A Method Selecting Antibiotics for Monitoring in Municipal Wastewater

Jaafar N. And Voulvoulıs N.

Centre for Environmental Policy, 15 Prince's Garden

South Kensington Campus, Imperial College London

London SW7 2AZ, United Kingdom Affiliation and address

*corresponding author:

e-mail: n.voulvoulis@imperial.ac.uk

Abstract

The widespread occurrence of emerging pollutants in aquatic environment, particularly in wastewater has been well documented in recent years. Pharmaceuticals have emerged as a major class of contaminants, where antibiotics are one of the most frequently observed classes. Of emerging concern is the relationship between the occurrence of antibiotics in the environment and the development of antimicrobial resistant pathogens. The incomplete metabolism and the improper disposal of unused antibiotics often leads to concentrations detected in wastewater, which lead to environmental and human health issues. However, there is currently no structured decision approach systems for making explicit and transparent decisions for antibiotics monitoring in wastewater. The paper presents findings of a recent study that prioritize and rank critically important antibiotics to wastewater treatment based on multi-criteria analysis (MCA) approach. A data set consisting of 14 antibiotics classes and seven evaluation criteria, considering antibiotics pathways into the environment (source, occurrence, fate, effect and toxicity) were used to select antibiotic classes for further study. Five critically important antibiotics were identified for further monitoring studies. The study presents an effective methodology to identify candidate antibiotics for monitoring in wastewater treatment considering usage data, fate in treatment and environmental concerns.

Keywords: antibiotics, multi-criteria analysis (MCA), wastewater, monitoring, ranking

1. Introduction

In recent years, a significant number of emerging pollutants have been frequently detected in all sectors of the environment. Emerging pollutants are defined as any synthetic or naturally occurring chemicals that are not commonly monitored in the environment but have the potential to enter the environment and cause known or suspected adverse ecological or human health effects. These contaminants mainly include chemicals found in pharmaceuticals, personal care products, pesticides, surfactants, and household products. Currently, emerging pollutants are not included in international routine monitoring programs, thus their fate, behavior and ecotoxicological effects are rarely well understood (Geissen *et al*., 2015).

Antibiotics are regarded as one of the most important class of pharmaceuticals utilized in human and veterinary medicine, as well as in improving growth rate of livestock (Sarmah *et al*., 2006). Antibiotics or antibacterial are a special group of human-made compounds of natural origin from sources such as fungi and bacteria. The presence of antibiotics in the ecosystem has been known for almost 30 years. The increase in the consumption of antibiotics depends heavily on the intensiveness of its application (Aminov, 2009). There are diverse classes of antibiotics that are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity.

Continuous exposure of antibiotics to the environment can enhance the selection and fostering of resistant bacterial strains (Kümmerer, 2004). In addition, due to their continual input into the environment and permanent presence, antibiotics are also considered to be pseudo-persistent contaminants (Hernando *et al*., 2006). It is now established that these compounds enter the environment through several sources and pathways. Figure 1 shows possible sources and pathways for the occurrence of antibiotics residues in the environment. The excretion of incompletely metabolized antibiotics by humans and animals is the primary source of antibiotics in the environment.

It has been demonstrated that antibiotics are, in general, poorly absorbed by the human body. Most antibiotics are not completely metabolized and between 30- 90% are excreted unchanged via urine and feces, eventually reaching municipal wastewater treatment plants (McArdell *et al*., 2003). The conventional wastewater treatment plants are insufficient for the complete removal of antibiotics from wastewater, indicating their ineffective treatment methods. Therefore, wastewater

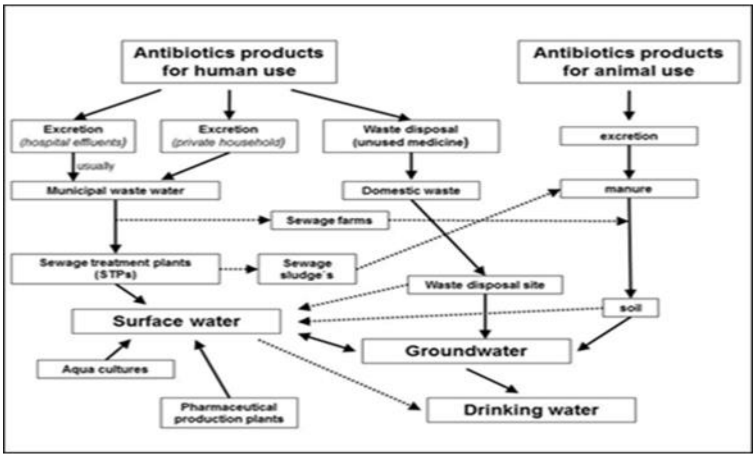

Figure 1. Possible sources and pathways of antibiotics into the environment

treatment plants act as the dominant point of pollution source and principal pathway for human antibiotics during their transfer process into environment (Gulkowska *et al*., 2008). Generally, the detected antibiotics concentration in wastewater influent and effluent are ranged from several hundred ng L-1 to several mg L-1. The introduction of antibiotics into the water environment through anthropogenic sources can constitute a potential risk for human health and stability of ecosystem (Kolpin *et al*., 2002). Until recently, previous studies mainly focused on the sources, occurrence and fate of antibiotics as well as their concentration and overall removal efficiencies in wastewater (Hirsch *et al*., 1999; Gulkowska *et al*., 2008; Rosmann *et al*., 2014). However, there have been almost no reliable studies on the systematic assessment for antibiotics monitoring, suggesting a need of a ranking procedure to be implemented. Consideration of a conceptual and holistic approach which combines different criteria and perspectives could provide a valuable tool for developing explicit and transparent decisions. The structured and justifiable tools would provide a valuable system of performance metrics quantifying both scientific and decision makers' values and views (Linkov *et al*., 2007). The rational decision making in the selection of critically important antibiotics is helpful to provide a comprehensive profile of antibiotics by considering interrelations and interdependencies between a set of different criteria. Multi-criteria analysis (MCA) has been indicated as the appropriate set of tools to compare alternatives that facilitate a fair discussion about different management options and to provide information about consequences of different options (Schuwirth *et al*., 2012). The approaches are diversely classified into measurement models, outranking models and reference-level models (Thokala and Duenas, 2012). MCA is a set of techniques that determines the performance of the alternatives with respect to each criterion and the relative importance of the evaluation criteria with respect to the overall objective of the problem. It is an operational evaluation and decision support approach that is suitable for addressing complex problems featuring high uncertainty, different forms of data and information, and conflicting objectives (Wang *et al*., 2009). The intent of this paper is to develop an effective ranking system to identify candidate antibiotics for monitoring in wastewater treatment using 7 criteria: (1) consumption, (2) excretion rate of original compound, (3) influent concentration, (4) log Kow value, (5) removal efficiency, (6) concentration in surface water, and (7) toxicity for different classes of antibiotics. The proposed system is expected to provide a comprehensive framework with clear information by making tradeoffs explicit.

2. Methodology

The following sections briefly present method for antibiotics ranking and prioritizing in environmental monitoring. Fourteen classes of antibiotics were considered. Antibiotic classes in this study cover various chemical groups such as penicillins, quinolones, sulfonamides, tetracyclines, macrolides, polypeptides, cephalosporines and lincosamides. Antibiotics classes were selected according to the information found in the literature on their occurrence and ubiquity in the aquatic environment, as well as on their existence in the market.

The present approach proposed a system which consists of alternatives, criteria and sub-criteria with the overall rank score for a set of different alternatives. The standard process requires (1) defining unstructured problems, (2) identifying alternatives and evaluation criteria, (3) measuring alternatives' performance; the alternatives are scored against the criteria in a performance matrix, (4) scoring alternatives and weighting criteria, (5) calculation of overall rank score, and (6) results interpretation. Figure 2 presents the overall framework of the antibiotics ranking system. The selected antibiotic classes will be scored and ranked where their overall performance will be calculated by means of a linear additive model, once weights and alternatives scores have been derived (Saaty, 2005).

2.1 Criteria Selection

To understand the environmental risks and effects of residual antibiotics in wastewater, appropriate risk assessment processes and related prioritization system must be developed. Environmental risk assessment is broadly defined as the combination of a probability of occurrence and fate of some exposure event with its associated hazard effects (Guillén *et al*., 2012). For antibiotic ranking, the development of criteria and sub-criteria are characterized by cause effect relationship approach and through the overall pathway of the antibiotics into environment after administration. Developing reliable evaluation criteria is a prerequisite for selecting the best alternative that requires parameters

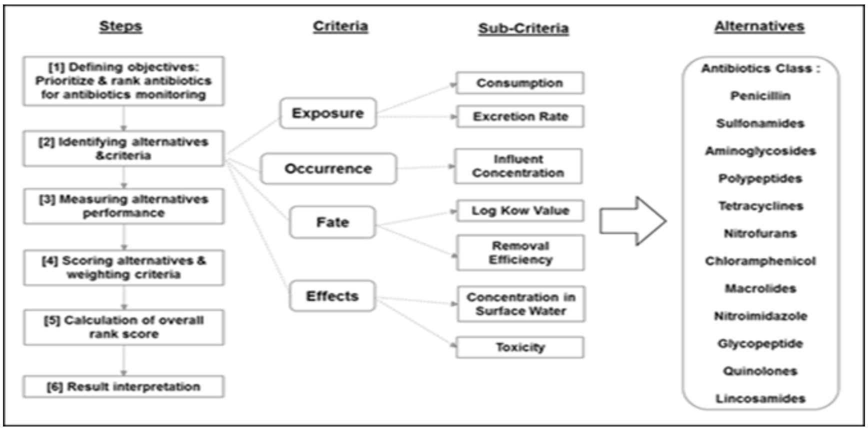

Figure 2. Overall framework of the antibiotics ranking system

related to the reliability, practicality and limitations of measurement (Wang *et al*. 2009). The selected criteria to evaluate in this study divide mainly into four aspects: source, occurrence, fate and effect. However, these main criteria categories are too broad to be used directly in evaluating antibiotics preference, and sub-criteria within each of these categories are developed (Figure 2). The first criterion ‘source’ is represented using two sub-criteria: (1) consumption, represented as antibiotics consumption (DDD per 1000 inhabitants per day) and (2) excretion rate, represented as percentage of antibiotics excretion from original compound. For the ‘occurrence’ criterion, the sub-criteria influent concentration (ng/L-1) has been selected to represent the highest concentration of antibiotics in wastewater influent reported from previous literature. The third criterion ‘fate’ is represented by two sub-criteria: (1) log Kow (octanol water partition coefficient) values, which commonly used as a measure of hydrophobicity, and (2) removal efficiency, represented as percentage of antibiotics removal in wastewater effluent. Finally, the criterion ‘effects’ is divided into two sub-criteria of: (1) antibiotics concentration in surface water (ng/L-1), and (2) toxicity, represented using lethal concentrations for 50% kill (LC50) for indicator species. This indicator describes the potential hazards of the active ingredient only due to acute exposure of chemical and are used in this study to get maximum value of the parameter.

3. Results

Multi-criteria analysis was conducted based on AHP method in identifying candidate antibiotics for antibiotics monitoring in wastewater. The input data to an MCA includes information on all alternatives and all criteria including sub-criteria. The alternatives are scored against the criteria in a performance matrix.

3.1 Performance Matrix

The performance matrix is a structured M x N matrix, where M is the number of alternatives and N is the number of criteria. In the resulting matrix = [aij]MxN, aij represents the relative performance of ith alternative in terms of the jth criterion based on Eq.1.

Performance matrix = [aij]MxN (1)

The alternatives are scored against the criteria in a performance matrix, which is shown in Table 1. Scores are developed from the performance of alternatives with respect to individual criteria and then aggregated into an overall score.

The weighting elicitation technique, namely the swing-weight procedure was chosen for this study. The criteria weights are determined directly by evaluating the impact of the swings from worst to best in each criterion. Swing weights express the relevance of the criteria by assigning highest weighting to the criterion which is considered will lead to the most important change in outcomes. This study used different weights value for each sub-criteria, which is 10% for consumption, excretion rate of original compound, log Kow value and removal efficiency, and 20% for the sub-criteria of influent concentration, concentration in surface water and toxicity. Once weighted, the criteria are standardized. Standardization are necessary for all attributes to have the same range of measurement and to compare scores. The scores are standardized to a dimensionless value between 0 and 1.

3.2 Overall Score

The main results of the decision support process of the MCA approach for developing antibiotics ranking list are presented in Table 2. In a typical priority list, an antibiotic with a low overall rank score requires immediate attention compared to an antibiotic with a relatively high overall rank score. Table 2 shows an overall rank score of 14 different classes of antibiotics by assuming the equal importance of all criteria for the situation under consideration based on the analytic hierarchical process.

The lowest overall score, indicates the antibiotics performance with the most unfavorable environmental effects. Antibiotics classes of sulfonamides, lincosamides and penicillins (equal overall score), quinolones, glycopeptides, and macrolides are considered as the critically important antibiotics, and are selected for future environmental monitoring purposes. The results provided a comprehensive list of critically important antibiotics for future consideration through a systematic and holistic approach.

Table 1. Performance matrix

	Exposure		Occurrence	Fate		Effects	
	Consumption (DDD)	Excretion rate (%)	Concentration in influent (ng/L-1)	Log K_{ow}	Removal efficiency (%)	Concentration surface water (ng/L^{-1})	Toxicity (LC_{50})
Penicillins	5.60	60	6940.00	0.87	99.23	9.91	15000
Sulfonamides	0.24	15	5597.00	0.89	65.70	11.40	6370
Aminoglycosides	0.13	90	7600.00	-7.30	54.75	69.38	5000
Polypeptides	1.10	97	8484.52	-4.20	70.82	69.38	3750
Tetracyclines	2.23	40	2480.00	-0.02	63.10	400.00	2000
Nitrofurans	0.88	40	8484.52	-0.47	70.82	69.38	604
Chloramphenicol	1.33	30	452.00	1.14	44.50	69.38	2500
Cephalosporins	0.50	75	64000.00	1.90	68.00	1.70	20000
Macrolides	1.90	60	1433.00	3.16	83.81	44.76	1270
Nitroimidazoles	1.10	70	3388.00	-3.92	70.82	30.30	3000
Glycopeptides	0.09	76	664.00	-0.48	52.00	11.69	10000
Trimethoprim	1.37	60	7900.00	0.91	69.62	96.50	200
Quinolones	0.46	20	4600.00	0.28	84.35	37.50	2000
Lincosamides	1.33	17.60	500.00	0.56	94.00	50.00	4000

Table 2. Partial score and overall score

	Exposure		Occurrence	Fate		Effects		Overall score
	Consumption	Excretion rate	Concentration in infuent	Log	Removal efficiency	Concentration surface water	Toxicity	
A1	1.0	0.5	0.1	0.2	0.0	0.0	0.3	**0.25**
A2	0.0	0.0	0.1	0.2	0.6	0.0	0.7	**0.24**
A3	0.0	0.9	0.1	1.0	0.8	0.2	0.8	0.48
A4	0.2	1.0	0.1	0.7	0.5	0.2	0.8	0.46
A5	0.4	0.3	0.0	0.3	0.7	1.0	0.9	0.55
A6	0.1	0.3	0.1	0.3	0.5	0.2	1.0	0.39
A7	0.2	0.2	0.0	0.2	1.0	0.2	0.9	0.37
A8	0.1	0.7	1.0	0.1	0.6	0.0	0.0	0.35
A9	0.3	0.5	0.0	0.0	0.3	0.1	0.9	**0.33**
A10	0.2	0.7	0.0	0.7	0.5	0.1	0.9	0.40
A11	0.0	0.7	0.0	0.3	0.9	0.0	0.5	**0.30**
A12	0.2	0.5	0.1	0.2	0.5	0.2	1.0	0.42
A13	0.1	0.1	0.1	0.3	0.3	0.1	0.9	**0.28**
A14	0.2	0.0	0.0	0.2	0.1	0.1	0.8	**0.25**

4. Discussion

The information for the criteria used in the MCA method was based on a broad review of literature and not from an implementation of any analytical processes. This study used all available occurrence and fate information for antibiotics in wastewater influent and effluent as well as in surface water. Due to lack of many full-scale antibiotics monitoring studies, it was difficult to obtain occurrence information of a given antibiotics in both wastewater influent and effluent, as well as in surface water in the same published study. Generally, previous studies have attempted to assess the environmental risks of antibiotics in water matrices using their occurrence, fate and effects criteria (Mutiyar and Mittal, 2014; Zhou *et al*., 2016). However, there is currently no available studies which consider a systematic method in developing antibiotics ranking for environmental monitoring. The multiple criteria-based ranking approach would provide comprehensive information on the antibiotic's pathways into the environment compared to other approaches. This ranking approach is recommended for prioritization purposes.

5. Conclusion

Effective antibiotics prioritization requires a transparent and systematic approach to jointly consider the exposure, occurrence, fate and effects that are relevant in evaluating alternatives and decision making. MCA yields the process ranking and overall scores of 14 different classes of antibiotics respectively, based on criteria which represent the antibiotics pathway from human body to surface water. Generally, antibiotic classes that recorded a low overall score indicate low environmental performance, and therefore the need for further monitoring. The rankings obtained in this study are only valid for the given set of alternatives, criteria, scores and weights, and can be revised if new and better data become available. The MCA method provides a framework for explicitly integrating information. The framework can also be used for other decisions, as well as other environmental monitoring fields. Finally, this study emphasizes that this procedure is a tool for supporting decision-making through a holistic approach, and thus can be useful for value of information analysis.

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