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Risk of Ceftriaxone (Antibiotic) in the Tigris River Water, Iraq

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Abstract: There are several causes of hemolytic diseases, such as viral or bacterial contamination, enlarged spleen, and typhoid fever, which can be transmitted through contaminated water. Polluted wastewater samples were collected for the period of June-2022 to (May-2023) from five stations in Baghdad City such as Al- Gureat, Al-Ahdamyah, Bab Al-Muhadum, Bab Al-Sharqy and Al-Jadryah stations on the Tigris Riverbanks for the studying of Ceftriaxone antibiotic risk. The concentrations of ceftriaxone have been detected using high-performance liquid chromatography (HPLC). The results reveal that concentrations of ceftriaxone in the water fluctuated via sampling stations and seasons; so the highest concentration was 8×10^{-5} ppm in site 2 at Ahdamyah station, while the lowest concentrations was 1×10^{-7} ppm in site 5 sites at Al-Jadryah station during wet season 2023. The results of the statistical analysis showed that there were no significant differences between the study stations, except for the control station. The detection of ceftriaxone in raw surface water confirms that sewage from health institutions reaches the river without any effective treatment.

Key words: Ceftriaxone, Tigris river, water pollution, Iraq, sewage.

Introduction

Therapeutic drugs vary in terms of the chemicals included in their composition, such as antibiotics, analgesics, laxatives, and others, where antibiotics are considered the most important of these types. Antibiotics are found in activated sludge, digested sludge, and daily sewage processes, depending on their sources. There are reports of antibiotics in wastewater treatment plants, lakes, rivers, groundwater, and even drinking water. If these antibiotics are not removed during water treatment, they can pose a significant threat to aquatic life when discharged (Meena et al., 2015; Niemi et al., 2020).

Antibiotics are considered one of the most important types of treatment in hospitals. The presence of antibiotics in water resources can cause the emergence of bacteria resistant to these antibiotics, which constitutes a serious threat to public health. Continuous exposure to antibiotics and their sub-inhibitory concentrations paves the way for bacterial resistance to many antibiotics, forming multidrug-resistant bacteria that not only cause resistance but also interfere with the biogeochemical cycle (Aydin et al., 2018). Along with hospital waste, municipal wastewater is one of the biggest "hot spots" for antibiotics (Shi et al., 2020). Human and animal feces and carcasses are the main sources of introduction of antibiotics, as well as antibiotic-resistant microbes,

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into aquatic ecosystems. These bacteria can transfer their genes to waterborne pathogenic microorganisms as well, thus inducing resistance. Thus, antibiotic resistance could become a crucial issue in modern medicine, as it poses the risk of catastrophic epidemics (Chandler, 2019).

Most developing countries respond to public health protection needs through pathogen management and water management (Bateganya et al., 2015; Hameed et al., 2019). The unsuitable disposal of these antibiotics in various ways leads to their access to water bodies. It becomes extremely necessary to ensure adequate treatment before releasing them into the environment; otherwise, these substances can cause severe pollution and disturb the natural balance. However, removing antibiotics from wastewater is a major challenge (Lien et al., 2015). Thus, antibiotic contamination has become a serious issue and a concern in many rivers and seas, as it can accumulate in aquatic organisms, leading to Biodiversity loss. The presence of antibiotics can pose a threat to the food chain, reduce soil decomposition and threaten marine/freshwater/terrestrial organisms (Huang et al., 2021).

The main contamination source of pharmaceutical residues in the aquatic environment is human excretion; they are released into the water bodies as parent compounds, metabolites products, as well as transformation byproducts (Mompelat et al., 2009). However, undesired traces of Active Pharmaceutical Ingredients (APIs) have been detected in the environment since the 1970s, when the first studies analysed the presence of pharmaceuticals and their metabolites in-home wastewater (Petrovic and Barceló, 2007). Pharmaceutical contamination of the aquatic environment is the most urgent concern due to its potential bio-accumulative and toxic characteristics (Aherne et al., 1985). Moreover, the extensive and rising use of pharmaceuticals is responsible for the continued leakage of these compounds into the aquatic environment (Sorengård et al., 2019).

The pharmaceutical residuals and their metabolites and degradation products have been detected in both surface and ground water across the globe (Golovko et al., 2021). Antibiotics contribute a higher proportion to this in pharmaceutical wastewater; this is because it is used to treat different diseases and bacterial infections in human beings and other animals (Zhong et al., 2019). Ceftriaxone is well known to cause various health problems like ceftriaxone-induced immune hemolytic anemia (Grimes et al., 2020); acute cholestatic hepatitis (Castellazzi et al., 2020); gastrointestinal disorders such as nausea, vomiting, and diarrhoea, biliary pseudolithiasis, urolithiasis (Leicht et al., 2018).

Recently, one of the most frequently used antibiotics, ceftriaxone sodium has been widely used in human treatment and animal husbandry, which leads to the release of residues via wastewater, causing different environmental, ecological, and health risks; it harmful to biota, and disrupting indigenous microbial populations (Castellazzi et al., 2020). During the COVID-19 pandemic, ceftriaxone has been used intensively for the treatment of infections (respiratory, skin, soft tissue, UTI, ENT) (Al-Sudani et al., 2022). The accumulation of ceftriaxone residual in the human body may cause various health disorders, some of which, biliary pseudolithiasis, urolithiasis, and haemolytic anaemia, are caused in children (Al-Sudani, 2021). Also, hemolysis was noticed in rare cases and the patient developed severe renal failure with a need for haemodialysis for 2 weeks after being injected with ceftriaxone (Al-Sudani & Arndt, 2020; Leger et al., 2014).

Ceftriaxone is a broad-spectrum cephalosporin antibiotic that is used for the treatment of different bacterial infections. It is known to cause hemolysis by inducing complement-activating drug-dependent antibodies, mainly immunoglobulin M (IgM)-type, resulting in “immune-complex” type immune hemolytic anaemia (Climate Knowledge Portal, 2023; Zhao et al., 2018). Pharmaceutical products used for human health, showing different characteristics and, consequently, producing different environmental exposure profiles, represent a group of widely used chemicals that contaminate the aquatic environment. Moreover, given their continuous discharging into the environment, their impact, both as stressors and by-products, is of great concern (Huang et al., 2020).

Iraq’s climate mode is mainly of the continental and subtropical semi-arid type. Rainfall in Iraq is seasonal and occurs mostly during the winter season from December through February, whereas the rainy season is from November to April. So we split the study results into two parts (wet season and dry season) to exclude the water quantities impacts (Amiri et al., 2020). The surface water of the water body is fed with daily discharging of millions of cubic meters of untreated sewage, some of which comes from health care complexes like Madent Al-Tub in the center of Baghdad “on the bank of the Tigris River”; and Abed Al-Muhsen Al-Khadumy sewage pump station. This leads to significant determination in water quality of this vital river (Mousa et al., 2019; Mohamed et al., 2023). Many studies deal with the assessment of the

water quality of the Tigris River; but most of them still concentrated on some water features far away from the traces of active pharmaceutical ingredients (APIs) (Castellazzi et al., 2022; Leicht et al., 2018; Zeng et al., 2020;).

The aim of our study is to search for traces of ceftriaxone in the Tigris River water in Baghdad city and to raise awareness about the risk of the presence of this compound in surface water; which may reach humans or biota by means or another. The research investigates the Ceftriaxone cause ability of hemolysis by inducing complement activating drug-dependent antibodies of mainly immunoglobulin M (IgM)-type, resulting in immune-complex type immune hemolytic anemia.

Material and Methods

Samples were taken using plastic tubes for sampling, and a pump was used to complete the process of drawing water samples, which were finally placed in pure bottles made of polypropylene for the purpose of transporting them to the laboratory.

Study Area

Five sampling stations were (Gureat, Ahdamyah, Bab Al-Muhadum, Bab Al-Sharqy and Jadryah) on the T.R main stream within Baghdad city (Figure 1). Sampling was conducted monthly basis (wet and dry seasons) from June-2022 to May-2023; sampling time was 10.30 am to 2.30 pm during the first week of the respective month.

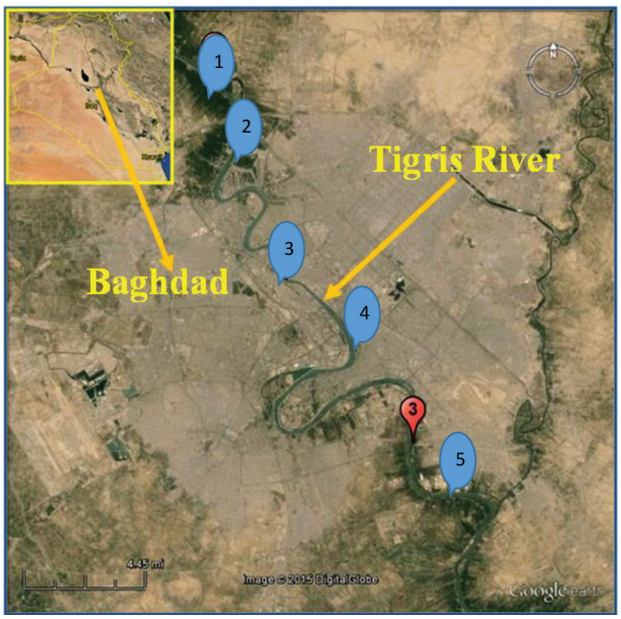

Figure 1: The map sampling site along the Tigris River - Baghdad City.

Water Sample Collection, Handling and Analysis

Water sampling from the five sampling stations has been collected to investigate and detect the Ceftriaxone residual in the water Tigris River samples after being kept in the refrigerator at 4°C. The high performance liquid chromatography (HPLC), Shimadzu was used for the water samples analysis via comparison with standard substrate of Ceftriaxone in certain operational conditions.

Statistical Analysis

The statistical approaches by ANOVA were used for measuring the variances among collected samples from the five stations from Tigris River.

Results and Discussion

The Ceftriaxone Residual Detection via HPLC

The collected water samples were analyzed using the Shimadzu instrument in certain operational conditions column of C18 (250 mm × 4.6 mm, 5µm particle size) at 25°C temperature. the elution pump ran an isocratic flow via 20 mM freshly prepared buffer solutions and mobile phases of ammonia acetate and methanol in the ratio of 80:20% v/v at 1ml/min flow rate. The investigation of water samples was collected during the wet season in 2023 with a run time of 8 min at λmax of 2.585 nm (Chen and Zhou, 2014; Shrivastava et al., 2009) as presented in Figure 2 for two stations (a for station and b for Al-Jadryia station.

Besides, Figure 3 shows the results of Ceftriaxone water samples collected during the dry season of 2022 in the five study sites as discussed.

Statistical Analysis via ANOVA Program for the Collected Water Sampling

The results were analysed using the Anova program as presented in Figure 4. The highest Ceftriaxone concentration was detected in site (3) as Bab Al-Muhadum in February with a value of 0.000007 ppm; while the lowest concentration with a value of 0.00000002 ppm in site (5) as Al-Jadryia site in April same year.

We note from the Figure 4 that the highest level of pollution for the year 2022 was in the Bab Al-Muhadum area for August and July, while the lowest station was at Al-Jadryia for the same months of the year.

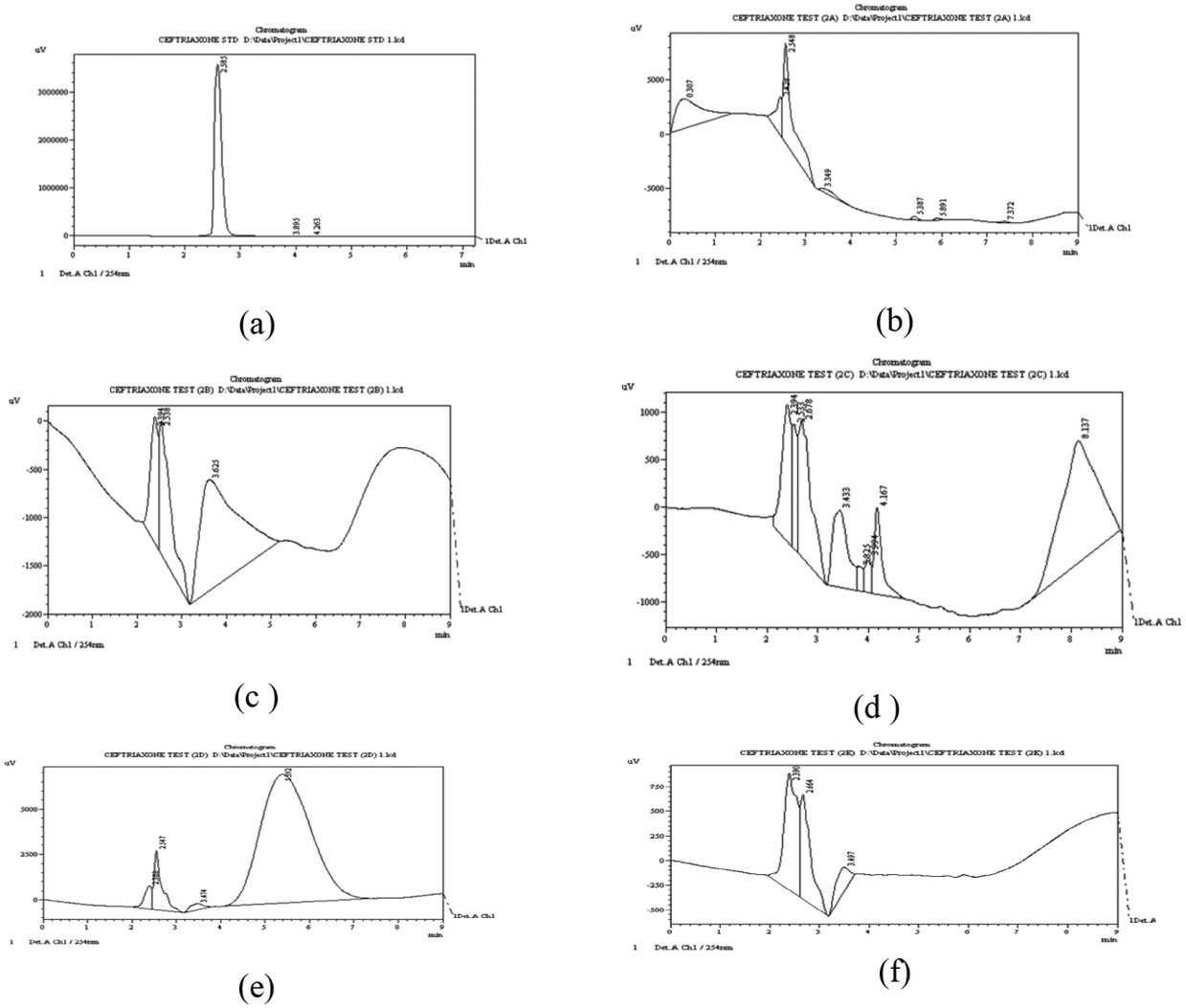

Figure 2: HPLC analysis of the collected samples detection of Ceftriaxone residual at λmax of 2.585 nm as (a) stander, (b) as Al-Gureat, (c) as Al-Ahdamyah, (d) as Bab Al-Muhadum, (e) as Bab Al-Sharqy and (f) as Al-Jadryah stations on the Tigris River, 2023 at wet season.

The Results of Wet Season at 2023 Studies

Figure 5 shows the result of Ceftriaxone concentration (ppm) during the wet season of the year 2023 in the five study sites. The results presented that the highest Ceftriaxone concentration was detected in site (2) in the Al-Ahdamyah area in February with value of 0.000008 ppm, while the lowest concentration with the value of 0.00000001 ppm in site (5) as Al-Jadriya area during April.

One of the most important results from the current study was the presence of Ceftriaxone residual in all the stations along the study period which may be due to the use of this antibiotic in Iraqi health institutions located on the dredged of the Tigris River. The results of the current study showed that there was a fluctuation in the concentrations of Ceftriaxone in the different study stations, and this may be due to the effect of the river water on the quantities coming from the top of the river during the wet season (winter) and then its decrease in summer so that the concentrations of dissolved substances in the water are relatively high. The results of the statistical analysis showed that there were no significant differences between the study stations, except for the control station (Station No.1). The detection of Ceftriaxone in raw surface water; perhaps the narrator's confirmation that the sewers of the health institutions reach the river without efficient treatment. This finding may increase the concern about

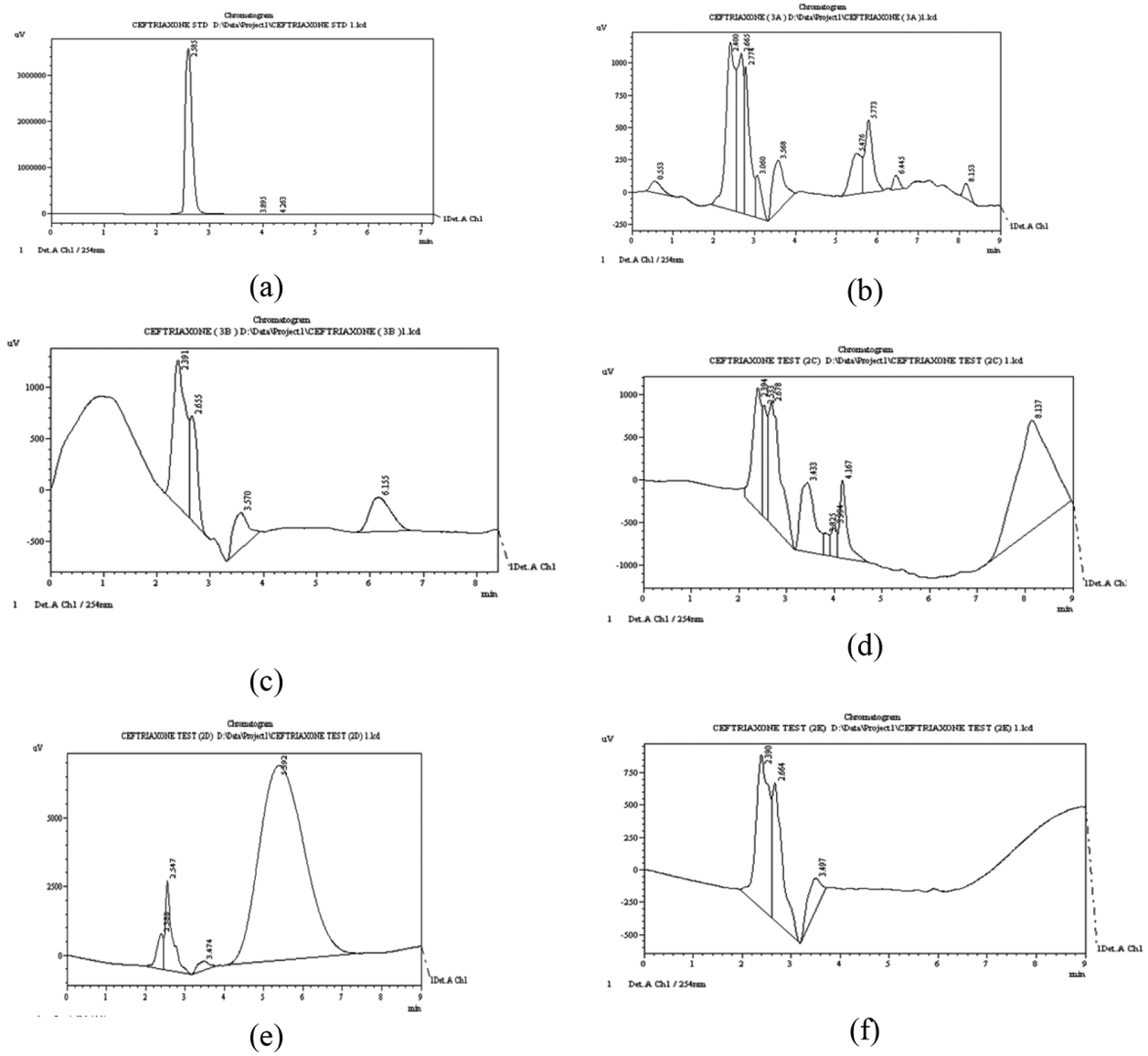

Figure 3: The HPLC analysis of the collected samples detection of Ceftriaxone residual at λmax of 2.585 nm as, (a) stander, (b) as Al-Gureat, (c) as Al-Ahdamyah, (d) as Bab Al-Muhadum, (e) as Bab Al-Sharqy and (f) as Al-Jadryah stations on the Tigris River, at dry season, 2022.

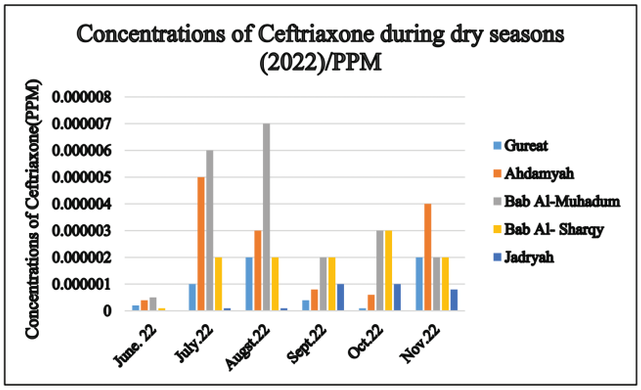

Figure 4: The Ceftriaxone concentration (ppm) in the dry season of the year 2022.

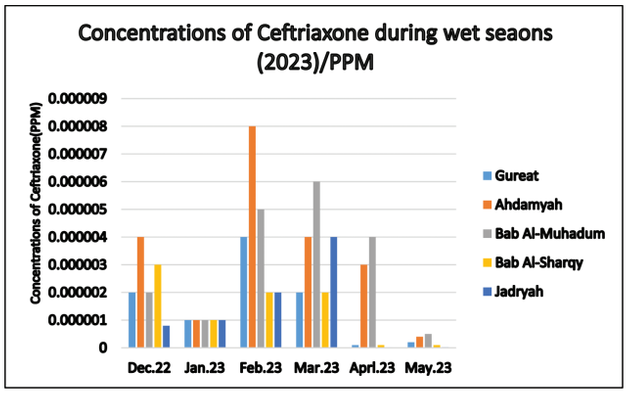

Figure 5: The Ceftriaxone concentration (ppm) in the wet season of the year 2023.

the Iraqi governmental efforts toward achieving progress in the implementation of goal (6) of the SDGs in hand; and alarming about the Iraqi people's health.

Conclusions

The detection of Ceftriaxone residual in the Tigris River was studied in the dry season of the year 2022 till the wet season of the year 2023. The water samples were improved in that all the study stations included the Ceftriaxone residual in the highest concentration of 0.000007 ppm during February at Bab Al-Muhadum area and the lowest concentration of 0.00000002 ppm in site (5) at Al-Jadryia site during April in the dry season of the same year. On the other hand, during the wet season in the year 2023, the highest concentration of Ceftriaxone was detected in site 2 at the Al-Ahdamyah area in February. With a value of 0.000008 ppm, while the lowest concentration with a value of 0.00000001 ppm in site (5) at the Al-Jadriya area during April. The detection of Ceftriaxone residual which affected the healthiness of the human being also may help to explain some illness diagnostic in some cases in Baghdad hospital. Totally active and standard sewage treatment is still needed urgently.

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