RADIOLYSIS AND OTHER ADVANCED OXIDATION PROCESSES FOR DEGRADATION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN DILUTE AQUEOUS SOLUTIONS

PhD Theses

Erzsébet Illés

Supervisors: Dr. Erzsébet Takács, doctor of Hungarian Academy of Sciences
Dr. Krisztina Schrantz, assistant professor

Doctoral School of Environmental Sciences

University of Szeged, Institute of Chemistry, Research Group of Environmental Chemistry, Szeged

Hungarian Academy of Sciences, Centre for Energy Research, Department of Radiation Chemistry, Budapest

Szeged
2014

Introduction and aims of the research

The removal of pollutants, especially organic pollutants by biological methods is more or less effective and economical. In these oxidative processes, microorganisms oxidize the pollutants at physiological temperature. Due to their low biodegradability, some of the pollutants are persistent, therefore, their elimination is not effective using conventional methods. Moreover, they can be poisonous for the microorganisms, causing their deaths. Therefore, the usual waste water treatment techniques are not effective enough in the removal of these harmful pollutants; there is the need to find proper ways for their elimination, and for the prevention of their accumulation in the natural reservoirs (e.g. rivers, lakes, etc.). In the last decades the concentrations of non-steroidal type pharmaceuticals has been increased in waste waters because of the large increase of their application and/or their high resistance. Incomplete efficiency of the elimination of toxic pollutants may result in their appearance in the natural water, where although their concentrations are quite low, their long-term effects on the ecosystem are not known. Combination of usual water purification methods with novel techniques such as advanced oxidation processes, AOPs, is very promising. Their operation is based on the formation of reactive radicals, especially $^{\bullet}OH$.

Nowadays, ozone-based techniques are widely used, they can be coupled with other techniques using reactive agents, such as H_2O_2 and/or ultraviolet (UV) light improving their efficiency. Heterogeneous photocatalytic processes, based on the photoactivity of semiconductors become increasingly important. With electromagnetic radiation, reactive agents can be generated using UV, or vacuum-UV (VUV) photolysis or radiolysis.

Although AOPs are widely used in waste water treatments, the chemical processes and the mechanisms of their reactions are not fully described. Their better understanding can help on their application, making this field of research a blossoming part of catalytic chemistry.

The main goal of my research is to suggest mechanism schemes and to compare different AOPs techniques in the removal of non-steroidal anti-inflammatory drugs in trace concentrations. Target molecules are such well-known compounds like ibuprofen (IBP) and ketoprofen (KET). Those non-steroidal anti-inflammatory drugs cannot be completely decomposed by the traditional waste water treatments. Thus, the effect of ozonation, combination of ozone and UV light radiation and high-energy ionizing radiation (radiolysis) are compared on the degradation of the two model compounds. Pseudo first-order rate coefficients of the degradations as well as the mineralization rate of the model compounds are

investigated using ozonation and O_3/UV combined techniques with the consideration of the similarities and differences in their structures.

In the reactions between the model compounds (IBP and KET) and the reactive radicals ($^{\bullet}OH$, $H^{\bullet}$ and e_{aq}^{-}), primary intermediates are determined using pulse radiolysis coupled with kinetic spectrophotometric detection system.

Using different conditions (N_2O, N_2, air, N_2 + tert-butanol), the role of the reactive particles, forming from the water, can be determined separately.

With kinetic studies, the reaction rate coefficients of $^{\bullet}OH$, $H^{\bullet}$ and e_{aq}^{-} with IBP or KET are determined, approving or disproving the varying different results described in the literature.

With the determination of the attacks of $^{\bullet}OH$ and e_{aq}^{-} on the IBP and KET molecules, it is possible to suggest mechanisms for the reactions of similar organic compounds.

Degradation products of the model compounds using different treatments are identified and their structures are described using HPLC-MS.

The model compounds are toxic substances, therefore following the change of toxicity of treated solutions are performed using several test organisms (*Pseudokirchneriella subcapitata* algae culture, *Daphnia magna* zooplankton and *Vibrio fischeri* luminescent bacteria) on the basis of ISO standards.

Materials and methods

The ketoprofen, ibuprofen and the reagents (HCl, NaOH) for pH setting to the testorganisms of toxicity measurements or used in Chemical Oxygen Demand (COD) and Total Organic Carbon (TOC, amount of carbon bound in an organic compound) measurements were purchased from Sigma-Aldrich and VWR. The solutions were prepared in ultrapure water in the $1 \times 10^{-5} - 4 \times 10^{-4}$ mol dm^{-3} concentration range (18 MΩ cm, Millipore Synergy185 apparatus). The treated samples were examined by UV-Visible spectrophotometry, HPLC (high-performance liquid chromatography) with UV and MS (mass spectrometry) detection, TOC and COD measurements. For chromatographic separation diluted acetic acid solution and acetonitrile were used as eluents in different proportions. The degree of degradation was followed by diode array detection and by mass spectrometer with ESI ionization. The COD measurements were performed on the basis of ISO Standard 6060:1989 with an HACH LANGE instrument. The TOC was measured with Analytik Jena equipment. The changes of the toxic effect of the parent compounds and of the degradation products were examined with standard toxicity tests of three testorganisms; *Pseudokirchneriella subcapitata* (formerly known as Selenastrum capricornutum) microalgae culture, *Daphnia magna* zooplankton and *Vibrio fischeri* luminescent bacterium.

The radiolysis of water gives a distribution of transient and stable products according to the following equation (1).

$$H_2O \longrightarrow {}^{\bullet}OH(0{,}28) + e_{aq}^{-}(0{,}27) + H^{\bullet}(0{,}06) + H_2(0{,}05) + H_2O_2(0{,}07) + H_3O^{+}(0{,}027) \quad (1)$$

The values in brackets in equation (1) are the yields in μmol J^{-1} units. In order to study the reactions of ${}^{\bullet}OH$, e_{aq}^{-} and $H^{\bullet}$ separately, different additives and techniques are applied. In N_2O saturated solutions due to transformation the reacting radicals and their yields are ${}^{\bullet}OH$ 0.55 μmol J^{-1} and $H^{\bullet}$ 0.06 μmol J^{-1}. The reactions of e_{aq}^{-} with KET and IBP are studied in N_2 saturated 5 vol% tert-butanol containing solution. In such solution ${}^{\bullet}OH$ reacts with t-butanol forming rather inactive radicals. $H^{\bullet}$ atoms, due to the low yield, give little contribution to the degradation above pH 4, therefore its effect was studied at pH 3.5.

Ozonation and O_3/UV combined treatment

I have already used ozonation method in my diploma work for KET degradation and I have completed these experiments in my doctoral thesis. During ozonation the home-made reactor, designed by our research group was filled every time with the same volume (300 cm^3) of solution made in phosphate buffer (pH 8) and circulated continuously with a peristaltic pump.

It operates with a low-pressure mercury vapour lamp with a high purity silica sleeve, which transmitted the 254 and 185 nm light. The lamp with an envelope was centered in a water-cooled, double walled glass tubular reactor. Oxygen flowed through a teflon ring between the wall of the lamp and the envelope, which separated the gas phase and the aqueous solution. The ozone generated from oxygen was then bubbled through the solution ($c_{O3,\ gas\ phase} = 3{,}50 \times 10^{-5}$ mol dm^{-3}, $c_{O3,\ liquid\ phase} = 4{,}94 \times 10^{-6}$ mol dm^{-3}). Depending on the material of the envelope, ozonation (perforated glass), and its combination with UV photolysis (perforated quartz) of KET or IBP was investigated. In this way the efficiency of these processes could be compared using the same light source.

Pulse radiolysis

A special advantage of the radiation technique is that it has an own method, the pulse radiolysis for examining the mechanism of the undergoing processes and for observation of intermediates.

Since the same or similar intermediates form in case of practically all AOPs, the radiolysis investigations can provide details for mechanisms of other AOPs.

For pulse radiolysis experiments as a radioactive source a TESLA LINAC LPR-4 type electron accelerator of the Department of Radiation Chemistry was used. A kinetic spectrophotometric detection system is connected to it, which allows to follow-up the concentration of the intermediates (radicals) with high time resolution.

The electron accelerator can release pulses with 800 and 2500 ns pulselength. The system can be used to study the intermediates in microsecond-millisecond time scale. The dose/pulse value can be varied between 10-300 Gy. The exact value is established with thiocyanate dosimetry before the measurements. The analysing light and the path of the accelerated electrons cross each other in the cell. The solution of KET or IBP was running continuously through the cell by a peristaltic pump. Time dependence of absorbance of the intermediates was followed by kinetic spectrophotometric measurements. Between the absorbance at definite time and the concentration of the intermediates, the connection is according to the Lambert-Beer law. The wavelength of the observation can be varied in the UV-Visible range (280–600 nm). From the kinetic curves taken at different wavelengths the transient absorption spectra of the intermediate can be produced.

Gammaradiolysis

In end product experiments the irradiation was done by a ^{60}Co γ-irradiation facility with 5 kGy h^{-1} dose rate. In case of gamma radiolysis experiments the dose was determined with alcoholic chlorobenzene dosimetry.

Novel scientific results

1. The direct reactions of ozonation have only negligible role in the degradation of ketoprofen and ibuprofen.

Neither of the compounds have strong electron donor groups, therefore the direct reactions of ozonation have little role in the degradation of both molecules. The main way of degradation is the indirect one, through the intermediates of ozone decomposition. The $^{\bullet}OH$ forming during the treatment has an important role in the decomposition of both compounds. During ozonation the degradation of the ibuprofen molecule is not so fast as that of ketoprofen. (*1st publication*)

2. By O_3/UV combined treatment the degradation of ketoprofen is faster than that of ibuprofen

There is one order of magnitude difference between the pseudo first order rate coefficients of IBP and KET in O_3/UV combined treatment. The efficiency of the KET decomposition by combined treatment was multiplied comparing to the ozonation, the pseudo first order rate coefficient was enhanced with two orders of magnitude by UV light. The efficiency of IBP degradation was increased to a smaller degree when using UV light. Because of the special structure of the molecule the photoionization gives the main contribution to the O_3/UV degradation of KET. $^{\bullet}OH$ reactions and especially molecular ozone reactions are less important. The photoionization of IBP molecule is not considerable, therefore the degradation of this molecule is mainly due to $^{\bullet}OH$ reactions in the combined method. (*1st publication*)

3. During radiolysis of aqueous solutions the decomposition of ibuprofen is more efficient in oxidative than reductive conditions

There are not considerable differences in the rate of the degradation of IBP and KET using solutions saturated with N_2O (oxidative condition) or with N_2 (oxidative/reductive). Investigating the reaction of e_{aq}^- solutions saturated with N_2 and contained tert-butanol (reductive condition) show higher rate coefficient in the case of KET, than IBP. The reason of the difference is the different place of the attack of e_{aq}^-. While e_{aq}^- attacks the KET via the carbonyl group, the IBP is attacked via the carboxyl group. *(2nd publication)*

4. Toxic effects of the ibuprofen and ketoprofen containing solution decrease to similar extent during radiolysis.

These results are based on the experiments using *Daphnia magna* and *Vibrio fischeri* as test organisms. The toxicity increased with the increasing concentration of the aromatic transformation products, then with their degradation, it decreased. The *Daphnia magna* was less sensitive to the presence of the aromatic transformation products. IBP exerted smaller toxic effect on these organisms than the KET. *(2nd publication)*

5. In the initial part of radiolysis, in the reaction of $^{\bullet}OH$ mostly ring-hydroxylated degradation products are formed from both ibuprofen and ketoprofen.

The observation is against to most of articles in this field, in which the authors described the possibility of the reaction with hydrogen distraction. Besides the appearance of mono- and double hydroxylated products, three and four times hydroxylated degradation products also form.

The results gained by pulse radiolysis prove that in the cases of both of the molecules the main initial reaction is the $^{\bullet}OH$ attack on the aromatic rings. This can be verified by the molar absorption coefficients of the degradation products. Rate coefficients of the reaction of IBP and KET with $^{\bullet}OH$ are somewhat smaller than the diffusion controlled value (1.1×10^{10} mol^{-1} dm^3 s^{-1}), because none of the molecules have such an electron donor group, which would be favourable to the reaction of the $^{\bullet}OH$. The KET also contains a carbonyl group, in which the carbon atom is strongly electrophyl. This is responsible for the further cutdown of the rate coefficient of KET and the $^{\bullet}OH$. *(2nd and 3rd publications)*

*The rate coefficients of KET and IBP with $^{\bullet}OH$, e_{aq}^- and $H^{\bullet}$ determined by pulse radiolysis (the value signed with * is a value from the literature in case of benzophenone)*

Reagent	Rate coefficient (mol^{-1} dm^3 s^{-1})	
	KET	IBP
$^{\bullet}OH$	5.5×10^9	7.0×10^9
e_{aq}^-	2.2×10^{10}	8.5×10^9
$H^{\bullet}$	$\sim 6.0 \times 10^9$*	4.0×10^9

6. No aromatic end products were found in the reaction of e_{aq}^- either in the case of ketoprofen, or ibuprofen.

The intermediates can easily recombine in the reaction of the e_{aq}^-. This is shown by the light-absorption spectra of IBP and KET during the continuous radiolysis. The light absorption of

the typical $\pi \rightarrow \pi^*$ aromatic band decreases without remaining absorbance, and more slowly than in other circumstances. The e_{aq}^- reacts with KET at the carbon atom of the carbonyl group and with IBP at the carbon atom of the carboxyl group. The carbonyl group is a strong electron acceptor; therefore, the e_{aq}^- attacks the KET at this group forming a ketyl radical anion and not at the carboxyl group. The anion is converted into a ketyl radical via protonation. It is reflected by the transient spectra of the intermediates and by the reaction rate coefficients: e_{aq}^- can attack IBP with much lower rate, than KET. *(2nd and 3rd publications)*

7. The well-known photosensitizing effect of ketoprofen is due to the photoionization.

In the radiolysis of solutions containing both KET and IBP, KET did not increase the degradation rate of IBP, as it was reported in photolysis experiments. It shows that the photosensitizing effect of KET is due to the photoionization of the molecule, because of the easy excitable carbonyl group, and not because of other radical (e.g. $^{\bullet}OH$) mechanisms.

Publication list

a) Papers related to the Thesis

1. Illés, E., Szabó, E., Takács, E., Wojnárovits, L., Dombi, A., Gajda-Schrantz, K., 2014. Ketoprofen removal by O_3 and O_3/UV processes: Kinetics, transformation products and ecotoxicity. Sci. Total Environ., 472, 178-184
   (IF = 3,26) Reference: 0

2. Illés, E., Takács, E., Dombi, A., Gajda-Schrantz, K., Rácz, G., Gonter, K., Wojnárovits, L., 2013. Hydroxyl radical induced degradation of ibuprofen. Sci. Total Environ., 447, 286-292
   (IF = 3,26) Reference: 6 (4)

3. Illés, E., Takács, E., Dombi, A., Gajda-Schrantz, K., Gonter, K., Wojnárovits, L., 2012. Radiation induced degradation of ketoprofen in dilute aqueous solution. Radiat. Phys. Chem., 81, 9, 1479-1483
   (IF = 1,38) Reference: 9 (4)

b) Papers not related to the Thesis

4. Csay, T., Homlok, R., Illés, E., Takács, E., Wojnárovits, L., 2014. The chemical background of Advanced Oxidation Processes. Isr. J. Chem., 53, 3, 233-241
   (IF = 3,03) Reference: 0

5. Gajda-Schrantz, K., Arany, E., Illés, E., Szabó, E., Pap, Z., Takács, E., Wojnárovits, L., 2013. Advanced Oxidation Processes for Ibuprofen Removal and Ecotoxicological Risk Assessment of Degradation Intermediates. *in* W. C. Carter and B. R. Brown, editors. Ibuprofen: Clinical Pharmacology, Medical Uses and Adverse Effects. Nova Science Publishers, Hauppauge, New York, United States.
   Reference: 0

6. D. Šojić, D., Despotović, V., Orčić, D., Szabó, E., Arany, E., Armaković, S., Illés, E., Gajda-Schrantz, K., Alapi, T., Sajben-Nagy, E., Palágyi, A., Vágvölgyi, Cs., Manczinger, L., Bjelica, L., Abramović, B., 2012. Degradation of thiamethoxam and metoprolol by UV, O_3 and UV/O_3 hybrid processes: Kinetics, reaction mechanism and toxicity. J. Hydrol., 472-473, 314-327
   (IF = 2,96) Reference: 10 (9)

7. Szabó, R.K., Megyeri, C., Illés, E., Gajda-Schrantz, K., Mazellier, P., Dombi, A., 2011. Phototransformation of ibuprofen and ketoprofen in aqueous solutions. Chemosphere 84, 1658-1663.
   IF = 3,206 Reference: 22 (19)

8. Illés, E., Gajda-Schrantz, K., Dombi, A. 2009. Ozonization and UV photolysis of ketoprofen. Pages 464-467 *in* The 16th International Symposium on Analytical and Environmental Problems, Szeged, Hungary.

9. Illés, E. 2010. A ketoprofen ózonos bontása. Pages 9-54 *in* A. Dombi, editor. Vizek szerves szennyezőinek eltávolítása nagyhatékonyságú oxidációs módszerekkel/Removal of Organic Contaminants of Waters by Advanced Oxidation Processes. InnoGeo Kft., Szeged.

10. Illés, E., Gajda-Schrantz, K., Dombi, A. 2010. Ozonization and UV Photolysis of Ketoprofen. Pages 155-160 *in* A. Dombi, editor. Vizek szerves szennyezőinek eltávolítása nagyhatékonyságú oxidációs módszerekkel/Removal of Organic Contaminants of waters by advanced Oxidation Processes. InnoGeo Kft., Szeged.

11. Illés, E., Szabó, R.K., Dombi, A., Oppenländer, T., Gajda-Schrantz, K., 2009. Ketoprofen bontása ózonozással (Degradation of Ketoprofen by ozonization). Dunaújvárosi Főiskola Kiadó, 8.

Total IF: 17,10

Number of references: 47 (independent: 36)

Conferences related to the Thesis

1. András Dombi, Krisztina Gajda-Schrantz, **Erzsébet Illés**, Emese Szabó: Ecotoxicity of ketoprofen degradation products, ISEAC36, Rome, Italy, 5-9. October 2010
2. Dombi András, Gajdáné Schrantz Krisztina, **Illés Erzsébet**, Szabó Emese, A ketoprofen bomlástermékeinek toxicitása, MKE 1. Nemzeti Konferencia, Sopron, 2011. máj. 22-25.
3. **Erzsébet Illés**, Erzsébet Takács, András Dombi, Krisztina Gajda-Schrantz, Katalin Gonter, László Wojnárovits, Radiation induced degradation of ketoprofen in dilute aqueous solution, 12th Tihany Symposium on Radiation Chemistry, Zalakaros, Hungary, 27. Augustus – 1. September 2011 (oral presentation, member of organizer team and co-chair in the Fundamental Prosesses in Radiation Chemistry I. session)
4. **Illés Erzsébet**, Takács Erzsébet, Dombi András, Gajdáné Schrantz Krisztina, Gonter Katalin, Wojnárovits László, A ketoprofen vizes oldatának bontása nagyenergiájú ionizáló sugárzással, MKE X. Környezetvédelmi Analitikai és Technológiai Konferencia, Sümeg, 2011. okt. 5-7.
5. **Illés Erzsébet**, Takács Erzsébet, Dombi András, Gajdáné Schrantz Krisztina, Gonter Katalin, Wojnárovits László, Nagyenergiájú ionizáló sugárzás alkalmazása ketoprofen vizes oldatának bontására, MKE Őszi Radiokémiai Napok, Sopron, 2011. okt. 26-28.
6. András Dombi, Krisztina Gajda-Schrantz, **Erzsébet Illés**, Emese Szabó**,** Ecotoxicity of ketoprofen degradation products formed during ozonization and O_3/UV combined method, Workshop on "Optimization of Cost Effective and Environmentally Friendly

Procedures for Treatment of Regional Water Resources", Hungary, Szeged, 1-2. December 2011

7. **Erzsébet Illés**, Erzsébet Takács, András Dombi, Krisztina Gajda-Schrantz, Katalin Gonter, László Wojnárovits, Efficient degradation of ketoprofen in dilute aqueous solution using high-energy ionizing radiation, Workshop on "Optimization of Cost Effective and Environmentally Friendly Procedures for Treatment of Regional Water Resources", Hungary, Szeged, 1-2. December 2011
8. **Illés Erzsébet**, Takács Erzsébet, Wojnárovits László, Dombi András, Gajdáné Schrantz Krisztina, A toxicitás változása ibuprofen és ketoprofen vizes oldatának radiolízise során, Környezettudományi Doktori Iskolák Konferenciája, Budapest, 2012. aug. 30-31.
9. **Illés Erzsébet**, Takács Erzsébet, Dombi András, Gajdáné Schrantz Krisztina, Rácz Gergely, Gonter Katalin, Wojnárovits László, Ibuprofen vizes oldatának radiolízise során keletkező köztitermékek és végtermékek vizsgálata, MKE Őszi Radiokémiai Napok, Siófok, 2012. okt. 08-10.
10. Arany Eszter, **Illés Erzsébet**, Farkas János, Szabó Emese, Alapi Tünde, Gajdáné Schrantz Krisztina, Dombi András, Takács Erzsébet, Wojnárovits László, Szerves mikroszennyezők bontása fotolízissel és radiolízissel, Első Környezetkémiai Szimpózium, Mátraháza, 2012. okt. 11-12.
11. **Erzsébet Illés**, Erzsébet Takács, András Dombi, Krisztina Gajda-Schrantz, Gergely Rácz, László Wojnárovits High energy ionizing radiation initiated degradation of ketoprofen and ibuprofen in dilute aqueous solution, The 28th Miller Conference on Radiation Chemistry, Israel, Dead Sea, 14-19. March 2013
12. **Illés Erzsébet**, Takács Erzsébet, Dombi András, Schrantz Krisztina, Rácz Gergely, Wojnárovits László, Nagyenergiájú ionizáló sugárzás alkalmazása ketoprofen és ibuprofen lebontására híg vizes oldatból, MKE XI. Környezetvédelmi Analitikai és Technológiai Konferencia, Hajdúszoboszló, 2013. okt. 2-4.
13. **Erzsébet Illés**, High energy ionizing radiation initiated degradation of ketoprofen and ibuprofen in dilute aqueous solution, Third Research Coordination Meeting of the Coordinated Research Project on"Radiation Treatment of Wastewater for Reuse with Particular Focus on Wastewaters Containing Organic Pollutants", Budapest, 18-23. May 2014