Modeling of Sorption and Degradation of selected Pharmaceuticals: case study of Belgrade Groundwater Source

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Abstract. The application of a mathematical model that analyzes the transport of selected pharmaceuticals from the Sava River to a corresponding radial collector well at Belgrade's groundwater source is assessed. The occurrence of the selected pharmaceuticals in surface water and the corresponding well was monitored from 2009 to 2015. The pharmaceuticals selected for the present study are carbamazepine, trimethoprim, and metamizole metabolites 4-AAA and 4-FAA. Transport is analyzed based on experimental data (sorption isotherms) and a field tracer experiment that includes injection of the selected pharmaceuticals. The analysis shows that sorption of carbamazepine is relatively low and that this pharmaceutical does not degrade under the studied conditions, so it is not possible to accurately determine the degradation half-life. Trimethoprim is detected in the Sava River with an average concentration 8.5 ng/L, but there is no positive detection in well Rb-16. The average concentration of 4-AAA in the surface water is 34 ng/L and of 4-FAA 13 ng/L. The average concentrations of 4-FAA and 4-AAA in the groundwater are in the range from 1 and 1.85 ng/L. The objective of the research is to use an existing hydrogeologic model and apply a transport model to determine the minimum degradation half-life of the investigated pharmaceuticals.

Key words: degradation, half-life, pharmaceuticals, sorption, model.

Апстракт. У раду је приказана примена математичког модела за анализу транспорта одабраних фармацеутика на путу од реке Саве до кореспондентног бунара са хоризонталним дреновима Београдског изворишта. У периоду између 2009 и 2015. праћена је појава испитиваних фармацеутика у Реци Сави и кореспондентном бунару. Одабрани фармацеутици за анализу транспорта од реке ка бунару су карбамазепин и метаболити метамизола 4-ААА и 4-ФАА. За анализу транспорта су коришћени подаци који су добијени експериментално (изотерме сорпције), као и резултати који су добијени на терену, спровођењем трасерског опита и накнадног упуштања одабраних фармацеутика. Утврђено је да карбамазепин има релативно малу сорпцију и не разграђује се у посматраним условима, тако да није било могуће прецизно утврдити период полураспада. Триметоприм је детектован у реци Сави са просечном концентрацијом од 8.5 ng/L, али није детектован у узорцима подземне воде бунара РБ-16. Просечна концентрација 4-ААА у површинској води је 34 ng/L, док је за 4-ФАА просечна концентрација 13 ng/L. Просечне концентрације 4-ААА и 4-ФАА у узорцима подземне воде су у интервалу од 1 до 1.85 ng/L. Циљ рада је да се на основу постојећег хидрогеолошког модела и модела транспорта фармацеутика од реке до кореспондентног бунара одреди минимални период полураспада одабраних фармацеутика за специфичне услове средине.

Кључне речи: деградација, полураспад, фармацеутици, сорпција, модел.

Introduction

Belgrade's groundwater source (BGS) is situated along the Sava River, for the most part within city lim- its, making the source vulnerable to anthropogenic pressures. Drinking water is treated at five plants, of which three plants are for groundwater treatment. The rate of maximum groundwater abstraction from the

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Sava alluvium is currently about 4.5 m³/s and the maximum designed capacity of the two treatment plant for mainstream river water is 5.5 m³/s (Dimkić et al., 2011b). As such, little less than half of the drinking water supply relies on alluvial groundwater of the Sava River.

In Serbia in general, about 70 % of drinking water originates from groundwater, of which 50% comes from alluvial aquifers (Dimkić et al., 2012).

The BGS alluvial aquifer ensures additional purification as groundwater flows through the aquifer during the course of riverbank filtration (RBF), in which case the aquifer can be considered as an extensive physical and biochemical reactor. This is an extremely important aspect from the perspective of river water treatment and mitigation of accidental pollution risks. There are several short-term studies that confirmed the presence of pharmaceuticals in groundwater in Serbia (Radović et al., 2012; Petrović et al., 2014; Radović et al., 2015). In these studies all investigated pharmaceuticals (carbamazepine, trimethoprim, metamizole metabolites N-acetyl-4-aminoantipyrine (4-AAA) and N-formyl-4-amino-antipyrine (4-FAA)), were detected in surface water samples. In all analyzed water samples, carbamazepine and metamizole metabolites were the most frequently detected analytes. Also a widespread occurrence of all investigated pharmaceuticals in analyzed surface waters was proven.

The occurrence of pharmaceuticals in groundwater affects the quality of the abstracted potable water, such that the implementation of RBF systems requires careful assessment. There are several recent studies that investigate the attenuation and transport of pharmaceuticals in groundwater (D'Alessio et al., 2015; Hamann et al., 2016). Objective of these studies was to determine the fate of organic micropollutants during river bank filtration, especially the effect of temperature, oxygen, and organic matter on the removal (D'Alessio et al., 2015) and the effect of the long-term/long-distance river bank filtration (Hamann et al. 2016). Study (D'Alessio et al. 2015) concludes that the local conditions (i.e., level of oxygen, temperature) are expected to play a key role in the removal of selected micropollutants. Long-term/long-distance study (Hamann et al., 2016), shows how temporal changes in the river and the time-shift caused by the groundwater travel time can sometimes lead to misinterpretation and indicate that the removal of micropollutansts during river bank filtration was flow path time-dependent.

Also, there are recent studies that address pharmaceutical transport models (Nham et al., 2015; Mustafa et al., 2016), in an attempt to simulate the fate, behavior and transport of pharmaceuticals in groundwater.

In a study conducted in Greece (Nham et al., 2015), four one-dimensional flow and transport models based on the data of a field scale experiment were constructed to investigate the transport behavior of sixteen organic trace pollutants during soil aquifer treatment. The simplification to 1D was unavoidable due to the lack of sufficient hydrological and hydrogeological data for constraining a 2D or 3D site model. In another study (Mustafa et al., 2016), analytical model was developed to simulate the influence of a pumping well on contaminant concentration in RBF systems. Both studies used simplified field hydrodynamic model because of the lack of data. This paper presents model simulation results of the transport of carbamazepine, trimethoprim and metamizole metabolites 4-AAA and 4-FAA from the Sava River to the corresponding well.

The selected pharmaceuticals belong to different pharmaceutical classes and the selection was based on the extent of administration of pharmaceuticals in Serbia and the review of occurrence in surface water and groundwater in Serbia (Radović et al., 2012; Petrović et al., 2014; Radović et al., 2015). Metamizole metabolites were selected for this study because metamizole is among the most popular analgesic and antipyretic pharmaceuticals (Moldovan et al., 2006). Although metamizole was not detected in surface water and groundwater, its metabolites are often found.

The objective of the research was to additionally explain the behavior of selected pharmaceuticals in alluvial aquifers, during riverbank filtration from the Sava River to the corresponding well. Periodic testing was undertaken in order to study the effect of the transport of a substance along with groundwater from the river to the well and to obtain input data for quantifying self-purification processes. The investigation covered seven years of periodic monitoring of pharmaceutical concentrations in the Sava River and corresponding well.

Besides monitoring of the pharmaceuticals, additional information about experimental linear sorption coefficients and linear sorption coefficients obtained during a field tracer test that included injection of pharmaceuticals were used for the model parameters. In our study numerical 3D model was applied. Based on available data for investigated pharmaceuticals concentration levels, hydrogeological and hydrodynamic conditions and sorption coefficients based on the field experiment data (Kovačević et al., 2016) and laboratory experiment data (Radović et al., 2016), previously developed numerical hydrodynamic 3D model and transport model were used to determine degradation potential of investigated pharmaceuticals. Based on the available results and existing hydrogeological model previously developed by the Jaroslav Černi Institute for the Development of Water Resources the transport model was used to determine the minimum degradation half-life of the investigated pharmaceuticals and conduct a spatial and temporal RBF analysis. Results for different sorption coeffi-

cients were compared and the diversity of the results indicates that most accurate results could be obtained based on the field experiment data for sorption coefficients.

Materials and methods

Sampling Locations and Sample Collection

Well RB-16 is located on the right bank of the Sava River, on a river island called Ada Ciganlija, within the city proper (Fig. 1). The well is outfitted with four relatively new laterals (horizontal screens, installed in 2007). The old laterals have been shut off and decommissioned. The laterals tap the lowest water-bearing layer of the aquifer system, at a depth of about 30 m. During the study period (2009–2015), a total of 14 surface water samples of the Sava River and eight groundwater samples from well Rb-16 were analyzed. Surface water was sampled mid-stream, at a depth of about one meter. Groundwater samples were taken directly from well Rb-16. All surface water and groundwater samples were collected using 1-liter amber glass bottles. The samples were stored unpreserved in refrigerators and frozen on the same day, until the time of analysis, generally 2–3 days after sampling.
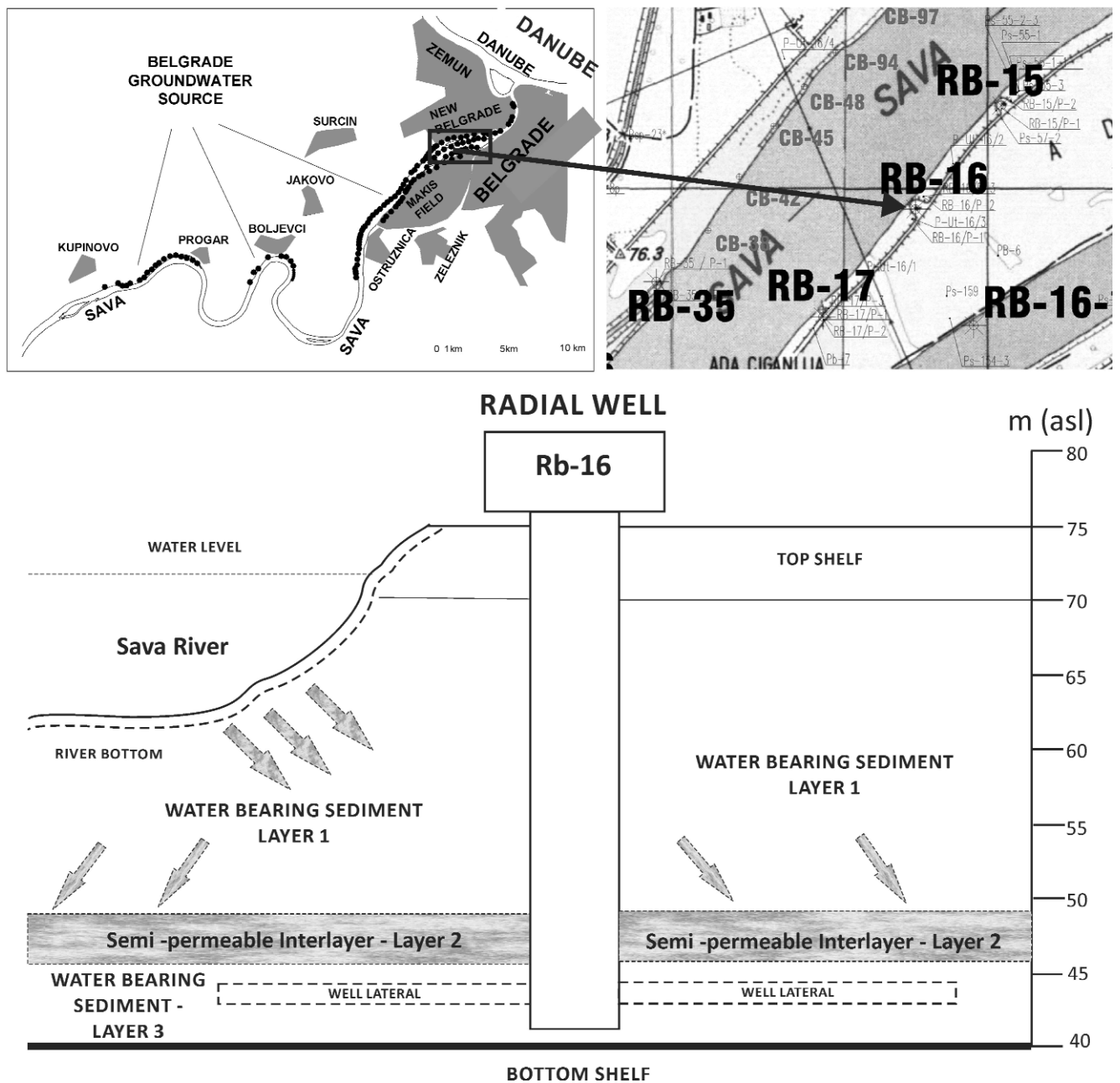

Fig. 1. Map of Belgrade Groundwater Source, well Rb-16 and schematic representation of the Sava River and the corresponding well Rb-16 (asl – above sea level).

Surface water and groundwater samples were sampled mainly in the autumn and spring every year. Both, surface water and groundwater samples were taken at the same time during the investigation period.

Minimum groundwater infiltration travel time from Sava River to corresponding well is approximately 100 days.

The particle size distribution was determined by sieving the materials using sets of sieves according to JUS L.J9.010, with the following mesh sizes in mm: 0.063; 0.090; 0.125; 0.250; 0.500; 0.710; 1.0; 2.0; 4.0; 8.0; 11.2; 16.0; 22.4; 31.5; 63.0; and 125.0. Based on the previously collected data, the theoretical hydraulic conductivity was calculated using the USBR empirical equation (Vukovic & Soro, 1992), where $d_{ef} = d_{20}$ (d_{ef} - the effective grain size diameter of the sediment; d_{20} – grain size diameter from 20 percent cumulative grain size distribution curve). Organic carbon was analyzed in the laboratory using a Shimadzu Total Organic Carbon Analyzer (TOC-5050a).

Sample preparation and analysis

High-purity (>95 %) analytical standards were obtained from local pharmaceutical companies (Hemofarm, Serbia, and Zorka-Pharma, Vršac, Serbia). Two metamizole (dipyrone) metabolites, 4-FAA and 4-AAA were procured from Sigma Aldrich. All the solvents were HPLC (high pressure liquid chromatography) grade from Fluka (Buchs, Switzerland) or Sigma-Aldrich (St. Louis, MO), and all the other reagents were of analytical grade. Concentrated acetic acid and ammonia were used for pH value adjustment of the water samples. Deionized water was made by passing tap water through a GenPure ultrapure water system (Niederelbert, Germany). Stock solutions of individual standards were prepared in methanol, in concentrations of 100 mg/l, every few months, and stored in a freezer.

The working standard solutions were prepared weekly in different concentrations, by mixing appropriate amounts of single standard stock solutions and dilution with methanol. All working solutions were preserved at –4° C.

During the period from 2009 to 2015 the water samples for pharmaceutical analyses were prepared applying the solid phase extraction (SPE) method and extracts were analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). The analytical method used for determining the selected pharmaceuticals has previously been described and validated.

Detailed information about the analytical procedure, instrument parameters, SPE recoveries, calibration curves, accuracy, precision, detection limits, and quantification limits is provided in a previously published study (Radović et al., 2015).

A Surveyor LC system (Thermo Fisher Scientific, Waltham, MA, USA) was used to separate the analytes on a reverse-phase Zorbax Eclipse® XDB–C18 column, 75 mm×4.6 mm ID and 3.5 μm particle size (Agilent Technologies, Santa Clara, CA, USA). A pre-column, 12.5 mm×4.6 mm ID and 5 μm particle size (Agilent Technologies), was also used.

For the LC–MS^n analyses of the pharmaceuticals in the positive ionization mode, the mobile phase was composed of methanol (A), deionized water (B), and 10% acetic acid (C). The mobile-phase gradient was varied as follows: 0 min, B 33%, C 2%; 12 min, B 98%, C 2%; 15 min, B 98%, C 2%. The initial conditions were then re-established and held for 15 minutes.

The flow rate of the mobile phase was 0.6 mL/min. The injection volume was 10 μL. Mass spectra were obtained using a LTQ Fleet linear ion trap mass spectrometer (Thermo Fisher Scientific). Electrospray ionization was used for mass spectrometric analysis.

The optimal source parameters for monitoring of all the ions were: source voltage (4.5 kV), sheath gas (25 au, i.e. 25 arbitrary units, from a scale of arbitrary units in the 0–100 range defined by the LCQ Advantage system), and capillary temperature (290° C). For each analyte, the precursor ion, optimal collision energy, and most abundant fragment ion were chosen in the selected reaction monitoring (SRM) mode, for quantification purposes. The additional fragmentation reaction was selected for confirmation purposes.

Sorption isotherm experimental setup

The sorption experiment was carried out using a BGS sediment sample, to determine the sorption equilibration time ($dC/dt = 0$), i.e. the contact time required to achieve a sorption and desorption equilibrium (batch kinetic experiment) (Sukul et al., 2008). All the experiments were performed in duplicate, to verify initial concentrations, and two blanks without sediments were run for each initial concentration to verify lack of laboratory contamination.

To ensure that photo degradation was not the cause of any poor results, the experiment was performed in the dark, by covering the tubes. The details of the sediment/solution ratio, mixing time, initial concentrations and experimental setup are described in study of Radović et al. (2016).

Briefly, a preliminary sediment/solution ratio experiment was performed and the optimum ratio for all the compounds was determined to be 1:20. The pH value of the solutions or sediment was not adjusted (Sanders et al., 2008). The mixture was shaken for 1, 2.5, 5, 16, 24 and 48h by a backward-and forward-moving shaker at 105 rpm and ambient temperature. At the end of each shaking period, the tubes were centrifuged at 4000 rpm for 10 min. The supernatants were decanted and the volumes measured and then filtered. To obtain all the

necessary data about the sorption and desorption equilibrium, the desorption experiment was carried out by adding an extra amount of deionized water to the sediment that remained in the centrifuge tubes, to achieve a total amount of the aqueous solution of exactly 20 mL. All the centrifuge tubes were returned to the shaker for a shaking period that corresponded to their adsorption studies (e.g. if the tubes were shaken for 5 h during the adsorption study, they were also shaken for 5 h for the desorption study), centrifuged, decanted and the desorbed solutions analyzed (SUKUL et al., 2008). The optimal sorption equilibration time was determined when the concentrations of the investigated compounds were stabilized in the supernatant. Initial concentrations of 10, 25, 50, 75, 100, 250, 500 and 1000 μg/L of all the compounds were employed to determine sorption isotherms because they covered the range of their concentrations found in river sediment, surface water and groundwater samples.

The concentrations of the pharmaceuticals sorbed to the material at equilibrium, S (ng/g), were calculated from the difference between the equilibrium concentration of the pharmaceuticals in the blanks, C_0 – initial concentration (ng/mL), and the equilibrium concentration in the solution, Ce (ng/mL), the mass of the sediment used in the experiment, m (g), and the volume of the solution, V (mL), applying the following equation (1):

$$S = (C_0 - Ce) \cdot \frac{V}{m} \qquad (1)$$

The experimental results were analyzed using the linear adsorption model:

$$S = Kd \cdot Ce \qquad (2)$$

where K_d is the linear sorption coefficient, mL/g.

Linear sorption model was used because of very low pharmaceutical concentrations (ng/L), and short equilibrium time, so for very small concentrations, especially in groundwater, linear sorption model is most applicable. With small initial concentration of solvents (ng/L) in solution other applicable sorption models (Langmuir, Freundlich) became linear.

In situ experiment setup

The monitored parameters and experimental conditions are described in detail in another study (KOVAČEVIĆ et al., 2016). The field experiment lasted for 16 days and the experimental parameters were monitored continuously. The tracer test was conducted under forced gradient conditions, induced by groundwater pumping.

Before the experiment started, baseline quality was monitored to determine initial conditions. The tracer test was conducted under forced gradient conditions, induced by groundwater pumping. The initial conditions were monitored continuously (every hour) and included monitoring of hydraulic head, flow and electrical conductivity. Additionally, pH, dissolved oxygen in the groundwater and the oxidation/reduction potential were monitored periodically. During the tracer test, the nonreactive tracer NaCl and the reactive pharmaceuticals were injected into the injection piezometer. A continuous-flow peristaltic pump was set up in an observation well at 6 L/s. Also, groundwater levels were monitored by data loggers (divers). At the beginning of the test, NaCl was dissolved in the injection tank. Following successful dissolution, the NaCl tracer was gradually injected. The maximum concentration of the NaCl tracer was established 200 minutes after the beginning of the test, which is consistent with the data obtained by analyzing the filtration properties of the aquifer and the average hydraulic conductivity of 7×10⁻⁴ m/s. The injection of pharmaceuticals commenced after successful injection of the NaCl tracer. The initial concentrations of the selected pharmaceuticals in a 100-liter injection tank were: trimethoprim 2.5 mg/L, carbamazepine 1 mg/l, diclofenac 1 mg/L, and 4–AAA 1 mg/l. Sampling was conducted based on a pre-defined program.

The following equation was used to calculate Kd – linear sorption coefficient, for all the analyzed pharmaceuticals:

$$Rd = \frac{v_{NaCl}}{v_{pharmaccutical}} = 1 + \frac{\rho_b}{Sy} Kd \qquad (3)$$

where: Rd is the retardation coefficient; v_{NaCl} is the velocity of the NaCl tracer [m/s]; $v_{pharmaceutical}$ is the velocity of the pharmaceutical [m/s]; ρ_b is the bulk density of the aquifer matrix [g/mL]; Sy is the effective porosity; and Kd is the linear sorption coefficient [mL/g].

Effective porosity was calculated based on the grain-size distribution curve and the results of hydrogeological model calibration. A theoretical soil bulk density of 1.65 g/mL for the aquifer gravel and sand (layer 1 and layer 3) and a value of 1.1 g/mL for a semi-permeable interlayer (layer 2) were used. The velocities of the NaCl tracer and the pharmaceuticals were calculated based on the results of the tracer test and monitoring of the behavior of the selected pharmaceuticals.

Groundwater model

The data on the well Rb-16 were analyzed and organized to form a hydrogeologic model of the terrain/simplified spatial model of the aquifer. Licensed software RockWorks (https://www.rockware.com/product/rockworks/) was used. The initial values of filtration

parameters, as the starting point for the development of the hydrodynamic model, were determined applying a two-fold approach: based on the grain-size distribution of the material sampled at different borehole depths, and based on interpretation of multiple well pumping tests.

Analysis and spatial data systematization related to the well RB-16, was carried out in order to form a 3D hydrogeological terrain model and a simplified spatial water bearing model of alluvial sediments. It was guided by the principle that the main hydrogeological unit represents the layer.

Groundwater flow was simulated using a new and original software WODA (Well Outline and Design Aid), a simulator of variably saturated well-driven groundwater flow in an anisotropic discontinuous environment with miscible displacements, heat transfer, variable density, sorption, degradation, etc. WODA

used for hydrogeological 3D model, and WODA was used for hydrodinamic 3D groundwater flow model and pharmaceutical groundwater transport model.

Geologic framework

The alluvial aquifer was developed through several sedimentation cycles and sequences: sandy gravel, sands of various grain sizes, and silty and clayey sediments. The thickness of the Quaternary strata is up to 25 m. With regard to the grain sizes of the sediments, two cross-sectional zones have been distinguished, Fig. 2: Lower zone: coarse-grain sediments, in which radial well laterals are installed. These sediments occasionally feature clay, sandy clay and silt interbeds and lenses; and Upper zone: fine-grain sediments, with poorer filtration properties.
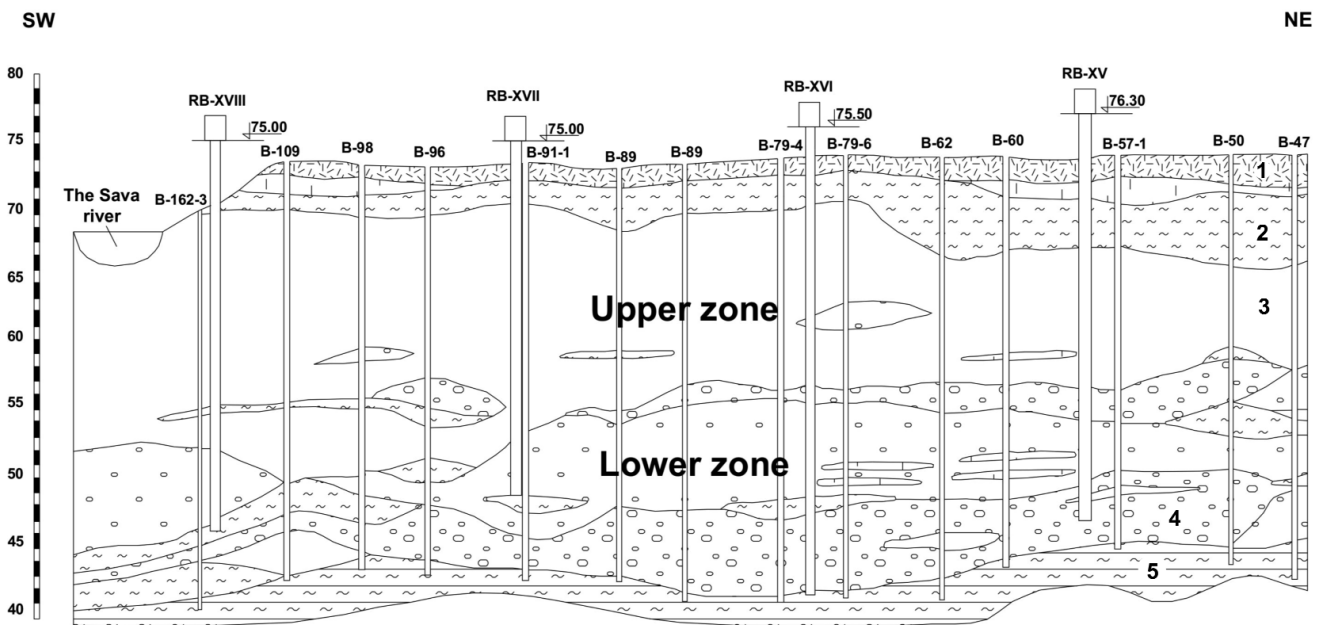

Fig. 2. Typical lithological section through the Sava riverbank. Legend: 1. surficial soil; 2. clay; 3. sand; 4. gravel; 5. bottom clay.

has been developed by the Numerical Analysis Group at the Jaroslav Černi Institute for the Development of Water Resources (JCI). It does not have its own graphical user interface, but can work with groundwater models constructed using a Lizza interface. Lizza was developed by JCI and the Bioengineering Research and Development Center – BioIRC from Kragujevac, Serbia. It supports full 3D modeling, stationary and non-stationary modeling, saturated and non-saturated environment simulations, as well as handling of mass and heat transport (Dimkić et al., 2011a, 2013; Dotlić, 2015).

Multiple software was used because of easier simplification and optimization of the existing data in order to obtain the most simple and accurate hydrogeological and hydrodynamic model. RockWorks was

It is a very intricate hydrogeological setting due to the presence of semi-permeable interlayers within the water-bearing complex.

Based on the vertical grain-size distribution in the zone of well Rb-16 (Fig. 3), it is apparent that there were several sedimentation cycles, which are schematically represented as a single semi-permeable interlayer for the purposes of the hydrodynamic analysis.

Groundwater model of well Rb-16

The previously-developed hydrogeologic model served as a basis for developing a pharmaceutical transport model in the region of well RB-16. Detailed information about the analysis and definition of input
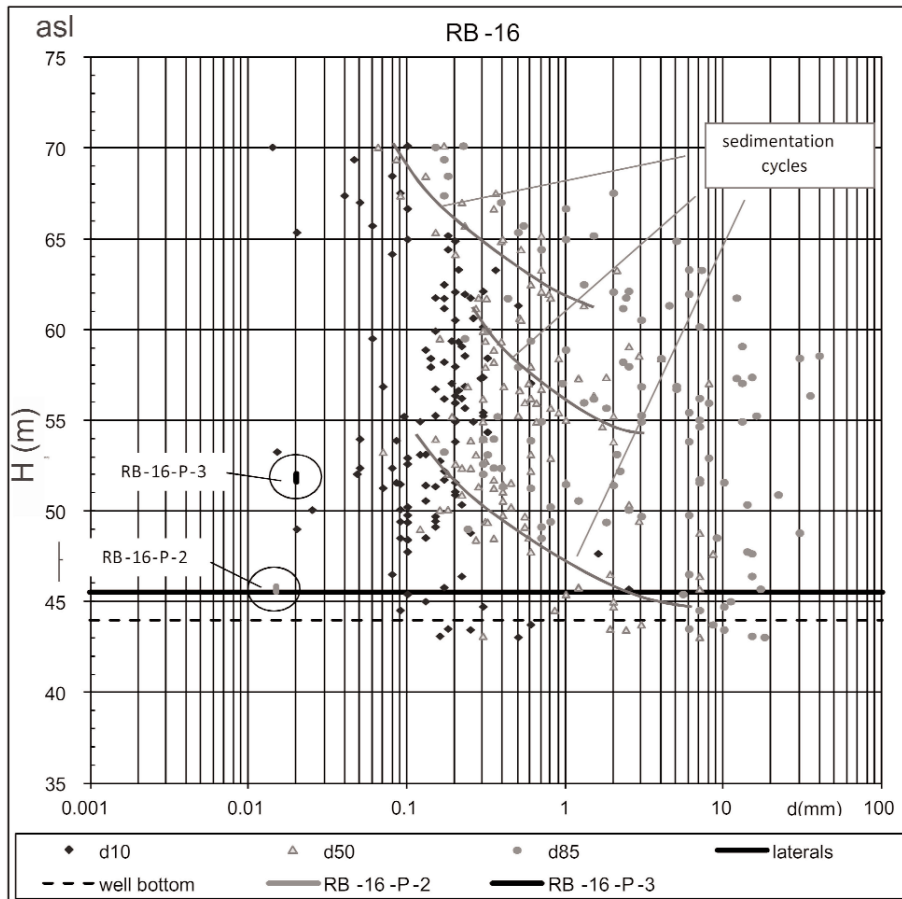
Fig. 3. Vertical profile of the selected grain-size fractions in the zone of well Rb-16.

Table 1. Model calibration results, average values of filtration parameters of schematized layers, riverbed, and lakebed.

	Khoriz (m/s)	Kvert (m/s)	S (1/m)	Sy (-)
Layer 1	3 E-04	2 E-06	7.E-05	1.5E-01
Layer 2	4.46 E-04	3.00 E-07	7.E-05	7.0E-02
Layer 3	6.5 E-04	6.5 E-04	7.E-05	1.2E-01
	K/d (1/s)			
Sava River	4 E-07			
Lake Sava	3 E-07			

ness, filtration rate) were extremely important aspects of the discharge capacity of both the well and the location as a whole. Datasets from three pumping tests (2007, 2011, and 2013) were used for calibration. Model tests revealed that the discharge capacity of well Rb-16 was the sum of inflows from the Sava River (95%), Lake Sava (4%) and the hinterland (1%). Based on the calibration of the well Rb-16 site, a model with three schematized layers provided representative, averaged values of filtration parameters of the porous medium and the permeability of the riverbed, where for Layer 1 – water-bearing sediments (Fig. 1), the horizontal hydraulic conductivity (Kh) was found to be about 3 E-04 m/s, the vertical hydraulic conductivity (Kv) roughly 2 E-06 m/s. For Layer 3, also water-bearing sediments (Fig. 1), the vertical and horizontal hydraulic conductivities were about 6.5 E-04 m/s. Layer 2, the semi-permeable interlayer (Fig. 1) acts as an isolator, whose horizontal hydraulic conductivity was determined to be about 4.46 E-04 m/s, vertical hydraulic conductivity some 3 E-07 m/s. Results of the hydraulic groundwater model calibration are presented in table 1.

The effect of the interlayer on the groundwater flow was manifested through the piezometric head difference between the upper and lower water-bearing layers. The conclusion was that it is extremely important

data, model optimization and model calibration is provided elsewhere.

Briefly, this model included schematized layers of the alluvial complex of the Sava River. The Sava River and Lake Sava were specified in the model using prior cross-sectional measurement data. The effect of the interbed on groundwater flow is reflected in a piezometric head difference between the upper and lower water-bearing layers. Distance from Sava River to well Rb-16 is approximately 50 meters and the laterals tap the lowest alluvial water-bearing stratum, at a depth of some 30 m.

The conclusion was that the hydrogeologic characteristics of the interlayer (position, areal extent, thick-

Fig. 4. Piezometric head difference between lower and upper layers (floor, roof, and interlayer).

for the discharge capacity of the well, and the site as a whole, to determine the hydrogeological characteristics of the interlayer (position, extent, thickness, filtration parameters). Fig. 4 shows the piezometric head difference between the upper and lower water-bearing layers, as a result of the presence of the schematized continuous interlayer, under the operating conditions of well RB-16.

Transport model of selected pharmaceuticals in groundwater

WODA was used to calculate sorption according to the following equation:

$$b = \frac{1 - Sy}{\rho_b Kd} \qquad (4)$$

where: b – distribution coefficient water/soil (-), Sy – effective porosity (-), ρ_b – bulk density (g/mL), Kd – experimentally-derived linear sorption coefficient (mL/g).

In the present study, an effective porosity of 0.15 was set for the first water-bearing layer (Layer 1) and 0.12 for the second water-bearing layer (Layer 3). For the semi-permeable interlayer (Layer 2), an effective porosity of 0.07 was specified based on calibration of the hydrodynamic model. The average concentrations of carbamazepine were approximately the same in the surface water and groundwater samples, such that it was not possible to accurately determine the degradation half-life with the transport model. Therefore, the conclusion was that carbamazepine did not degrade in groundwater or, in other words, that its degradation half-life was much longer than the groundwater travel time from the river to the well under the considered site conditions (TERNES et al., 2007; HAMANN et al., 2016).

Since the model comprised three layers, a different sorption coefficient was specified for each one. Layer 2 was the semi-permeable interlayer and its sorption coefficient was set as equal to that of the river sediment (Table 1) for both models. For Layer 1 and Layer 3, Kd values were set for different models; batch experiment values (Table 1) – water bearing sediment (model 1) and field experiment values (model 2) were assigned (Table 1).

Experimentally-derived data were specified as the boundary conditions in the transport model and served as a basis for defining the minimum degradation half-life of the selected pharmaceuticals. For the Sava River, the boundary condition was the average concentration of the selected pharmaceuticals, and the degradation half-life was determined by transient simulations, where the experimentally-derived sorption coefficients Kd were specified in the existing hydro-

dynamic model. Half-life was calibrated until the obtained value for concentration in well Rb-16 was equal to the average monitored concentration at well Rb-16 (in the case of detected pharmaceuticals). For pharmaceuticals that were not detected in well Rb-16, the half-life was calibrated until the obtained concentration in well Rb-16 reached the value equal to ½ LOD.

Results and discussion

Monitoring of selected pharmaceuticals

During the long-term study (seven years), the two metamizole metabolites, 4-FAA and 4-AAA, were the most frequently (64%) detected pharmaceuticals in the Sava River samples. The average concentrations were 34 ng/L (4-FAA) and 13 ng/L (4-AAA). However, the detection frequencies in the groundwater were relatively low. The detection frequency of 4-FAA was 25%, with an average concentration of 1.85 ng/L, and that of 4-AAA 12.5% with an average concentration of 1 ng/L. Higher concentrations of 4-AAA have been detected in surface water samples of the Velika Morava River (Serbia) – 512 ng/L (KOVAČEVIĆ et al. 2016), as well as in Spain – 811 ng/L (GRACIA-LOR et al. 2011). Previously, 4-FAA was detected in the Tisa River in Serbia, with a concentration of 186 ng/L (RADOVIĆ et al., 2015) and in considerably higher concentrations in Spain – 871 ng/L (GRACIA-LOR et al., 2014). 4-AAA and 4-FAA were detected in low concentrations in BGS well Rb-16, compared to other studies (TEIJON et al., 2010; DE JONGH et al., 2012). Carbamazepine was detected in 50% of the surface water samples, with an average concentration 6 ng/L. In the groundwater samples from well Rb-16, carbamazepine was detected in 75% of the samples and the average concentration was the same as in the surface water (6 ng/L). Other studies report much higher carbamazepine concentrations in surface water. Carbamazepine had previously been detected in higher concentrations in surface water in Serbia – 35 ng/L (PETROVIĆ et al., 2014) and 94 ng/L (KOVAČEVIĆ et al., 2016), as well as in groundwater in Serbia – 4 ng/L (PETROVIĆ et al., 2014) and 41 ng/L (KOVAČEVIĆ et al., 2016). Trimethoprim was detected in 14% of the Sava River samples with an average concentration of 8.7 ng/l, but there was no positive detection in the groundwater samples. These concentrations of trimethoprim were similar to previously reported concentrations in Serbia (PETROVIĆ et al., 2014). Consequently, a value of ½ LOD (limit of detection) was adopted for average concentration calculations where the selected pharmaceuticals were not detected in the samples. This value was assumed when the transport model inputs were defined.

The results showed that carbamazepine was detected in roughly the same concentrations in the river and

the corresponding well (about 6 ng/L on average). However, the detected concentrations of carbamazepine were so low that averaging errors were likely. River discharge during the study period varied from 300 to 2100 m³/s, as did the concentrations of diluted pharmaceuticals of anthropogenic origin, such that generally higher concentrations were detected at low discharges. The metamizole metabolites 4-AAA and 4-FAA were detected in both surface water and groundwater. The concentrations of trimethoprim, 4-AAA and 4-FAA detected in the Sava River were several times higher than those detected in well Rb-16, so that it was possible to determine the degradation half-life with the transport model.

Results of the sorption experiment

The sorption equilibration time was determined when the concentrations of the investigated compounds were stabilized in the supernatant. The results demonstrated that sorption largely increased gradually with the passage of shaking time and the optimal sorption equilibrium was reached after 24 h and within 48 h, so 48 h was chosen as the equilibrium time for all the compounds (RADOVIĆ et al., 2016). The obtained data fitted well with the linear model (2), as indicated by mainly high regression coefficients for all the pharmaceutical compounds, $R^2 = 0.68$–0.92. The lowest regression coefficient R^2 was obtained for carbamazepine ($R^2 = 0.68$) and 4-FAA ($R^2 = 0.69$), in the case of river sediment samples. The individual linear sorption coefficients are listed in Table 2.

organic carbon content could be the main driver of the sorption process; and results showed a significantly higher sorption coefficient, Kd. The dominant fraction of the river sediment sample was 0.032–0.063 mm and consisted of: clay (0%), silt (93.5%), sand (5.22%), and gravel (0%).

The sorption coefficients ranged from Kd = 0.87 mL/g for 4-FAA to Kd = 6.74 mL/g for carbamazepine in the water-bearing sample (BGS), and from Kd = 5.57 mL/g for carbamazepine to Kd = 15.61 mL/g for trimethoprim in the river sediment sample, indicating the minimum and maximum sorption capacities of the particular compounds in different sediments.

The results showed that the sorption coefficients of the same compounds could be appreciably different for different sediments, which could be caused by the complex structure of the sediments, diverse ratios of their constituents (clay, silt, sand, etc.), and different organic carbon content of the sediment samples.

Results of the *in situ* experiment

The linear sorption coefficients (Kd) and retardation coefficients (Rd), based on the results of an *in situ* experiment described in more detail in a previous study (KOVAČEVIĆ et al., 2016), are presented in Table 3.

The sediment sample from the new borehole was analyzed and the organic carbon content found to be approximately 0.229%. The organic carbon content was relatively low, so it was not the predominant driver of the sorption process. The dominant fraction of the sample was 2–16 mm and consisted of: clay (0%), silt (0.42%), sand (38.83%), and gravel (60.52%).

Table 2. Linear sorption coefficients Kd of all the investigated pharmaceuticals.

Pharmaceutical	Water-bearing sample (Belgrade Groundwater Source)		River sediment	
	R^2	Kd (ml/g)	R^2	Kd (ml/g)
Trimethoprim	0.84	6.21	0.71	15.59
4-AAA	0.82	1.56	0.81	10.58
4-FAA	0.98	0.87	0.68	14.33
Carbamazepine	0.71	6.74	0.69	5.57

The results showed that the values derived from the *in situ* experiment were considerably lower than those from the batch experiment. Trimethoprim had the highest Kd value and Kd of carbamazepine was higher than that of 4-AAA. According to these results, the fastest moving pharmaceuticals in the *in situ* experiment were 4-AAA and carbamazepine, and trimethoprim and 4-FAA were the slowest.

The first sediment sample from a new borehole was analyzed and the organic carbon content found to be 0% in the water-bearing layer sample. It was clear that the organic carbon content was not the predominant driver of the sorption process. The dominant fraction of the water-bearing layer sample was 0.032–0.063 mm and consisted of: clay (0%), silt (0%), sand (94.74%), and gravel (5.26%). The second sediment sample from the riverbed was analyzed and the organic carbon content found to be 1.28 %. In this sample the

Field experimental conditions significantly differ from laboratory batch experimental conditions. Besides different scale ratio between filed experiment (*in situ*) and batch experiment, there is a natural flow of groundwater along preferably flow paths during filed experiment, which have significant influence on the groundwater velocity in aquifer. Besides, sediment sample analyzed during batch experiment has several times smaller grain size diameter and sorption process is more pronounced. The in-situ sample is gravel dominated and

Table 3. Linear sorption coefficients Kd and retardation coefficients Rd of the analyzed pharmaceuticals.

Pharmaceutical	Rd	Kd (ml/g)
Trimethoprim	7.7	0.64
Carbamazepine	2.2	0.18
4–AAA	1.88	0.15
4–FAA	6.87	0.57

Fig. 5. Results of trimethoprim simulation.

it has lower sorption potential than the sand dominated batch sediment sample. Sediment samples from filed experiment usually have several times smaller fraction of organic matter in relation to sediment samples analyzed during batch experiment, and sorption process on organic matter is more pronounced in laboratory conditions which influence the final result, respectively higher obtained linear sorption coefficients.

Calculation of minimum half-life of the selected pharmaceuticals

Table 4 show minimum half-life results based on model calculations and linear sorption coefficients of the BGS water-bearing sediment sample (model 1), as well as the results of the field experiment (model 2).

When the sorption parameters based on the batch experiment with the sample from the BGS water-bearing layer (model 1) were specified under transient conditions, the minimum degradation half-life of trimethoprim could not be calculated. According to the sorption coefficient derived from the field experiment (model 2), the minimum half-life was ≈ 600 days. Fig. 5 shows simulation results, with a trimethoprim breakthrough curve without sorption or degradation on the way from the river to the well (tracer – no sorption and degradation), and the time difference
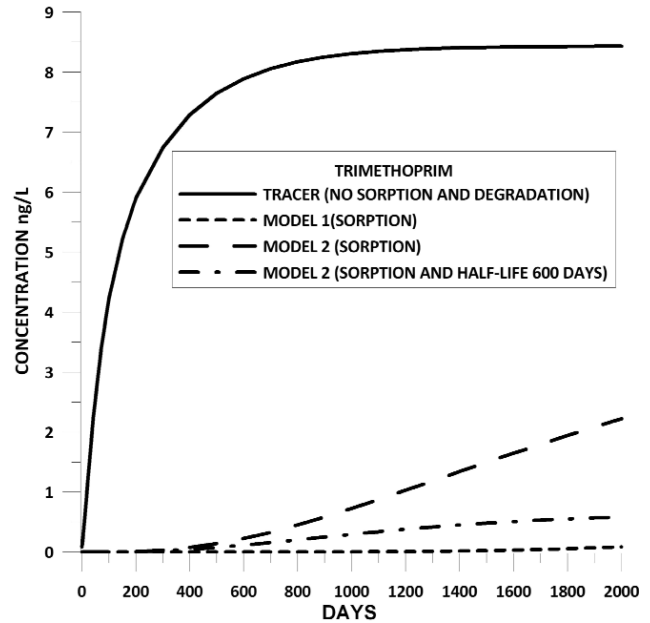
between the occurrence of trimethoprim for different models and minimum half-life. The experimental half-life of trimethoprim in other studies is considerably shorter, ≈ 1 hour (BERTELKAMP et al., 2014), so the result obtained with this model could not be used in practice because trimethoprim was readily degradable (STORCK et al., 2012).

According to the simulation results, 4-AAA has a minimum half-life ≈ 1000 days for model 1 parameters and a minimum half-life ≈ 300 days for model 2 parameters (Fig. 6). It is clear that model 2 yielded a minimum half-life which was shorter than that of model 1 by a factor of three.

In the case of 4-FAA, model 1 gave a half-life ≈ 550 days and model 2 a minimum half-life ≈ 420 days (Fig. 7). There was no half-life data on the metamizole metabolites 4-AAA and 4-FAA during the field expe-

Table 4. Transport model parameters and results of minimum half-life calculations (n.c. – not calculated).

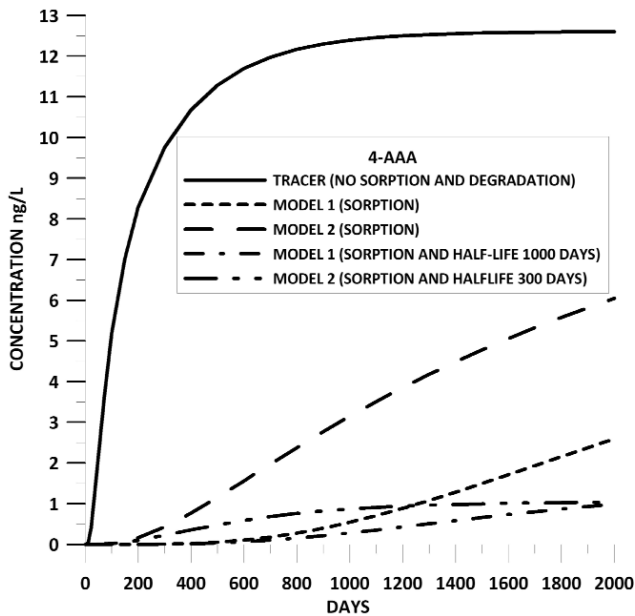| Pharmaceutical	Average concentration in Sava River	Average concentration in well Rb-16	Layer	Distribution coefficient b (-)		Calculated minimum half-life (days)	
				Model 1	Model 2	Model 1	Model 2
Trimethoprim	8.4 ng/l	–	1	0.09	0.88	n. c	≈ 600
			2	0.05	0.05		
			3	0.09	0.88		
4-AAA	13 ng/l	1 ng/l	1	0.34	3.56	≈ 1000	≈ 300
			2	0.08	0.08		
			3	0.34	3.56		
4-FAA	34 ng/l	1.84 ng/l	1	0.61	0.99	≈ 550	≈ 420
			2	0.06	0.06		
			3	0.61	0.99		

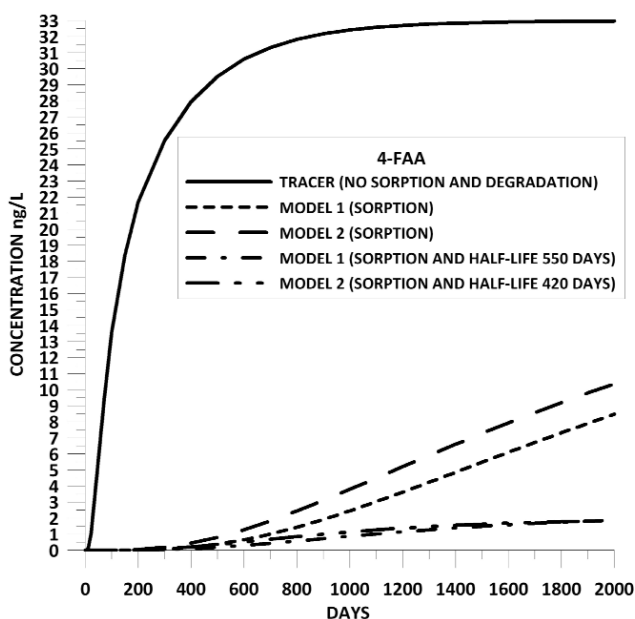Fig. 6. Results of 4-AAA simulation.

Fig. 7. Results of 4-FAA simulation.

riment, so that these results were obtained for the first time from model calculations.

Obtained results have several uncertainties. Calculated half-life for the selected pharmaceuticals represents only minimum calculated value. In practice, half-life is certainly lower. Also very low pharmaceutical concentrations are limiting factor, as input data in transport model, because analytical method and low concentrations significantly influence on the precise final result. Besides that, in this case pharmaceutical were detected with very low concentrations and frequency of occurrence in analyzed groundwater sam-

ples. Result are site specific and in other studies with different input data for groundwater pharmaceutical transport model and different natural conditions (for example oxic conditions in groundwater, dilution from hinterland of well ect.), final result can significantly differ. Calculated half-life for analyzed pharmaceuticals could be used for different sites and field studies with similar natural conditions, such as alluvial aquifers with similar sediment, travel time longer than 100 days, anoxic groundwater and no dilution of water in the well with groundwater from the hinterland.

In further research, groundwater transport model should be used for other regulated pollutants with higher concentrations and frequency of occurrence in surface water and groundwater, and the final result will have less uncertainties. Application of studied groundwater transport model, provide data on the potential for degradation that reflect natural conditions, with respect to batch degradation kinetic experiments in laboratory conditions.

Conclusions

Based on the transport results, it is clear that all the investigated pharmaceuticals, except the persistent carbamazepine, degraded during riverbank filtration from the Sava River to the corresponding well Rb-16. During the study period, the monitored concentrations of non-persistent pharmaceuticals were much lower in groundwater than in surface water, suggesting that there is a significant effect of sorption and degradation processes on the occurrence of non-persistent pharmaceuticals.

However, field conditions differed from laboratory conditions. Given that the effect of scale is very important, this had a significant impact on the final results. Apart from the experiment scale, the semi-permeable layer affected groundwater velocity and groundwater flow under natural conditions, and consequently influenced the final results.

According to the results, information relating to the sorption coefficient was a very important factor. Considerably different results were obtained with the various samples used to experimentally determine linear sorption coefficients. The results indicated that other sorption mechanisms are equally important for the transport of pharmaceuticals in groundwater, because the organic content in the analyzed samples was negligible. The field data (model 2) yielded a sorption coefficient that closely reflected natural conditions. According to the sorption coefficients obtained from the batch experiment (model 1), the minimum degradation half-life was significantly longer, which would have a considerable effect on the travel time from the Sava River to the radial collector well Rb-16. Such data are highly relevant for delineating sanitary protection zones and predicting potential impacts of pollution from anthropogenic sources.

Besides, the results indicated that the degradation half-life was directly related to the sensitivity of the analytical methods used to determine the concentrations of the pharmaceuticals, due to very low concentrations and limits of detection, as well as to the data used to develop the hydrogeological and hydrodynamic model (boundary conditions).

Acknowledgement

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Резиме

Модел сорпције и деградације одабраних фармацеутика: студија случаја Београдског изворишта подземних вода

Извориште подземних вода Београда се налази у приобаљу реке Саве и већим делом на територији града Београда, што чини извориште рањивим на антропогене утицаје. Око половине укупне количине воде за пиће града Београда представља воду која је пореклом из савских алувијалних подземних вода. У Републици Србији од укупне количине воде за пиће око 70 % се захвата из издани, од чега више од 50 % чине алувијални аквифери. Применом обалске филтрације речна вода се додатно пречишћава филтрацијом кроз аквифер, који се може се третирати као екстензивни физичко – биохемијски реактор, што је веома важно са аспекта третмана речне воде и смањења ризика од акциденталног загађења.

У сврху испитивања транспорта материје подземном водом од реке ка бунару, спроведено је периодично испитивање појаве одабраних фармацеутика, како би се добили улазни подаци за квантификацију процеса самопречишћавања. Поред тога, спроведена су и експериментална одређивања коефицијената сорпције, као и теренски опит ињектирања трасера – NaCl, а затим и одабраних фармацеутика, како би се добило кашњење у односу на трасер.

У раду је приказана примена математичког 3Д модела за анализу транспорта одабраних фармацеутика на путу од реке Саве до коресподентног бунара РБ-16 са хоризонталним дреновима београдског изворишта, који се налази у анизотропној средини са издвојеним слабопропусним слојем, испод кога се захвата подземна вода.

На основу хидрогеолошког модела, који је претходно развијен у Институту за водопривреду "Јарослав Черни" и података који су добијени експерименталним и теренским одређивањем коефицијента сорбирања, анализиран је период полураспада за поменуте фармацеутике и приказана је просторно – временска анализа транспорта у подземним водама од реке ка бунару.

Резултати показују да је одређивање периода полураспада у директној вези са осетљивошћу аналитичких метода за одређивање концентрације фармацеутика, због веома малих концентрација и осетљивости прага детекције, као и са подацима који се односе на формирање хидрогеолошког модела (гранични услови). Други битан фактор је податак који се односи на коефицијент сорбирања. Може се видети да за различите узорке, за које је експериментално и теренски одређивана изотерма сорпције, добијамо знатно различите резултате. Подаци, који су добијени теренским експериментом, дају коефицијент сорбирања који најприближније одговара условима у природи, односно на основу експерименталних података добијамо већи период полураспада, што значајно утиче на време транспорта. Наведени подаци су веома значајни са становишта одређивања концепције за формирање зона санитарне заштите и предвиђања могућег антропогеног загађења.