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Photocatalytic degradation of metoprolol tartrate in suspensions of two TiO_2-based photocatalysts with different surface area. Identification of intermediates and proposal of degradation pathways

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ABSTRACT

This study investigates the efficiency of the photocatalytic degradation of metoprolol tartrate (MET), a widely used β_1-blocker, in TiO_2 suspensions of Wackherr's "Oxyde de titane standard" and Degussa P25. The study encompasses transformation kinetics and efficiency, identification of intermediates and reaction pathways. In the investigated range of initial concentrations (0.01–0.1 mM), the photocatalytic degradation of MET in the first stage of the reaction followed approximately a pseudo-first order kinetics. The TiO_2 Wackherr induced a significantly faster MET degradation compared to TiO_2 Degussa P25 when relatively high substrate concentrations were used. By examining the effect of ethanol as a scavenger of hydroxyl radicals ($^{\bullet}OH$), it was shown that the reaction with $^{\bullet}OH$ played the main role in the photocatalytic degradation of MET. After 240 min of irradiation the reaction intermediates were almost completely mineralized to CO_2 and H_2O, while the nitrogen was predominantly present as NH_4^+. Reaction intermediates were studied in detail and a number of them were identified using LC–MS/MS (ESI+), which allowed the proposal of a tentative pathway for the photocatalytic transformation of MET as a function of the TiO_2 specimen.

1. Introduction

When speaking of pollutants in the environment one usually thinks of chemicals that are used to treat plants and soil, of radioactive wastes and of exhaust gases. Active components of drugs have slowly – one might say, 'by the back door', entered the environment, primarily aimed at helping people. The notion of active pharmaceutical ingredients (APIs) includes highly bioactive compounds that are used in the treatment or prevention of diseases, thanks to their reaction with specific targets in the animal or human body such as receptors or enzymes. Due to their increasing consumption, growing emissions of APIs affect the natural environment from hospitals, pharmaceutical industries or domestic waters. In the latter case, incorrect disposal of non-used or expired drugs and human excretions after partial metabolism of the drugs by the body are the main pathways involved [1]. The use of antibiotics in cattle breeding is a further important route of pharmaceuticals to the environment [2].

APIs have been detected in ground and surface water [3–5], drinking water [6,7], ocean water, sediment and soil [8]. In the latest years there has been a tendency to synthesize drugs that are resistant to common biotransformation processes, with the purpose of protracting their persistence in the organism. However, very stable molecules are obtained as a result [9,10], the environmental occurrence of which, at either low or high concentrations, can bring harmful toxicological effects [11,12].

The metoprolol tartrate salt {MET, *1-[4-(2-methoxyethyl) phenoxy]-3-(propan-2-ylamino)propan-2-ol tartrate (2: 1)*} is a selective β-blocker that is used to treat a variety of cardiovascular diseases, such as hypertension, coronary artery disease and arrhythmias [13]. MET is characterized by an increasing use in recent years and, as a consequence, its occurrence in aqueous effluents is expected to increase as well [14,15]. MET shows slow direct phototransformation and/or hydrolysis [16,17]. An efficient way to deal with this problem is the degradation of the drug by advanced oxidation processes (AOPs) based on the formation of hydroxy ($^{\bullet}OH$) and other radicals [18]. MET contains a secondary amine group and a weakly/moderately activated aromatic ring that are

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likely targets of molecular ozone and of $^{\bullet}$OH [13]. Yang et al. investigated the degradation of selected β-blockers (atenolol, metoprolol and propranolol) in aqueous suspensions of TiO_2 Degussa P25 and proposed a preliminary mechanism of degradation of these compounds [19]. Romero et al. have also investigated and compared the intermediates of the degradation of metoprolol and propranolol by AOPs [20].

The aim of this work was to make a detailed comparison of the kinetics and mechanism of photodegradation of MET, sensitized by TiO_2 Wackherr and Degussa P25 in aqueous solutions under a variety of experimental conditions. The effects of the initial concentration of MET and of catalyst loading were studied, along with the presence of $^{\bullet}$OH scavengers. An attempt has also been made to identify the intermediates formed during the photooxidation process and to propose possible reaction pathways for the photocatalytic degradation of MET in UV-irradiated aqueous suspensions of TiO_2.

2. Materials and methods

2.1. Chemicals and solutions

All chemicals were of reagent grade and were used without further purification. The drug (±)-Metoprolol(+)-tartrate salt, ≥99%, was purchased from Sigma–Aldrich; 85% H_3PO_4 was purchased from Lachema, Neratovice; 96% ethanol was obtained from Centrohem, Stara Pazova; 99.8% acetonitrile (ACN) was a product of J.T. Baker. All solutions were made using doubly distilled water. The TiO_2 Degussa P25 (75% anatase and 25% rutile, surface area $50 \pm 1.0\,m^2\,g^{-1}$, crystallite size about 20 nm, non-porous) and Wackherr's "Oxyde de titane standard" (100% anatase, surface area $8.5 \pm 1.0\,m^2\,g^{-1}$, crystallite size 300 nm, hereafter "TiO_2 Wackherr"), produced by the sulfate process were used as photocatalysts [21].

2.2. Photodegradation procedures

Photocatalytic degradation was carried out as described previously [22]. In a typical experiment, and unless otherwise stated, the initial MET concentration was 0.05 mM and the TiO_2 loading (Degussa P25 or Wackherr) was $1.0\,mg\,mL^{-1}$. All experiments were performed at the natural pH (*ca.* 7).

2.3. Analytical procedures

For the LC–DAD kinetic studies of MET photodegradation, aliquots of 0.50 mL were taken from the reaction mixture at the beginning of the experiment and at regular time intervals. Aliquot sampling caused a maximum volume variation of *ca.* 10% in the reaction mixture. The suspensions were filtered through Millipore (Millex-GV, 0.22 μm) membranes. Lack of adsorption of MET on the filters was preliminarily checked. After that, a 20-μL sample was injected and analyzed on an Agilent Technologies 1100 Series liquid chromatograph, equipped with an Eclypse XDB-C18 column (150 mm × 4.6 mm i.d., particle size 5 μm, 25 °C). The UV/vis DAD detector was set at 225 nm (wavelength of MET maximum absorption). The mobile phase (flow rate $0.8\,mL\,min^{-1}$) was a mixture of ACN and water, the latter acidified with 0.1% H_3PO_4, with the following gradient: 0 min 15% ACN which increased to 30% ACN in 5 min, after which 30% ACN was constant for 5 min; post time was 3 min. Reproducibility of repeated runs was around 3−10%.

Kinetics of the aromatic ring degradation was monitored spectrophotometrically at 225 nm [23].

For ion chromatographic determinations, aliquots of 3 mL of the reaction mixture were taken at regular time intervals, filtered through membrane filters and analyzed on an ion chromatograph Dionex ICS 3000 Reagent Free IC system with conductometric detector [22].

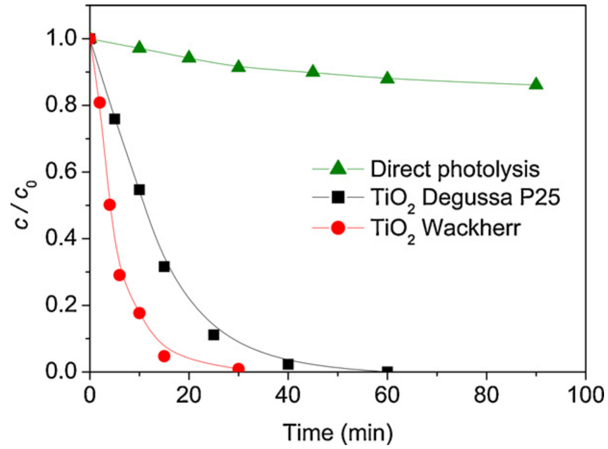

Fig. 1. Kinetics of the photolytic (no TiO_2) and photocatalytic degradation of MET (initial concentration $c_0 = 0.05$ mM). When present, the TiO_2 loading was $1.0\,mg\,mL^{-1}$.

For the LC–MS/MS (ESI+) evaluation of intermediates, the initial MET concentration was 3 mM. The selected reaction monitoring (SRM) mode (parameters are given in Table 1) was used for obtaining peak areas of the analytes, in order to track the reaction kinetics. Detailed information on experimental conditions can be found in the Supplementary Material.

For total organic carbon (TOC) analysis, aliquots of 10 mL of the reaction mixture were taken at regular time intervals, diluted to 25 mL and analyzed after filtration on an Elementar Liqui TOC II analyzer according to Standard US 120 EPA Method 9060A.

3. Results and discussion

3.1. Effect of the kind of TiO_2

The photocatalytic activity of TiO_2 Wackherr was compared to that of the most often used TiO_2 Degussa P25 under UV irradiation (Fig. 1). Significant MET degradation could be observed under UV, and the process involving TiO_2 Wackherr was significantly faster than direct photolysis or transformation with Degussa P25. Furthermore, the variety and amount of intermediates depended on the type of catalyst (Fig. 2). The faster degradation of MET with TiO_2 Wackherr compared to Degussa P25 is an interesting result, although it is hardly unexpected [21,22,24]. Note that TiO_2 Wackherr has much larger particles than Degussa P25 (3–4 times larger average radii in solution), which produces a surface area that is

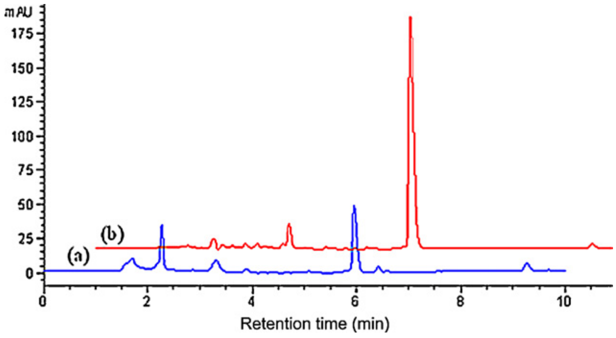

Fig. 2. Chromatograms obtained after 10 min of MET ($c_0 = 0.05$ mM) degradation under UV irradiation in the presence of TiO_2 Wackherr (a) and Degussa P25 (b). $\lambda_{det} = 225$ nm, $t_R(MET) = 5.8$ min.