



Removal of Fexofenadine and Montelukast Drugs from Aquatic Environment Using a Rhodotron Accelerator

Omid Abouee Mehrizi¹, Seid Kamal Ghadiri², Fatemeh Anvari³, Parinaz Mehnati^{4*}

¹ Department of Medical Physics, Medical School, Tabriz University of Medical Sciences, Tabriz, Iran.

² Department of Environmental Health Engineering, School of Public Health, Shahroud University of Medical Sciences, Shahroud, Environmental and Occupational Health Research Center, Shahroud University of Medical Sciences, Shahroud, Iran.

³ Central Iran Radiation Processing Complex, Nuclear Science and Technology Research Institute, Yazd, Iran.

⁴ Radiation Medical Sciences Research Center, Department of Medical Physics, Tabriz University of Medical Sciences, Tabriz, Iran.

ARTICLE INFO

ORIGINAL ARTICLE

Article History:

Received: 23 February 2024

Accepted: 20 May 2024

*Corresponding Author:

Parinaz Mehnati

Email:

parinazmehnati8@gmail.com

Tel:

+98 914 313 4485

Keywords:

Aqueous Solution,
Rhodotron Accelerate,
Drug,
Kinetics.

ABSTRACT

Introduction: Nowadays, the management of drug effluents, as emerging pollutants, has attracted great attention due to human health and ecological adverse effects. During the COVID-19 pandemic, two drugs, Fexofenadine and Montelukast, have been used in large quantities for patients with lung involvement. The aim of this study is to investigate the feasibility of removing Fexofenadine and Montelukast and determine the removal kinetics.

Material and methods: In this study, we used Rhodotron accelerator to determine kinetic coefficients for the removal of drugs. Our research focused on studying the kinetics of E-Beam radiation reactions and the generation of significant amounts of free radicals during these processes. We employed first-order and second-order kinetic models under laboratory conditions, taking into account various influencing factors to establish the rate of removal.

Results: The results showed that the decomposition of Fexofenadine and Montelukast drugs by high-energy E-Beam bending process is a pseudo-first-order reaction with a coefficient of more than 0.9105 and 0.998, respectively. The results showed that the reaction rate constant depended significantly on the initial concentration of Fexofenadine and Montelukast drugs and their molecular structure.

Conclusion: Using a Rhodotron accelerator is important for removing Fexofenadine and Montelukast from the aquatic environment.

Citation: Abouee Mehrizi O, Kamal Ghadiri S, Anvari F, et al. *Removal of Fexofenadine and Montelukast Drugs from Aquatic Environment Using a Rhodotron Accelerator*. J Environ Health Sustain Dev. 2024; 9(2): 2257-69.

Introduction

The primary aim of wastewater treatment is to generate environmentally suitable effluent for discharge, ensuring compliance with wastewater discharge standards and preventing harm to the environment^{1, 2}. Current research focuses on emerging pollutants, particularly polar compounds that can easily dissolve in water and spread through the water cycle originating from various

human activities like industry, agriculture, domestic use, and sewage^{3, 4}. Attention is also given to the transformation of these compounds during water treatment and natural processes¹. Optimizing analytical methods is crucial due to the toxicity of many emerging pollutants and their by-products even at low concentrations. Water and wastewater treatment involves the removal of pollutants, including new compounds like drugs, to

ensure water quality⁵. Pharmaceuticals with diverse characteristics contribute to water and soil pollution through production⁶. Accidental releases, household disposal, and livestock treatment impact humans and other organisms^{7, 8}. The continuous release of prescription and non-prescription drugs into the environment also has led to increased scrutiny of the presence of drugs and their metabolites⁹. Concerns arise from the evidence suggesting incomplete drug metabolism and their entry into the environment through sewage treatment facilities, with effluents reaching waters potentially used for drinking¹⁰. Efficient drug removal is crucial as some drugs have demonstrated negative effects on both humans and aquatic species¹¹. Therefore, although these drugs are found in small amounts in surface water, false resistance due to continuous human excretion can lead to health-related problems⁵. The removal efficiency of drugs depends on their biodegradability and other physicochemical properties, such as the possibility of absorption or non-absorption by activated sludge, solubility in water, and their tendency to escape^{12, 13}. Moreover, the design of wastewater treatment plants (WWTPs) and the treatment processes used in each WWTP can affect the removal efficiency of target compounds¹⁴. Anti-inflammatory and respiratory drugs, including Fexofenadine and Montelukast, are common drugs prescribed with or without a doctor's prescription to reduce fever, pain, and inflammation. During the COVID-19 pandemic, these two drugs have been used in large quantities for patients with lung involvement¹⁵. The contaminations in treated wastewater show that these compounds cannot be removed by common treatment methods and are often discharged without treatment in the environment¹⁶. Advanced oxidation process and absorption can be mentioned among the corrective methods of removing these substances in water and wastewater¹⁷. Electron Beam radiation (E-Beam) for water and wastewater refinement is particularly important compared to other methods for various reasons¹⁸. Irradiation of aqueous solutions with E-Beams causes the formation of excited species and free

radicals^{19, 20}. In the process of E-Beam, a stream of high-energy electrons is used, which is directed into a thin layer of the solution²¹. High-energy E-Beams are ionizing energy characterized by low penetration and high dose. A concentrated and highly charged stream of electrons is produced by converting speed into electricity²². These electrons are produced by accelerators, capable of producing alternating and continuous beams. Electron accelerators are devices that accelerate the electron produced by a filament (as the main part of the electron gun) in a vacuum environment and a strong electric field, and finally, by an oscillating magnetic field, to the target^{19, 22}.

Considering that no study has been done on determining the kinetic coefficients of drug removal using the Rhodotron accelerator in the aquatic environment, we decided to investigate the feasibility of removing Fexofenadine and Montelukast, along with determining the kinetics of the removal reaction.

Materials and methods

Materials

The examined samples containing Fexofenadine (98 % Assay, Sigma Aldrich, USA) and Montelukast (99/7% Assay, Sigma Aldrich, USA) were prepared synthetically by dissolving the pure powder of these two drugs in double distilled water, 0.1 normal sodium, and hydrochloric acid.

Preparation of samples and chemicals

After preparing the stock solution, different concentrations of Fexofenadine and Montelukast drugs were prepared. The prepared samples were transferred to polystyrene containers, and after being sealed by parafilm, they were exposed to radiation by E-Beams. The solution was placed in an ultrasonic bath for five minutes to ensure sample mixing. The sample volume was 50 ml, and the water height was 1 cm.

Characteristics of the reaction reactor

The samples were irradiated by a TT200 Rhodotron electron accelerator manufactured by IBA Belgium in Yazd Institute of Nuclear Sciences and Technologies affiliated with the

Atomic Energy Organization, which produces an E-Beam with an energy of 10 MeV. The electron accelerator of this laboratory is one of the newest and most powerful accelerators available in the world. This Rhodotron accelerator has four vertical and horizontal outputs and 5 and 10 MeV energies. The absolute power of this device

is 100 kW and can be doubled. Furthermore, it can also produce X-rays and electrons. Like all accelerators, Rhodotron operates on the same basic principle of passing electrons through a strong electric field to increase energy (Figure 1).

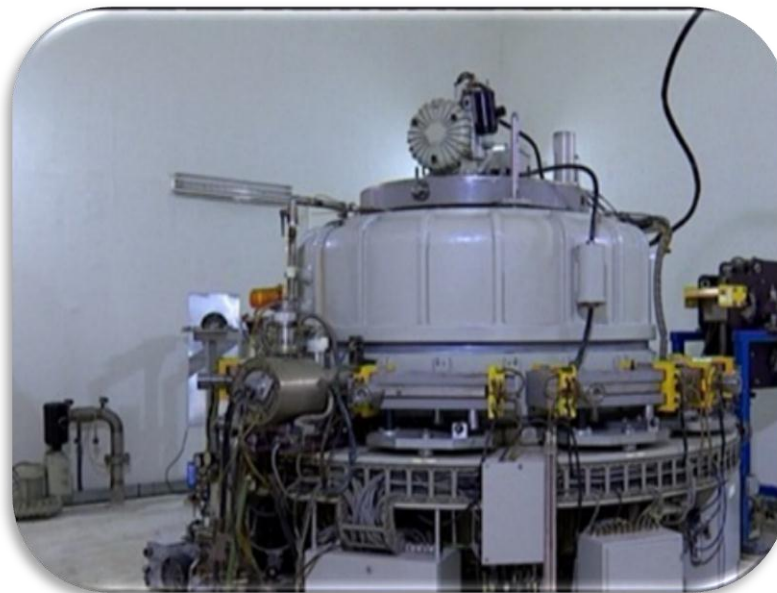


Figure 1: Rhodotron accelerator

Calculating the sample size

This study investigated removal efficiency pH, absorbed dose rate, initial concentration of Fexofenadine, and Montelukast drugs. The samples were measured twice. There were a total of 30 samples used for the main tests, resulting in 60 test cases. Additionally, 12 tests were conducted to determine a more accurate range of variables, and these were analyzed with Simplex software.

Design method

The approach employed in this study for designing and conducting experiments was the one-factor-at-a-time approach. After all the tests are done, a set of graphs is usually prepared, which shows how the response variable is affected by the change in one of the factors when the other factors are kept constant. At the end of each step, solution sampling is done, and the concentration of the residual pollutant is measured. To this end, to determine the effect of pH, different pHs of 3, 10,

8, 6, and 5 were investigated at a concentration of 75 mg/liter each of Fexofenadine and Montelukast drugs. The tests of this stage were done at a dose of 10 kGy. After determining the pH levels, we investigated different concentrations (100, 85, 75, 65, and 50 mg/L) of Fexofenadine and Montelukast at the optimal pH. The absorbed dose was 10 kGy. Also, to investigate the effect of different absorption doses of high-energy E-Beams in the removal of two drugs, Fexofenadine and Montelukast, the absorption doses of 8.5, 15, 10, and 20 kGy were investigated in the optimal concentration in terms of milligrams per liter and the optimal pH.

Kinetic models

Synthetic models express the removal rate of Fexofenadine and Montelukast drugs during irradiation with high-energy E-Beams. In order to investigate the elimination kinetics of Fexofenadine and Montelukast in the presence of

high-energy E-Beams, the fields related to first-order kinetics (Changes in $\ln C/C_0$ against absorbed dose) and the second-order kinetics (changes $1/(C) - 1/C_0$ against the absorbed dose) was drawn. The data obtained from the reactions were analyzed by comparing the fitting lines and using the correlation coefficient (R^2). Equations related to the first and second-order kinematics are presented as follows:

$$\ln \frac{C}{C_0} = -kD \quad (1)$$

$$\frac{1}{C} - \frac{1}{C_0} = kD \quad (2)$$

C and C_0 are the remaining and initial concentrations of Fexofenadine and Montelukast drugs (mg/L), respectively, and D is the absorbed dose (kGy). K is the first-order (kGy-1) and second-order kinetics (mg-1kGy-1) constant²³.

Statistical analysis

During the research, standardized samples and various concentrations of Fexofenadine and Montelukast were prepared. Predetermined E-Beam doses were applied to these samples. The level of light absorption at 259 nm wavelength for Fexofenadine and 311 nm for Montelukast was measured using a UV/Visible spectrophotometer.^{24, 25} Subsequently, vital data and information were collected through experiments and the use of lab equipment. After the experiments were completed and the results were obtained, Microsoft Excel and SPSS version 18 software were employed to analyze the data and create detailed tables and

visual representations. The Kruskal-Wallis statistical test was employed to determine means and discern the impact of independent variables. Moreover, linear regression was employed to assess the efficacy of removal and ascertain the kinetics of elimination for Fexofenadine and Montelukast pharmaceutical agents.

Results

In this study, we identified the most influential factors in the analysis and used simplex modeling to conduct 12 test runs to precisely determine the range of these factors. Simplex mathematical modeling accurately transforms given data into the unknown and studies the effects of variables within a specified range.

The effect of pH on the removal efficiency of Fexofenadine and Montelukast

At the beginning of the research, as stated, pH was measured and analyzed under the specified conditions. The effect of the absorbed dose of 10 kGy and the initial concentration of Fexofenadine and Montelukast 75 mg/liter was performed at different pHs of 3, 5, 10, 8, and 6. The highest efficiencies in pHs of 3, 8, and 10 were 92.25 ± 1.8 , 91.80 ± 2.7 , and 90.52 ± 1.9 for Fexofenadine and 86.43 ± 1.2 , 86.04 ± 1.7 and 84.77 ± 1.3 for Montelukast, respectively (Figure 2). In order to determine the optimal pH, the removal efficiency of drugs at different pHs was checked using the Kruskal-Wallis test.

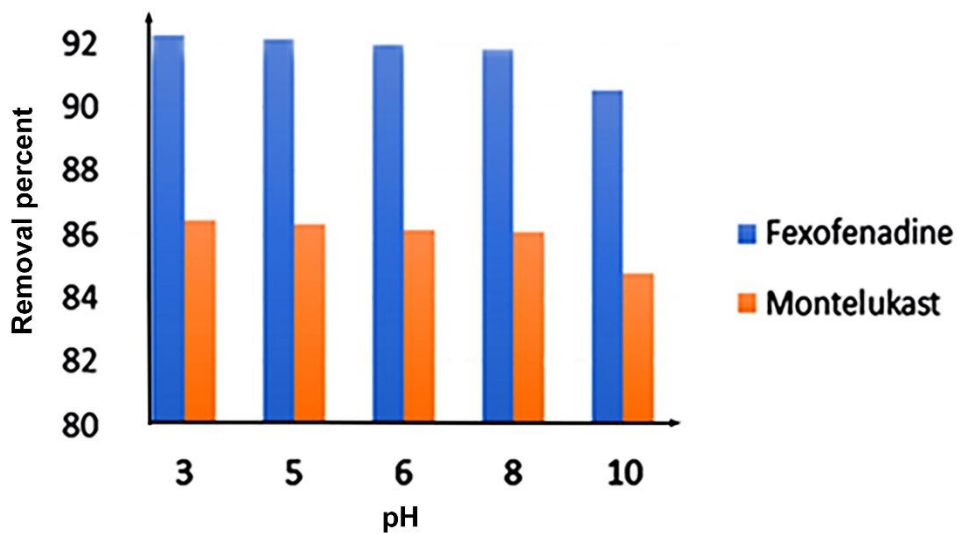


Figure 2: Effect of pH level on removal efficiency of Fexofenadine and Montelukast

The effect of pollutant concentration on the removal efficiency of Fexofenadine and Montelukast

The effect of pollutant concentration on removal efficiency of Fexofenadine and Montelukast at pH = 8 and absorbed dose of 10 kGy. Based on the results shown in Figure 3, by increasing the initial concentration of Fexofenadine and Montelukast drugs from 50 to 100 mg/L, the efficiency of removing high-energy E-Beams decreased due to the production of more degradation by-products. By increasing

the concentration of Fexofenadine from 50 to 100 mg/liter, the removal efficiency in the presence of high-energy E-Beams decreased from 93.23% to 82.39%. Also, by increasing the concentration of Montelukast from 50 to 100 mg/liter, the removal efficiency in the presence of high-energy E-Beams decreased from 87.1% to 78.43% (Figure 3). According to the typical concentrations in wastewater and water sources and the maximum efficiency, the optimal and base concentration was considered 50 mg/liter.

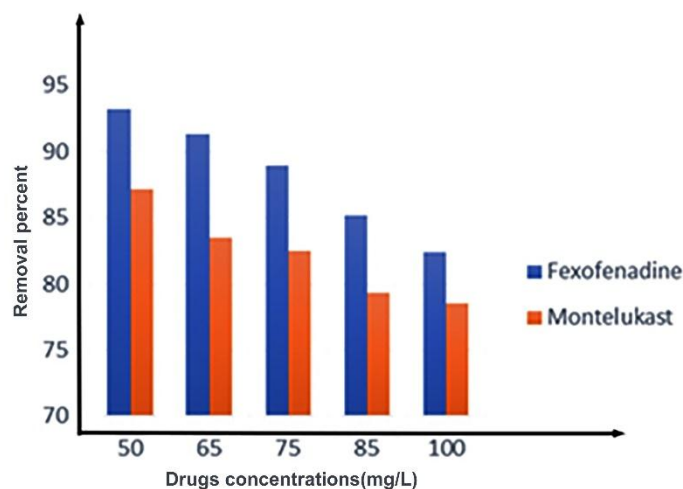


Figure 3: Effect of drug concentrations on removal efficiency of Fexofenadine and Montelukast

The effect of absorbed dose of high energy E-Beams on the removal of Fexofenadine and Montelukast drugs

The effect of different absorption doses of 5, 8, 10, 15, and 20 for the concentration of 50 mg/L of Fexofenadine and Montelukast drugs at the optimal pH of 8 was investigated. The reason for investigating the effect of higher doses in this study was the possible removal of higher production by-products. This study found that the removal efficiency of Fexofenadine and Montelukast drugs increased with the increase of the absorbed dose. 15 kGy was the optimal dose because of its maximum ability to remove the two drugs.

Determining the elimination kinetics of Fexofenadine and Montelukast drugs in the presence of E-Beams

In order to determine the kinetics of the decomposition reaction of Fexofenadine and Montelukast drugs in the high-energy E-Beam irradiation process, the curves of the linear equations of the first and second-order reactions were designed and drawn based on the linear regression equation. During the irradiation

processes, the concentration of the desired pollutants decreased with the increase of the absorption dose, which is expressed in Equation 3.

$$C = C_0 e^{-kD} \quad (3)$$

where

C: was the initial drug concentration after irradiation,

C_0 : the initial concentration of the drug,

K: the reaction rate is constant, and

D: was the absorbed dose

The reaction rate constant depends significantly on the initial concentration of Fexofenadine and Montelukast drugs and their molecular structure. In this phase of the study, the data obtained from the absorption doses of 5, 8, 10, 15, and 20 kGy of high-energy E-Beams to remove the concentrations of 75, 65, 50, 85, and 100 mg/liter to determine the kinetics of removal were examined. The pseudo-first-order kinetic equation related to the removal of various pollutants is shown in Equation 1 (Figure 4).

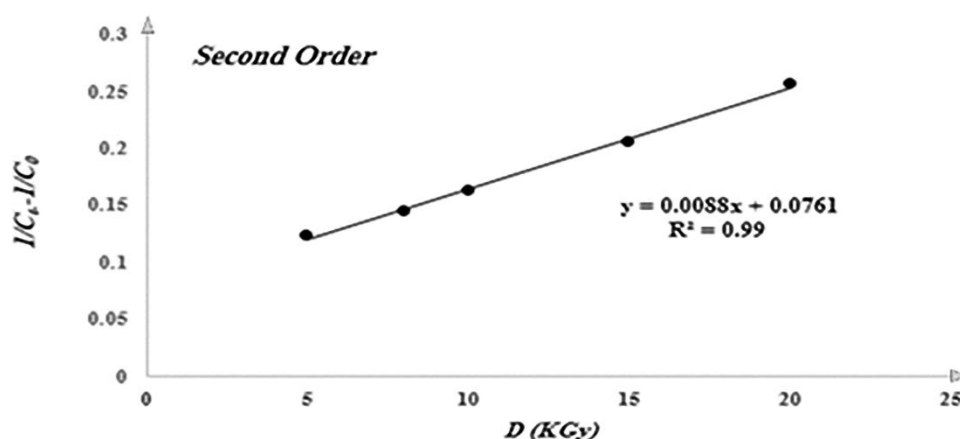


Figure 4: Second-order kinetic model of fexofenadine drug removal during irradiation by high-energy E-beams

Based on what was obtained from the literature review ²⁶, most of the studies in the irradiation field followed first-order kinetics. However, in

minor cases, the removal of pollutants during the irradiation process followed second-order kinetics equation 2 (Figure 5).

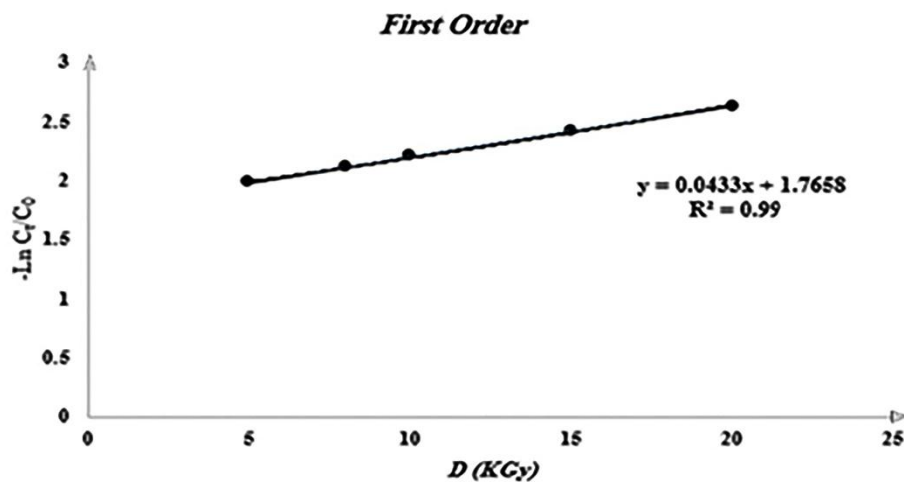


Figure 5: First-order kinetic model of montelukast removal during irradiation by high-energy E-beams

In the present study, the results of the reaction of high-energy E-Beam radiation in removing Fexofenadine and Montelukast were investigated

using the kinetics of pseudo-first and second-order reactions. (Figure 6).

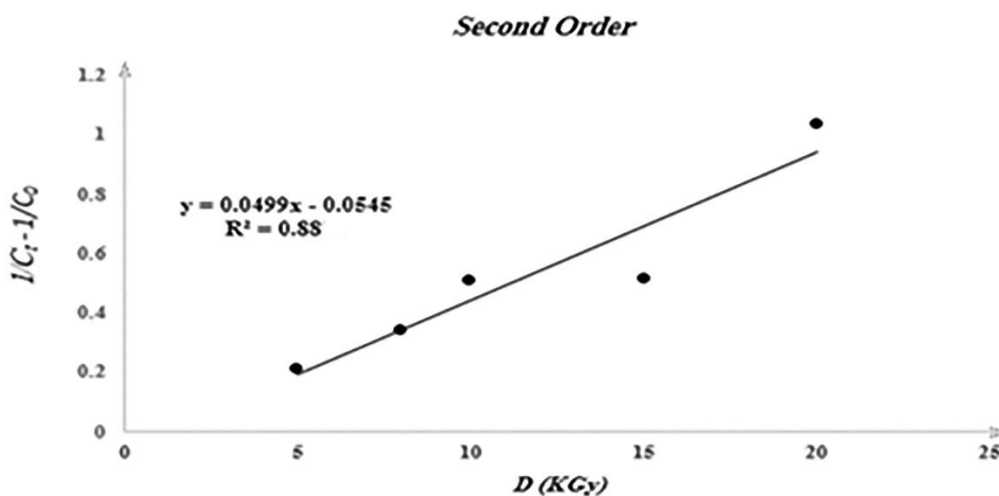


Figure 6: Second-order kinetic model of Montelukast drug removal during irradiation by high-energy E-beams

Efficiency of E-Beam for Removing Fexofenadine and Montelukast from Real Samples

To achieve the study's objectives related to the efficiency of the process of removing Fexofenadine and Montelukast in practical settings, multiple samples of hospital wastewater were examined. These samples had a pH level and

electrical conductivity of 815 mS/cm and were evaluated under optimal kinetic conditions (pH of 8, a dose of 15 kGy) with concentrations of 3 mg/L and 8 mg/L for Fexofenadine and Montelukast, respectively. The study's results showed that in actual conditions, the removal efficiency of Fexofenadine was 81.8 ± 2.1 , and the removal efficiency of Montelukast reached 77.5 ± 1.6 .

Production of Hydroxyl Radicals in Fexofenadine Decomposition by High-Energy E-Beam with Radical Scavengers

As mentioned earlier, one of the significant advantages of advanced oxidation processes was the generation of radicals, especially hydroxyl radicals. To ensure the production of hydroxyl

radical in the optimal conditions of high-energy E-Beam irradiation, the high-energy E-Beam irradiation reaction was repeated using one molar concentration of tert-butanol radical scavenger. The findings from this phase of the study are illustrated in Figure 7.

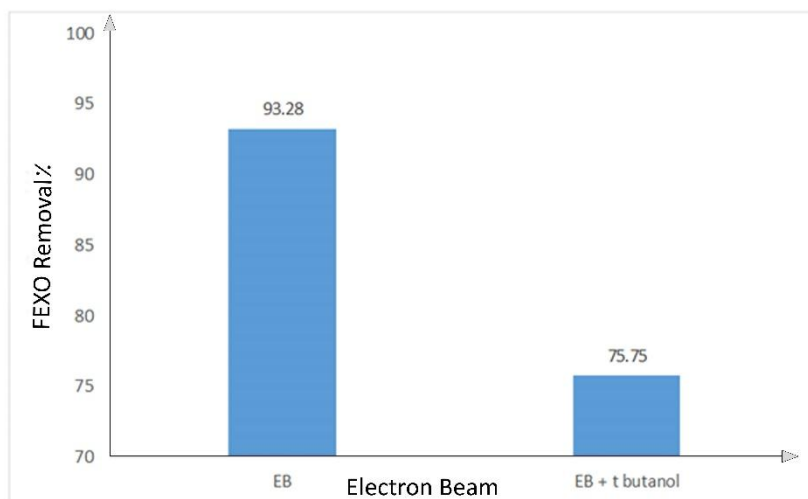


Figure 7: The effect of scavengers on the removal of fexofenadine by high-energy E-beam method using scavengers

Discussion

The research delved into the application of the high-energy E-Beam process for the elimination of two pharmaceuticals, namely Fexofenadine and Montelukast. The advantages of utilizing E-Beam (electron accelerator) over other ionizing radiation methods, such as gamma rays and traditional purification techniques, are manifold. E-Beams eliminate the need for chemical additives, prevent the generation of harmful byproducts, and avoid additional expenses associated with source replacement^{19, 21}. This process, via advanced oxidation methods, disintegrates contaminants through a cascading reaction mechanism that yields reactive radicals. Emerging pollutants, including pharmaceuticals, are subjects of scrutiny as well. Even at low concentrations, prolonged exposure to pharmaceutical residues can lead to adverse effects like drug resistance and metabolic

side products within organisms. In a study conducted in 2022 on the application of water radiolysis by E-Beams to purify sewage sludge, purification by high-energy E-Beams was considered a successful approach to disinfecting sewage and sewage sludge²⁷. In removal efficiency studies, a model can be adjusted to fit the data and then used to analyze options for process improvement. However, these analyses were only used to develop experiments containing pertinent data for fitting the model. Models may be used to analyze data obtained from similar surveys. Achieving this goal requires choosing models that specifically describe the processes under investigation before determining which interpretation is better or best, that is, which interpretation is more general^{23, 28}.

Pharmaceuticals enter ecosystems when they remain unmetabolized in both human and animal

bodies, releasing their active compounds. In a 2021 study by Flavio Kiyoshi et al., it was found that the use of high-energy E-Beams could be a promising alternative for biological pre-treatment and post-treatment processes.²⁴

High-Energy E-Beam Analysis for Removing Fexofenadine and Montelukast - pH Effect Analysis on Removal Efficiency

The obtained results showed that pH change slightly affected the removal efficiency of Fexofenadine and Montelukast in the presence of high-energy E-Beams. The disintegration of the two drugs at pH of 3 was slightly more than 8 and more than other pH levels. The data obtained from this stage showed slight changes in the removal efficiency of Fexofenadine and Montelukast at different pH values. However, the process's performance in removing Fexofenadine was shown to be higher than Montelukast. Based on the ionic dissociation coefficient, organic substances are dissolved in water in two molecular or ionic forms. When the pH of the aqueous solution is higher than the ionic dissociation coefficient, the organic matter dissolves in the aqueous solution in an ionic form considering that the pH of the medium is lower than its ion dissociation coefficient. Organic matter dissolves molecularly in water. The drugs studied in aqueous environments with acidic pH dissolve molecularly in water. While in alkaline conditions, they dissolve in water in an ionic form. Studies demonstrated that the ionic form of drugs tended to be highly reactive with hydroxyl radicals compared to its molecular form. The comparison of the average removal efficiencies at different pH using the Kruskal-Wallis test showed no statistically significant difference (P value > 0.05) between efficiency values at different pHs. Although the pH level of 8 is slightly higher than 3, acidic byproducts generated during E-Beam irradiation reduced the pH. As there was no statistically significant difference in efficiency across pH levels and water sources typically have pH levels of 7 to 8, a pH of 8 was deemed optimal for this study. Due to the low production of hydroxyl radicals and the non-ionic nature of an important part of drugs at a pH of less than 8,

efficiency was the lowest at these pH levels. In this study, the wide-ranging effect of pH on the process was investigated due to the small initial pH changes. Therefore, the optimal pH was selected at 10 kGy, and an initial concentration of 75 mg/L of Fexofenadine and Montelukast was estimated to be 8. This was while in other studies where the irradiation method was used to remove pollutants, it was found that pH greatly affected the efficiency of the process. For example, a study conducted by Gu. et al used the gamma-ray irradiation method to remove trihalomethanes with low concentration in drinking water; they found that at an absorption dose of 3 kGy with increasing pH, the removal of all of the trihalomethanes also increased²⁹. Krikoit et al. 2010 investigated high-energy E-Beams in the decomposition of citric acid solutions containing sodium persulfate. Their study showed that with an increase in pH level from 4 to 11, the efficiency of forming active radicals during the water radiolysis process did not depend on pH. At a pH level of higher than 10, relatively less hydroxyl free radicals were formed. In the present study, it became neutral after being exposed to radiation at a dose of 10 kGy.²². In their study, Behjat et al. (2008) studied the degradability of the blue solution of reactive dyes by high-energy E-Beams with an energy of 10 megaelectron volts. They concluded that the pH level of solutions decreased after irradiation. Also, with increasing radiation dose, pH decreased. This study measured the effect of high-energy E-Beams on the pH value of samples before and after irradiation. Due to the production of organic and inorganic acid anions during irradiation, the pH value of treated solutions decreased²¹.

- Analysis of the effect of different concentrations of Fexofenadine and Montelukast on removal efficiency during irradiation process with high-energy E-Beams

Another influencing variable in the irradiation process with high-energy E-Beams was the drug concentration. Based on the results, by increasing the initial concentration of Fexofenadine and Montelukast from 50 to 100 mg/liter, the efficiency

of removing high-energy E-Beams decreased due to the production of more degradation by-products. By increasing the concentration of Fexofenadine from 50 to 100 mg/liter, the removal efficiency in the presence of high-energy E-Beams decreased from 93.23% to 82.39%. Moreover, by increasing the concentration of Montelukast from 50 to 100 mg/liter, the removal efficiency in the presence of high-energy E-Beams decreased from 87.1% to 78.43%. According to the common concentrations in wastewater and water sources and the maximum efficiency, the optimal and base concentration was considered 50 mg/liter. In high concentrations of medicinal pollutants, the probability of a reaction between free radicals and oxidizing species with Fexofenadine and Montelukast molecules increased, thus increasing the removal percentage. After that, however, due to the formation of intermediates and side products, the possibility of the reaction of molecules of the examined drugs with oxidizing species decreased due to competition with formed intermediate substances, and the amount of its removal increased with a gentle slope. The intermediate compounds resulting from the decomposition of drugs were a type of OH radicals, so the efficiency was higher at low concentrations of the drug; for higher concentrations, more radical concentration was needed, and the reaction time was long. In 2011, in a study comparing the efficiency of high-energy E-Beams and Gamma rays to remove color solutions, Abdou et al. concluded that the percentage of color removal decreased with the increase in color concentration. In this study, it was found that the initial concentration of the drug was an important factor in the purification process³⁰.

- Analysis of the absorption dose effect of high-energy E-Beams in the removal of Fexofenadine and Montelukast

The results indicated that with the increase in pH, the dose used in the specific process increased the production of various radicals, including hydroxyl radical, and these radicals act non-selectively due to their high power of oxidation. In addition to drugs, they also oxidized intermediate compounds of production. Increasing the dose at

low pH levels was more important than at high pH levels. Therefore, if a high pH level was used as the optimal pH, it was better to use the low dose of the process as the optimal dose. With the increase in the dose of the process, as an oxidizing agent, the production of hydroxyl radicals in the medicinal solution increased, which increased molecular mass transfer and the efficiency of the irradiation process significantly. The results of the present study were consistent with the results of a study conducted by Parsaian et al. in 2008. In this research, the aqueous solutions of both drugs with a concentration of 100 ppm were irradiated in different doses of 1, 3, 6, and 9 kGy. The results showed that the desired polluted solutions were effectively destroyed and treated by high-energy E-Beams. The absorption band of the desired drugs decreased rapidly at a dose of 1 kGy and disappeared completely at a dose of approximately 9 kGy³¹. In the present study, with the increase of absorption dose from 1 to 15 kGy, the removal efficiency of the two drugs, Fexofenadine and Montelukast, increased. However, these two drugs were not completely removed at 15 kGy.

Kinetic analysis of elimination reaction of Fexofenadine and Montelukast in the presence of E-Beams

According to the obtained data, the degradation of Montelukast and Fexofenadine was compatible with pseudo-first-order reactions with a coefficient of more than 0.9105 and 0.998, respectively. The decomposition of drugs by high-energy E-Beams is shown in Equation 4.



The decomposition rate of Fexofenadine and Montelukast by high-energy E-Beams was written as Equation 5. Hence, the reaction rate depended on the concentrations of the drug and hydroxyl radicals and was expected to be quadratic. However, due to the hydroxyl radical's highly active and reactive nature, it did not accumulate in the solution. Therefore, its concentration was considered constant during decomposition.

$$[\text{drugs}]/d t = - k \bullet\text{OH} [\text{drugs}] \quad (5)$$

Given the constant concentration of $\bullet\text{OH}$, the next equation could be obtained by substituting k_{app} for $[k_{abs}]\bullet\text{OH}$, where, k_{app} was the apparent reaction coefficient. According to this relationship, the decomposition of Fexofenadine and Montelukast by high-energy E-Beam bending process was a first-order reaction, but due to the fixed coefficient and the use of the apparent constant, it was called a false first-order

$$[\text{drugs}]/dt = -k_{app} [\text{drugs}] \quad (6)$$

$$\frac{([\text{drugs}]_t / [\text{drugs}]_0) = -k_{app} t \rightarrow ([\text{drugs}]_0 / [\text{drugs}]_t) = +k_{app} t \quad (7)$$

Yavuz et al. conducted a study on the electro-chemical removal of phenol from oil refinery wastewater; they concluded that the removal of phenol by Electro Fenton Process (EFP) followed a false first-order reaction²⁹. In 2012, Mousavi et al. removed formaldehyde using EFP and announced that the decomposition of formaldehyde followed pseudo-first-order kinetics²³. In 2013, Sahinkaya et al. reported that removing dye from textile wastewater by EFP followed a first-order reaction³².

Investigating the production of hydroxyl radical in the decomposition of Fexofenadine by the process of high-energy E-Beam irradiation using radical scavengers

According to Figure 6, the reduction in the efficiency of the high-energy E-Beam radiation process in the presence of tert-butanol scavengers was 17.53% for Fexofenadine. This reduction in the performance of the high-energy E-Beam irradiation process in the presence of radical-eating compounds indicated that the high-energy E-Beam irradiation process through the production of hydroxyl radicals led to the elimination of Fexofenadine and Montelukast. The reaction rate constant of tert-butanol with hydroxyl radical was very high therefore, this compound was widely used in advanced oxidation processes as a radical scavenger to determine the role of hydroxyl radical²³.

Conclusion

This research investigated the removal of drugs

from aqueous solutions using high-energy E-Beams. The drugs Fexofenadine and Montelukast are among emerging pollutants whose presence in water harms water quality, the environment, and human health. The research showed that high-energy E-Beam technology effectively removed non-steroidal anti-inflammatory drugs. After preparing the sample, the influencing variables were determined and analyzed. Optimum conditions, a pH value of 8, a concentration of 50 mg/l, and a dose of 15 kGy were determined. The maximum efficiency in the EB process was calculated to remove Fexofenadine at 93.28% and Montelukast at 88.13%. The high removal efficiency of Fexofenadine compared to Montelukast in the investigated process is its higher solubility in aqueous environments. Increasing the radiation dose and decreasing the initial concentration of these two drugs, increases removal efficiency. According to the study results, the EB process effectively removes drugs. Due to the short reaction time, it can be used to remove compounds resistant to common decomposition, taking into account other considerations.

Acknowledgments

The authors would like to thank Tabriz University of Medical Sciences for financial and technical support of this research (Grant No: 69774).

Conflict of interest

The authors declared no conflict of interest.

Funding

None

Ethical Considerations

None

Code of Ethics

IR.TBZMED.VCR.RCE.1401.119

Authors' Contributions

Omid Abouee (PhD student) was involved with data collection manuscript preparation. Kamal Ghadiri (Associate Professor) analyzed data and cooperated in writing the manuscript.

Fatemeh Anvari (M.S. Chemistry) collected data

and helped with writing the manuscript.

Parinaz Mehnati (Professor) designed the research, analyzed data, and edited the manuscript.

This is an Open-Access article distributed following the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt, and build upon this work for commercial use.

References

1. Dos Santos DM, Buruaem L, Gonçalves RM, et al. Multiresidue determination and predicted risk assessment of contaminants of emerging concern in marine sediments from the vicinities of submarine sewage outfalls. *Mar Pollut Bull.* 2018;129(1):299-307.
2. Bonyadi Z, Noghani F, Dehghan A, et al. Biomass-derived porous aminated graphitic nanosheets for removal of the pharmaceutical metronidazole: optimization of physicochemical features and exploration of process mechanisms. *Colloids Surf A Physicochem Eng Asp.* 2021;611:125791.
3. Christensen ER, Wang Y, Huo J, et al. Properties and fate and transport of persistent and mobile polar organic water pollutants: a review. *J Environ Chem Eng.* 2022;10(2):107201.
4. Vázquez-Tapia I, Salazar-Martínez T, Acosta-Castro M, et al. Occurrence of emerging organic contaminants and endocrine disruptors in different water compartments in Mexico—A review. *Chemosphere.* 2022;308:136285.
5. Husain Khan A, Abdul Aziz H, Khan NA, et al. Pharmaceuticals of emerging concern in hospital wastewater: removal of Ibuprofen and Ofloxacin drugs using MBBR method. *Int J Environ Anal Chem.* 2023;103(1):140-54.
6. Morin-Crini N, Lichtfouse E, Liu G, et al. Worldwide cases of water pollution by emerging contaminants: a review. *Environ Chem Lett.* 2022;20(4):2311-38.
7. Fairbairn DJ, Elliott SM, Kiesling RL, et al. Contaminants of emerging concern in urban stormwater: spatiotemporal patterns and removal by iron-enhanced sand filters (IESFs). *Water Research.* 2018;145:332-45.
8. Lima EC. Removal of emerging contaminants from the environment by adsorption. *Ecotoxicol Environ Saf.* 2018;150:1-17.
9. Tran NH, Reinhard M, Gin KY-H. Occurrence and fate of emerging contaminants in municipal wastewater treatment plants from different geographical regions—a review. *Water research.* 2018;133:182-207.
10. Tijani JO, Fatoba OO, Petrik LF. A review of pharmaceuticals and endocrine-disrupting compounds: sources, effects, removal, and detections. *Water, Air, & Soil Pollution.* 2013;224:1-29.
11. Sundararaman S, Kumar JA, Deivasigamani P, et al. Emerging pharma residue contaminants: occurrence, monitoring, risk and fate assessment—a challenge to water resource management. *Science of the Total Environment.* 2022;825:153897.
12. Edwards QA, Sultana T, Kulikov SM, et al. Contaminants of emerging concern in wastewaters in Barbados, West Indies. *Bull Environ Contam Toxicol.* 2018;101:1-6.
13. Ayyami Y, Dastgir M, Ghorbani M, et al. Characterization and application of targeted MnO₂/CS@ ALA-MTX nano-radiosensitizers for boosting X-ray radiotherapy of brain tumors. *Colloids Surf A Physicochem Eng Asp.* 2024;692:133975.
14. Tang Y, Yin M, Yang W, et al. Emerging pollutants in water environment: occurrence, monitoring, fate, and risk assessment. *Water Environment Research.* 2019;91(10):984-91.
15. Barré J, Sabatier JM, Annweiler C. Montelukast drug may improve COVID-19 prognosis: a review of evidence. *Frontiers in pharmacology.* 2020;11:1344.
16. Henning N, Falås P, Castronovo S, et al. Biological transformation of fexofenadine and sitagliptin by carrier-attached biomass and suspended sludge from a hybrid moving bed biofilm reactor. *Water research.* 2019;167:115034.
17. Jiménez JJ, Pardo R, Sánchez MI, et al. Photochemical, thermal, biological and long-term degradation of celecoxib in river water.

- Degradation products and adsorption to sediment. *Journal of hazardous materials*. 2018;342:252-9.
18. Emami-Meibodi M, Parsaeian M, Amraei R, et al. An experimental investigation of wastewater treatment using electron beam irradiation. *Radiation Physics and Chemistry*. 2016;125:82-7.
 19. Zhang J, Zheng Z, Luan J, et al. Degradation of hexachlorobenzene by electron beam irradiation. *Journal of Hazardous Materials*. 2007;142(1-2):431-6.
 20. Ayyami Y, Ghorbani M, Dastgir M, et al. Chitosan-modified manganese oxide-conjugated methotrexate nanoparticles delivering 5-aminolevulinic acid as a dual-modal T1–T2* MRI contrast agent in U87MG cell detection. *MAGMA*. 2024:1-16.
 21. Behjat A, Mozaheb S, Khalili MB, et al. Advanced oxidation treatment of drinking water and wastewater using high-energy electron beam irradiation. *Water and Wastewater*[Internet]. 2007;18(1 (61)):60-68. Available from: <https://sid.ir/paper/103457/en>. [cited Jul 11, 2007].
 22. Criquet J, Leitner NKV. Electron beam irradiation of citric acid aqueous solutions containing persulfate. *Sep Purif Technol*. 2012;88:168-73.
 23. Moussavi G, Bagheri A, Khavanin A. The investigation of degradation and mineralization of high concentrations of formaldehyde in an electro-Fenton process combined with the biodegradation. *Journal of hazardous materials*. 2012;237:147-52.
 24. Ehrampoush MH, Taghi M, Jasemizad T, et al. Evaluation of the efficiency of electron beam irradiation for removal of humic acid from aqueous solutions. *Toloo-E-Behdasht*, [online]. 2017;16(1):61.
 25. Yavuz Y, Koparal AS, Öğütveren ÜB. Treatment of petroleum refinery wastewater by electrochemical methods. *Desalination*. 2010;258(1-3):201-5.
 26. Tominaga FK, Silva TT, Boiani NF, et al. Is ionizing radiation effective in removing pharmaceuticals from wastewater? *Environmental Science and Pollution Research*. 2021;28:23975-83.
 27. Selambakkannu S, Bakar K, Ting T, et al. Assessment of pathogenic microorganisms inactivation by electron beam irradiation and physico-chemical characteristics evaluation in sewage sludge. *Radiation Physics and Chemistry*. 2022;199:110358.
 28. Yektamanesh M, Ayyami Y, Ghorbani M, et al. Characterization of multifunctional β -cyclodextrin-coated Bi₂O₃ nanoparticles conjugated with curcumin for CT imaging-guided synergetic chemo-radiotherapy in breast cancer. *Int J Pharm*. 2024:124264.
 29. Guo Z, Zheng Z, Gu C, et al. Radiation removals of low-concentration halomethanes in drinking water. *Journal of Hazardous Materials*. 2009;164(2-3):900-3.
 30. Abdou L, Hakeim O, Mahmoud M, et al. Comparative study between the efficiency of electron beam and gamma irradiation for treatment of dye solutions. *Chemical engineering journal*. 2011;168(2):752-8.
 31. Almomani FA, Shawaqfah M, Bhosale RR, et al. Removal of emerging pharmaceuticals from wastewater by ozone-based advanced oxidation processes. *Environ Prog Sustain Energy*. 2016;35(4):982-95.
 32. Şahinkaya S. COD and color removal from synthetic textile wastewater by ultrasound assisted electro-Fenton oxidation process. *Journal of Industrial and Engineering Chemistry*. 2013;19(2):601-5.