

Ph.D. Thesis

Decomposition of some pharmaceuticals by Advanced Oxidation Processes

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1. Introduction

During the last three decades the pollution of the aquatic environment has become an important issue. However, the attention of society and researchers was focused almost exclusively on the conventional “priority” pollutants listed in the EU Water Framework. Beside these recognised pollutants however, numerous other chemicals are released into the environment with unforeseen consequences. This group, classified as so called emerging contaminants, is mainly composed of products used in every day’s life, such as surfactants, pharmaceuticals and personal care products, as well as gasoline additives, fire retardants, plasticizers etc. This work is focused on pharmaceuticals. Although some of them are not persistent, they can still cause negative effects to living organisms, due to their continuous introduction into the environment. Since wastewater treatment plants are not able to remove most of them completely from wastewaters, they can reach the surface waters. There are even some reports about their presence in drinking water. Although they are found in these waters in very low concentrations, in the lower ppb range, they can represent a risk to the non target organisms and even to humans, due to the long-term exposure. There are already reports on the mutagenic effects of some hormones and Non Steroidal Anti-Inflammatory Drugs (NSAIDs) in trace concentrations on fishes, causing dysfunction of the reproductive organs. In Europe, the three most often prescribed NSAIDs are ibuprofen, ketoprofen and naproxen.

One group of the intensively studied procedures to remove the emerging contaminants and other organic pollutants from water are the Advanced Oxidation Processes (AOPs), mostly based on generation of the hydroxyl radical. It is one of the most reactive and non selective species which can react very rapidly with almost any organic substance. Among others, these processes include direct ultraviolet photolysis, ultraviolet photolysis combined with vacuum-ultraviolet photolysis and vacuum-ultraviolet photolysis, which are available methods for removing contaminants from drinking water, without the addition of other reagents.

2. Objectives

The goal of this work was the investigation of the degradation of three NSAIDs ibuprofen, ketoprofen and naproxen. UV photolysis, UV/VUV photolysis and VUV photolysis have been applied as elimination processes. The efficiency of these processes has also been compared. Same experimental setup and a low-pressure mercury vapour light sources with identical geometrical and electrical parameters have been used in the case of UV

and UV/VUV photolysis. In case of the VUV photolysis Xe-excimer lamp with the same electrical output has been used as the previous lamps.

Further objectives were the determination of the kinetical parameters of these photodegradations, as well as the identification of the formed photoproducts. To get information about the mechanism of the degradation of these compounds radical scavenging has been carried out and the influence of the dissolved molecular oxygen was investigated. The photosensitizing characteristics of benzophenone type compounds, such as ketoprofen, are well known on living organisms (e.g. skin diseases). Whether this effect influences in some way the degradation of another pharmaceutical compound has not been investigated yet. In this work, our aim was to examine the antagonistic or synergistic effect of the investigated compounds on each others photodegradation.

3. Material and Methods

3.1 UV and UV/VUV photolysis of the selected compounds

Low-pressure mercury vapour lamps can be used as a water treatment technology for disinfection of drinking water. The emission spectrum of the low-pressure mercury lamps is very narrow in UV range at the wavelength of 254 nm and VUV range at 185 nm. Special high purity quartz (Suprasil quartz) sleeve must be used to ensure that the 185 nm radiation passes through the wall of the lamp.

During the UV photolysis of ibuprofen, ketoprofen and naproxen two types of reactor and lamps were used.

For the experiments, low pressure mercury vapour lamps from LightTech were used. A low pressure mercury vapour lamp was used for the UV photolysis experiments (GCL307T5/CELL) with a normal quartz sleeve transmitting the UV light over 200 nm. For UV/VUV experiments, a second low pressure mercury lamp was used (GCL307T5VH/CELL) with a high purity quartz sleeve.

3.2 The VUV photolysis of the selected compounds by Xe-excimer lamp

The xenon excimer lamp (15 W, Osram) emitting 172 nm light, has been placed inside the reactor. The entire apparatus is described as xenon excimer flow-through photoreactor. The temperature of the reactor was regulated at 25 °C, the flow rate of 300 cm³ min⁻¹ was used and the solutions were continuously stirred inside the reservoir.

4. Results

4.1 During UV photolysis

A. The degradation rate of the investigated substances is in direct relevance to their light absorbing characteristics (molar absorbance). This degradation can be described with first order kinetics.

B. The presence of dissolved molecular oxygen in the solution has no significant influence on the degradation rate with the exception of ibuprofen where there is a deviation from first order kinetics in oxygen free solutions. As we head towards smaller concentrations the relative degradation rate decreases.

C. Methanol, as OH-radical scavenger and the azide-ion as a broad spectrum radical scavenger has no notable inhibiting effect on the degradation of either of the investigated compounds, therefore photolytic degradation is the primary way of degradation.

4.2 During UV/VUV photolysis

A. Where 185 nm light was also used beside the 254 nm light, insignificant increase of the degradation rate was measured in case of ketoprofen, while for ibuprofen and naproxen this increase became quite significant. The relative degradation rate rises at higher initial concentrations. This can be explained by the increased ratio of radicals that contribute to the reaction.

B. Dissolved oxygen had a minor effect on the degradation rate of ketoprofen, while in case of ibuprofen and naproxen this effect is significant.

C. In accordance with the previous statement, methanol as an OH-radical scavenger has a slight influence on the degradation of ketoprofen while it is a significant inhibitor for the degradation of ibuprofen and naproxen. For Na-azide this effect is more explicit, especially in solutions where dissolved oxygen is present. This means that other species than OH-radical take part in the degradation process, like peroxyde- and hydroperoxyde radical ions.

4.3 During VUV photolysis using Xe-excimer lamp

A. Photons with much larger energy are absorbed by water, generating radicals which react with the target molecules. This is indicated by the fact that the degradation rate is independent of the initial concentration; at smaller concentrations the degradation rate is slow. This shows that the rate at which the radicals are generated by VUV irradiation determines the rate of the degradation process.

B. The presence of dissolved oxygen influenced the reaction rate less than expected. Based on the “cage-effect” which was experienced during the examination of other substances, we can state that the excited water molecule leaves this cage not because of dissolved oxygen, but due to the target molecule, generating more radicals.

C. Radical scavengers inhibit the process during VUV photolysis in slightly different way. These slight alternations can be explained by the fact that these molecules compete for the radicals differently. Na-azide as a universal radical scavenger inhibits these degradation processes more than methanol.

4.4 Ketoprofen is known to be *photosensitizer* when in interaction with a biological system. It was investigated whether this effect is also true for non-biological systems, by combining ibuprofen and ketoprofen in the same photolytic reaction, using all three methods previously mentioned.

A. In the case of UV photolysis ketoprofen accelerated the degradation of ibuprofen both in oxygenated and oxygen free solutions. The other way around this was not true, the degradation of ketoprofen was not influenced by ibuprofen.

B. Under UV/VUV photolysis this effect of ketoprofen was also noted, although not to the scale measured in UV. The photosensitizing effect of ketoprofen was somewhat smaller in oxygenated solutions than in oxygen free solutions.

C. In the case of VUV photolysis, based on the previous experiments, this effect of ketoprofen was not expected. On the contrary, according to general reaction kinetic expectations both compounds inhibited each others degradation.

D. The usage of radical scavengers reinforced our prior statement, when used in UV photolysis they have no inhibiting effect. In UV/VUV photolysis we can experience some inhibition in the degradation of ibuprofen, this inhibition is somewhat smaller, than when ibuprofen was photolysed alone. Ketoprofen had no notable influence on the degradation of ibuprofen when the reactions were inhibited by radical scavengers during VUV photolysis.

4.5 By-products formed during UV and UV/VUV photolysis were determined and their evolution in time in oxygenated and oxygen free solutions was followed. The most important by-products in case of ibuprofen are (1-ethyl-4-(2-methylpropyl)-benzene, 1-ethenyl-4-(2-methylpropyl)-benzene, 1-(1-hydroxyethyl)-4-isobutyl-benzene, 4’-(2-methylpropyl)acetophenone). Based on these findings we can say that the degradation starts with decarboxylation. During the degradation of ketoprofen we determined four intermediates, 3-

acetylbenzophenone, 3-ethylbenzophenone, 3-hydroxyethyl benzophenone, and 3-hydroperoxyethyl benzophenone. In the case of naproxen we followed the evolution of four intermediers, and determined the structure of three of them. These intermediers were 1-(2-methoxy naphthalene-6-yl)ethane-1,2 diol, 2-methoxy-6-vinylnaphthalene, 1-(2-methoxy naphthalene-6-yl)ethanone.

It was also found that the degradation of these intermediers results in the formation of aliphatic compounds containing oxygen, mainly carboxylic acids.

4.6 The *mineralisation process* of the target compounds was followed by measuring the total organic carbon (TOC) content. The measurements showed that the degree of mineralisation is small during the complete conversion of the substances. The mineralisation is the smallest during UV photolysis, and in the case of ketoprofen, for all the three methods.

From the three methods investigated, with the applied experimental conditions, the mineralisation of the target molecules was most efficient in the case of UV/VUV photolysis.

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08-12. November 2010, Dunaújváros, Hungary

oral presentation

Coauthor's declaration

I hereby certify that I am familiar with the thesis of the applicant Ms Rita Katalin Szabó entitled Decomposition of some pharmaceuticals by Advanced Oxidation Processes.

Regarding our joint results referred to in this thesis, the following ones were obtained as the result of joint contribution by the applicant and me.

date, signature

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