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BETA-ADRENERGIC DRUGS (β-BLOCKERS) IN THE ENVIRONMENT – NEW METHODS OF REMOVAL

LEKI BETA-ADRENOLITYCZNE (β-BLOKERY) W ŚRODOWISKU – NOWE METODY ELIMINACJI

A b s t r a c t

This paper is part of a series of publications discussing the prevalence of pharmaceuticals in the aquatic environment and the effectiveness of their removal and degradation during wastewater and water treatment processes. It presents the most commonly used β-blockers and their parameters related to their metabolism and excretion from a body. In the paper, the authors review the literature data on the presence of β-blockers in wastewater and surface waters and present new solutions which have been developed to increase the efficiency of removal of these compounds from wastewater and potable water.

Keywords: β-*blockers*, *wastewater*, *surface water*, *wastewater treatment*, *water treatment*

S t r e s z c z e n i e

Artykuł jest częścią serii publikacji obejmujących zagadnienia występowania farmaceutyków w środowisku wodnym oraz skuteczności ich eliminacji i degradacji w procesach oczyszczania ścieków i uzdatniania wody. W pracy przedstawiono najczęściej stosowane leki β-adrenolityczne oraz ich parametry dotyczące metabolizmu i usuwania z organizmu. Dokonano przeglądu literatury dotyczącej występowania β-blokerów w ściekach i wodach powierzchniowych oraz nowych rozwiązań mających na celu zwiększenie skuteczności eliminacji tych związków ze ścieków i uzdatnianej wody.

Słowa kluczowe: β-*blokery*, *ścieki*, *wody powierzchniowe*, *oczyszczanie ścieków*, *uzdatnianie wody*

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1. Introduction

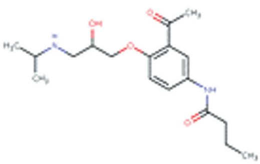
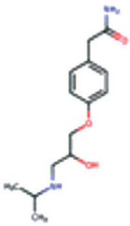
Economic factors effectively limit the range of solutions that would ultimately prevent a discharge of drugs and other organic substances into rivers. The application of some methods used in water treatment could enhance the degradation of pharmaceuticals during wastewater treatment, but at the same time, it would significantly increase the treatment costs of municipal wastewater. Therefore, articles reporting the presence of specific pharmaceuticals in aqueous environments are regularly published. They not only address the issue of popular and over-the-counter pharmaceuticals such as non-steroidal anti-inflammatory drugs [17], but also cytostatic drugs used in chemotherapy and the treatment of autoimmune diseases [2]. According to Wegrzyn et. al. [22] β-blocker drugs are ranked third among pharmaceuticals most commonly present in the aquatic environment. Due to the nature of β-blockers, they should not be present in water intended for human consumption.

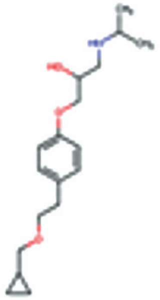
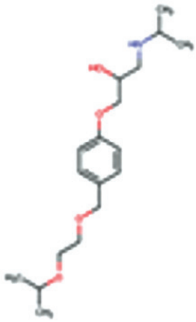
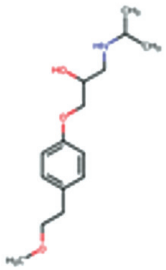
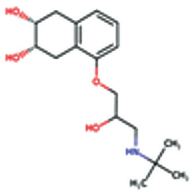
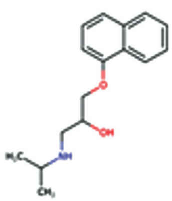
2. Characteristic of β-blockers

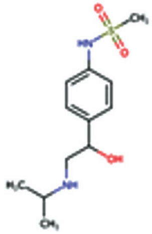
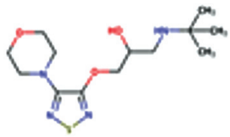
β-adrenergic receptor blockers are pharmaceuticals that block β-1 and β-2 adrenergic receptors to reduce the effects caused by adrenaline and noradrenaline i.e. they act upon the sympathetic nervous system. Their action results in a slower heartrate, lower blood pressure and smooth muscle contraction. They are divided into two groups: non-selective (generally affecting adrenergic receptors) and selective, mainly blocking β-1 receptors (described as cardio selective). β-blockers are used not only in the treatment of diseases such as coronary heart disease, hypertension, heart rhythm disorders and glaucoma, but also in anxiety disorders and neuroses. Table 1 shows the most common β-blockers.

Table 1

Characteristics of β-blockers [25–33]

Name	Formula	Structure	CAS	Metabolism	Half-life	Excretion
Acebutolol	$C_{18}H_{28}N_2O_4$		37517-30-9	Hepatic	3–4 h	30-40% Renal 60% Billary
Atenolol	$C_{14}H_{22}N_2O_3$		29122-68-7	Hepatic 90% not metabolised	6–7 h	50% Renal 50% Faeces

Betaxolol	$C_{18}H_{29}NO_3$		63659-18-7	Hepatic 15% not metabolised	14–22 h	Renal
Bisoprolol	$C_{18}H_{31}NO_4$		66722-44-9	Hepatic 50% not metabolised	9–12 h	50% Renal 2% Faeces
Metoprolol	$C_{15}H_{25}NO_3$		37350-58-6	Hepatic 5% not metabolised	3–7 h	Renal
Nadolol	$C_{17}H_{27}NO_4$		42200-33-9	Not metabolised	14–24 h	Renal
Propranolol	$C_{16}H_{21}NO_2$		525-66-6	Hepatic < 1% not metabolised	4 h	Renal

Sotalol	$C_{12}H_{20}N_2O_3S$		3930-20-9	Not metabolised	12 h	Renal Lactic
Timolol	$C_{13}H_{24}N_4O_3S$		26839-75-8	Hepatic 20% not metabolised	2.5–5 h	Renal

3. β-blockers in the environment

Both common and uncommon sources of pharmaceuticals in the aquatic environment and soil are shown in Figure 1 [10]. β-blockers, as drugs used primarily in treatments of a cardiac nature, should be expected primarily in wastewater from households and hospitals.

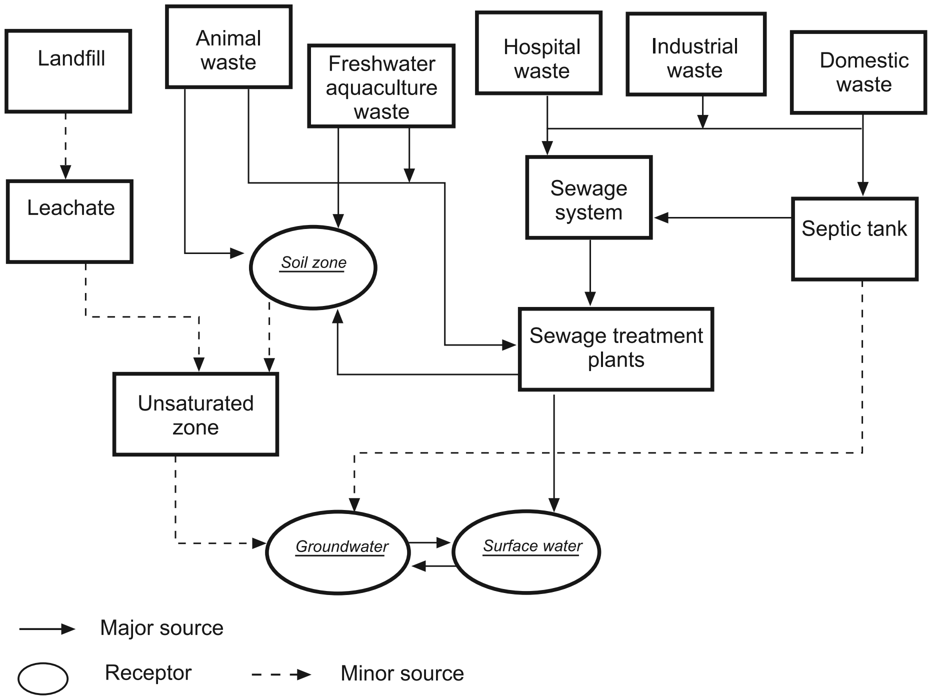


Fig. 1. Pharmaceuticals in water and soil

The concentration of the drugs may vary significantly, due to its prevalence, dose and its metabolic pathway in the body (some of them, such as nadolol or sotalol, are not metabolised). Therefore, there may not be an actual relationship between the occurrence of a particular drug in a given area and its concentrations discharged to wastewater treatment plants (WWTP). A good example of such cases are the results reported at the WWTP in Bitz, where the following drugs were found (max/mean): atenolol (ATE) 590/74 ng/l, metoprolol (MET) 4340/2430 ng/l and sotalol (SOT) 6010/2150 ng/l [15]. The data could suggest, that sotalol was the β-blocker the most widely used by the inhabitants of Bitz. However, when considering the excretion of the unchanged drug (MET 5%, SOT 100%), metoprolol was found to be the most common. In Spain, analyses [5] showed the presence of numerous β-blockers in raw and treated sewage (average concentrations in influent / effluent): atenolol 2359/1060 ng/l, metoprolol 2408/375 ng/l, propranolol (PRO) 117/104 ng/l and sotalol 311/268 ng/l. In the United Arab Emirates, the analysis of effluents from municipal treatment plants confirmed the presence of acebutolol, atenolol, metoprolol and propranolol in the range of 3 to 234 ng/l; researchers attributed their presence to insufficient removal of these compounds during the wastewater treatment process [18]. The concentrations of β-blocker pharmaceuticals in wastewater and surface water reported in the literature are presented in Tab. 2.

Table 2

Concentrations in ng/l (min-max or mean ± σ) of detected β-blockers in WWTP influent, WWTP effluent and surface water

Compound	Influent	Effluent	Surface water
Atenolol	100–33100[12] 971±30[13] 12913–14223[16] 1800–2400[20]	664±22[13] 550–980[20] 2123–2870[16] 130–7600[12]	0.25–122[1] 3.5–64[15] 1–487[16]
Metoprolol	2–1520[12] 411±15[13] 75–110[16] 2–32[19] 220–290[20]	1–1200[7] 3–250[12] 375±24[13] 41–69[16] 1–4[19] 130–210[20]	3–380[6] 5–107[9] 4.1–563[15] 0.5–10[16] 4–33[19]
Nadolol	51±2[13] 1–16[20]	10–360[7] 20±0.5[13]	–
Propranolol	10±1[13] 14–45[20] 60–638[16]	26–1900[7] 45±1[13] 13–26[20] 93–388[16]	0.5–561[1] 20–450[4] 0.5–107[16]
Sotalol	529±10[13] 370–640[20]	466±24[13] 210–470[20],	4.8–103[15]
Timolol	10–16[20]	1–13[20]	–

Recent studies have shown that β-blockers are poorly adsorbable by soil structure and show good water solubility [14]; therefore, there is a risk of their penetration to groundwater.

This view is supported by the literature, since the metabolites of atenolol (6.4 ng/l) [8] and propranolol (5–21.4 ng/l) [11] have been detected in groundwater. The presence of β-blockers in the water coming to water treatment plants could threaten to reach the consumers of drinking water – such cases were confirmed by studies showing the presence of atenolol, among other pharmaceuticals, in water for human consumption (0.82–23 ng/l) [3].

4. New methods of β-blocker removal

One of the newest methods of β-blockers degradation is the application of $K_2Fe^{VI}O_4$ used in the advanced oxidation of actual hospital wastewater [23]. Studies have shown a more than 90% degradation of ATE, MET and PRO. However, during the process, many pharmaceutical oxidation by-products were formed, while the biodegradability of the system was only slightly increased. According to the authors [23], the proposed method can be implemented in water or wastewater treatment only after thorough research on process mechanisms and advanced oxidation by-products formed during the process.

Photocatalysis also appears to be an effective tool in the degradation of pharmaceuticals. 100% elimination of MET after 2 h of irradiation was achieved using a new nanocomposite consisting of $Ag–Bi_2–WO_6$ and graphene [24], which the authors define as a motivating factor for the development of new photocatalysts and their use in wastewater treatment.

In [21], the authors compared the efficiency of advanced oxidation in removing pharmaceuticals from hospital wastewater. In the case of atenolol, bisoprolol, metoprolol, propranolol and sotalol, the most effective method of removal was H_2O_2-assisted ozonation. The process was continued for over 15 minutes at ozone concentrations of 450 mgO_3/l and 200 mgH_2O_2/l. With the exception of bisoprolol (76% elimination), all β-blockers were removed with an efficiency of over 97%.

5. Conclusions

- Pharmaceuticals are commonly found in wastewater and surface waters.
- The efficiency of β-blocker degradation is related to the efficiency of wastewater treatment processes which reduce the pollution of the aquatic environment.
- β-blockers, as drugs that are water soluble and poorly adsorbable on soil, can penetrate into groundwater and accumulate in plants.
- Since there is no research data on the long-term impact of β-blockers on the human body, attempts should be made to fully eliminate these substances during water treatment processes.
- Newly developed technological solutions for β-blocker degradation are a good prognostic for the safety of drinking water in the future.

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