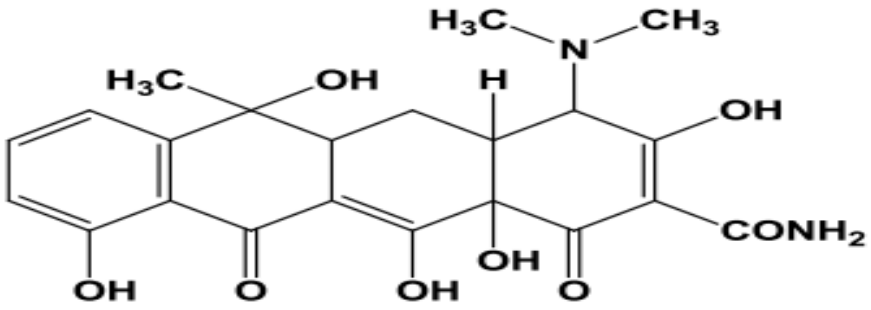


Figure (1) Chemical structure of tetracycline

Tetracycline is used to treat infections of the respiratory system, middle ear, sinuses, and urinary tract, in addition to its use in treating skin infections . Tetracyclines, a large family of antibiotics, were discovered by Benjamin Duggar in 1948 as natural products, and were first described in 1948. (1) Benjamin Dugar, working under Yellapragada Subaru at Lederle Laboratories, discovered the first tetracycline antibiotic, chlortetracycline, in 1945. (2) The structure of aureomycin was elucidated in 1952 and published in 1954 by the Pfizer-Woodward group after the discovery of the structure. , researchers at Pfizer began by chemically modifying Aureomycin by treating it with hydrogen in the presence of a carbon catalyst. This chemical reaction replaced the chlorine charge with hydrogen, creating a compound called tetracycline by hydrogenolysis (3). Tetracyclines offered higher potency, better solubility, and were more convenient than other antibiotics in their class. The new compound was one of the first commercially successful antibiotics to be used to develop sancycline, minocycline, and glycylcyclines. And then tetracyclines have a broad spectrum of antibiotic action. Originally, they possessed some level of bactericidal activity against almost all

medically relevant bacterial genera, both Gram-positive and Gram-negative, with a few exceptions, such as Pseudomonas aeruginosa and Protease spp. Which displays internal resistance. However, the inherent resistance acquired has spread in many pathogenic organisms and has greatly eroded the broad diversity of this group of antibiotics. Resistance has become common among Staphylococcus aureus. Tetracyclines are particularly useful in the management of infections by certain intracellular bacterial pathogens such as Chlamydia, Mycoplasma, and Rickettsia. It is also valuable in plochaetal infections such as syphilis and Lyme disease. Some rare or exotic infections, including anthrax, plague, and graminoidea, are also susceptible to tracycline. Tetracycline tablets were used in a plague outbreak in India in 1994 (4) Tetracycline is one of a group of antibiotics that can be used together to treat peptic ulcers caused by bacterial infections. The mechanism of action for the antibacterial effect of tetracycline is based on disrupting protein translation in bacteria, thus damaging the ability of microbes to grow and repair (5) (6).

Ciprofloxacin (CIP) is a widely used antibiotic that belongs to the fluoroquinolone family and is widely used in human and veterinary medicine (7). Its molecular formula is (C17H18FN3O3), partial weight 331.346 g/mole, boiling point 581.8°C, and its chemical composition is shown in the following figure (8)

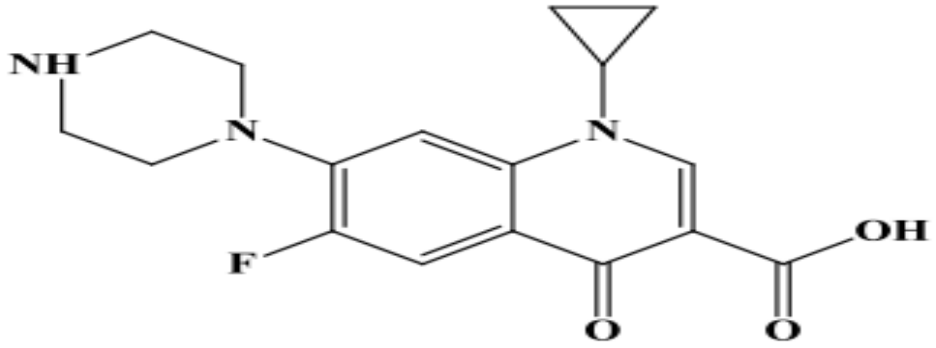


Figure (2) Chemical structure of ciprofloxacin

Ciprofloxacin is used as a therapeutic agent in the treatment of many bacterial infections in humans and animals (9) and is also primarily used in the treatment of urinary tract infections (10). This medication has side effects, as it can cause health problems such as headache, diarrhea, vomiting, and nausea (11). Ciprofloxacin has an important role in treatment guidelines issued by major medical societies for the treatment of serious infections, especially those likely caused by Gram-negative bacteria, including Pseudomonas Aeruginosa. For example, ciprofloxacin in combination with metronidazole is one of the regimens. First-line antibiotics recommended by the Infectious Diseases Society of America for the treatment of community-acquired abdominal infections in adults (12). It also features prominently in treatment guidelines for acute pelvic nephritis, complicated or hospital-acquired urinary tract infections, acute or chronic prostatitis(13), certain types of endocarditis(14) some dermatitis(15) and prosthetic joint infections(16) in... In other cases, treatment guidelines are more restrictive, in most cases recommending older, narrower medications as first-line treatment for less severe infections to reduce the development of fluoroquinolone resistance. For example, the Infectious Diseases Society of America recommends the use of ciprofloxacin and other fluoroquinolones in urinary tract infections in cases of proven or predicted resistance to narrower-spectrum drugs such as nitrofurantoin or trimethoprim/sulfamethoxazole. The European Association of Urology recommends ciprofloxacin as a regimen. An alternative to treat uncomplicated urinary tract infections, But warns that the "potential" for adverse events must be considered. Although it has been approved by regulatory authorities for the treatment of respiratory infections, it is not recommended for respiratory infections by most treatment guidelines due to its modest activity against the common respiratory pathogen pneumonia because (Ciprofloxacin) is a lipid profile, it has the ability to cross the blood barrier and cause inflammation (17). The 2013 FDA label warns of nervous system effects. Ciprofloxacin, like other fluoroquinolones, is known to provoke seizures or lower the seizure threshold, and may cause other adverse central nervous system effects. Headache, dizziness, and insomnia have been reported as

occurring fairly commonly in post-approval review articles, along with a low incidence of serious CNS adverse effects such as tremors, psychosis, anxiety, hallucinations, paranoia, and suicide attempts, especially at higher doses (18). Like other fluoroquinolones, it is also known to cause potentially irreversible peripheral neuropathy such as weakness, burning pain, tingling, or numbness (19).

Material and methods

Devices used

Devices used	Origin
Centrifuge	DuPont - Germany
Incubator	BDH
Hot plate	Japan
HPLC	SYKAMAN

Analysis methods using HPLC device

After both the sample solution to be separated and the phase solution are prepared and placed in the place designated for them in the device, and the required separation column is installed according to the type of separation and the material to be separated in the place designated for it inside the device, then the mobile phase is passed over the separation column for a period of no less than Half an hour, then the device injects a small, known amount of the sample solution in microliters, so that the sample moves to the column and passes through the mobile phase through the separation column, in which the substance is separated, which then comes out and the result appears in the form of a chromatogram to the detector, and the result appears in the form of a peak and an indication for each component of the sample. The area enclosed under the top of the separated substance is calculated and compared with the area enclosed under the top of a standard substance with the same concentration. Thus, the concentration of the separated substance can be known. If the separation is successful, each peak represents a component of the mixture to be separated. All recorded peaks are called chromatograms. To obtain an excellent result, a high pressure exceeding 100 par must be applied. Through the work that took place, the results were collected in the form of graphs, chromatograms, peaks, and tables for each sample separately. As well as the standard material to show some statistical values, detention time, peak area, percentage, height, quantity and type of unit used.

Samples Collection

Samples were collected from wastewater from several hospitals in Diyala Governorate, namely (Baquba General Hospital, Al-Batoul Hospital, Al-Muqdadiya General Hospital, Al-Zahraa Hospital, Jalawla General Hospital), one sample for each hospital on 3/1/2023 for a period of one month, using clean glass bottles. The container has a capacity of 250 ml and is kept in a cool, dry place until the medication is evaluated.

Preparation the sample

100mg of each substance was taken separately, then each substance was placed in a 100ml volumetric vial, and the volume was completed to the mark, where the initial concentration became 100ppm for each of them. Using the dilution law C1V1=C2V2, the concentrations injected into the device were prepared, where 1ml of the prepared standard solution was taken and the volume was completed. Up to 10ml in a volumetric vial, and the second concentration became 10ppm and injected into the HPLC device. 100µm of the standard solution was injected with the same volume of the sample.

Extraction Procedure of tetracycline

Extraction method: 100 ml of the sample was taken and 10 ml of methanol and Citrate buffer were added to it in a volumetric ratio of 7:3 v/v. Then the mixture was stirred for five minutes. The samples were placed in the incubator and at room temperature for five minutes, after which the separation was done in a quickly refrigerated centrifuge. 3,500 rmp for ten minutes. The extraction was repeated for the second time using 2 ml of buffer solution. The clear solution was filtered and an SPE cartridge containing 10 ml of methanol and 4 ml of water was placed in it. The sample was then washed with 5 ml of water. 3 ml of mixed tetracycline was taken and filtered using a nylon fitter filter with a pore capacity of 0.45 µm, and then 100 µm of it was taken from it. It was injected into an HPLC device. The separation was conducted using an HPLC device at the Ministry of Science and Technology - Department of Water and Soil, according to the specifications below.

Mobile phace:methanol:D.W 70:30 ,Colommn:C18.Ops(25 cm ,4.6 mm)

Detector Florescence =Ex=310 nm, Em=420 nm, Flow rate=1.2 ml/min

Extraction Procedure of

Take 0.1 g of standard Ciprofloxacin and put it in a 250 ml volumetric vial and add an appropriate amount of solvent using the dilution rule. The solution becomes 400 ppm and then inject the sample into the analysis device.

The separation was conducted using an HPLC device at the Ministry of Science and Technology - Department of Water and Soil with the specifications below: SYKAMN model with a 100 ml injection system and a UV/Vis detector, then set at 278 nm, reversed phase, 25 cm, 4.6 mm, 3.5 µm C18 column, and a mobile phase consisting of a mixture of

0.025M Phosphoric acid to PH_3 with triethanolamine)

B= acetonitrile , C= methanol 40:40:20 Flow speed

, 1.0 ml/min

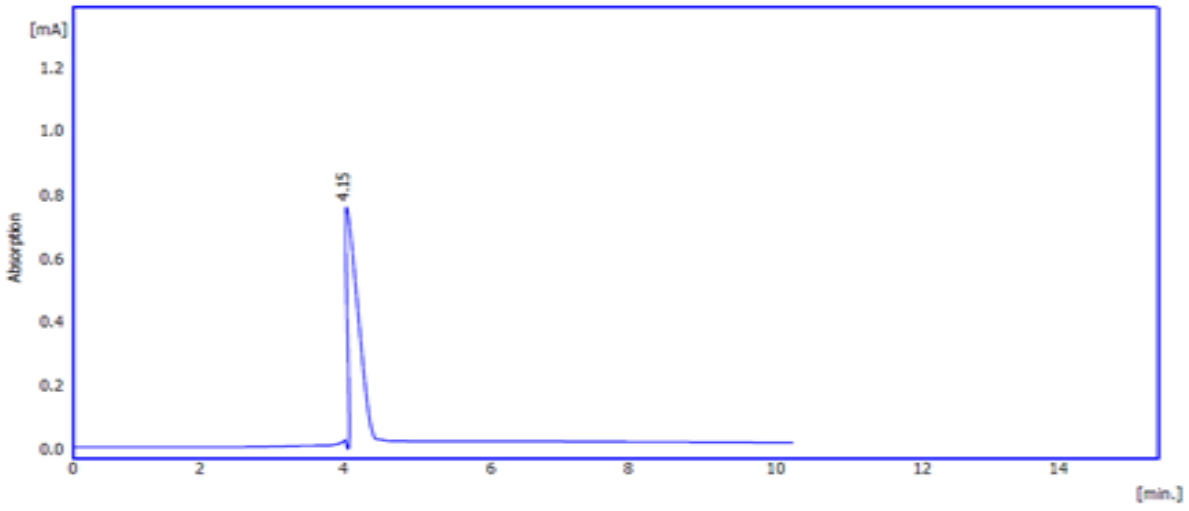
Calculation

The concentration of the following drugs, tetracycline and ciprofloxacin, was calculated by using the following formula: -

$$Csam = \frac{Cst \times Asam}{Asta}$$

Result and discussion

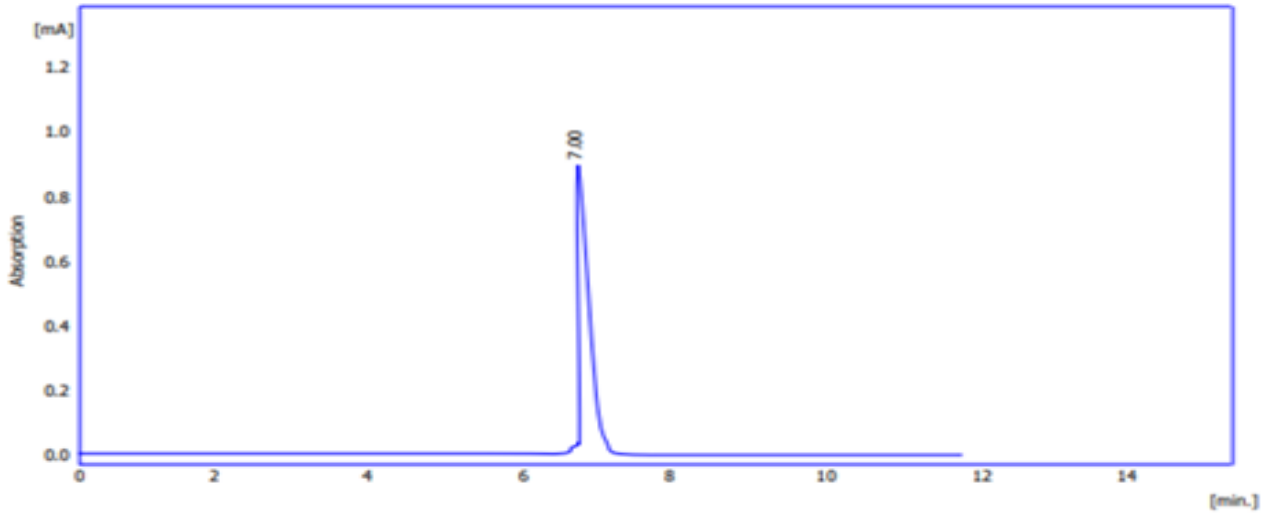
In this study, HPLC technology was used to detect the antibiotics tetracycline and ciprofloxacin in wastewater from the previously mentioned hospitals and the results are shown in Tables (1) (2) below. Figures (3)(4) are chromatograms of the standard substance for tetracycline and ciprofloxacin, respectively, with a summary table of the peaks and some statistical values of retention time, peak area, percentage, height, and the quantity and type of unit used.



Result chromatography Table (Uncal - F:\ tetracycline (10 PPM)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.15	2541.59	791.25	100.00	100.00	0.25	Tetracycline
	Total	2541.59	791.25	100.00	100.00		

Figure (3) Chromatogram of the standard substance tetracycline.

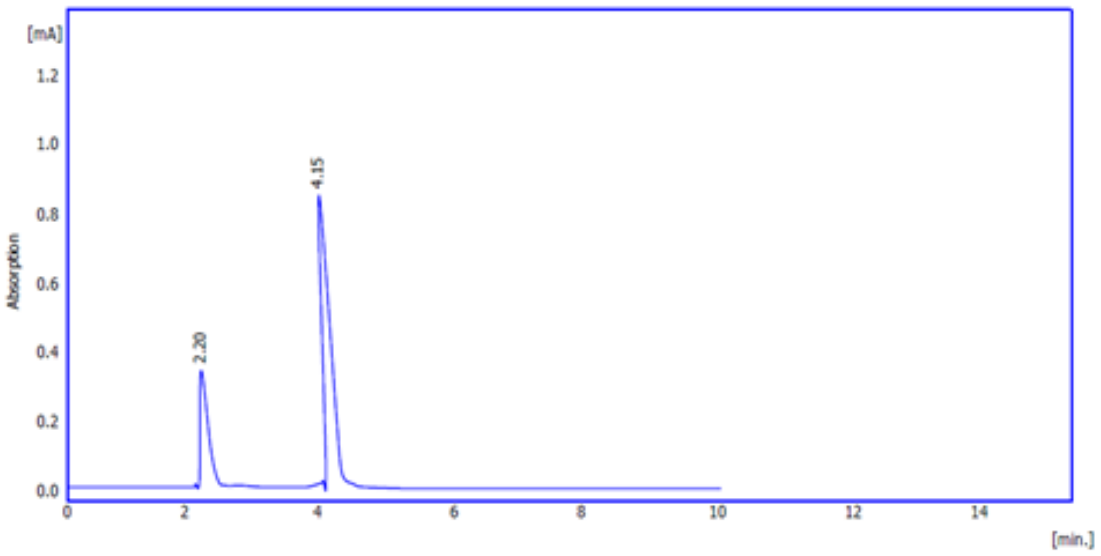


Result chromatography Table (Uncal - F:\ ciprofloxacin 10 ppm)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.00	2554.18	820.46	100.00	100.00	0.25	Ciprofloxacin
	Total	2554.18	820.46	100.00	100.00		

Figure (4) Chromatogram of the standard substance for ciprofloxacin.

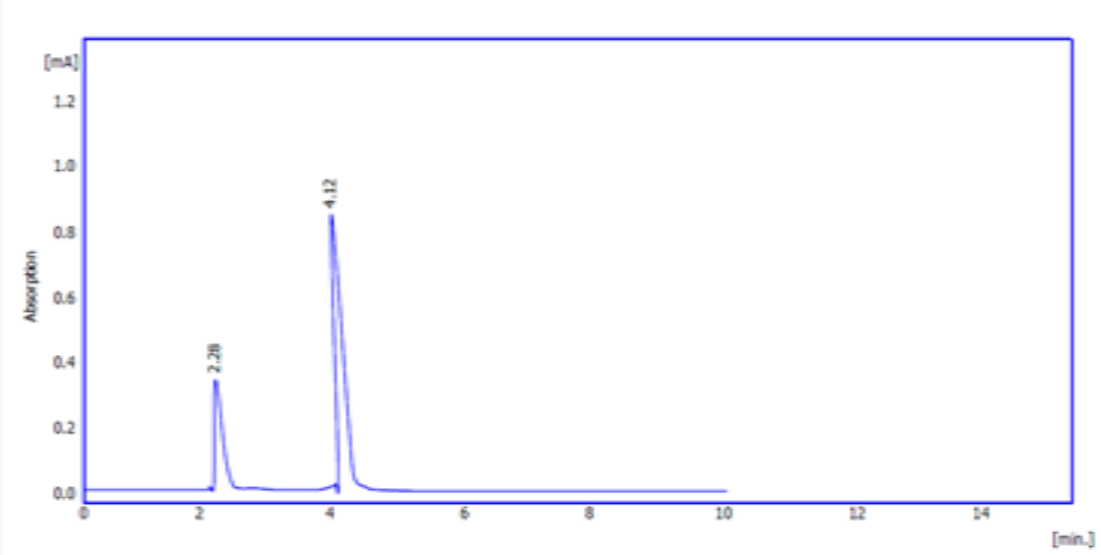
Figures (5) to (9) and (10) to (14) indicate chromatograms showing the percentages of presence of tetracycline and ciprofloxacin, respectively, with a summary table of the peaks and some statistical values of retention time, peak area, percentage, and height. The quantity and type of unit used in samples taken from the wastewater of the aforementioned hospitals



Result chromatography Table (Uncal - F:\ sample 1

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.20	4256.98	388.59	30.00	30.00	0.15	
2	4.15	98547.28	811.25	70.00	70.00	0.25	Tetracycline
	Total	102804.58	1199.84	100.00	100.00		

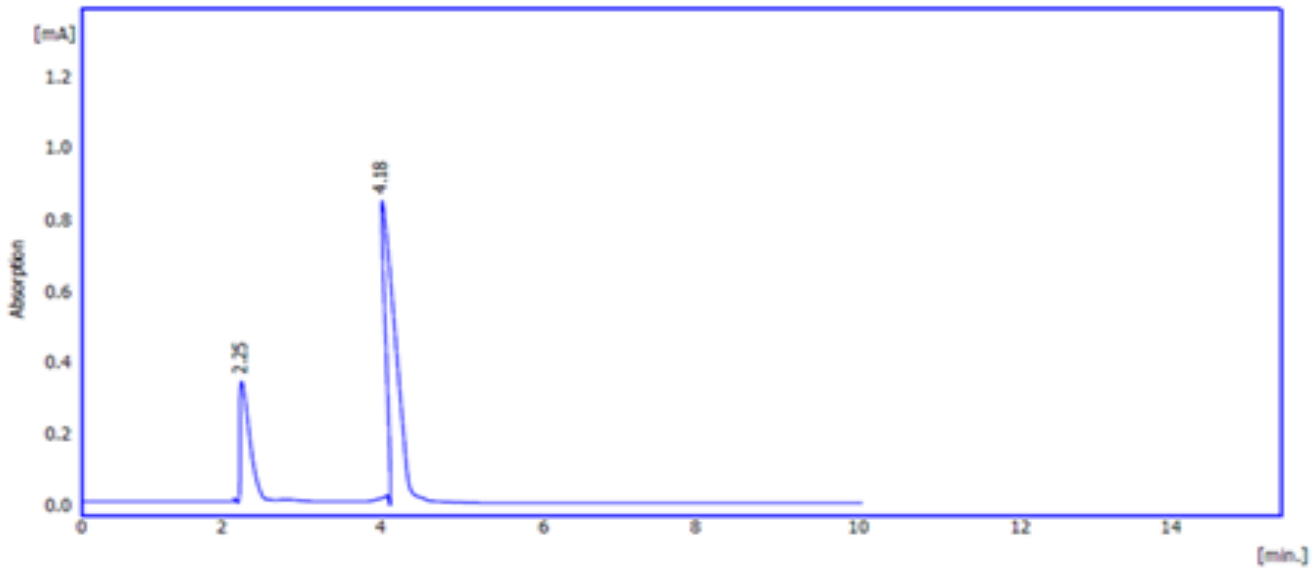
Figure (5) Chromatogram of the test sample from Al Zahra Hospital for tetracycline



Result chromatography Table (Uncal - F:\ sample 2)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.28	4355.19	381.05	30.00	30.00	0.15	
2	4.12	79582.14	812.45	70.00	70.00	0.25	Tetracycline
	Total	86215.02	1190.22	100.00	100.00		

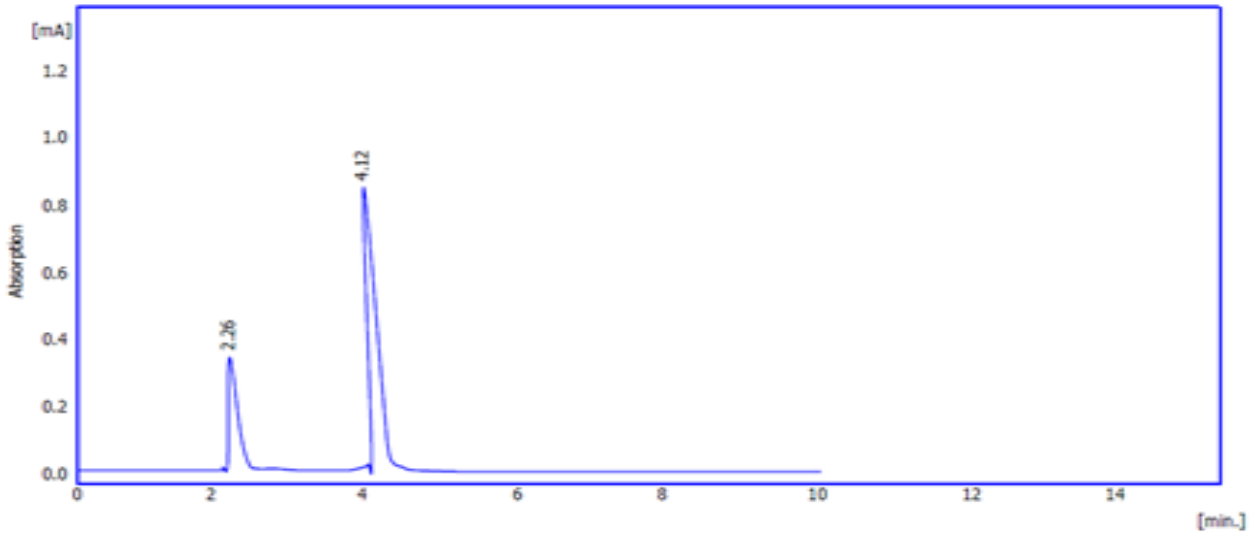
Figure (6) Chromatogram of the test sample from Al-Muqdadiya Hospital for tetracycline.



Result chromatography Table (Uncal - F:\ sample 3)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.25	4952.12	381.05	30.00	30.00	0.15	
2	4.18	91255.25	812.65	70.00	70.00	0.25	Tetracycline
	Total	90672.37	1190.22	100.00	100.00		

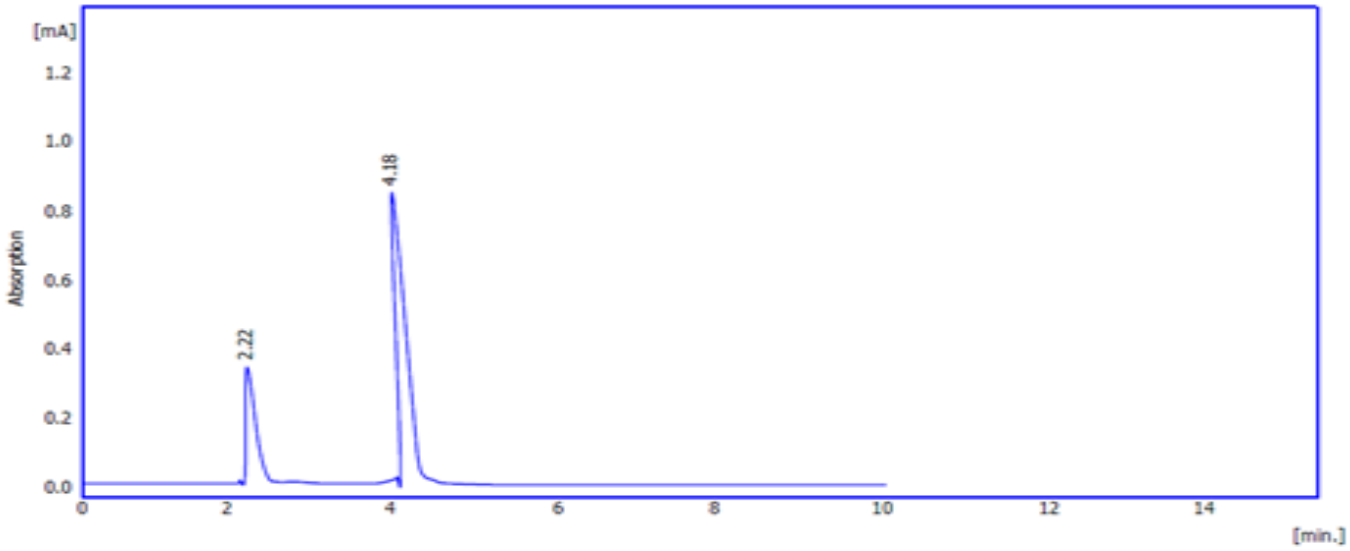
Figure (7) Chromatogram of the test sample from Jalawla Hospital for tetracycline.



Result chromatography Table (Uncal - F:\ sample 4)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.26	4452.08	381.25	30.00	30.00	0.15	
2	4.12	99682.05	812.60	70.00	70.00	0.25	Tetracycline
	Total	10413.59	1193.85	100.00	100.00		

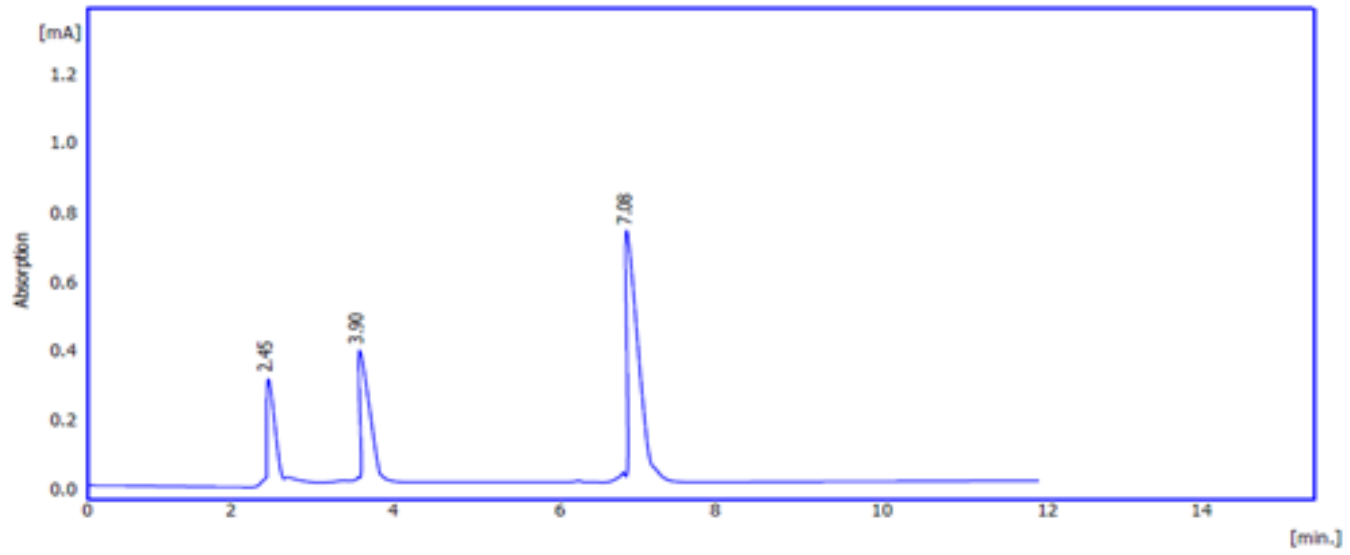
Figure (8) Chromatogram of the test sample from Al-Batoul Hospital for tetracycline.



Result chromatography Table (Uncal - F:\ sample 5)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.22	4921.08	382.55	30.00	30.00	0.15	
2	4.18	96254.08	811.44	70.00	70.00	0.25	Tetracycline
	Total	101225.16	1193.99	100.00	100.00		

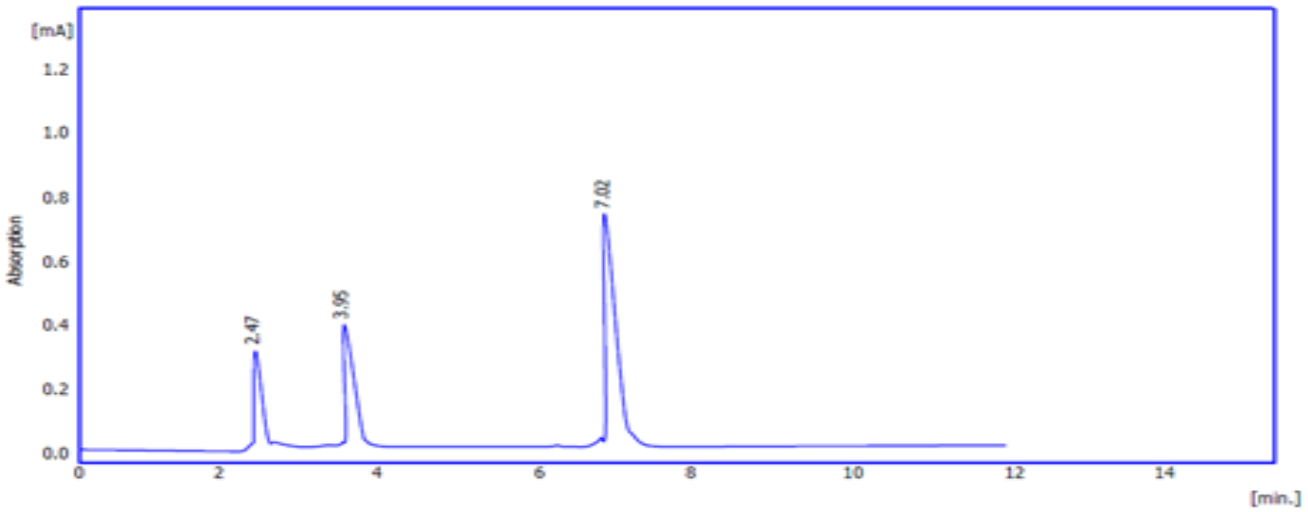
Figure (9) Baqubah Hospital test sample chromatogram for tetracycline.



Result chromatography Table (Uncal - F:\ sample 1)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.45	2154.89	360.25	20.00	20.00	0.15	
2	3.90	3205.64	377.49	20.00	20.00	0.15	
3	7.08	88964.25	784.25	60.00	60.00	0.25	Ciprofloxacin
	Total	94256.29	1521.99	100.00	100.00		

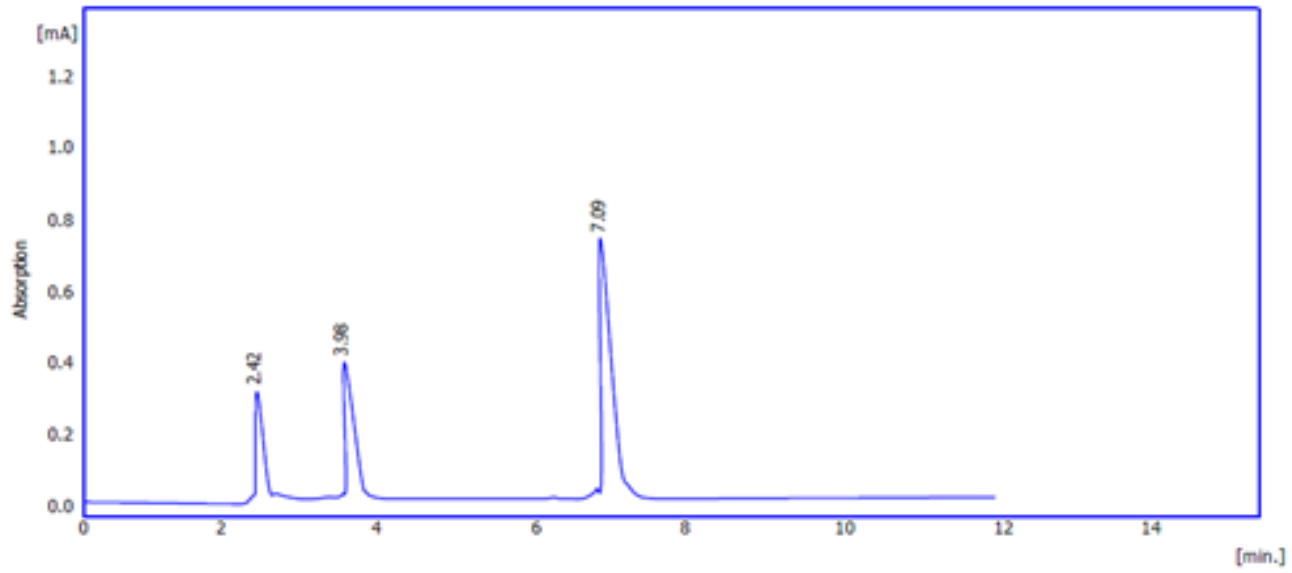
Figure (10) Chromatogram of the test sample from Al Zahra Hospital for ciprofloxacin.



Result chromatography Table (Uncal - F:\ sample 2)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.47	2256.98	361.45	20.00	20.00	0.15	
2	3.95	3365.22	378.99	20.00	20.00	0.15	
3	7.02	93554.89	785.49	60.00	60.00	0.25	Ciprofloxacin
	Total	99652.25	1525.98	100.00	100.00		

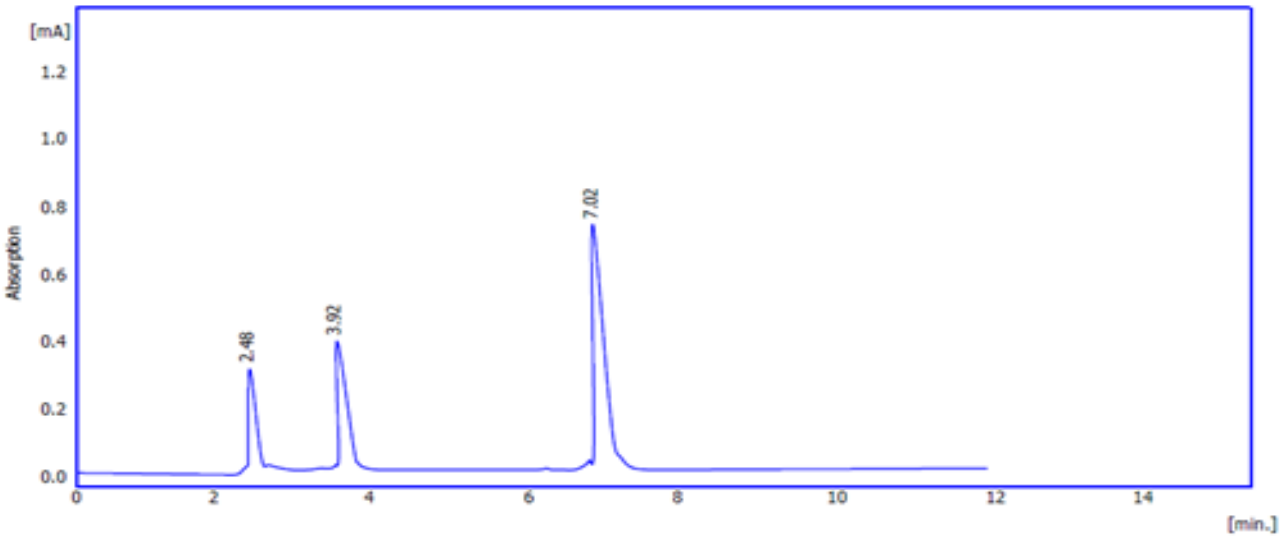
Figure (11) Chromatogram of the test sample from Al-Muqdadiya Hospital for ciprofloxacin.



Result chromatography Table (Uncal - F:\ sample 3)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.42	2965.08	360.15	20.00	20.00	0.15	
2	3.98	3995.08	377.98	20.00	20.00	0.15	
3	7.09	96542.08	784.98	60.00	60.00	0.25	Ciprofloxacin
	Total	100256.58	1522.66	100.00	100.00		

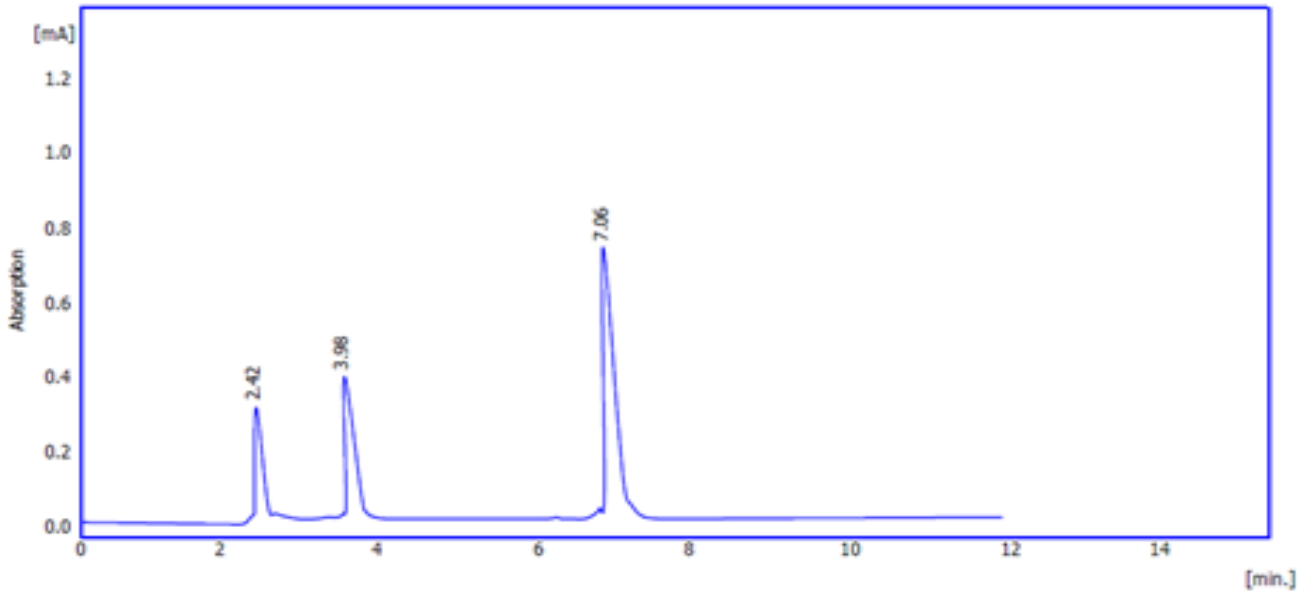
Figure (12) Chromatogram of the test sample from Jalawla Hospital for ciprofloxacin.



Result chromatography Table (Uncal - F:\ sample 4)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.48	2754.08	363.55	20.00	20.00	0.15	
2	3.92	3854.11	378.98	20.00	20.00	0.15	
3	7.02	98952.66	784.55	60.00	60.00	0.25	Ciprofloxacin
	Total	102256.85	1523.98	100.00	100.00		

Figure (13) Chromatogram of the test sample from Al-Batoul Hospital for ciprofloxacin.



Result chromatography Table (Uncal - F:\ sample 5)

No	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	2.42	3012.58	365.98	20.00	20.00	0.15	
2	3.98	3966.12	371.49	20.00	20.00	0.15	
3	7.06	92456.08	785.00	60.00	60.00	0.25	Ciprofloxacin
	Total	99434.56	1525.98	100.00	100.00		

Figure (14) Chromatogram of the test sample from Baquba Hospital for ciprofloxacin.

The results below shown in Table (1) (2) for the concentrations of tetracycline and ciprofloxacin, respectively:

Table (1) Tetracycline concentrations in ppm for a number of hospitals in the governorate.

No	Name	Con (ppm)
1	Al Zahra	**174.5**
2	Al-Muqdadiya	**165.0**
3	Jalawla	**180.6**
4	Al-Batoul	**142.5**
5	Baquba	**201.1**

Table (2) Ciprofloxacin concentrations in ppm for a number of hospitals in the governorate

NO	Name	Con (ppm)
1	Al Zahra	**95.58**
2	Al-Muqdadiya	**80.22**
3	Jalawla	**105.64**
4	Al-Batoul	**78.99**
5	Baquba	**156.98**

Conclusion:

Samples from several hospitals were analyzed to estimate the residues of the antibiotics tetracycline and ciprofloxacin in wastewater in the governorate using the (solid) phase extraction method, and then estimated using the high-performance liquid chromatography technique, with a fluorescence detector Em = 420, Ex = 310, a C18 column 25 cm, 4.6 mm, and a mobile phase Methanol: Dw 70. :30 for tetracycline.

The extraction method used a 25cm, 4.6mm and 3.5mm C18 column, a UV/Vis detector with a wavelength of 278nm, and a mobile phase of a mixture of phosphoric acid, acetonitrile, and methanol in ratios of 40:40:20.

It was noted that the concentrations of the studied antibiotics ranged from tetracycline concentrations to 201.1 - 142.5 ppm and ciprofloxacin concentrations from 156 to 80.22 ppm. Therefore, it is necessary to monitor these concentrations leaking into the water as long as they affect the environment and human and animal health. Therefore, the leakage of these antibiotics through wastewater or through purification or treatment methods by adsorption or photodegradation must be minimized to get rid of them. Therefore, the person must adhere to the doctor’s instructions when using treatment when he is afflicted with diseases caused by these antibiotics.

References

1. Klajn R. "Chemistry and chemical biology of tetracyclines". Archived from the original on 2007-06-17. Retrieved 20 June 2007. Better source needed.
2. Jukes TH (1985). "Some historical notes on chlortetracycline". Reviews of Infectious Diseases. 7 (5): 702–707. doi:10.1093/clinids/7.5.702. JSTOR 4453725. PMID 3903946.
3. Conover LH, Moreland WT, English AR, Stephens CR, Pilgrim FJ (September 1953). "Terramycin. Xi. Tetracycline". Journal of the American Chemical Society. 75 (18): 4622–4623. Doi: 10.1021/ja01114a537. ISSN 0002-7863.
4. Lippincott has Illustrated Reviews: Pharmacology, 4th ed. Harvery RA, Champe, PC. Lippincott, Williams & Wilkins, 2009.
5. Moullan N, Mouchiroud L, Wang X, Ryu D, Williams EG, Mottis A, et al. (March 2015). "Tetracyclines Disturb Mitochondrial Function across Eukaryotic Models: A Call for Caution in Biomedical Research". Cell Reports. 10 (10): 1681–1691. doi:10.1016/j.celrep.2015.02.034. PMC 4565776. PMID 25772356.

6. Chatzispyrou IA, Held NM, Mouchiroud L, Auwerx J, Houtkooper RH (November 2015). "Tetracycline antibiotics impair mitochondrial function and its experimental use confounds research". Cancer Research. 75 (21): 4446–4449. doi:10.1158/0008-5472.CAN-15-1626. PMC 4631686. PMID 26475870.

7. N. Dhiman and N. Sharma, ―Removal of ciprofloxacin hydrochloride from aqueous solution using vertical bed and sequential bed columns,‖ J. Environ. Chem. Eng., vol. 6, no.4, pp. 8381–4391, 2018.

8. X. Peng, F. Hu, H. Dai, Q. Xiong, and C. Xu, ―Study of the adsorption mechanisms of ciprofloxacin antibiotics onto graphitic ordered mesoporous carbons,‖ J. Taiwan Inst. Chem. Eng., vol. 65, pp. 472–481, 2016.

9. E. S. I. El-Shafey, H. Al-Lawati, and A. S. Al-Sumri, ―Ciprofloxacin adsorption from aqueous solution onto chemically prepared carbon from date palm leaflets,‖ J. Environ. Sci. (China), vol. 24, no.9, pp. 1579–1586, 2012.

10. R. E. Ionescu, N. Renault, L. Bouffie, C. Gondran, S. Cosnier, D.G. Pinacho, M. P. Marco, F.J. S´anchez-Baeza, T. Healy, C. Martelet, ―Impedimetric immunosensor for the specific label free detection of ciprofloxacin antibiotic,‖ Biosens. Bioelectron., vol. 23, no. 4, pp. 549–555, 2007.

11. Solomkin JS, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJ, Baron EJ, O'Neill PJ, Chow AW, Dellinger EP, Eachempati SR, Gorbach S, Hilfiker M, May AK, Nathens AB, Sawyer RG, Bartlett JG (January 2010). "Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America". Clinical Infectious Diseases. 50 (2): 133–64. Doi: 10.1086/649554. PMID 20034345.

12. Jump up to:a b Grabe M, Bjerklund-Johansen TE, Botto H, Çek M, Naber KG, Pickard RS, Tenke P, Wagenlehner F, Wullt B (2013). "Guidelines on Urological Infections" (PDF). European Association of Urology. Archived from the original (PDF) on 31 December 2013.

13. Baddour LM, Wilson WR, Bayer AS, Fowler VG, Bolger AF, Levison ME, et al. (June 2005). "Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America". Circulation. 111 (23): e394–434. doi:10.1161/CIRCULATIONAHA.105.165564. PMID 15956145.

14. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan EL, Montoya JG, Wade JC (November 2005). "Practice guidelines for the diagnosis and management of skin and soft-tissue infections". Clinical Infectious Diseases. 41 (10): 1373–406. Doi: 10.1086/497143. PMID 16231249.

15. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR (January 2013). "Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America". Clinical Infectious Diseases. 56 (1): e1–e25. doi:10.1093/cid/cis803. PMID 23223583.

16. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Moran GJ, Nicolle LE, Raz R, Schaeffer AJ, Soper DE (March 2011). "International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases". Clinical Infectious Diseases. 52 (5): e103–20. doi:10.1093/cid/ciq257. PMID 21292654.

17. Jump up to:a b c Heidelbaugh JJ, Holmstrom H (April 2013). "The perils of prescribing fluoroquinolones". The Journal of Family Practice. 62 (4): 191–197. PMID 23570031.

18. Babar SM (October 2013). "SIADH associated with ciprofloxacin". The Annals of Pharmacotherapy. 47 (10): 1359–63. Doi: 10.1177/1060028013502457. PMID 24259701. S2CID 36759747.

19. R. S. Alkizwini and S. S. Alquzweeni, ―Modeling natural bentonite, thermal-modified bentonite and iron-modified bentonite with artificial neural network, sorption kinetics and sorption isotherms for simulated sorption tetracycline, Int. J. Environ. Sci. Technol., vol. 18, no. 9, pp. 2633–2650, 2021.