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Emerging Pollutants

Some Strategies for the Quality Preservation of Our Environment

Edited by Sonia Soloneski
and Marcelo L. Larramendy

EMERGING POLLUTANTS - SOME STRATEGIES FOR THE QUALITY PRESERVATION OF OUR ENVIRONMENT

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Meet the editors

Sonia Soloneski received her PhD degree in Natural Sciences and is an Assistant professor of Molecular Cell Biology at the Faculty of Natural Sciences and Museum of La Plata, National University of La Plata, Argentina. She became a member of the National Scientific and Technological Research Council (CONICET) of Argentina in genetic toxicology field. Presently, she is a member of the Latin American Association of Environmental Mutagenesis, Teratogenesis and Carcinogenesis (ALAMCTA), the Society of Environmental Toxicology and Chemistry, the Argentinean Society of Toxicology (ATA), and the Argentinean Society of Genetics (SAG). She is authored of more than 320 scientific publications in the field, including scientific publications in research papers, reviewed journals and conferences worldwide. She is a referent for on issues related to genetic toxicology, mutagenesis and ecotoxicology field.

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Contents

Preface

Environmental contamination is a serious problem for our society worldwide, which continuously needs new monitoring and implementation of strategies for the preservation of environmental quality on the best plausible mode. Although a wise terminology with no strict definition is given for emerging pollutants, they can be defined as xenobiotic, synthetic or natural. In addition, different microbial communities that are not usually monitored or regulated have the possibility to introduce, by themselves, into the different environments and, then, exert unfavorable ecological and/or human health consequences.

Emerging pollutants are closely associated with multiple man-made activities such as industry, transport, food production and urbanization, which are necessary for the development of our modern society. In several cases, discharge of emerging pollutants into the environment has likely occurred for an extensive period of time, but detection, identification and quantification may not have been performed until new strategies and methodologies for recognition were developed. In other cases, synthesis of new chemicals or novel applications are forms of use for known contaminants, and final disposal of preexisting chemicals, not necessarily toxic, can generate new sources of emerging pollutants in multiple environmental compartments.

Few regulatory agencies have proposed methods for establishing provisional safety levels of emerging pollutants. According to the United Nations Educational, Scientific, and Cultural Organization (UNESCO), these xenobiotics include mainly "…compounds found in pharmaceuticals, personal care products, pesticides, industrial and household products, metals, surfactants, industrial additives and solvents". The US Environment Protection Agency (US EPA) states that an emerging pollutant "… is a chemical or material that is characterized by a perceived, potential, or real threat to human health or the environment or a lack of published health standards….". However, today there is no international consensus on the term "emerging pollutants" and it remains problematic. It is not easy to conclude which type of xenobiotic, belonging to different classes, should or should not be included in the list of these contaminants because they represent a changing reality, dependent on perspective as well as timing. Emerging pollutants are currently not included in international legislation mostly because there is not enough information on toxicity, behavior and ecotoxicological effects to establish threshold values. In general, the chemical structure of emerging pollutants comprises diverse, and origin, and they can be released from either point or diffuse pollution sources, i.e., effluents of wastewater treatment plants from urban or industrial areas and atmospheric deposition or from crop and animal activities. Despite the rate of scientific publications covering the problematic of "emerging pollutants" input into the environment, the frequency of occurrence, the last fate and the deleterious effects, the knowledge of the real effects of this particular type of xenobiotic remains fragmentary.

Although a vast literature is available on emerging pollutants, this book contains important investigations into the diverse chemical hazards encountered in both anthropogenic and natural environments and provides valuable information about the genotoxicity of several xenobiotics that can negatively influence the health of humans and ecosystems.

This book begins with a chapter presenting an overview of the current advantages and disadvantages of the employ of the rough set theory as a mathematical approach employed for data analysis in the field of air pollution management including the main methodological and operational contributions as an integrated approach for climate risk evaluation as well as management when developing air quality management strategies. The second chapter provides a review of data concerning the employment of exogenous and endogenous nitrogen oxide species implicated in a large diversity of vital functions as well as their use in the medical field against pathogens' infection highlighting the versatility of these nitrosative compounds. The third chapter describes a study employing a simple, fast, and inexpensive method combining solid-phase extraction and ultraviolet spectrophotometry for simultaneous preconcentration and determination of benzophenone and sulisobenzone compounds in wastewater samples. The fourth chapter is focused on the removal of pollutants from wastewater samples by employing magnetic nanomaterials, particularly affected by heavy metals and dyestuffs. Lastly, this book includes a final chapter presenting an approach combining solar photodecomposition and biocarbon adsorption for removing a mixture of antibiotics, e.g., enrofloxacin, oxytetracycline, cephalexin and amoxicillin from the polluted surface water.

The editors of *Emerging Pollutants - Some Strategies for the Quality Preservation of Our Environment* are enormously grateful to all the contributing authors for sharing their knowledge and insight into this book project. They have made an extensive effort to arrange the information included in every chapter. This book is designed to provide some strategies for the preservation of our environmental quality focusing on the different categories of environmental pollutants and their negative consequences on living organisms. The contributions made by the specialists in this field of research are gratefully acknowledged. We hope that the information presented in this book will continue to meet the expectations and needs of all those interested in the different aspects of the ecotoxicology field. The publication of this book is of high importance for those scientists, chemists, technologists, as well as engineers belonging to academia, governmental and nongovernmental institutions and environmental entities, who make use of these different investigations to understand both basic and applied aspects of how the known and newly emerging pollutants can affect our society and to guide them in the future investigations.

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Chapter 1

Rough Set Applied to Air Pollution: A New Approach to Manage Pollutions in High Risk Rate Industrial Areas

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Additional information is available at the end of the chapter

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Abstract

This study presents a rough set application, using together the ideas of classical rough set approach, based on the indiscernibility relation and the dominance-based rough set approach (DRSA), to air micro-pollution management in an industrial site with a high environmental risk rate, such as the industrial area of Syracuse, located in the South of Italy (Sicily). This new data analysis tool has been applied to different decision problems in various fields with considerable success, since it is able to deal both with quantitative and with qualitative data and the results are expressed in terms of decision rules understandable by the decision-maker. In this chapter, some issue related to multi-attribute sorting (i.e. preference-ordered classification) of air pollution risk is presented, considering some meteorological variables, both qualitative and quantitative as attributes, and criteria describing the different objects (pollution occurrences) to be classified, that is, different levels of sulfur oxides (SOx), nitrogen oxides (NOx), and methane (CH_4) as pollution indicators. The most significant results obtained from this particular application are presented and discussed: examples of 'if, … then' decision rules, attribute relevance as output of the data analysis also in terms of exchangeable or indispensable attributes/criteria, of qualitative substitution effect and interaction between them.

Keywords: industrial areas, air pollution, meteorological attributes, rough set approach

1. Introduction

Air pollution in a region depends mainly on the emission of pollutants and on local meteorological conditions. The probability of air pollution occurrences may be estimated by simple atmospheric dispersion models with proper meteorological data and predefined typical air pollution sources [1, 2].

A lot of studies, however, do not give enough information about the possible relationships between sampling and meteorological parameters, as well as their optimal correspondence formal tools in order to enable modeling and determination of patterns which are characteristic of the investigated area. Proposing conceptual models enables decision-makers at many levels to assess and manage air quality as a whole, rather than on a pollutant-by-pollutant concentration. By developing a holistic approach to air quality, it is possible to evaluate its extensive benefits of more effective developments in existing air-quality features, thereby avoiding the growth of air-quality ceilings, and to consider air quality within its wider meteorological context [3, 4]. By establishing why and when air pollution occasions may occur across a region, strategies should be designed and implemented so as to deal with such episodes. The possibility of forecasting pollutant concentration near the ground with high spatial detail offers the opportunity of constantly monitoring and managing the territory. Air-quality modeling procedures can forecast the behavior and the effects of the substances emitted from identified sources, particularly using data from meteorological instruments. These models can supply the distribution of pollutant concentrations on the ground, and are used for thermoelectric power plant management, being very useful in the case of exceptional events, such as when a highly dangerous pollutant escapes [5].

This study analyses the main relationships between air micro-pollution and meteorological conditions of the area surrounding Siracusa, a city located in Sicily. This was done by measuring air samples from a receiving station near a small town called Melilli, a Sicilian industrial area with a high environmental risk rate [6, 7].

This station has been chosen because it allows the production of a complete picture with respect to the amount of micro-pollution data and meteorological variables descriptions [8]. Then the most reliable parameters for the phenomena of the dispersion of micro-pollutants were identified and also the various critical scenarios were checked, so that all available air pollution sources were considered [9–11]. In particular, a specially designed model, with forecasting abilities of air pollution, has been developed, working independently from the knowledge of the local sources [12]. This monitoring model uses temperature and wind vertical profiles, measured by Radar Analysis Support System (RASS, a radar manufacturer-independent system for evaluating the different elements of a radar by connecting to signals) and SOnic Detection And Ranging (SODAR, a meteorological instrument used as a wind profiler to measure the scattering of sound waves by atmospheric turbulence) and concentration data from ground stations. The local values are correlated with the characteristics of the thermal profile and the direction and intensity of the wind at a selected altitude. On the basis of stored and statistically analyzed data, the model is able to forecast the pollution in the area surrounding the ground station [13] and to give useful information about the management of its main sources.

From the methodological point of view, the proposed approach is in the framework of multicriteria decision analysis, where a lot of different points of views, often conflicting one other, are explicitly considered together to support effective decisions. The utility or, better, the necessity of a multicriteria evaluation in public policies has been recently underlined by Munda [14].

The novel method of data analysis applied to the study of air micro-pollution management, the rough set approach (RSA), considers objects described by a lot of both qualitative and/or quantitative attributes and criteria (that is their 'profile'). In this context, inconsistencies between descriptions and risk classes assignments need not be removed prior to the analysis, therefore giving useful information about the quality of the inferred decision rules; moreover, the RSA also allows for highlighting the attributes which most contribute to air pollution among those taken into account for the assessment, giving too some useful information about the management of pollution.

Furthermore, this method is able to identify redundant attributes. This concerns the elimination of superfluous data from the data table, without deteriorating the quality of the results, that is, obtaining the same information of that inferred from the original table, therefore permitting enormous savings in data collection. Additionally, the rough set theory also shows a posteriori the relative importance of the considered attributes and criteria, without requiring a priori any elicitation or assessment of technical parameters (such as importance weights, trade-off, etc.), which are often very difficult to provide and never easily understandable by decision-makers.

The results hereby obtained are just an example of the RSA application, in order to understand how and why it is possible to apply this approach to environmental problems.

This chapter contains other five sections; Section 2 explains the basic principles of rough set theory and its main methodological features; Section 3 shows air micro-pollution analyzed data; Section 4 presents the main decision rules obtained; Section 5 discusses the interpretations of the results from the methodological and operational points of view; and lastly, Section 6 concludes this chapter.

2. The rough set theory

The rough set theory (RST), introduced by Pawlak [15–17], has proved to be an excellent tool for data analysis, even in the presence of inconsistencies and ambiguities. The main idea of the RSA is that every object in the universe U (data to be analyzed) is associated a certain amount of information (data, knowledge), expressed by means of some attributes used for their description (e.g. if the objects are air pollution observed by monitoring stations, attributes may be air temperature, the relative humidity index, direction and wind speed, quantities of some micro-pollutants, etc.). Objects having the same description [18] in terms of these attributes are called indiscernible (similar); the indiscernibility relation thus generated induces a partition of the universe U into blocks of indiscernible objects, called elementary sets or granules of knowledge, which therefore result in information granulation. If set U is divided in some classes, objects indiscernible should belong to the same class to be consistent with the indiscernibility principle.

From the universe U, any subset X can be expressed either precisely (as a union of elementary sets) or approximately. In the latter case, the subset X may be characterized by two ordinary sets, called the lower and upper approximations. The lower approximation of X is composed of all the elementary sets included in X (whose elements, therefore, certainly belong to X), while the upper approximation of X consists of all the elementary sets which have a non-empty intersection with X (whose elements, therefore, may belong to X). A rough set is defined by means of these two approximations, which coincide in the case of an ordinary set. The difference between the two approximations represents the boundary region, whose elements cannot be characterized with certainty as belonging or not to X. The information about objects from the boundary region is, therefore, inconsistent or ambiguous.

The original RSA based on the indiscernibility relation (usually called classical rough set approach) is not, however, able to deal with preference ordered attribute domains (so-called criteria) and preference ordered decision classes (sorting problem), very often crucial for application to real problems in the field of multicriteria decision analysis.

To be able to deal with criteria and ordered decision classes, Greco et al. [19–25] have proposed an extension of the original rough set theory, called dominance-based rough set approach (DRSA), mainly based on the substitution of the indiscernibility relation by a dominance relation: object *a* dominates object *b*, if and only if *a* is at least as good as *b* with respect to all considered conditional criteria. In a similar way, the decision attribute *d* makes a partition of U into a finite number of preference ordered classes, Cl = {Clt, t = 1,…, *n*}, each *x*∈U belonging to one and only one class, Clt∈Cl. We can therefore state a basic consistency principle with respect to the dominance relation: if object *a* dominates object *b* with respect to a set of criteria and *b* belong to class Clt, *a* should belong at least to class Clt (upward union of Clt). Otherwise, there is an inconsistency with respect to the dominance principle. Therefore, *x* belongs to the lower approximation of any subset X of U if all objects dominating *x* belong to at least the same class of *x*, that is, *x* belongs to Clt or better without any ambiguity; x belongs to the upper approximation of X if among the objects dominated by x there is at least an object y belonging to Clt or better. In a similar way, it is possible to define lower and upper approximation of downward union of classes. Also in DRSA, the difference between the two approximations represents the boundary region.

The objects from U can be split into some decision classes by decisional criterion d, obtaining a decision table (DT), where each object x is described using some independent variables, called conditional attributes/criteria, and each object is assigned to a class of this partition, considered as a dependent variable. The quality of classification expresses the ratio between the objects which have been correctly classified and the total number of the elements of the DT, it lies between 0 (any object is not correctly classified) and 1 (all the objects of the universe are correctly classified), and therefore it can measure the goodness of the classification.

Besides, the classification quality may be unaltered if certain conditioned attributes are eliminated because they are superfluous. The minimal sets of the attributes which maintain the same classification quality of the entire table are called reducts. The intersection among all the reducts generates the core (the set of the most important attributes, which consequently cannot be eliminated without deteriorating the quality of the classification). Therefore, the attributes belonging to the core are indispensable, while the attributes belonging to the reducts are exchangeable with one another; the others are actually superfluous.

The relations existing among conditional attributes/criteria and decisional classes in the multicriteria sorting problem are expressed by decision rules. These are logical statements of the type 'if…, then…', where the antecedent (condition part) specifies values assumed by one or more condition attributes/criteria and the consequence specifies an assignment to one or more decision classes. If there is only one possible consequence, then the rule is said to be certain, otherwise, it is said to be approximate or ambiguous. An object $x \in U$ supports decision rule r if its description is matching both the condition part and the decision part of the rule; certain rules are supported only by objects from the lower approximation of the corresponding decision class; approximate rules are supported only by objects from the boundaries of the corresponding decision classes.

Procedures for the generation of decision rules from a decision are complex tasks, and a number of procedures have been proposed to solve it [18, 25–27].

The existing induction algorithms use one of the following strategies:

- the generation of a minimal set of rules covering all objects from a decision table;
- the generation of an exhaustive set of rules consisting of all possible rules for a decision table; and
- the generation of a set of 'strong' decision rules, even partly discriminant, covering relatively many objects from the decision table (but not necessarily all of them).

In this chapter to infer the rules, the jMAF software has been used, that is available for free in the Internet: RSES – Rough Set Exploration System, http://logic.mimuw.edu.pl/~rses , ROSE – ROugh Set data Explorer http://idss.cs.put.poznan.pl/site/rose.html, –jMAF, java Multicriteria and Multi-attribute Analysis Framework http://www.cs.put.poznan.pl/jblaszczynski/Site/jRS.html, and jRank – ranking generator using Dominance-based Rough Set Approach http://www.cs.put.poznan.pl/mszelag/Software/jRank/jRank.html [28].

The rules inferred by DRSA can use also the 'at least' and 'at most' terms in their conditional and decisional parts. All these rules are expressed in a natural language, simple to understand the studied phenomenon and for decision support [22]. This means that the proposed approach actually is also able to explain the reasons of a particular pollution situation, moreover showing the real examples of these (traceability of decisions), and is able to support the management in preventing pollution damages, presenting them the situations where some critical events are most probable. Moreover, parameters like the support (the number of the objects which satisfy both the conditional part and the decisional part of the rule) and the confidence (the ratio between support and the number of the objects which satisfy only the conditional part of the rule, expressed in percentage) help the decision-maker in their choice of the most relevant rules.

We can summarize the main characteristics of the rough set approach as follows. With respect to input information (object description), both quantitative and qualitative data can be considered, even if they present some inconsistencies. With reference to output, information about the relevance of attributes and the quality of approximation can be acquired, and the final results are expressed in the form of 'if…, then…' decision rules, which are sentences that decision-makers find easier to understand [29–31] and using only the most relevant attributes/criteria (i.e. some reduct).

In the case of air pollution problem at hand, for example, we can consider some different decision classes of pollution according to an increasing level of some micro-pollutants (SOx, NOx,…). Since some meteorological variables (conditional attributes/criteria) present a monotonic relationship with the degree of pollution (e.g. the air temperature, the degree of humidity) and other no (e.g. wind direction, etc.), it is very important from both the operational and methodological points of view to take into consideration and to exploit in the appropriate way in the description of the objects and in the rule induction attributes and criteria distinctly. Therefore, we have to consider the indiscernibility relation with respect to the former, the dominance relation with respect to the latter, and the assignment to ordered classes with respect to the decision.

Greco et al. [26] proposed an approach for this kind of real-life multicriteria problems. This can be easily modeled by introducing some appropriate thresholds to discretize the conditional attributes and to characterize different levels of air pollution, for the decision classes. No discretization is required with respect to criteria, using the DRSA.

Consequently, the rough sets could be very efficiently applied in the case of uncertainty derived from the granularity of information. Actually, granules of condition attributes/criteria (objects having the same descriptions or respectively belonging to the same dominating/dominated sets) are used to approximate granules of decision (assignment to some decision classes).

The RSA is therefore very different with respect to the fuzzy sets, where the linguistic imprecision due to the use of natural language is mainly considered, and the membership function aims at indicating in what degree each object belongs to a particular class. Of course, the two approaches are not mutually exclusive, but they can actually be used in a complementary way [32–34]. Using a terminology from image representation, we could say that rough sets are related to the number of pixels of an image (its resolution), while the fuzzy sets represent the number of gray levels between black and white. At an operational level, the implementation of fuzzy sets always requires the definition and specification of particular membership functions, one for each attribute, not easy to specify analytically. Therefore, both classical rough set approach and fuzzy sets are sensitive to the specification of these values and both interesting and useful sensitivity and robustness analysis are actually useful and recommended by moving the level of the thresholds and other parameters [30, 35, 36]. It is not the case of DRSA, where actually no parameter should be elicited, but only some example of decision (from the past experiences of from expert knowledge) is needed to model the preference of the decision-maker.

3. Data description

Air micro-pollution-analyzed data come from an air monitoring network, working since 1975, covering an industrial area of 500 km^2, including the towns of Priolo–Melilli–Siracusa, situated in the province of Siracusa, in the region of Sicily. This industrial area was declared 'a high environmental risk rate place' by the Law 349/86 and covers six surrounding towns (Augusta, Priolo, Melilli, Siracusa, Floridia, Solarino); the landscape is very varied and is formed by sandy hills, mountains, and plains near the coast [37, 38].

In this territory, a lot of chemical plants, energy production industries, and oil refineries are found, as well as members of a private organization, the industrial trust for environmental safety (CIPA, Consorzio Industriale Protezione Ambiente–Environmental Protection Industrial Consortium). In its operative center, CIPA assembles and works out different micro-pollution parameters and various meteorological variables, measured by 12 different monitoring stations. Data collection and processing is useful in statistical analysis and in upgrading air pollution management in order to avoid the air-tested-exceeding threshold qualities, previously established [38–42].

This chapter studies monitoring station in Melilli only, because in this place, data concerning air micro-pollution quantities and weather conditions, present at the moment of pollution sample construction, are thoroughly collected. In fact, in Melilli, monitoring station hourly quantities of some micro-pollutants, such as sulfur oxide, nitric oxide, non-methanic hydrocarbon, ozone, sulfonyl hydrogen, and different meteorological conditions present at the moment of their observations, such as air temperature, relative humidity index, wind direction, and speed are observed and stored. Some previous studies show the evident correlation between these environmental variables and the quantity of air micro-pollution found in the samples. Because of the complete data present in the samples studied, levels of four micro-pollutants (SOx, CH_4, NMHC, NOx) in correlation with the meteorological variables previously mentioned [42, 43] are analyzed in this chapter.

Data recovered from the Melilli monitoring station during 2 weeks, more precisely 1 week in January and 1 in August 2010, have been studied, in order to observe differences of analysis results also on the basis of the different seasons of the year. Daily available recorded 'objects' described both by meteorological variables (condition attributes) and by micro-pollution quantity (decision attribute) have been considered. More than 1000 data records have been analyzed, as an example to which the RSA could be applied.

The selected condition attributes/criteria (descriptors) considered in this analysis are the hour of observation (attribute), wind speed (criterion) and wind direction (attribute), air temperature (criterion), and the relative humidity index (criterion), whereas the levels of the aforementioned micro-pollutants are the decision classes. The descriptors have been chosen because in previous studies [36, 42] they looked like some very important factors, at a local level, influencing air micro-pollution quantity.

4. Results

In spite of the fact that data samples used are restricted to a relatively short period of time (each one only 2 weeks), their analysis allowed us to obtain some interesting results, both from methodological and from operational points of view, which give an idea of the knowledge extraction (in terms of decision rules) from available data using the considered approach and the possibility to use this new method to improve air pollution management. As mentioned before, the final results are expressed in the form of 'if…, then…' decision rules, using at any time a particular (relevant) subset of attributes (reducts), according to the season and the micro-pollutant considered at each time.

In the following sections of this chapter, just some examples of decision rules obtained in our study are presented, useful for understanding and describing concisely pollution effects caused by particular combinations of conditional attribute/criteria values. Such rules, as mentioned before, are very useful in explaining the main reasons of some particular pollution events and can be also used in forecast analysis and for decision support too. The rules were chosen as the most representative among those with the highest degree of confidence, indicating the relative frequency of antecedent ('if' part of the rule) also matching the consequent ('then' part of the same rule) of the considered rule. Apart from the analysis of SOx, CH_4, and NMHC with respect to the January observations (**Tables 1–4**), the considered rules have a confidence equal to one, that means that all the objects match both the antecedent and the consequent in each rule [37, 41, 43].

These decision rules are presented in the form of tables which are very easy to read, showing in the first column the number of the rule and in the other columns the values of the conditional attributes/criteria characterizing that rule. These values are expressed as intervals with respect to attributes (corresponding to the partition of their domain) and as real numbers ('vertices' of dominance cones) with respect to criteria. The last columns of **Tables 1–3** display the confidence of each rule; in the other tables, the confidence of the rules is one. In particular, **Tables 1–4** show results from Melilli Monitoring Station during the month of January, and **Tables 5–7** show the results in Melilli Monitoring Station during the month of August. Each table concerns a different micro-pollutant.

The threshold interval values for the conditional attribute were chosen as following: hour: 0, 1, … 23 and wind direction: N (North), S (South), E (East), W (West), as main direction ±45°. On the contrary, the criteria values were automatically determined by the method applied for

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction	Confidence
1		≥11.55					0.54
2					E		0.54
3						81.9–137.7	0.46
4	13–16				E		0.58
5			≥52.3		E		0.58
6			≥52.3			81.9–117.9	0.58
7					E	81.9–117.9	0.58

Table 1. Melilli monitoring station, January 2010 SOx; threshold = 70 μg/Nm^3.

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction	Confidence
8	13–17	≥9.5					0.21
9	14–17				N		0.21
10	13–17					134.2–190.2	0.21

Table 2. Melilli monitoring station, January 2010 CH_4; threshold = 950 μg/Nm^3.

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction	Confidence
11		≥11					0.36
12					E		0.40
13						107.3–149.7	0.37
14					E	107.3–149.7	0.42

Table 3. Melilli monitoring station, January 2010 NMHC, threshold = 90 μg/Nm^3.

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction
15					E	
16						66.4–111.5
17	11–14	≥ 10.5				
18	10–21		≥ 75.5			
19		≥ 9.7				18.8–117.9
20			≥ 49.6		E	
21			≥ 53.8			67.3–111.5
22				≤ 3.4	E	

Table 4. Melilli monitoring station, January 2010 NOx, threshold = 20 μg/Nm^3, confidence = 1.

them (DRSA). Since the dominance approach is also used for the decisional attribute, pollution is reached 'by definition' depending whether or not the observed value of micro-pollutant is at least equal to the threshold value defined by law and indicated in each table. They are usually some threshold values that it is not allowed to exceed more than three times a year.

In each table, the conditional attributes/criteria are the following: Attribute 1: hour of observation; Criterion 1: air temperature (°C); Criterion 2: air relative humidity index (%); Criterion 3: wind speed (m/s); Attribute 2: wind direction; Attribute 6: wind direction (degrees) with respect to wind speed (measured by SODAR).

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction	Risk Class
23			≥72.8				B–C
24				≤4.8	E		A
25		≥31.3	≥54	≤3.9			A
26			≥37.2	≥3.3			B–C
27			≥33	≥3.7			B–C
28			≥37		N		C
29			≥31.9		N		C

Table 5. Melilli monitoring station, august 2010 SOx, confidence = 1.

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction
30	14–20		≥37.2			
31	6–14					132.5–269.1
32		≥26.3	≥37.1			
33		≥25.9	≥37.6, ≤42.9			

Table 6. Melilli monitoring station, August 2010 CH$_4$ threshold =845 μg/Nm^3, confidence = 1.

Rule	Hour	Air temperature	Humidity	Wind speed	Wind direction	Wind speed and direction
34					E	
35						88.9–103.8
36				≥3.7	E	
37					E	90.5–103

Table 7. Melilli monitoring station, August 2010 NOx, threshold = 20 μg/Nm^3, confidence = 1.

With respect to the decision, in **Table 5**, we consider three decisional classes, coded as following according to the law: A (Emergency), B (Alarm), C (Alert). The corresponding decision rules are expressed in terms of 'at least (≥)' or 'at most (≤)'; therefore, for example, B–C means 'at most Alarm' and A means '(at least) Emergency'. In all the other tables, the decision rules indicate if the considered threshold values are overtaken or not.

The rules in all the above tables represent only a few of several rules obtained by applying the RSA and they are presented here just as examples of easily understandable samples of the results of this analysis. All these rules are of the type 'At least' with respect to the decision, in the sense that if the antecedence is verified, the level of the corresponding micro-pollution is greater than the threshold value. We observe that the selected rules involve in the conditional part only few attributes/criteria each time.

In the following lines, some examples of how reading the decisional rules are presented from **Tables 1–7**. Rule 18 (**Table 4**): between hours 10.00 and 21.00, if the air relative humidity index is at least 75.5%, then the NOx is at least 20 μg/Nm^3, with a confidence of 1. Rule 33 (**Table 6**): if the air temperature is at least 25.9°C and air relative humidity index lies in the interval 37.6–42.9%, then the CH_4 level is at least 845 μg/Nm^3 with a confidence of 1.

5. Discussions

The decision rules concerning CH_4 and NMHC of January 2010 (**Tables 2** and **3**) have a very low confidence level; this means that the considered attributes are not sufficient to explain the phenomenon. Perhaps some attributes are missing and therefore, in order to improve this result, it would be useful to consider further attributes. This is another important methodological feature of the rough set approach, underlining that sometimes more information is needed to better describe some object in order to be able to arrive at well-founded conclusions, that is with a high degree of confidence. On the other hand, the same analysis regarding the observations of August gives very interesting results; we can observe the particular relevance of the degree of humidity in the CH_4 level (**Table 6**) and the crucial role of the wind direction and speed in NOx analysis (**Table 7**). We can also observe that sometimes (e.g. rules 12, 15, 23) it is possible to explain a result using only one attribute, that is with very short and simple decision rules. It should be remembered that a general property of the rough set approach is one that uses all conditional attributes; instead of only attributes from a reduct, we can obtain more concise rules, that is with a greater variety a fewer number of attributes in the conditional part of the rules.

With respect to SOx, we used a greater value for the threshold in January than in August both in order to present the relative pollution level more clearly and to obtain an acceptable confidence degree for same decision rules. Both the analyses of NOx (**Tables 4** and **7**) give excellent results in terms of confidence with respect to all the decision rules obtained, where we can observe a greater relevance of the attributes hour of observation, air temperature, and humidity degree in the analysis of the January data, while a crucial role in the August results is played by winds.

Actually, a first idea about the relevance of the conditional attributes can be directly revealed by the presence frequency of each conditional attribute in the decisional rules, as shown in the **Tables 1–7** (see, e.g. how important the conditional attribute for air relative humidity is in **Table 5**). Some more sophisticatedly important indices can also be computed, for example, according to the Shapley value in the cooperative games in the framework of game theory; the main idea is to compute the contribution to the quality of results by adding another attribute/criterion in the conditional part of the rules, in other words, a degree of the involvement of each attribute in all coalitions of attributes, measuring therefore also the interaction (synergy or redundancy) between the considered attributes [20] (Greco, S. et al., 2001 b). It should be observed that this kind of importance is therefore an output of the analysis within the rough set approach, and not an input information, as usually happens when we use other approaches, as, for example, weighted sum or outranking methods for the comparative evaluation of some objects.

Moreover, the results also show interesting interpretations in terms of a particular kind of trade-off. From the analysis of the couples of decision rules (26,27) (32,33) we can easily observe some cases of trade-off between the values of the couple of attributes in the classical meaning of 'compensation'. From rules (32,33), there is a relationship between air temperature and degree of humidity, in the sense that the different values of air temperature can be compensated by the different degrees of humidity obtaining the same results in terms of pollution. A similar relationship can be observed in the pair of decision rules (26,27) with respect to the degree of humidity and wind speed. This means that a certain capacity of compensation is allowed (trade-off) between the performances of a couple of attributes: a better value on one attribute is able to compensate the worst value on the other and vice-versa.

By observing the following couples of rules (5,6) (9,10) (20,21), we can see that it is possible to obtain the same results in terms of level of pollution considering the combination of one (fixed) attribute/criterion and step by step another one associated with it (example of exchangeable attributes/criteria). In other words, the same decision could be described and explained by different rules, where at each time are present different combinations (in this case, couple) of attributes/criteria that, therefore, are able to describe the same phenomenon independently one another. So, for example, from the couple of rules (5,6), it can be observed that the same result in terms of level of pollution, with the same degree of confidence, is the consequence of the degree of humidity ≥52.3 and wind direction E (rule 5) or the consequence of the same degree of humidity associated with the wind speed and wind direction between 81.9 and 117.9 (rule 6).

Another similar observation can be made comparing rules 6 and 7, where again the phenomenon of exchangeable attributes can be observed that in this case are the air humidity and the wind direction. This means that using the RSA the same effect in the pollution class assignment can be obtained as a result of a combination of an attribute/criterion value each time with other different attributes/criteria, as a particular very interesting 'qualitative substitution effect' between different attributes/criteria. The exchangeable role played independently by some conditional attributes/criteria in combination with a given level of another conditional attribute/criterion (in the previous example, the degree of humidity or the wind direction and speed) results therefore in the assignment of an object to the same decision class of pollution.

With respect to the operational aspect of this approach, it is important to emphasize how obtained results can be used to capably support the decision-maker to manage the pollution risk. Actually, the information given by decision rules can help to understand the main reasons of a pollution event, giving us the explanation of this (its 'traceability') but also for preventing or forecasting dangerous situations, very probable when meteorological conditions similar to those described by the obtained decision rules are approaching (air temperature, humidity degree, wind direction, …).

Another very interesting result using this approach concerns the information we can receive by so-called non-activated rules in improving or in deteriorating the results of a decision. See, for example, rules from **Table 5** and at levels of air relative humidity index. It can be observed that if this value is smaller than 31.9, the SOx will never be at a level higher than the threshold of 10/gr/Nm^3. These rules, therefore, are able to give us useful information about 'critical values' of the conditional criterion air of relative humidity.

More generally, we can say that using this approach we are able to detect some threshold values of one or more condition criteria that can be considered as boundary values to be reached or to be avoided and the combination of two or more attributes/criteria that can be really dangerous for the air pollution. Of course, the meteorological variables cannot be changed by decision-makers. But the rules inferred using the rough set approach can be actually used as guidelines for forecasting in some areas particular cases of pollution events (e.g. emergency, alarm, alert), consequently giving people useful information and suggestions concerning the probable danger of air pollution.

6. Conclusions

The aim of this chapter is to give a first idea of the possibilities offered by rough sets data analysis in the field of air pollution management. In the following, we summarize its main methodological and operational contributions of this exemplary application.

From the methodological point of view, the RSA allows us to take into consideration quantitative and qualitative data, without being in need of their arbitrary transformations.

The relevance of each subset of attributes/criteria is an output of the analysis, and not an input, and therefore does not require elicitation of a priori subjective weights.

It is possible to underline the role of each attribute/criterion in terms of reducts and core; the attributes belonging to the core are indispensable, while the attributes belonging to the reducts are exchangeable with one another; the others are actually superfluous or redundant.

The significance of the results can be measured by peculiar indicators (quality, strength, support, confidence, etc.).

The results are presented in the form of 'if… then…' logical statements, decision rules expressed in simple language and very understandable for the decision-makers.

It is not necessary to remove a priori some inconsistency in the data to be analyzed, but—on the contrary—also these inconsistencies are an important piece of information about the degree of uncertainty of the decision rules inferred (certain or approximate rules, degree of confidence, etc.).

From the operational point of view, the decision rules inferred can be used immediately for managerial purposes as guidelines for preventing or warning people about the risk of air pollution (emergency, alarm, or alert situations), when the weather conditions match or are similar to those shown on the tables and to other rules not included in this chapter.

The decision rules are also able to explain the reasons of particular pollution occurrences, describing the consequences of different meteorological scenarios and their giving a traceability of possible decisions.

Moreover, the results obtained point out other relevant profiles of the phenomenon considered. They clearly show, for example, the more or less important role played by each meteorological variable in the assignment of the actions to different pollution classes, the fundamental relationships between the antecedent (attributes and conditional criteria), and the consequent (ordered decision class). Furthermore, they provide interesting information about the semantic importance of quantitative and qualitative trade-offs between attribute/criteria, that is the role of combination of different levels and/or different pollutants considered together, showing therefore also the main interaction among some meteorological factors. Finally, using the RSA it is also possible to detect some particularly interesting threshold values, of one or more condition criteria, that can be considered as boundary values to be reached or to be avoided.

The decision rules, in fact, could be the basis for the development of air-quality management strategies under the impacts of climate change, that is fundamentally a risk valuation and risk management process involving priority assessment of the impacts of climate change and associated uncertainties, including determination of air-quality targets, the selection of potential management options, and identification of effective air-quality management strategies through decision-support models.

The simple application of the method presented in this chapter shows how it can effectively help decision-makers in making appropriate responses to climate change, since it provides an integrated approach for climate risk assessment and management when developing air-quality management strategies. The risk-based decision-making framework can also be applied to develop climate-responsive management strategies for the other environmental dimensions and appraise costs and benefits of future environmental management policies.

Like any study, this could be improved and a more in-depth study can be carried out. For example, the original database could be enlarged, both in time limits and with reference to the variables considered. If we take into consideration data concerning different years or places, and analyze them by using the same methodology, we can, for instance, eliminate the peculiar effects related occasionally to atypical weather conditions. Moreover, if we extend the analysis to other meteorological variables we could obtain decisional rules which are sometimes easier, more intuitive, and more precise than those obtained by using a smaller number of descriptors.

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Chapter 2

The Hidden Face of Nitrogen Oxides Species: From Toxic Effects to Potential Cure?

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Additional information is available at the end of the chapter

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Abstract

Nitrogen oxide (NOx) species represent ones of the most threatening air pollutants due to their prevalence and harmful impact on the environment and human health. The term NOx gathers mainly nitric oxide (NO) and nitrogen dioxide (NO_2), mostly produced by anthropogenic activities such as transport and industries. Several cellular constituents were already described as NOx targets. These include membranes, proteins, respiratory chain enzymes, lipids, and DNA. Such damages lead to pathologies of lungs, cardiovascular system, and skin because these organs represent the first barrier toward the environment. On the other hand, NOx is also naturally synthetized by several organisms, playing a mediator role in essential cellular functions. However, few data are yet available on NOx activity toward microorganisms. Here, we review data concerning the double face of NOx, including their use in the medical field against pathogens' infections that highlight the versatility of these compounds.

Keywords: NOx, pollutants, signalization, physiopathology, treatment

1. NOx species: the genesis of a major air pollutant

"Yet, pollution is the largest environmental cause of disease and death in the world today, responsible for an estimated 9 million premature deaths" stated The Lancet Commission in 2017. This phenomenon represents an alarming threat for human health, as a major cause of respiratory and cardiovascular pathologies as well as infertility. Moreover, those atmospheric pollutants have severe impacts on the environment and participate in climatic change, acidification, eutrophication, and ecosystem disturbances. Several international and national organizations (e.g. WHO, EEA, and INERIS) aim at reducing the global emission of pollutants, thanks to environmental policies as Kyoto and Gothenburg protocols signed in 1997 and 1999, respectively. After that, an encouraging decrease in air pollutants' levels was measured between 2000 and 2015 [1].

Atmospheric pollutants can be classified into four families: classical, indoor, and organic or inorganic air pollutants. Among the classical ones, which are the principle in amount, sulfur dioxide (SO_2), particle matter, ozone (O_3), and nitrogen oxide (NOx) species are found [2]. The term NOx refers to a wide range of nitrogen-derived compounds, where nitric oxide (NO) and nitrogen dioxide (NO_2) are predominant [3]. Those compounds can be naturally produced at low level by lightnings [4] and volcanic eruptions [5]. However, NOx is mainly generated by anthropogenic activity (e.g., road transport, energy production, industry, and agriculture) (**Figure 1**) [6].

Even if NO and NO_2 represent the main species of NOx, nitrogen exists in several oxidation states in the environment, from N (−III) to N (+V). NO takes a central place in the series of reactive nitrogen species (RNS) [7]. Oxidation and reduction of NO result in the formation of several RNS, including nitrate or ammonium. NO_2 is formed by the reaction of NO with O_2 and can be dimerized to give N_2O_4. The formed reactive species can, in turn, be involved in a wide range of reactions (**Figure 2**).

Nitrogen is an essential constituent of vital macromolecules (nucleic acids and proteins). This atom also constitutes the dinitrogen (N_2) gas, usually abbreviated nitrogen. This gas represents 78% of atmospheric air and is continuously recycled in our environment. First, the atmospheric nitrogen is fixed in the soil by prokaryotes to form ammonia (NH_3), which could be taken up by plants. NH_3 is then converted into ammonium (NH_4^+). Ammonium could be also

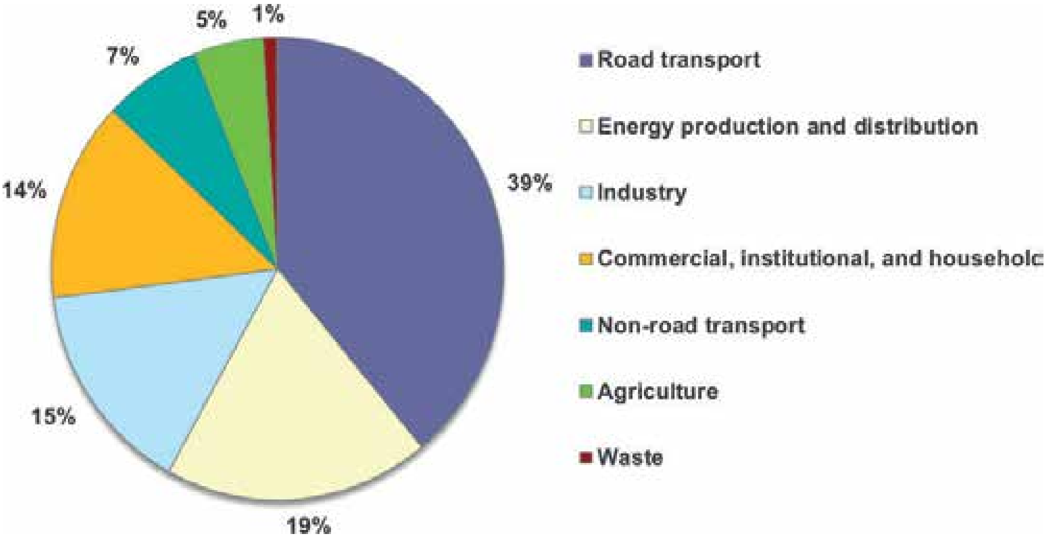


Figure 1. NOx sources linked to anthropogenic activities (according to [1]).

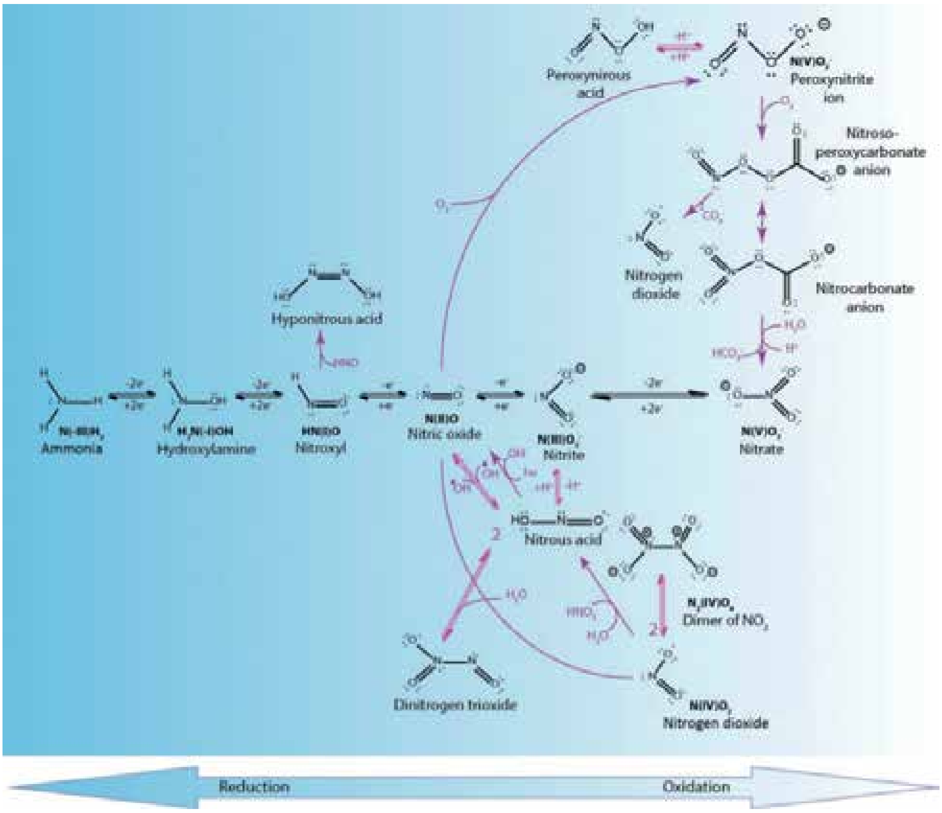


Figure 2. Redox relationships of NOx with other RNS. Black arrow: oxidation and reduction of NO; purple arrow: a wide range of reactions; roman numbers: oxidation state of the nitrogen atom; color gradient: reduction/oxidation state from (−III) to (V).

formed by mineralization of organic matter by decomposers (fungi, worms, and prokaryotes). The second part of the nitrogen cycle is the nitrification of ammonium by prokaryotes leading to nitrite (NO_2^-) formation, which is then further oxidized into nitrate (NO_3^-). Finally, nitrate could be assimilated by plants for their growth or converted into N_2 by denitrifying bacteria (**Figure 3**).

Moreover, nitrogen is also the precursor of NOx. Indeed, NOx formation can be separated into four steps. First, NO is formed in the atmosphere in combination with nitrogen, resulting from the global biogeochemical nitrogen cycle, and oxygen, following combustion (natural or anthropic). Then, this highly reactive compound can be oxidized by oxygen (O_2) to form NO_2. Alternatively, nitrogen dioxide can also be directly formed through catalytic ammonia combustion or nitrosyl chloride oxidation. Then, a temperature-dependent equilibrium is establishing between NO_2 and its dimeric form, nitrogen tetroxide ($N_2O_4^-$). Finally, a photochemical reaction between NO_2 and hydroxyl radicals leads to the generation of ozone (O_3^-) (**Figure 4**).

Even if NO and NO_2 are classified as RNS, their characteristics are very different suggesting their diverse behavior and reactivity. For example, the solubility of NO is very low

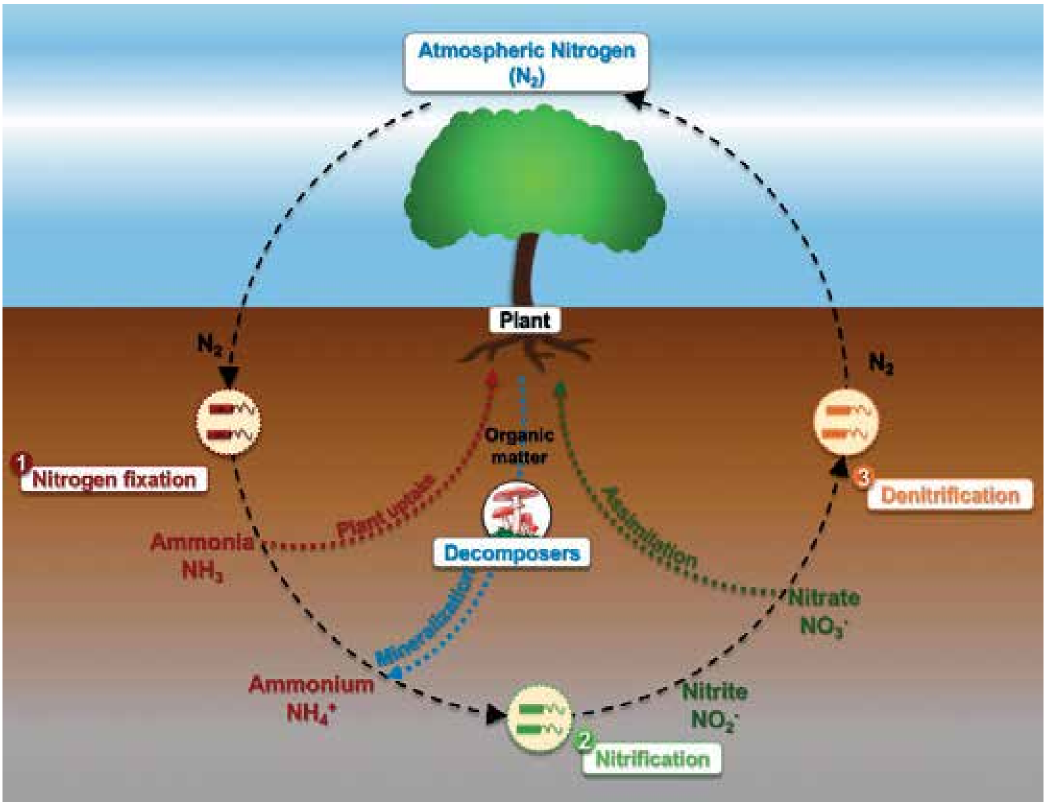


Figure 3. Nitrogen cycle at the interfaces among air, soil, and ecosystem. (1) Fixation of gaseous nitrogen by prokaryotes leading to ammonia (NH_3) and ammonium (NH_4^+); (2) nitrification of NH_4^+ by prokaryotes resulting in nitrite formation (NO_2^-) subsequently oxidized into nitrate (NO_3^-); (3) denitrifying prokaryotes catalyzing the conversion of nitrate into gaseous N_2.

(5.7×10^2 g/L), and NO_2 is highly reactive in water resulting in the formation of HNO_2 and HNO_3 [8]. Moreover, the half-life time of those compounds highly differs because NO_2 half-life is around 35 h, whereas that of NO is almost impossible to determine because of its high reactivity [9]. The permeability of both compounds is also totally unrelated: NO has a lipophilic behavior with consequently a high-membrane permeability. This can be illustrated by the high-diffusion ability of NO toward the membrane. Conversely, the permeability coefficient of NO_2 is estimated about 5 cm s^{-1} suggesting a lower diffusion power toward biological membranes [10]. In spite of these differences, the penetration of NO and NO_2 inside cells and their high reactivity are at the origin of their pathogenic potential on human health, particularly when physiological elimination thresholds are exceeded. Since skin, respiratory tract, and lungs are the first barrier toward those gases, these organs are evidently the principle targets of these compounds and their derived species [11–13]. However, their diffusion deeper in the organism can lead afterward to other severe effects, for instance, on the cardiovascular and immune systems [12, 14]. Human health effects range from reversible (nausea, breathing difficulties, and asthma symptoms) to irreversible (cardiovascular defects, emphysema, and immunopathologies), including cancer induction in the worst cases (**Figure 5**) [15].

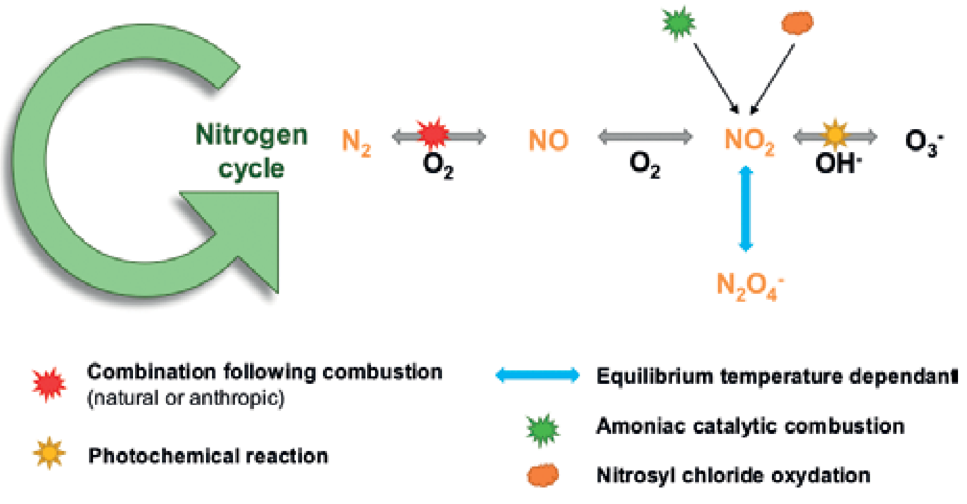


Figure 4. Atmospheric genesis of NOx (adapted from [3]).

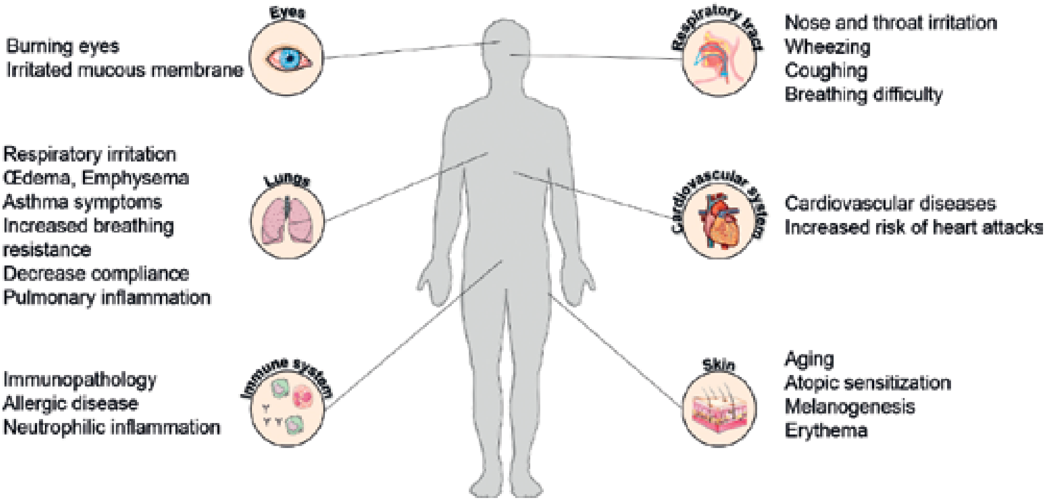
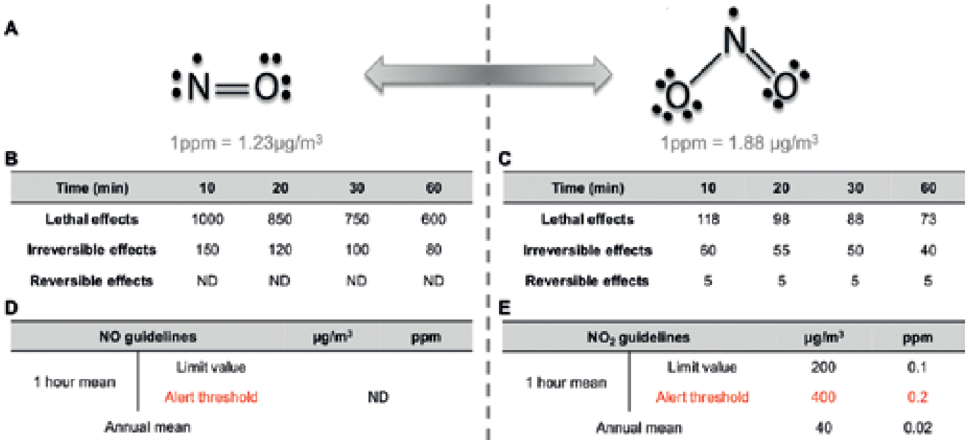


Figure 5. Representation of NOx targets and associated pathologies [11–15].

Thanks to epidemiological and clinical studies, thresholds of NO and NO_2, whose chemical structure and conversion factors are represented **Figure 6A**, have been determined for different human health effects (**Figure 6B** and **C**, respectively). However, no guideline values are available for NO (**Figure 6D**) due to its complete and rapid reaction [16]. Thus, in order to limit health issues, international organizations, such as WHO, set up guidelines for atmospheric NO_2 limit value (**Figure 6E**).

NOx is then highly toxic compounds and has a myriad of deleterious impacts on the human physiology when the bearable thresholds are exceeded. However, NOx is also naturally produced by cellular processes in a wide range of living organisms. In this case, NOx can have totally different effects as discussed later.



Time (min)	10	20	30	60
Lethal effects	1000	850	750	600
Irreversible effects	150	120	100	80
Reversible effects	ND	ND	ND	ND

Time (min)	10	20	30	60
Lethal effects	118	98	88	73
Irreversible effects	60	55	50	40
Reversible effects	5	5	5	5

NO guidelines		µg/m³	ppm
1 hour mean	Limit value		
	Alert threshold	ND	
Annual mean			

NO_2 guidelines		µg/m³	ppm
1 hour mean	Limit value	200	0.1
	Alert threshold	400	0.2
Annual mean		40	0.02

Figure 6. Key features concerning NOx. (A) Lewis structure of NOx and conversion factors; (B) NO threshold (ppm) according to [9]; (C) NO_2 threshold (ppm) according to [9]; (D) and (E) NO and NO_2 guideline values, respectively, according to [1]. ppm, parts per million; ND, not determined.

2. The double face of NOx in the eukaryotic world

To better understand why NOx impact on so many organs, it is essential to focus on the units forming each part of our body: the eukaryotic cells themselves.

2.1. Exogenous NOx: a hostile intruder inside the eukaryotic cells

Much work was already performed on NOx targets at the cell scale. NO and NO_2, thanks to their chemistry properties mentioned earlier, are highly diffusible through living membranes and exhibit a strong reactivity. It is easy to imagine the potential of such compounds. Since NO is highly reactive in lipophilic media, it can react inside the lipid bilayer, first protection of cells against the environment. Indeed, polyunsaturated fatty acids (PUFAs) are susceptible to NO in the presence of O_2 and $ONOO^-$ [17]. The interaction of these toxic compounds with PUFA double bounds leads to the formation of nitrated FA. This process is considered as a protective strategy because it redirects O_2^- and $ONOO^-$-mediated cytotoxic reactions to other oxidative pathways. Post-translational modification of several proteins is also observed in the presence of NOx and RNS. For example, tyrosine nitration on phenol residue mediated by peroxynitrite derived from OH and NO_2 leads to 3-nitrotyrosine formation [18]. This molecule represents a useful biomarker of nitrosative stress in various pathologies such as atherosclerosis [19]. Protein thiol residues are highly susceptible to NO and $ONOO^-$ leading to the formation of nitrosothiol (RS-NO) and nitrothiol (RS-ONO), respectively [20]. This reversible modification modulates the activity of several proteins similar to phosphorylation. For example, S-nitrosylated cysteine thiol residue can be denitrosylated by S-nitrosoglutathione reductase or thioredoxin systems [21]. NO and other RNS can also nitrosylate [Fe—S] cluster of transition metal centers, which are essential for protein function. This modification can activate a wide range of enzymes such as the soluble guanylate cyclase (sGC) mentioned below

[22]. On the contrary, this reaction can also alter the protein function, for example, in the case of hemoglobin [23]. NO and other higher RNS products ($ONOO^-$ or NO_2) are able to generate nitration, nitrosation, or deamination reactions on DNA bases leading to mutagenesis [24]. This phenomenon is enhanced by the inhibition of DNA repair triggered by NO [25]. More recently, a role of NO in epigenetic modification was suggested. To be more precise, this simple molecule seems to modulate histone acetylation and methylation through direct and indirect modulations of histone acetyltransferases and deacetylases, lysine demethylases, histone methyltransferases activity, thus modifying the expression of several genes [26]. These pleiotropic activities of NO and derived compounds highlight here the necessity of fine regulation pathways to prevent the development of several diseases.

2.2. Endogenous NO: an essential mediator of cellular signalization

Interestingly, NO can also be produced by several living organisms: plants, animals, and bacteria, thanks to a specific enzyme called nitric oxide synthase (NOS) [27, 28]. The large distribution of this enzyme through the different reigns emphasizes the importance of NO synthesis. Evolutionary studies highlight the necessity for the first living organisms during primitive era to eradicate toxic O_3 present in the paleoatmosphere as a survival strategy. Indeed, the liberation of gaseous NO in extracellular environment could have subsequently neutralized O_3, thus limiting harmful oxidative reactions [29]. In eukaryotic cells, three isoforms of NOS have been described [30]. The neuronal nNOS (NOS-1) and the endothelial eNOS (NOS-3) are constitutively expressed but are only activated through calcium-dependent mechanisms. The third one is the inducible iNOS (NOS-2) expressed in macrophages following infection by pathogens, virus, or tumors. Contrary to NOS-1 and 3, NOS-2 is constitutively functional. Interestingly, these NOSs have high structural similarities with an oxygenase and a reductase domain (**Figure 7**) [27].

To be fully functional, NOS requires to associate with homodimers, and this form of NOS is crucial for the generation of NO [32]. When conditions are favorable (high level of L-arginine

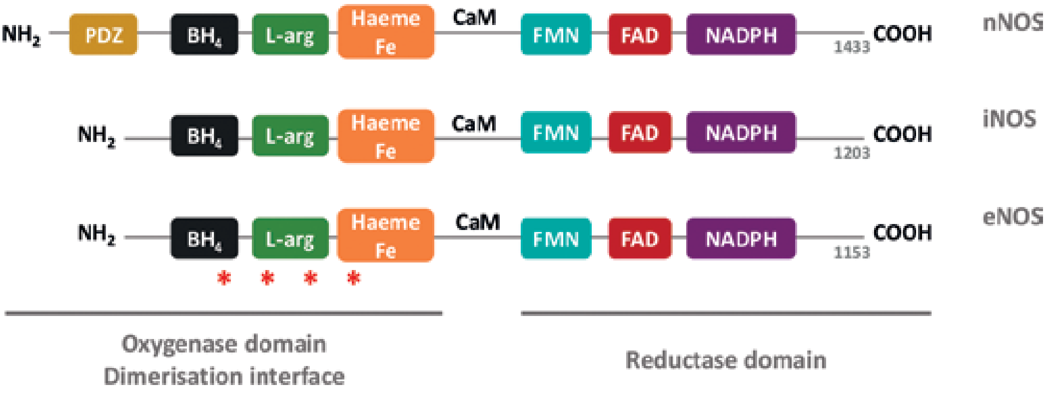


Figure 7. The structural similarities of NOS (adapted from [31]). BH_4, tetrahydrobiopterin; L-arg, L-arginine-binding site; Heme Fe, iron protoporphyrin IX; CaM, calmodulin-binding site; FMN, flavin mononucleotide-binding site; FAD, flavin adenine dinucleotide-binding site; NADPH, nicotinamide adenine dinucleotide phosphate-binding site; *, palmitoylation and myristoylation of eNOS oxygenase domain.

and cofactors like BH_4), this enzyme catalyzes the conversion of L-arginine into L-citrulline using O_2 and leading to NO formation with a ratio of 1:1 [33]. However, if these parameters are not available or if NOS remains monomeric, the enzyme only produces superoxide (O_2^-) [32]. Even if NOS isoforms catalyze the same reaction, their distribution is largely related to their respective functions.

2.2.1. The endothelial eNOS and vasodilatation

Endothelial nitric oxide synthase (eNOS) can be activated through calcium-dependent and independent pathways. On the one hand, through activation of specific receptors, such as acetylcholine muscarinic receptors, bradykinin receptors, and H1 histamine receptors, distributed in the endothelial cell membrane, agonists can trigger an increase in intracellular concentration of calcium (Ca^{2+}) through the well-known polyphophoinosides pathway. Indeed, activation of those receptors stimulates membrane-associated PLCϒ and PI3K activation. This results into inositol trisphosphate (IP3) formation, which induces the release of intracellular calcium stock from endoplasmic reticulum [34]. Then, Ca^{2+} binds to calmodulin (CaM), which could later fix on the calmodulin-binding domain of eNOS controlling its enzymatic activity. On the other hand, in response to hormones or growth factors acting on their corresponding receptors, phosphate kinase A (PKA) or B (AKT) pathway can be induced mediating a phosphorylation cascade. The post-translational phosphorylation of eNOS on three specific sites (Ser617 and Ser1179 for AKt, Ser635 and Ser1177 for PKA) enhances the activity of the enzyme [35]. Moreover, the lipidation of eNOS (palmitoylation and myristoylation) could also enhance its activity [36]. This other post-translational modification promotes eNOS association with cell membrane and is stabilized by interaction with membrane chaperone proteins (caveolin-1 and HSP70/90). Both mechanisms are essential for linking upstream signal transduction pathway to eNOS activity in cells [37]. eNOS could then produce a large amount of NO, which latter diffuses freely inside smooth muscles. Herein, NO activates soluble guanylate cyclase (sGC) by reaction with the heme of the enzyme leading to the increase of cyclic guanosine monophosphate level (cGMP). cGMP subsequently activates phosphate kinase G (PKG) favoring a cytosolic Ca^{2+} reuptake into sarcoplasmic reticulum [38]. The decrease of intracellular level of Ca^{2+} leads to the relaxation of smooth muscle. Moreover, NO can inhibit caspases 3 and 8 and thus apoptosis through protein nitrosylation. NO released by endothelium is also reducing platelet aggregation and platelet or leukocyte adhesion (**Figure 8**) [39, 40].

Another source of NO inside endothelial cells was also described. Indeed, nitrite and nitrate reservoirs could be converted into NO by several enzymes such as cytochrome P450, hemoglobin, myoglobin, and others, under specific conditions [42]. However, several pathways could abolish NO production. Indeed, NO can be eliminated in combination with reactive oxygen species (ROS). eNOS could be inactivated by several phosphatases. The removal of eNOS membrane sequestration by interaction between NOS-interacting protein (NOSIP) and NOS-traffic inducer (NOSTRIN) complex favors eNOS recycling [36]. Since NO plays a central role in this phenomenon, any abnormality altering its production leads to pathogenesis and vascular disorders such as atherosclerosis and hypertension [43].

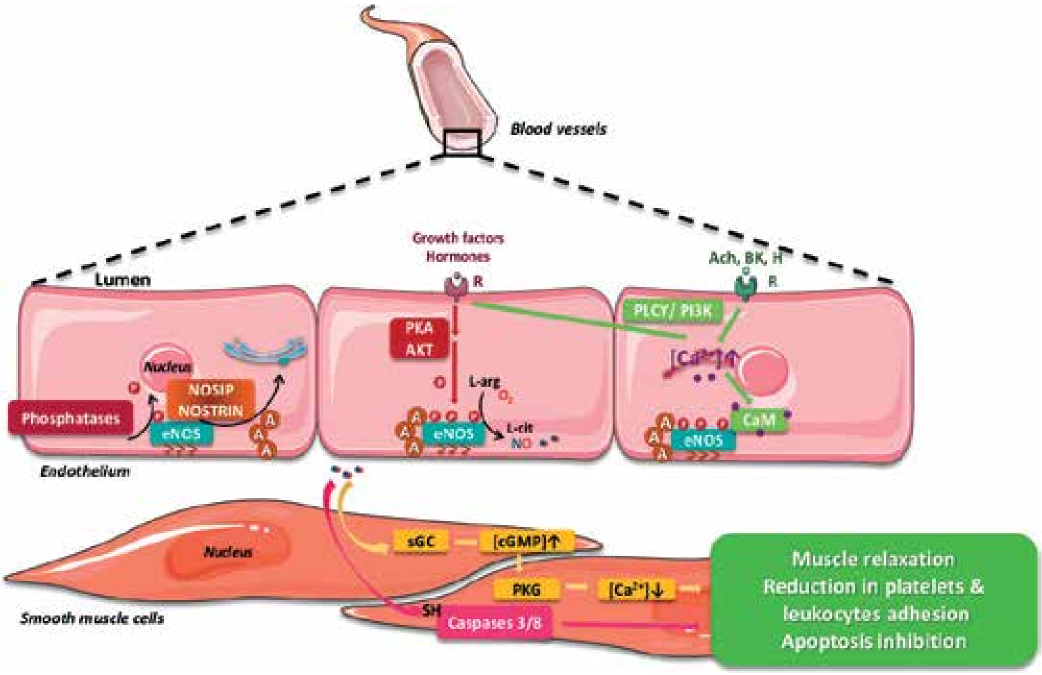


Figure 8. Physiology of vasodilatation: implication of eNOS and NO (adapted from [41]). eNOS, endothelial nitric oxide synthase; ach, acetylcholine; BK, bradykinin; H, histamine; R, receptor; CaM, calmodulin; PLCϒ, phospholipase C ϒ; PI3K, phosphoinositide 3-kinase; PKA, phosphate kinase A; AKT, phosphate kinase B (PKB); sGC, soluble guanylate cyclase; cGMP, cyclic guanosine monophosphate; PKG, phosphate kinase G; A, protein complex of HSP70, HSP90, and caveolin-1; NOSIP, NOS-interacting protein; NOSTRIN, NOS traffic inducer.

2.2.2. The neuronal nNOS: a crucial element in neurotransmission

nNOS, also called NOS-1, was the first isoform discovered in the neuronal tissue. It should be distinguished between two subfamilies: nNOSα and nNOSμ, thanks to their locations and functions. Indeed, nNOSα is found in central nervous system and plays a major role in the neurotransmission at neuronal synapses, whereas nNOSμ is found in skeletal and cardiac muscle where NO controls muscle contractility and local blood flow.

2.2.2.1. nNOSα in the central nervous system

Glutamate is the major excitatory neurotransmitter in the brain. When deliver into the synapse, this molecule is activating a specific receptor (NMDAR) located inside the postsynaptic membrane. Activated NMDAR thus allows the entry of calcium. Ca^{2+} are able to activate calmodulin by physical interaction [44]. Afterward calmodulin binds to nNOSα, which, in turn, is activated. Interestingly, nNOSα can indirectly interact with the NMDAR through its fixation on an adapter protein PSD95 by their PDZ interaction domain [45]. This allows the high speed of NO synthesis in response to NMDAR activation. Thereafter, NO can diffuse back to the presynaptic area leading to an increase glutamate release in the synaptic cleft and thus neurotransmission. CAPON, a chaperon protein of DexRas, was found altering the level of nNOSα present at the membrane [46]. Indeed, CAPON competes with the PDZ domain of nNOSα and thus promotes its detachment from the NMDAR-PSD95 complex. nNOSα interaction with CAPON-DexRas complex allows the activation of DexRas, a small protein G, through s-nitrosylation on its thiol residue [47]. Then, DexRas activates the MAPK cascade and the transcription of several genes [47]. Several shutdown systems are available to limit this process, which could dramatically affect the brain physiology by synapses hyperactivation. Indeed, kinases, such as PKC or PKII, can phosphorylate nNOSα leading to its loss of activity [48]. nNOSα can also be sequestrated by two membrane proteins (caveolins 1 and 3) preventing its interaction with calmodulin (**Figure 9**).

As mentioned above, any disorder affecting NO synthesis can lead to dramatic consequences in the brain. Indeed, a lack of NO could impair the neurotransmission and hence the neuronal plasticity, such as long-term potentiation (LTP) in the hippocampus or long-term depression (LTD) in the cerebellum [50]. NO ensures also the correct irrigation of brain by its vasodilator effect on peripheral blood vessel. The synthesis of NO can be altered by a deficiency or a loss of activity of nNOS. Other regulatory elements, such as the decrease of L-arginine precursor availability or cofactors crucial for the catalytic activity of NOS, contribute also to nNOS inactivation. Conversely, in some several brain pathologies (ischemia, strokes, neurodegenerative disorders including Parkinson's and Huntington's diseases, and amyotrophic lateral sclerosis), a large amount of NO is produced [51]. It is hypothesized that NO or derived nitrogen species interact with various proteins inducing several toxic effects. Thus, pharmacological regulation of NO synthesis offers important strategies for the treatment of neurodegenerative and muscle diseases.

2.2.2.2. nNOSμ in peripheral neurotransmission

On the other hand, nNOSμ is located in skeletal and cardiac muscle where NO controls muscle contractility and local blood flow essential to support muscular effort. When the excitatory neurotransmitter acetylcholine (Ach) is released at the neuromuscular junction, it is activating specific acetylcholine nicotinic receptors present on muscle cells [52]. Activation of these receptors allows the release in the cell sarcoplasm of calcium from exogenous and/or endogenous

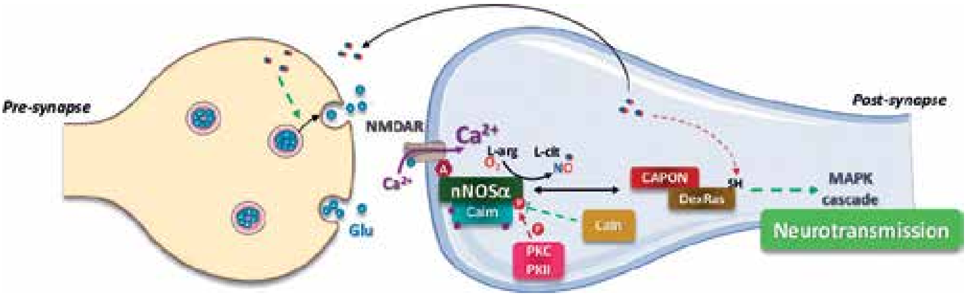


Figure 9. The neurotransmission mediated by NOSα in central nervous system (CNS) (adapted from [49]). Glu, glutamate neurotransmitter; NMDAR, N-methyl D-aspartate type-glutamate receptor; A, PSD95 protein adapter between nNOSα and NMDAR; CaM, calmodulin; PKC, phosphate kinase C; PKII, Ca2+/CaM-dependent protein kinase II; CaN, calcineurin; CAPON, C-terminal PDZ domain ligand of neuronal nitric oxide synthase; MAPK, mitogen-activated protein kinase.

sources. This process is also enhanced by the activation of a voltage-dependent Ca^{2+} channel (CaCn) [53]. The increase of Ca^{2+} from exogenous origin activates ryanodine receptor present on the sarcoplasmic reticulum, which, in turn, delivers a large amount of Ca^{2+}. When the Ca^{2+} threshold is reached, it is binding on the calmodulin protein. Calmodulin can then interact with the nNOSμ to activate the generation of NO. Interestingly, nNOSμ interacts through its PDZ domain with adapter proteins (syntrophins) linked to a membrane protein complex called dystrophin [54]. Produced NO could then diffuse back to the motor neuron to enhance the liberation of neurotransmitters or the vasodilatation of blood vessels, thus increasing the local blood flow to support muscle needs during contraction efforts (**Figure 10**) [55].

NO synthesis is also well regulated by calpain (Calp). Indeed, this protein interacts with the PDZ domain nNOSμ provoking its detachment from the dystrophin/syntrophin membrane complex [56]. Interestingly, in muscular Duchenne dystrophy, the damages caused by dystrophin absence are enhanced in case of simultaneous lack of nNOSμ [57]. Thus, NO donors may offer a potential avenue for therapy.

2.2.3. The inducible iNOS and the innate immunity

NO also takes an important part in innate immunity. Indeed, NO and derived compounds are cytotoxic weapon against tumor cells, microorganisms, and viruses [58]. NO is generated by inducible nitric oxide synthases (iNOS and NOS2) within macrophages. However, more recently, studies have shown that this enzyme is also expressed in other cell line (vascular endothelial cells, hepatocytes, pulmonary, and colonic epithelial cells) [59]. Unlike nNOS or eNOS, its expression is stimulated by several pathways after activation of specific receptors by endotoxins (LPS) or cytokines (TNFα, IFNϒ, and IL1β). Briefly, the LPS endotoxins are carried by an LPS-binding (LPB) protein to its specific Toll-like receptor 4 (TLR4). Then, the transduction

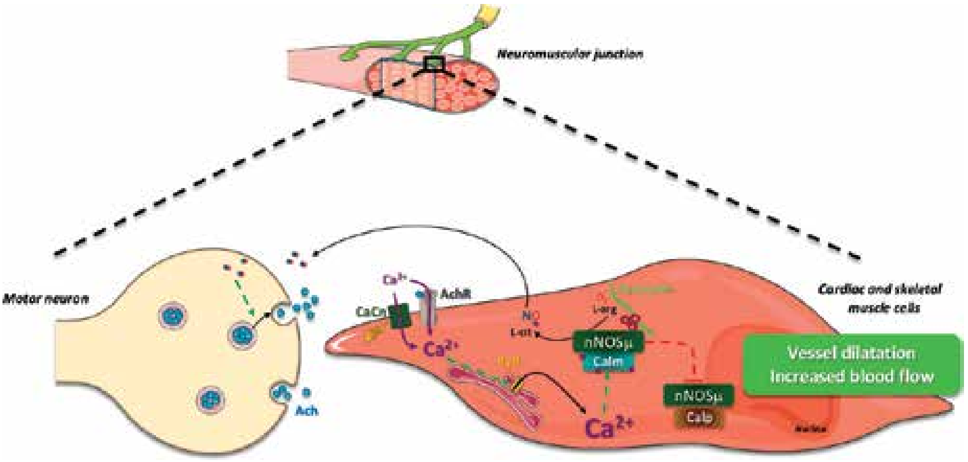


Figure 10. nNOSμ activity at the neuromuscular junction (adapted from [49]). Ach, acetylcholine; CaCn, voltage-dependent Ca^{2+} channel; AchR, acetylcholine receptor; yellow lightning symbols, membrane depolarization; Ca^{2+}, calcium; RyR, ryanodine receptor; L-cit, L-citrulline; L-arg, L-arginine; CaM, calmodulin; A, syntrophin α1, β1 and β2 adapter between dystrophin and nNOSμ; Calp, calpain.

of the signal leads to the transcription of NF-κB [60]. This transcription factor is essential for the expression of *iNOS* gene. On the other hand, cytokines produced by infected cells activate pathways responsible for the expression of several transcription factors (NF-κB, AP1, and IRF1) also involved in the transcription of iNOS [61]. Both pathways are necessary to fully upregulate iNOS expression. Moreover, iNOS is constitutively active and exhibits a high affinity for calcium explaining its Ca^{2+}-independent activity. iNOS produces a large amount of NO until substrate depletion [62]. Then, NO acts directly or through derived compounds (mostly $ONOO^{-}$ and NO_2) generated through the reaction of NO with ROS formed by NADPH oxidase. These molecules can be generated inside (phagosome) or outside the cells. Altogether, NO and derivatives could act in synergy on several components within the targeted hostile elements such as proteins (thiols, metal centers, and tyrosine residues), nucleic acids, and lipids [63, 64]. Altogether, these modifications lead to irreversible damages impairing cellular metabolism and ultimately inhibit growth and replication mechanisms and even cell death (**Figure 11**).

After infection, NO generation is abolished by neutralization of iNOS activity. Indeed, iNOS undergoes a posttranslational modification called polyubiquitination leading to its proteasomal degradation. Physiological aggresome, an alternative pathway for protein degradation, is also involved in iNOS inactivation [66]. The degradation of NO can also be modulated by its own interaction with ROS. The depletion of ʟ-arginine precursor also shuts down iNOS activity.

Overexpression of iNOS is observed during chronic infection leading to an excessive level of NO and RNS. This phenomenon can impair the host physiology because these high reactive compounds represent mutagenic sources. Thus, the NO balance is a crucial point to

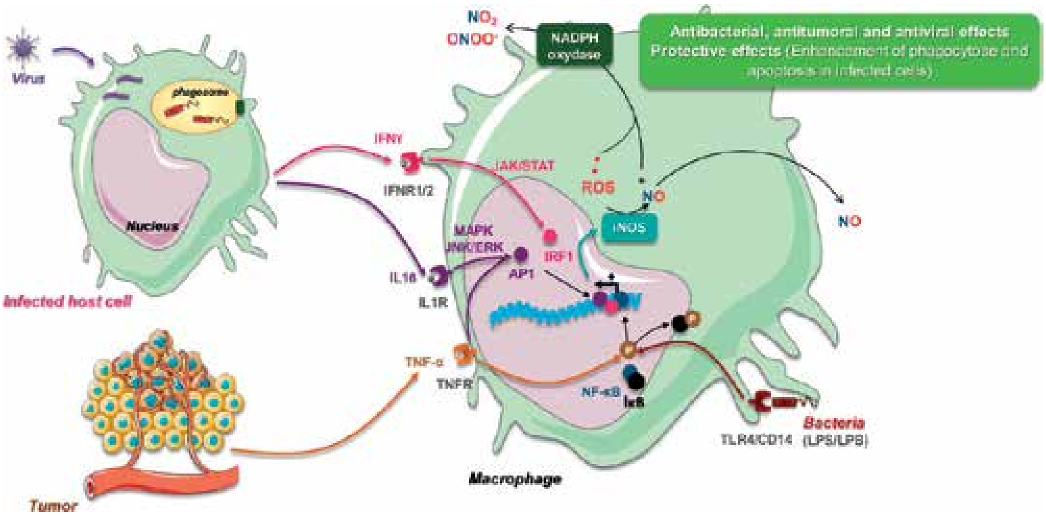


Figure 11. Implication of iNOS in the innate immunity (adapted from [65]). IFNϒ, interferon ϒ; IFNR1/2, IFNϒ receptors 1 and 2; JAK, Janus kinase; STAT, signal transducer and activator of transcription; IRF1, interferon response factor 1; IL1β, interleukin 1β; IL1R, IL1β receptor; MAPK, mitogen-activated protein kinase; JNK, C-Jun N-terminal kinase; ERK, extracellular signal-regulated kinase; AP1, activator protein 1; TNF-α, tumor necrosis factor α; TNFR, tumor necrosis factor receptor; NF-κB, nuclear factor κB; TLR4, Toll-like receptor 4; CD14, cluster of differentiation 14; LPS, lipopolysaccharide; LPB, LPS-binding protein; ROS, reactive oxygen species.

control in order to limit its tumorigenic potential. The development of iNOS inhibitors and NO-releasing agents offers interesting therapeutic strategies to struggle against cancer and microbial infections.

3. NOx versus prokaryote: “Catch me if you can”

3.1. NOx at the center of prokaryotic life, virulence, and death

Several environmental, commensal, and pathogenic prokaryotes possess an arsenal of proteins dedicated to the nitrogen metabolism under anaerobic conditions [67]. Indeed, an enzymatic chain is involved in the denitrification pathway responsible for the production of NO through nitrite reductase (NIR) as an intermediate. The outcome of this mechanism is the formation of dinitrogen (N_2). This process is crucial for the growth of bacteria in the absence of oxygen because it is coupled with ATP generation (**Figure 12**).

Interestingly, a shortened NOS-like protein called bNOS was discovered in Gram-positive bacteria [28]. This enzyme is deprived of the classical reductase domain already described in other NOS isoforms. However, bNOS is able to recruit other proteins exhibiting a reductase catalytic activity [69]. Similar to mammalian isoforms, bNOS catalyzes the production of NO using L-arginine precursor. However, NOx is key elements in the innate immunity to avoid infection. Indeed, similar to eukaryotic cells, prokaryotes are also sensitive to NOx activity. Thence, such compounds could alter DNA, proteins, and metal centers leading to severe alterations of bacterial growth and replication.

As previously described, NO could be endogenously produced by bacteria but is also a powerful exogenous antimicrobial agent. This highlights the requirement of systems to manage a bearable threshold of NOx within the cell. First, bacteria have developed NO sensing system

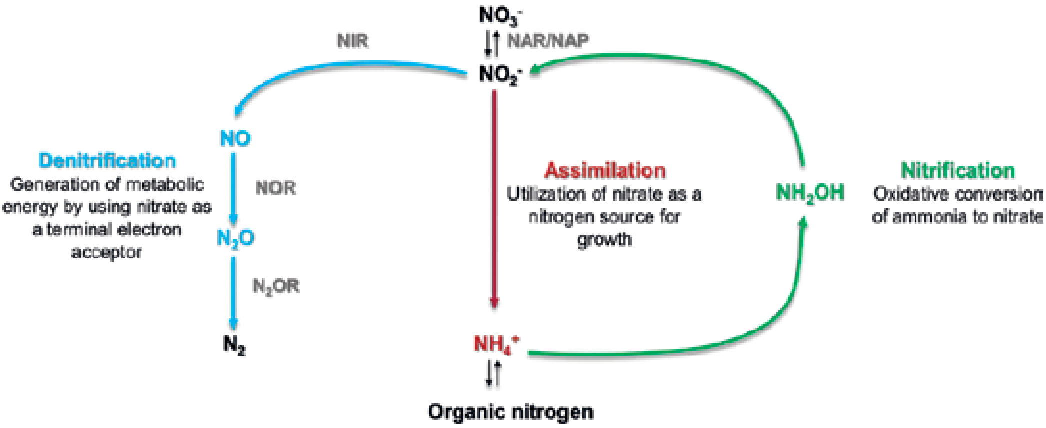


Figure 12. Bacterial nitrogen cycle (adapted from [68]). NO_3^-, nitrate; NO_2^-, nitrite; NO, nitric oxide; N_2O, nitrous oxide; N_2, dinitrogen; NH_2OH, hydroxylamine; NH_4^+, ammonia; NAR/NAP, nitrate reductase; NIR, nitrite reductase; NOR, nitric oxide reductase; N_2OR, nitrous oxide reductase.

through non-heme iron cluster conjugated with a wide range of detoxification mechanisms. Several pathways involving reaction of NO with non-heme iron cluster were described, mainly in *Escherichia coli* [70]. Indeed, NO can lead to a raise of the repression of sulfur assimilation operon (*suf*) exerted by ferric uptake regulator protein (Fur). This reaction is mediated by Fur nitrosylation through NO-derived S-nitrosoglutathione (GSNO). *Suf* products are required for the biogenesis of the [Fe—S] cluster, which, in turn, gives a lure to get rid of NOx collateral damages. The flavohemoglobin (hmpA) is another response against the nitrosative stress. This enzyme catalyzes the conversion of NO into nitrous oxide (N_2O) under anaerobic conditions. Interestingly, in the presence of NO, the S-nitrosylation of cysteine residues on MetR and FNR inactivates both the proteins. Thus, the repression exerted by MetR and the fumarate and nitrate reductase regulatory protein (FNR) is raised by *hmpA* allowing its transcription. Furthermore, NO-responsive transcriptional factor (NorR) is directly activated by NO and enhances the expression of NorVW protein catalyzing the reduction of NO into N_2O. Redox-sensitive cysteines also take part in the NO-sensing systems. Indeed, NO-activated superoxide regulon (SoxR) protein leads to the transcription increase of superoxide dismutase (*sodA*) removing O_2^- that may react with NO to form NO_2 and $ONOO^-$ [71]. Similar to SoxR, peroxide regulon (OxyR) protein is activated by S-nitrosylation. This protein induces gene expression for protective products against nitrosative stress at least by limiting the S-nitrosylation [72]. For example, the expression of catalase KatA, which could buffer free NO, is activated by OxyR [73]. Altogether, these sensing systems lead to the efficient detoxification by generation of less toxic compounds or scavenger molecules.

Moreover, bacteria also develop repairing system of DNA and [Fe—S] cluster damages related to nitrosative stress. Similar to eukaryotic cells, five DNA repair pathways are available in prokaryotes. Among them, the base excision repair (BER), to repair deaminated base, and the nucleotide excision repair (NER), to remove cross-linking in DNA, are predominant [74]. Concerning the [Fe—S] cluster repair, the iron sulfur cluster S protein (IscS), a cysteine desulfurase, can denytrosylate these protein clusters in the presence of L-cysteine [75]. Moreover, Isc regulator (IscR) protein is able to sense nitrosylated [Fe—S] cluster and thus enhances the formation and/or repair of [Fe—S] cluster [76, 77].

NO could also alter tricarboxylic acid (TCA) metabolic pathway and bacterial respiration through reaction with aconitase and cytochromes of the electron transfer chain, respectively [78]. However, these mechanisms are crucial for the generation of ATP and hence the energetic needs of bacteria [79]. To counteract the inefficiency of this enzyme, some bacteria are able to reprogram their metabolism. For example, *Pseudomonas* spp. uses the citrate lyase, phosphoenolpyruvate carboxylase, and pyruvate phosphate dikinase to convert citrate into pyruvate and ATP [80].

In nonlethal concentrations, NO interplays a signaling role in bacteria through several proteins possessing heme-nitric oxide/oxygen-binding domain and is referred under the name H-NOX proteins. H-NOX exhibits a highly conserved domain among bacteria and also shared in mammals (sGC) [81]. All H-NOX are histidine-ligated protoporphyrin IX hemoprotein able to fix NO on its ferrous iron. The H-NOX-encoding genes are found in operons with diverse bacterial signaling genes [82], whose majority is now divided in two classes: containing (i) histidine kinase (HK) or (ii) diguanylate cyclase (DGCs) and phosphodiesterase (PDE). H-NOX could modify the function of proteins implicated in virulence such as biofilm formation and motility or even *quorum sensing* [83]. For example, H-NOX alters the function of diguanylate cyclase and enhances the phosphodiesterase activity. Altogether, this leads to the biofilm dispersion through the decrease of c-di-GMP, an essential mediator in this process. On the contrary, a more sophisticated system relative to histidine kinase (HnoK) activity leads to the accumulation of c-di-GMP in response to NO favoring the biofilm adhesion and formation. Another important virulence trait could be also modulated by H-NOX as in *Vibrio* species a cross-talk with QS seems to exist. However, a few studies are yet available.

More recently, an antibiotic resistance modulation was promoted by a bacterial NO_2 gaseous exposure. Indeed, an upregulation in expression of MexEF-OprN efflux pump was observed coupled with an increase in related antibiotic resistance [84]. The link between NO_2 and this efflux pump is yet not established, but the authors suggest here a potential role of this protein in the releasing of NOx outside the cells. Previous studies also highlight a correlation between NO endogenously generated by bNOS and increase aminoglycoside resistance [85]. NO and NO_2 could directly interact with antibiotic leading to a less toxic compound and exerted a repression of bacterial respiration preventing drug uptake.

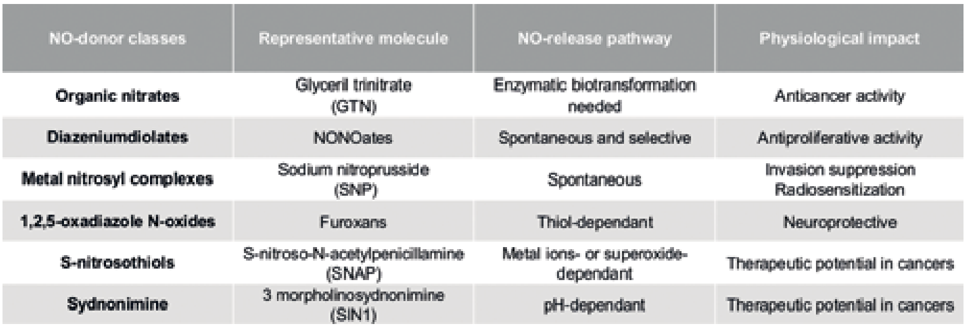
To resume, bacteria are able to produce NO and RNS. Following endogenous burst or exogenous aggression (pollution, inflammation reactions), a physiological threshold is exceeded. However, bacteria developed an ingenious system to counteract the potential effects of NO and derived products. Various interconnected signaling pathways are implicated in this phenomenon: (i) NO detection, (ii) detoxification, (iii) repairing mechanisms, and (iv) metabolic reprogramming. Finally, these fundamental modifications modulate bacterial community behavior (QS) and virulence traits, such as biofilm and antibiotic resistance. This last point is particularly attractive in medicine. Indeed, the emergence of several antibiotic multiresistant pathogens represents a big threat for human that brings us to the last question of this review: "Does NOx therapy represent the new trends in human health care?"

3.2. The novel therapeutic strategies mediated by NOx

A lot of therapeutic strategies exploiting NOx-mediated pathways has recently emerged, particularly to treat cancer. Here we propose to classify them in three families: (i) NO-donor compounds, materials, or nanoparticles; (ii) modulators of NOS activity; and (iii) last but not least, generators of gaseous NO.

The first family NO donors consist of NO-chelating compounds that can release NO under specific conditions within the organism after administration. As shown below, several NO donors have been developed during the last decade. Their global—direct or not—anticancer effects have been exploited in the case of various carcinoma (**Table 1**).

For further information, we strongly recommend to read the review of Huang et al. [86]. Another extension of the use of NO-donor compounds is their graft on material and nanoparticles. Indeed, prosthetic biomaterials used in medical devices were modified through covalent or noncovalent binding of two NO donors (diazeniumdiolates and S-nitrosothiols).



NO-donor classes	Representative molecule	NO-release pathway	Physiological impact
Organic nitrates	Glyceril trinitrate (GTN)	Enzymatic biotransformation needed	Anticancer activity
Diazeniumdiolates	NONOates	Spontaneous and selective	Antiproliferative activity
Metal nitrosyl complexes	Sodium nitroprusside (SNP)	Spontaneous	Invasion suppression Radiosensitization
1,2,5-oxadiazole N-oxides	Furoxans	Thiol-dependant	Neuroprotective
S-nitrosothiols	S-nitroso-N-acetylpenicillamine (SNAP)	Metal ions- or superoxide-dependant	Therapeutic potential in cancers
Sydnonimine	3 morpholinosydnonimine (SIN1)	pH-dependant	Therapeutic potential in cancers

Table 1. The different classes of NO donor (adapted from [86]).

Several clinical trials have shown their usefulness in the context of preventing thrombus formation [87]. NO-donating nanoparticle systems represent a new promising tumoricidal agents, thanks to their unique properties: (i) strengthening NO-donor stability, (ii) loading a large amount of NO, and (iii) possibility to trigger NO releasing [88].

The modulation of NOS activity is another interesting strategy. In some pathologies inducing exacerbating inflammation (sepsis), a localized "nitrosative burst" occurs, and inhibition of NOS function is a crucial element. Thus, several L-arginine precursor analogs (N^{ω}-substituted L-arginine) were developed and tested. However, since L-arginine is the common point between all NOS isoforms, these analogs represent nonselective drugs. Moreover, such therapy did not reach clinical studies on human stage despite its effects on canine vascular tone [89]. Thus, investigation on a more selective inhibition of iNOS, crucial for inflammation, was conducted through transgenic animals. Unfortunately, iNOS knockout mice exhibit an increase in mortality following polymicrobial sepsis [90]. More recently, researcher focused on increasing NO delivery within cancers. Thus, thanks to technical progress and scientific knowledge updating, iNOS-based suicide gene therapy was investigated through viral vector use. This treatment exhibits promising tumoricidal effects and appears interesting for its specific and localized iNOS expression on animal models [91].

The third strategy is the direct gaseous delivery of NO in the treatment of various infection diseases related to antibiotic resistant bacteria. Ghaffari et al. provided a considerable work on this topic. First, they developed an ingenious delivery system usefulness for the monitoring of gNO effects on microorganisms (bacteria and fungi) and eukaryotic cells [92]. Then, they reported an effective concentration of gNO up to 200 ppm in continuous 4 h delivery exhibiting bacteriostatic effects on a representative group of microorganisms (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli*, *Candida albicans*, and *Group B Streptococcus*). Moreover, no toxic effects were observed on representative mammalian cell lines (dermal fibroblasts) of wound-healing pathology such as leg ulcer or burn injuries [93]. Thus, these promising results placed gNO as a potential topical antibiotic agent [94]. Later, they also investigated the potential use of inhaled gNO in the treatment of pathogenic infection in the case of cystic fibrosis. Indeed, this pathology is a threatening pulmonary disease where microbial infection could be lethal. However, a continuous exposure of gNO at such concentration can lead to severe impact on the human health, particularly through methemoglobinemia. This phenomenon occurs when hemoglobin losses its vital function of oxygen carrier following the saturation of its iron heme with NO. Thus, an intermittent high-dose short-duration exposure was tested to determine the dose/duration most effective treatment. An adapted lung mammalian model was also used (macrophages and monocytes and pulmonary epithelial cells) to appreciate the potential effects of this cure on human health [95]. This study reached phase I clinical studies using a promising NO treatment at 160 ppm for 30 min three times daily for two periods of 5 days [96]. However, as reviewed by Petit et al., it is important to keep in mind that "administration of inhaled NO is associated with and unavoidable codelivery of NO_2," thanks to the spontaneous high reactivity of NO with O_2 [97]. They also reported that the higher NO doses are used, the faster is the formation rate of NO_2. In contrast, a direct gaseous NO_2 exposure could also be benefit in the struggle against undesirable microorganism because it seems to impact their metabolism, social behavior, and growth [84]. Moreover, a continuous high-dose NO_2 exposure seems to lead in membrane alteration through an increased permeability [98].

4. Conclusion

In summary, this review of the literature shows that NOx is ubiquitous and essential in our lives. We are exposed to these compounds through environmental contaminations, but they also result from physiological processes, infections, diseases, or even drugs. NO and derivatives are implicated in a large diversity of vital functions including brain functions; motricity; cardiac, vascular, and pulmonary functions; and immunity. For these reasons, NOx is key molecules of major biochemical interest. As all active substances, NOx can exert both beneficial and adverse effects with regard to the exposition dose. The physiological adaptation to NOx results from a fine-tuned equilibrium where detoxification plays crucial roles. Myriad of finely regulated processes has emerged in response to nitrosative stress. Our knowledge still remains incomplete, and future studies are necessary to finely precise the synergy of each NOx implemented in nitrosative stress, especially when they are presented in gaseous phase that remains less explored. However, in spite of all previously described mechanisms to counteract the nitrosative stress, abnormal NOx thresholds could trigger a wide range of pathologies and even death. These antagonists, positive and negative effects, of NOx are actually intriguing. So, many researches are now focusing on NOx producing pathways to find the most effective treatments and drugs. More investigations are still needed to better understand the real potential of NOx as antitumor, antibacterial agents, and their safe clinical use.

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Conflict of interest

We have no conflict of interest to declare.

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Multivariate-Assisted Solid Phase Extraction Procedure for Simultaneous Preconcentration and Assessment of UV-Filters in Wastewater Prior to UV-Vis Spectrophotometric Determination

Anele Mpupa and Philiswa N. Nomngongo

Additional information is available at the end of the chapter

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Abstract

Determination of emerging pollutants such as UV-filters in environmental samples is very important because they have been proven to have harmful effects on human and aquatic life. In this study, a simple, fast and inexpensive method combining solid phase extraction (SPE) and UV spectrophotometry was developed for simultaneous preconcentration and determination of benzophenone and sulisobenzone in wastewater samples. The effect of factors affecting the preconcentration of UV-filters was optimized using univariate and multivariate approach. Under optimized conditions, the limits of detection (LOD), limits of quantification (LOQ) and preconcetration factors were in the range of 0.15–0.28 and 0.50–0.93 μg L^{-1}, 50–55, respectively. The dynamic linear range was up to 250 μg L^{-1} for benzophenone and sulisobenzone. In addition, the intra- and inter-day precisions were 3.1–3.3 and 4.5–5.2%, respectively. The developed method was successfully applied to determine UV filters in wastewater samples attaining satisfactory recoveries over the range of 99.3–100.7%. The concentration of the target pollutants in wastewater samples ranged from 6.83 to 85.67 μg L^{-1}.

Keywords: solid phase extraction, emerging organic pollutants, UV-filters, response surface methodology, UV-Vis spectrophotometry, endocrine disruptors

1. Introduction

Ultraviolet filters are chemical agents that are used in a variety of cosmetics, specifically those used for sun protection such as sunscreen lotions, creams and sprays [1]. These compounds often contain single or multiple aromatic structures (**Figure 1**), sometimes conjugated with

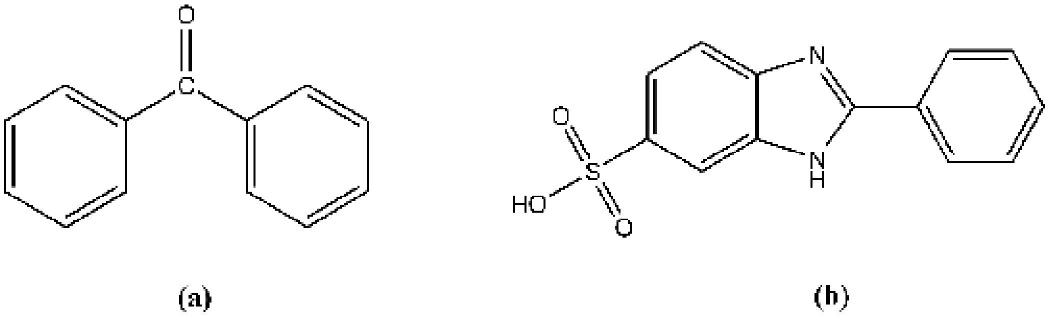

Figure 1. Chemical structures of (a) benzophenone and (b) sulisobenzone.

carbon-carbon double bonds and carbonyl moieties [2]. The presence of these functional groups affords UV filters the ability to absorb photons and rapidly return to the ground state by thermally emitting the energy through vibrational relaxation [3]. This makes the compound to be able to mitigate the deleterious effects of UV radiation [1, 2].

After application, UV-filters are washed off and enter the aquatic environmental directly or indirectly via wastewater effluent and recreational water systems [4]. They are also used as sun blocking agents in materials such as plastics, adhesive and rubber, this suggests that these compounds can also leach into the environmental matrices [5–7]. The amount and type of UV-filter used depends on the desired degree of protection, however combined concentrations should not exceed 10% with other organic or inorganic UV-filters [8].

The main concern of the presence of these compounds is their potential toxicity and their effects as xenohormones (effect on reproductive activity) [9, 10]. These effects include estrogenic activity [11], effects on cell proliferation by 4-methylbenzylidene camphor (4-MBC), benzophenones, and octyl methoxycinnamate (OMC) [12]. Several studies have shown hormonal disruption in both in vivo and in vitro test systems in fish and mammals [13–16]. It has also been recently shown that besides estrogens, there are other hormonal targets affected by UV-filters in fish and mammals [17, 18].

A number of detection techniques have been used to quantify UV-filters in environmental water samples. These include techniques high performance liquid chromatography (HPLC) with UV or mass spectrometry detection [19, 20], HPLC-MS/MS [21], gas chromatography-mass spectrometry (GC-MS) and GC-MS/MS [22, 23]. However, the levels of these compounds in environmental waters are usual in the $\mu g\ L^{-1}$ range. Therefore, sample cleanup/preconcentration techniques such stir-bar sorptive extraction [20], pressurised liquid extraction [1], dispersive liquid-liquid phase extraction [24], solid phase extraction [25], among others, have been used to improve sensitivity, LODs and to remove interferences prior to quantification with the different analytical techniques.

Solid phase extraction is one of the most established preconcentration techniques used for the simultaneous extraction and analysis of organic compounds [26]. Mainly silica bonded phases such as C18 were formerly used for SPE, however recently modified and tuned solid phases can be used to achieve more specificity [27]. Advantages of SPE include the potential of simultaneous extraction, reduced labour and cost. Of the advantages of solid phase extraction, scientists are mostly attracted to the possibility of using reduced amount of organic solvents and the fact that SPE is highly tuneable with regards to the adsorbents used [28].

Thus the aim of this study was to develop a multivariate assisted solid phase extraction method for the simultaneous preconcentration of UV- filters in wastewater samples prior to their spectrophotometric quantification. The main advantage of the method relies on the use of multivariate optimization approach which led to the reduction of the number of experiments and analysis time as well as the use of a simple, fast and cost effective instrumentation. UV-Vis spectrophotometry was chosen due its simplicity and high availability. The factors (such as sample pH, flow rates, eluent and adsorbent types) affecting the preconcentration step method were optimized using univariate and multivariate approach. The developed SPE/spectrophometric method was applied to the preconcentration and determination of two UV filters from the wastewater samples collected from Daspoort wastewater treatment plant (WWTP) in Pretoria, Gauteng, South Africa. According to our literature search there are limited reports on the application of UV-Vis spectrophotometry for quantification of UV filters [29]. In addition, to the best of our knowledge, the application of SPE/UV-Vis spectrophotometry for simultaneous preconcentration and determination of Benzophenone and sulisobenzone has been reported for the first time.

2. Experimental

2.1. Materials and reagents

Benzophenone (Reagent plus, 99%), sulisobenzone (5-benzoyl-4-hydroxy-2-methoxy-benzenesulfonic acid) (HPLC, ≥97.0%) and acetonitrile (for HPLC Plus) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Ethyl acetate was purchased from Merck (Merck, Darmstadt, Germany), ethanol and methanol were purchased from Associated Chemical Enterprises (Johannesburg, South Africa). Stock solutions of benzophenone and 5-benzoyl-4-hydroxy-2-methoxy-benzenesulfonic acid (10 mg L^{-1}) were prepared in ultra-pure water (Direct-Q® 3UV-R purifier system, Millipore, Merck). Working standards of 100 μg L^{-1} were prepared daily by diluting appropriate volumes of the stock solution in ultra-pure water. The ion exchange resins used in this study as packing materials were Dowex 1x8 (Chloride form) (Sigma Aldrich).

2.2. Instrumentation

A Shimadzu UV-2450 high performance single monochromator UV-VIS spectrophotometer (Shimadzu Corporation, Tokyo, Japan) was used for all analysis of the samples. Solid phase extraction (SPE) was carried out in a VacMaster-24 sample SPE station (VacMaster, Biotage, Sweden). The latter was used to control the sample loading and elution flow rate in the range of 1–3.0 mL min^{-1}. An OHAUS starter 2100 pH meter (Pine Brook, NJ, USA) was used for pH adjustments of the reagents and to measure the pH of samples

2.3. Sampling and sample collection

Influent (after sediment removal) and effluent wastewater samples were collected from Daspoort wastewater treatment plant (WWTP, Pretoria, Gauteng, south Africa). The samples were collected in pre-cleaned 500 mL glass bottles. The samples were then refrigerated at 4°C.

Factors	Low level (−1)	Central point (0)	High level (+1)
Sample pH	4	7	10
Sample flow rate (SFR) (mL min^{-1})	2	3.5	5
Eluent flow rate (EFR) (mL min^{-1})	1	2	3

Table 1. Factors and levels used in 2^3 factorial design for extraction and preconcentration of UV filters.

2.4. Solid phase extraction procedure

The columns were prepared according to [30]. Briefly, polyethylene columns of diameter 1.0 cm and 6 cm in height were used for preconcentration. Slurries of 0.5 g of Dowex 1x8 in double distilled deionized water were prepared and packed to columns to heights of about 1 cm. A porous frit was placed at the bottom of the column and at the top of the packing material to hold and confine the adsorbent within the designated capacity/volume. The columns were washed with 6 mL of double distilled deionized water followed by conditioning with 3 mL organic solvent (methanol, ethanol, ethyl acetate or mixture of methanol and acetonitrile) and then 3 mL of double distilled deionized water. Due to the scarcity of reference materials for UV-filters, a commercial sunscreen lotion was used as a reference material for the validation of the SPE/UV method. An appropriate amount of the sunscreen lotion was accurately weighed and dissolved using a small volume of methanol (2 mL) and made to the mark with double distilled deionized water and used for validation experiments.

An aliquot (10 mL) of model solution containing benzophenone and sulisobenzone at a concentration of 100 μg L^{-1} was passed through a packed column at a flow rate of 2–5 mL min^{-1}. After percolating the synthetic samples through, the cartridges were washed with 3 mL double distilled deionised water. Then retained analytes were eluted with 2 mL organic solvents. The optimization of the solid phase extraction method was carried out using a 23 full factorial design involving three variables such as pH, sample flow rate (SFR) and eluent flow rate (EFR). Maximum, central point and minimum levels are presented in **Table 1**. The second step of the optimization strategy involved the application of a response surface methodology (RSM) based on a central composite design. All the experiments were carried out in random order and the experimental data was processed by using the Minitab 17 software program.

3. Results and discussion

3.1. Optimization of separation and preconcentration method

3.1.1. Selection of adsorbent and eluent type: univariate approach

Selection of the adsorbent and eluent type was achieved by packing columns using the ion exchange adsorbent (Dowex 1x8). Each experiment was done in triplicates for each solvent type and adsorbent combination. The flow rates and the sample pH were fixed at 2 mL min^{-1}

for both the sample loading and elution and 7, respectively. The results obtained are presented in **Figure 2**.

Selection of the adsorbent and eluent was done using the absorbance of benzophenone and sulisobenzone at the wavelengths of 260 and 220 nm, respectively. Since the absorbance is directly proportional to concentration, a higher absorbance can be related to higher concentration. Thus, from the univariate optimization, the most effective adsorbent and eluent combination was found to be Dowex 1x8 and methanol (**Figure 2**). This combination was further used for the optimization of the solid phase extraction procedure for both benzophenone (UV-01) and sulisobenzone (UV-02).

Due to the overall charge of adsorbents, the extraction and preconcentration of the analytes was possible by means of ionic interactions. Dowex 1x8 has an overall positive charge, thus the negatively charged analytes could interact with the positive charges of the adsorbent. This resulted in higher absorbances and Dowex 1x8 resin was selected as the suitable adsorbent for further studies.

The polarity of the solvent was the contributing factor on the elution of the analytes, the more polar solvent resulted in better elution from the SPE column, and hence higher absorbances for methanol were observed when used in combination with Dowex 1x8. This was a consequence of the methanol having the ability to displace the analytes from the positively charged Dowex 1x8 adsorbent. The 1:1 mixture of acetonitrile and methanol also had promising results, but did not perform better than the methanol alone. Acetonitrile could not be used for this study even though it is more polar than methanol, there are dangers associated with the use of pure acetonitrile like the risk of cyanide poisoning as a result of its decomposition products.

Experimental conditions; mass of adsorbent 0.5 g, sample volume 10 mL at 100 μg L^{-1}, eluent volume 2 mL, pH 7, flow rates 2 mL min^{-1}. MeOH = methanol, ACN = acetonitrile, EtOH = ethanol.

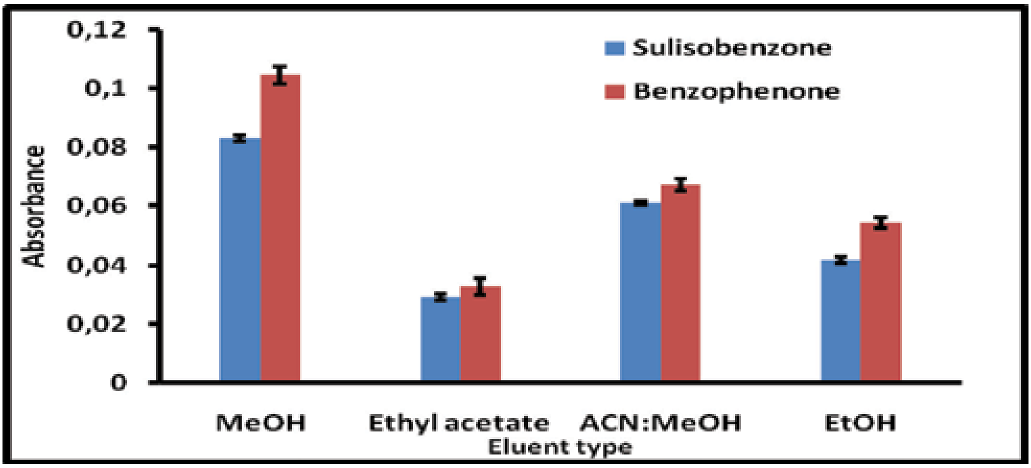

Figure 2. Selection of suitable adsorbent and eluent combination in model aqueous solution.

3.1.2. Optimization of the SPE operation parameters: Multivariate approach

In order to achieve quantitative preconcentration of analytes by SPE system, the optimization of the most influential parameters, such as sample pH, sample and eluent flow rates, was carried out using 2^3 full factorial design and response surface methodology (RSM) based on a central composite design. Two level full factorial design (FFD), involving 11 experiments was used for screening of the significant factors for the extraction and preconcentration of UV filters. **Table 2** presents the factorial design matrix and the analytical responses (expressed as average percentage recovery, %R) obtained in each experiment. Analysis of variance (ANOVA) reproduced in the form of Pareto chart was used to investigate the significance of the effects SPE procedure. The Pareto chart of main effects and their interactions produced are shown in **Figure 3**.

It can be seen from **Figure 3** that for simultaneous preconcentration of UV filters, sample pH and EFR and their interactions were statistically significant. The effect of sample flow rate on the analytical response (%R) was not significant at 95% confidence level. The overall results obtained for the screening step indicated that sample pH and EFR required further optimization. Whereas, sample flow rate was fixed at 3.5 mL min^{-1}.

A central composite design matrix consisting of 14 experiments and analytical response based on each of the experimental runs (**Table 3**) was used for further optimization of the SPE method. The analysis of variance (ANOVA) of the predicted response surface quadratic model for the recoveries of UV filters was obtained. The ANOVA results were analysed using quadratic equations (not included) for the models to illustrate the dependence of the analytical response with respect to the evaluated main effects [31].

The 3D response surface plots (**Figure 4**) were used to access the interactive relationship between individual variables (sample pH and EFR) and analytical response [31]. Based on

Expt.	pH	SFR (mL/min)	EVR (mL/min)	UV-01 (%R)	UV-02 (%R)
1	4	2	1	34.39	33.7
2	10	2	1	39.63	39.1
3	4	5	1	51.01	53.5
4	10	5	1	72.71	75.4
5	4	2	3	12.22	16.0
6	10	2	3	8.84	9.1
7	4	5	3	11.58	10.6
8	10	5	3	10.24	17.6
9	7	3.5	2	83.55	72.8
10	7	3.5	2	78.88	77.5
11	7	3.5	2	81.08	78.6

Table 2. Two level (2^3) full factorial design matrix and analytical response.

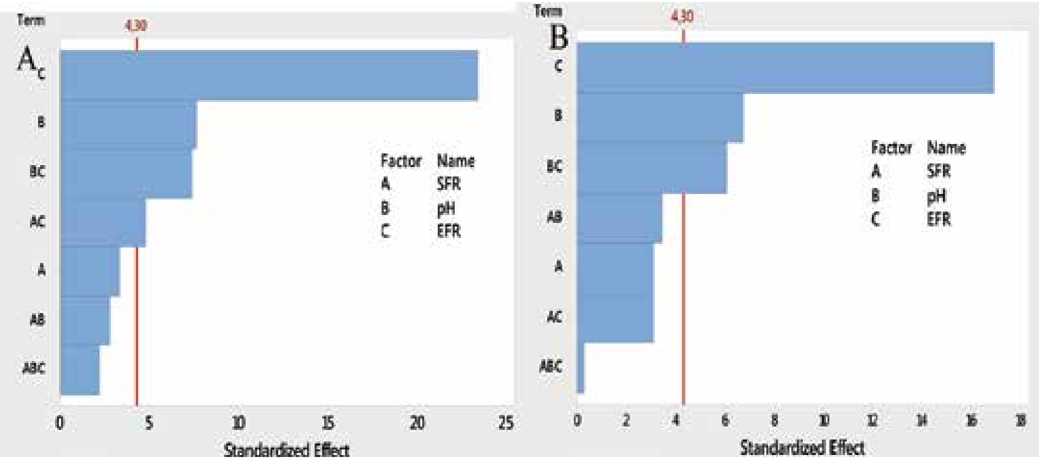

Figure 3. Pareto charts of standardized effects for variables in the preconcentration of (A) benzophenone and (B) sulisobenzone.

quadratic equations and 3D surface response plots, the calculation indicated that pH = 7.5 and EFR = 2 mL min^{-1} provided maximum retention and recovery of the studied analytes. Therefore, the results obtained from both designs, illustrated that the optimum conditions that led to quantitative extraction and preconcetration of UV filters were 7.5, 3.5, 2 mL min^{-1} for sample pH, sample and eluent flow rates, respectively.

Sample	pH	SFR (mL/min)	EFR (mL/min)	UV-01 %R	UV-02 %R
1	4	3.5	1	66.1	63.4
2	10	3.5	1	65.7	44.5
3	4	3.5	3	49.7	16.6
4	10	3.5	3	25.9	19.2
5	7	3.5	2	61.3	51.9
6	7	3.5	2	54.8	59.2
7	7	3.5	2	49.7	49.7
8	2.8	3.5	2	78.8	49.6
9	11.2	3.5	2	42.0	66.0
10	7	3.5	0.5	100.1	103.1
11	7	3.5	3.4	32.2	17.4
12	7	3.5	2	75.0	81.5
13	7	3.5	2	74.8	82.0
14	7	3.5	2	75.1	81.8

Table 3. Central composite design matrix and analytical response.

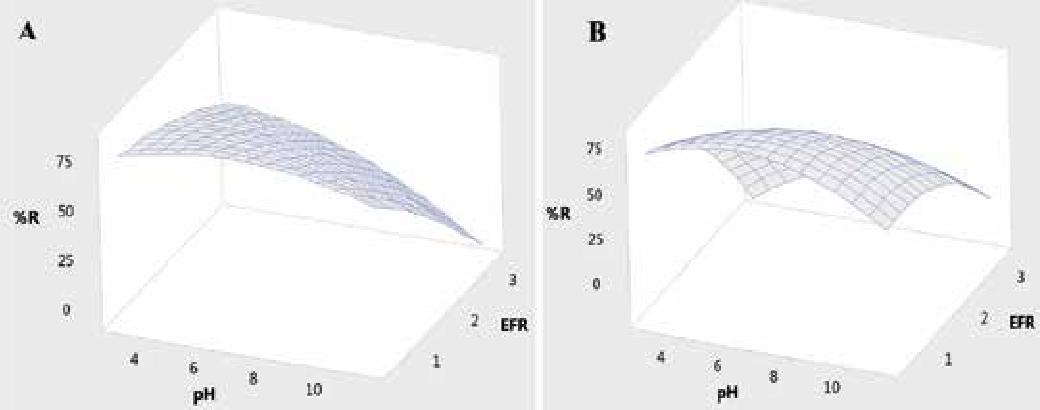

Figure 4. Response surfaces obtained for (A) benzophenone and (B) sulisobenzone after extraction and preconcentration by SPE.

The effect of pH on the extraction and preconcentration of UV filters can be seen from **Tables 2** and **3**. Acidic pH resulted in lower recoveries. This is because benzophenone and sulisobenzone have pKa values of 7.5 and 7.6, respectively, meaning that in acidic pH they are more likely to accept H^+ ions resulting in lower recoveries as they end up with an overall positive charge. In more alkaline conditions (pH 10), the analytes are easily displaced on the adsorbent, resulting in little or no adsorption.

The central pH (7) showed the highest recoveries for both UV-filters. This is a result of the interaction of the analytes' negative charge with the positive charges of the adsorbent prior to elution with methanol.

The optimum conditions obtained by the multivariate approach were confirmed experimentally. Under these conditions (7.5, 3.5, 2 mL min^{-1} for sample pH, sample and eluent flow rates, respectively), quantitative recoveries ranging from 96 to 98.6% were obtained. These recoveries were compared with the predicted recoveries values (95.6 and 98.1% for benzophenone and sulisobenzone) obtained using the RSM model. It was then concluded that the results obtained by RSM model were valid since there was no significant difference at a 95% confidence level between the experimental and predicted values.

3.2. Analytical performance

Under the determined optimum experimental conditions, the analytical performances of the developed method for preconcentration and determination of UV-filters were investigated. The calibration curves were obtained after a set of standard solutions (0 to 350 µg L^{-1}) was processed using the described SPE procedure. The concentrations of the analytes in the eluent solutions were quantified with the aid of a UV spectrophotometer. The limits of detection and quantification were calculated using the expressions: LOD = $^{3Sd}/_{b}$ and LOQ= $^{10Sd}/_{b}$, where *Sd* is the standard deviation of 10 replicate measurements at lower concentrations of calibration curves and *b* is the slope of each calibration curves. Dynamic linear ranges (DLR), correlation coefficient (R^2), enrichment factor (EF), LOD and LOQ for benzophenone were determined to be LOQ-250 µg L^{-1}, 0.9990, 50, 0.28 µg L^{-1} and 0.93 µg L^{-1}, respectively. Whereas for sulisobenzone, the DLR, R^2, LOD, LOQ, and EF were found to be LOQ-250 μg L^{-1}, 0.9991, 0.15 μg L^{-1}, 0.50 μg L^{-1} and 55, respectively. Furthermore, the intraday (repeatability; n = 10) and interday (reproducibility; n = 7 working days) precisions of the SPE method, expressed in terms of relative standard deviation (% RSD), ranged 3.1–3.3 and 4.5–5.2%, respectively. The analytical performance of the proposed method was compared to other methods that reported in the literature **Table 4**. It can be seen that the performance of the current method was comparable or better that those reported in the literature. In addition, the LODs obtained using the current method were lower compared to [25, 32].

3.3. Validation and application

The accuracy of the SPE/UV procedure was evaluated using a sunscreen lotion with a sulisobenzone content of 1.75% (w/w). The recovered sulisobenzone was 1.69 ± 0.07% (w/w) meaning that the percentage recovery was 96.6%. Therefore, the determined values by SPE/UV were in the acceptable range. In addition, the accuracy and matrix effects were investigated by analysing spiked real waste water samples and the results are shown in **Table 5**. From the recoveries shown in **Table 4**, it can be seen that the SPE/UV procedure described was not affected by the matrix effects as the recoveries for both benzophenone and sulisobenzone ranged from 99.3 to 100.7%.

As seen on **Tables 5** and **6**, there was a significant amount of both UV filters on the influent. This can be explained by the fact that the Daspoort waste water treatment plant treats domestic waste water. Therefore as explained by [37], personal care products are usually applied to

Analyte(s)	Matrix	Analytical method	DLDLR (μg L^{-1})	LOD (μg L^{-1})	EF	% RSD	Refs.
Octicrylene	Wastewater	MEPS-GC-MS	0.25–20	0.081	-	7	[33]
Benzophenone-3	Water	CE-ESI-MS	300–20000	150	3400	1.5–6.5	[25]
Benzophenone-3	Water	SBSE-LC-MS/MS	0.005–0.5	0.0009	-	3–7	[34]
Benzophenone-2	Human serum	DLLME-UPLC-MS/MS	0.6–40	0.2	-	1.9–13.1	[35]
Benzophenone-3	Sea water	DLLME-GC-MS	0.1–0.5	0.03	262	<15	[25]
Benzophenone	Tap water	DDA-IL-DLLME	0.002–1.5	0.0013	-	3.5–5.3	[32]
Benzophenone	Sunscreen	SPE-GC-MS	10–2000	4.4	25.3	4.6–5.5	[36]
Benzophenone and sulisobenzone	Wastewater	SPE-UV/vis	0.50–250	0.15-0.28	50 and 55	3.1–5.2	Current work

MEPS = microextraction in packed syringe, CE-ESI = capillary electrophoresis-electro spray ionisation, SBSE-LC-MS/MS = stirbar sorptive extraction-liquid chromatography tandem mass spectroscopy, DLLME-UPLC = dispersive liquid-liquid microextraction-ultra pressure liquid chromatography, GC-MS = gas chromatography-mass spectroscopy, SPE = solid phase extraction, DDA-IL =double dispersant assisted-ionic liquid, UV/vis = ultraviolet-visible spectrophotometry.

Table 4. Comparison of the analytical figures of merit of the current method and those reported in the literature.

Sample	**Added (μg/L)**	**Benzophenone**		**Sulisobenzone**	
		Found (μg/L)	**% R**	**Found (μg/L)**	**% R**
Influent 1	0	85.8 ± 1.3		69.4 ± 1.2	
	50	135.3 ± 2.3	99.3	119.7 ± 3.5	100.7
	100	186.3 ± 2.5	100.6	169.4 ± 4.2	100.0
Effluent 1	0	6.83 ± 0.92		19.8 ± 0.9	
	50	56.7 ± 1.2	99.8	69.6 ± 1.3	99.7
	100	106.9 ± 3.1	100.0	119.1 ± 2.7	99.3

Table 5. Analysis of wastewater samples (influent and effluent) spiked and unspiked from Daspoort (Pretoria, Gauteng, South Africa) wastewater treatment plant.

Samples	**Months**	**Benzophenone**		**Sulisobenzone**	
		SPE/UV	SPE/HPLC	SPE/UV	SPE/HPLC
Influent	August	78.6 ± 1.2	79.4 ± 1.5	56.3 ± 2.1	58.0 ± 1.8
	September	155.3 ± 2.4	157.2 ± 2.2	171.3 ± 3.1	172.2 ± 2.8
	October	327.3 ± 4.3	328.9 ± 4.0	337.3 ± 3.6	337.6 ± 3.6
Effluent	August	18.5 ± 0.7	19.5 ± 0.5	14.5 ± 0.7	15.1 ± 0.5
	September	57.9 ± 1.3	59.0 ± 1.5	23.6 ± 0.9	24.2 ± 0.8
	October	134.5 ± 1.5	135.1 ± 1.2	45.3 ± 0.5	46.0 ± 0.2

Table 6. Analysis of influent and effluent over from Daspoort (Pretoria, Gauteng, South Africa) wastewater treatment plant a period of 3 months.

the skin and later washed off into drains which are connected to wastewater treatment plants. From wastewater treatment plants, the water is discharged into rivers [3]. This has resulted in the occurrence of UV-filters in surface waters [22], sediments [38, 39], drinking water and even fish [4, 12, 40].

The presence of UV-filter in different water bodies does not only have an effect in humans as suspected endocrine disrupters [18]. Their effects spans into aquatic life, as reported by [3], benzophenone can cause cell membrane impairments in fresh water protozoa. Benzophenone was also found in other fresh water species in percentages ranging from 50 to 80% by [41].

The described method was applied in the analysis of real water samples collected over a period of three months as expressed in **Table 6**. The influent and effluent samples were collected over two seasons, namely winter (one month) and spring (two months). From **Table 6**, it was observed that between the three months, October showed the highest concentrations for both the influent and effluent. This was because it was significantly warmer during spring when compared to August. It is also worthy to note that the concentrations of benzophenone were higher than those of sulisobenzone. This could be the consequence of the degradation of sulisobenzone during the water treatment process. This is possible because benzophenone forms the backbone of sulisobenzone, this means that when the sulisobenzone losses the methoxy and sulfonic acid side chains, traces of the benzophenone can remain in the water.

The described SPE/UV procedure was compared with a reference method, SPE/HPLC method using the same extraction conditions. The obtained results from the SPE/UV methods were comparable with the SPE coupled with HPLC method. According to the paired student t-test, there was no significant difference between the two methods at 95% confidence level. Therefore, the SPE/UV procedure can be utilised as a rapid, cheap and effective method for the determination of UV-filters in water samples.

4. Conclusions

The combination of SPE and UV-Vis spectrophotometry offers a simple, inexpensive and selective procedure for the assessment of UV-filters in wastewater samples. With the aid of multivariate optimisation of key parameters in the solid phase extraction procedure, it was possible to achieve satisfactory analytical performance. Real sample analysis showed that as explained by [27], wastewater treatment plant processes are not exhaustive enough to completely remove emerging organic pollutants. There were still some traces of benzophenone and sulisobenzone found in the effluent which is released into the nearby river. This means that the flora and fauna in the river is exposed to these potentially toxic compounds. Thus, the next step would be to study the distribution of these UV-filters in the river where the effluent is released into.

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Chapter 4

Study on Magnetic Materials for Removal of Water Pollutants

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Additional information is available at the end of the chapter

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Abstract

Water is a primary element for all living things, and we need water for each and every day-to-day activity related to agricultural, industrial, and domestic cares and, thus, its quality influences all aspects of human life including energy, food, health, and economy. Safe drinking water is our primary need to protect our life and thus developing efficient and affordable techniques for water treatment to access potable water to the humanity. Water pollution is one of the severe environmental and health problems worldwide. Pollutants in water can be of organic, inorganic, heavy metals, microbial, and radioactive species, which may be in different forms viz. suspended, dissolved, or dispersed materials. The water quality is mainly affected by industrial discharges, agricultural activities, mismanagement of hazardous materials, etc. Nowadays, nanotechnology offers the possibility of an efficient removal of water pollutants including metals, organic dyes, bacteria, parasites, etc. Magnetic nanomaterials like iron oxide (Fe_3O_4) are very promising materials used in water decontamination particularly for heavy metals and dyestuffs because of their ease of separation through external magnet, high surface area, unique morphology as well as their high stability. These materials can be used as adsorbent, photocatalyst, and coagulating agents for water remediation based on their composite materials or surface functionalities.

Keywords: magnetic nanomaterials, water treatment, water pollution

1. Introduction

Water, i.e., 2 mol of hydrogen and 1 mol of oxygen or simply called H_2O plays a vital role in our everyday life. Without water no one can think of life on earth. About 71% of earth is covered with water. Of that 71% water about 97% resides in oceans and only 3% of water is fresh water (**Figure 1a**) and of that 3% about 68.7% of freshwater is locked up in icecaps and glaciers (**Figure 1b**), and it is quite a surprising fact that almost all the remaining fresh water is below the ground. Of all the freshwater on the surface of earth only 0.3% is contained in fresh lakes, and rivers [1].

As the population is increasing day by day the water availability per capita is decreasing. So the challenge of limited amount of freshwater and its decreasing per capita availability is an issue of concern but another major challenge is water pollution that has not only environmental impact but also have a major effect on human health. As per the statistics 783 million people do not have access to clean and safe water worldwide [2]. Around 319 million people in Sub-Saharan Africa are without the access to improved reliable drinking water sources. One in nine people worldwide do not have access to safe and clean drinking water. 443 million school days are lost each year due to water-related diseases [3]. In developing countries, as much as 80% of illnesses are linked to poor water and sanitation conditions [4]. 2.6 billion people in the world lack adequate sanitation and which contributes to about 10% of the global disease burden [5]. Half of the world's hospitals beds are filled with people suffering from a water-related disease [6].

There are various type of illnesses due to water and are summarized in **Table 1**.

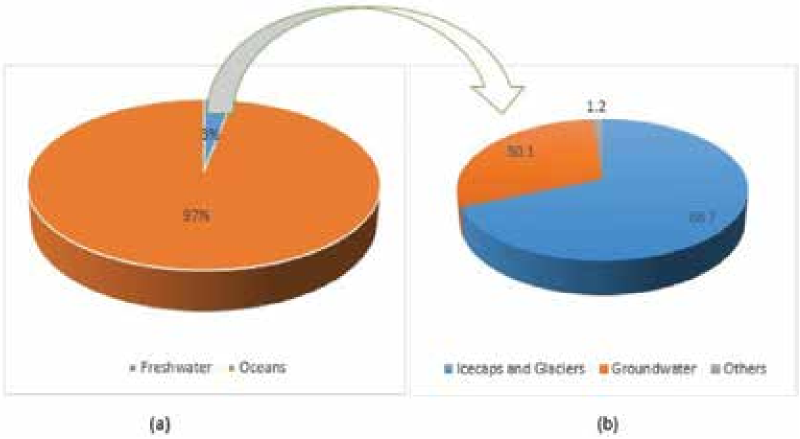

Figure 1. (a) Water distribution on the earth and (b) freshwater distribution on the earth.

Type of diseases	Source	Example	References
Water borne	Human or animal waste	Cholera, typhoid, and dysentery,	[7]
Water washed	Lack of clean water for washing	Skin and eye infections	[8]
Water based	Organism developed in water and then become parasite	Schistosomiasis	[9]
Water-related insect vector	Mosquitoes breed in water	Malaria and dengue	[9]

Table 1. Various types of illness due to water.

As we have seen that the contaminated water has a very bad impact on human health even some heavy metals that if taken for long time it can cause cancer such as arsenic is considered as one the carcinogenic contaminant in water. After understanding the health issues related to contaminant water there is need to understand the source of contamination and major contaminants that pollute the water.

In recent years, magnetic materials have been potentially used for removal of water pollutants, particularly organic contaminates (dyes, chlorinated hydrocarbons, aromatics), pesticides, as well as heavy metals [10]. There are a large number of techniques available for water treatment for safe drinking water including adsorption, precipitation, solvent extraction, ion exchange, reverse osmosis, membrane separation, evaporation, and photocatalysis. The development of nanoscience and nanotechnology shows their potentiality in removing toxic elements from water bodies with better water treatment process. The design and development of nanomaterials which belong to the size range of 1–100 nm exhibiting unique properties as compared to the bulk materials leads to the enormous improvements in many sectors including, health, manufacturing, electronics, environmental remediation as well. The magnetic nanomaterials (paramagnetic or ferromagnetic or superparamagnetic) with tailored surface chemistry have already expanded their scope of application in water treatment. In this chapter, various processes of drinking water treatment and waste water treatment using advanced magnetic materials in removing toxic metal ions, organic and inorganic solutes, bacteria and viruses has been discussed.

1.1. Major sources of water contamination

There are many sources of drinking water and the main sources are ground water, lakes, canals, reservoirs, rain water, fog water and sea water. These sources are contaminated in different ways and broadly the source of contamination can be divided in to two categories:

- Direct sources or point sources
- Indirect sources or non-point sources

Direct sources basically include effluent from industries, treatment plants, refineries, factories, etc. However, indirect sources or non-point sources include the water contamination entering to the water body through a number of processes, e.g., while putting the fertilizers and pesticides to the agricultural field, the elements presents in the chemical percolates down to the groundwater and ultimately pollute the water.

1.2. Different types of water contaminants

There are various types of water contaminants, however in the following subsections organic contaminants, inorganic contaminants and pathogens are briefly discussed.

1.2.1. Organic contaminants

Organic contaminants present in drinking water create severe problem on human health. Pollution by organic chemicals in water bodies occurs by various mechanisms. Industrial waste containing various organic chemical contaminants pollutes the water bodies. Volatile organic compounds (VOCs), pesticides, phenolic compounds, phthalates, and nitrogen-containing compounds, are often detected in polluted water [11]. Many of these compounds have been found to be carcinogenic, even in very low concentrations. WHO Guidelines for drinking water quality, levels are set for 28 organic constituents (i.e., microcystin-LR, chlorinated alkanes, chlorinated benzenes and miscellaneous), 33 pesticides, and 9 disinfectant by-products, due to their health effects on humans [12]. It is noteworthy to mention that, occurrence of pharmaceutical and personal care products and perfluoroalkyl acids in aquatic environment has been recognized as emerging issue in environmental chemistry [13].

1.2.2. Inorganic contaminants

Inorganic contaminants include metals, salts and other compounds that do not contain carbon. Many of them are naturally occurring and should be considered as an integral part of those waters, e.g., calcium carbonate and bicarbonate in hard water. The metal ions such as Hg(II), Pb(II), Cr(III), Cr(VI), Ni(II), Co(II), Cu(II), Cd(II), Ag(I), As(V) and As(III) are toxic from eco toxicological point of view. Besides, the pollution by the radioactive elements is of major concern looking into their long-term hazardous impacts.

1.2.3. Pathogens

Pathogens such as bacteria, viruses and parasites may be present in very low concentration in drinking water; but cause many infectious diseases and are considered as one of the major risk factors with drinking water safety [14]. The pathogenic microorganisms enter in to water body through sewage discharge as a major source or through the wastewater from industries like slaughterhouses. Water-borne pathogens have been the causes of many disease outbreaks such as diarrhea, cholera, gastro-intestinal illness [15]. The recurrence of water-borne pathogens is due to a number of reasons like heavy water contamination, population explosion, change in potable water treatment methods, globalization of commerce and travel. It has been made possible to detect pathogen based water contamination to a large extent owing to the improved methods for detection and source tracking [16, 17]. The most serious health risk is related with ingestion of water which is contaminated with fecal matter and the discharge of wastewater into various ambient water bodies is what contributes to the multiplication of numbers of such pathogens (bacteria, viruses, protozoa and helminthes) [18].

2. Techniques for water treatment

Water treatment is defined as the removal of the above contaminants using some specific process. In most of the water treatment processes, conventional adsorption process with activated carbon is adopted and the adsorption capacity is substantially decreased in presence of high concentration of organic matters in water where the active sites are mostly occupied by these materials. In recent times, there are various technologies have been employed for the removal of water contaminants such as filtration (ceramic, bio sand, membrane, and activated carbon based filtration), heat and UV radiation, chemical treatment (coagulation-flocculation, chemical disinfection), and desalination (reverse osmosis, distillation). The various techniques in water treatment can categorized into following six classes [19]:

- Adsorption
- Biotechnology
- Catalytic processes
- Membrane processes
- Ionizing radiation processes
- Magnetically assisted processes.

There are specific advantages and disadvantages for a particular process. The nanotech based processes are promising option in current water treatment processes because of their target specificity, ease of separation, high adsorption per unit area, as well as less maintenance.

3. Magnetic materials for water treatment

There has been increased interest in using magnetic materials in water treatment which are basically composed of magnetic core of iron oxides organic compounds, carbon materials, etc. Recently, nanomaterials in different shapes, morphologies, forms, e.g., metal-containing nanoparticles, carbonaceous nanomaterials, zeolites, dendrimers, carbon nanotubes, nanofibers have been used for water purification [20]. However, the difficulty arises in using these materials is the separation of solid materials from liquid and which is more difficult as the particle size decreases in nanoscale. On the other hand, the using of magnetic, particularly the magnetic nanoparticles (MNPs) materials have the advantage of magnetic filtration in separation of solid from liquid and are more efficient [21].

However solid/liquid (S/L) separation is more difficult as the particle size decreases. On the other side, in case of magnetic sorbents based on Fe oxides, the magnetic filtration may be applied for S/L separation. Furthermore, the removal of particles from solution with the use of magnetic fields is more selective and efficient (and often much faster) than centrifugation or filtration (Yauvuz et al.) [21]. Here are the advantages of using MNPs adsorbent for water treatment processes:

- Small size and thus high surface to volume ratio
- Solid/liquid separation through magnetic filtration is selective, faster than centrifugation and filtration techniques
- Reusability
- Greater biocompatibility
- Magnetic separation

3.1. Different types of magnetic materials for water treatment

Different types of magnetic materials have been synthesized and designed for development of advanced materials and applied effectively in widespread uses such as biomedicine, magnetic resonance imaging (MRI), catalysis, spintronics, robotics, engineering, environmental remediation, etc. [22] There are different synthesizing methods viz. co-precipitation, solvothermal, hydrothermal, microemulsion, sonochemical, etc. which determine their particle size, distribution, morphology, surface functionality, and magnetic properties and in turn of their various application [22]. Magnetic materials are made from mixtures of metals of iron, cobalt, nickel, and alloys and their oxides (of the type MFe_2O_4, where M is a metal). Out of these materials, iron (zero valent iron) and its oxides, i.e., usually γ-Fe_2O_3 (maghemite) and Fe_3O_4 (magnetite) nanoparticles have attained significant interest in recent years and have been used for water treatment processes. The various composite magnetic materials such as Fe_3O_4@C [23, 24], Fe@SiO_2 [25], Fe_3O_4@TiO_2 [26], Fe_3O_4@PPO (poly(propylene oxide)), PEO (poly(ethylene oxide) [27], Fe_3O_4@PDA (polydopamine) [28], Fe_3O_4@PNIPAM (poly(N-isopropylacrylamide)) [29], Fe_3O_4@MIPs (molecularly imprinted polymer-encapsulated particles) [30], Fe_3O_4@CNTs (multi-walled carbon nanotubes) [31], Fe@CS (carbon spheres) [32], Fe/iron oxide-oxyhydroxide/rGO (grapheme) [33], etc. have been used for environmental applications. Singh and his co-workers synthesized a series of magnetic nanocomposites such as $CoFe_2O_4$–ZnS [34], Fe_3O_4@GTPs (green tea polyphenols) [35], Fe_3O_4–Cr_2O_3 [36], $CoFe_2O_4$-Cr_2O_3-SiO_2 [37] and applied for wastewater treatment.

In addition to their suitable magnetic properties, i.e., ferrimagnetic, ferromagnetic and superparamagnetic (nanoparticle size less than 10 nm), their synthesis procedure is simple and cost-effective and they can be easily functionalized as desired for many applications. The size and shape and magnetism of these magnetic materials can be easily controlled based on their application and thus they can be easily dispersed in liquid medium and their stability can be retained for multiple uses. Moreover, these materials are non-toxic or less toxic, chemically inert, thermally stable as well as biocompatible.

3.2. Use of magnetic materials for clean water technology

Appearance of water pollution as a global threat demands the development of low-cost and reliable materials for effective waste water remediation. The magnetic materials have been used for clean water technology for both in laboratory as well as field scale [38, 39]. In recent years, iron oxide nanomaterials have been used as adsorbent or immobilizing agent and photocatalyst or the both depending on nature of contaminants in water [40].

3.2.1. MNPs for the removal of metals

Heavy metal contamination in water such as cadmium, zinc, lead, chromium, nickel, copper, vanadium, platinum, silver and titanium due to industrial activities is significantly increasing which is detrimental to human beings and animals. Magnetic nanomaterial adsorbents have been potentially used for removal of metallic ions such as Cr(VI), Cu(II), Co(II),Cd(II), As(V), As(III) and Hg(II) in water [41, 42] which are more effective as compared to micron size particles. The magnetic chelating resin based materials have been used for effective removal of Cu(II), Co(II), and Ni(II) ions [43]. The magnetic hydrogels based on 2-acrylamine-2-methyl-1-propansulfonic acid can be used for removal of many heavy metal ions such Cd(II), Co(II), Fe (II), Pb(II), Ni(II), Cu(II) and Cr(III) from water in repeated cycles [44]. The Cu(II) can also be effectively removed by functionalized mesostructured silica containing magnetite [45]. The acrylate-based polymer composites with magnetite can be used in selective removal of heavy metals from water (selectivity: Cu > Cr > Zn > Ni) [46]. Layered double hydroxide (LDH) prepared from Fe^{3+} and Ni^{2+} shows good adsorption of As and subsequent magnetic separation [47]. The magnetic zeolite composites are used for decontamination of heavy metals from water [48]. The composite materials of mesoporous magnetic MCM-41 with aminopropyls are used for selective removal of As(V), and Cr(VI) in presence of Cu(II) [49].

3.2.2. MNPs for removal of organic contaminants

Magnetic nanoparticles are used as an adsorbent for the removal of various dyes and dyes stuff from aqueous solution. Removal of dyes from waste water has become a serious issue of concern because of its harmful impact on human. Dyes basically can be classified in to two categories, i.e., anionic dyes and cationic dyes.

3.2.3. MNPs for the removal of anionic dyes

Long et al. [50] synthesized Fe_3O_4@catechol/polyethylenimine (PEI) nanoparticles and tested for adsorption of three different kind of anionic dyes, i.e., methyl blue, orange G and amaranth and found the maximum adsorption capacities of 344.8, 192.3 and 146.2 mg/g, respectively. Saksornchai et al. [51] synthesized magnetite (Fe_3O_4) coated with cetyltrimethylammonium bromide (CTAB) and tested for the adsorption of anionic dye Congo red (CR) removal. They found maximum adsorption capacity for CR dye to be 93.46 mg/g. Faraji et al. [52] synthesized triazine-based nitrogen-rich network-modified magnetic nanoparticles were synthesized for the adsorption of methyl orange. Sahraei et al. [53] reported the synthesis of magnetic bio-sorbent hydrogel beads based on modified gum tragacanth/graphene oxide for the removal of heavy metals and dyes from water. They found the adsorption capacity of 101.7 mg/g for Congo red dye. Ge et al. [54] fabricated Fe@MgO magnetic nanocomposites for the removal of heavy metal ions and dye from water. They found that the synthesized nanocomposite showed excellent adsorption capacity of 6947.9 mg/g for methylene orange. Wu et al. [55] fabricated multi-functional magnetic nanoparticle core covered with polyethylenimine (PEI) derived quaternary ammonium compounds (QAC) corona through electrostatic attraction for the removal of dyes and metal ion adsorption. The adsorption results corresponding to synthesized nanoparticle showed the maximum adsorption capacity of 653 mg/g for AF as a representative of dyes. Konicki et al. [56] synthesized Fe@graphite core shell nanocomposite for the removal of anionic dyes from aqueous solution. The synthesized nanoparticles were tested for the adsorption of two anionic dyes namely acid red 88 (AR88) and direct orange 26 (DO26) and the maximum adsorption capacity was found to be 63.7 mg/g and 42.7 for AR88 and DO26, respectively. Zhang et al. [57] synthesized the Fe_3O_4 nanoparticle modified with 3-glycidoxypropyltrimethoxysilane (GPTMS) and poly-lysine (P-Lys). They found that the synthesized MNPs could effectively remove anionic dyes including methyl blue (MB), orange I (OR-I), amaranth (AM) and acid red 18 (AR-18) from water solution.

3.2.4. MNPs for the removal of cationic dyes

Cationic dyes are most toxic because they can easily interact with negatively charged cell membrane surfaces, and also they can enter in to the cells and can concentrate in cytoplasm (Bayramoglu et al.) [58]. Ge et al. [59] have studied the adsorption of cationic dyes such as crystal violet, methylene blue and alkali blue 6B from aqueous solutions by use of polymer-modified magnetic nanoparticles. The cationic dyes could be quickly removed from water solution with high efficiency at pH 5–12. More significantly, the MNP showed high efficiency as a reusable adsorbent for fast and convenient removal of cationic dyes from water solution. Yan et al. [60] have synthesized full biodegradable magnetic adsorbent based on glutamic acid modified chitosan and silica coated Fe_3O_4 nanoparticles for removal of three different kinds of cationic dyes, methylene blue, crystal violet and cationic light yellow 7GL, from aqueous solutions. Chen et al. [61] have prepared magnetic adsorbent by fabrication of chitosan/ polyacrylic acid multilayer onto magnetic Fe_3O_4 microspheres for removal of adsorption of two cationic dyes, methylene blue and crystal violet from aqueous solution. Amiri et al. [62] synthesized cobalt ferrite silica magnetic nanocomposite for the adsorption of Malachite green dye and found the adsorption capacity of 75.5 mg/g for that dye. Li et al. [63] synthesized wettable magnetic hypercrosslinked microporous nanoparticle for the water treatment. The synthesized nanoparticle consists of microporous organic polymer which combine sodium acrylate functionalized hypercrosslinked polymer with magnetic Fe_3O_4 nanoparticle to form a hybrid. They tested the synthesized hybrid for the adsorption of Rhodamine B dye and found the maximum adsorption capacity of 216 mg/g. Singh et al. [64] had synthesized the superparamagnetic nanoparticles coated with green tea polyphenol by wet chemical method. They found that the particles have a very high adsorption capacity of (7.25 mg/g) for removal of methylene blue (MB) dye in wastewater treatment. Li et al. [65] synthesized magnetic peach gum bead bio-sorbent for the adsorption of MB dye and found the maximum adsorption capacity of 231.5 mg/g.

3.2.5. MNPs for the removal of pharmaceutical products

The presence of pharmaceuticals such as antibiotics, anticonvulsants, antipyretics drugs, hormones in surface and ground water possesses a major environmental challenge. Their contamination even at trace amount is a serious concern to the aquatic organisms as well.

Attia et al. [66] synthesized magnetic nanoparticles coated zeolite for the adsorption of pharmaceutical compounds from aqueous solution. They found that the synthesized magnetic nanoparticles can remove more that 95% of PPCPs in 10 min. Reddy et al. [67] reviewed spinal ferrite nanoparticles and found that SF and its derivatives can be used for remediation of various pollutants. Nadim et al. [68] Synthesized gallic acid coated magnetic nanoparticles (GA-MNP) and used as a photocatalyst for degradation of meloxicam; a commonly prescribed nonsteroidal anti-inflammatory drug.

Recently, M. Hayasi and his coworker described the use of magnetic poly (styrene-2-acrylamido-2-methyl propanesulfonic acid) (St-AMPS) as adsorbent for removal of the pharmaceuticals viz. ceftriaxone sodium, diclofenac sodium, and atenolol from water [69].

Liu [70] discussed the use of various magnetic nanoparticles (MNPs) in pharmaceutical removal from waste water their recent review which are outlined below (**Table 2**).

3.2.6. MNPs for removal of pathogens

Xu et al. [82] demonstrated that poly-allylamine-hydrochloride (PAAH) stabilized magnetic nanoparticles are powerful tools to remove pathogenic bacteria from drinking water with high efficiency and no significant toxicity was observed in the MNPs treated water. Over 99.5% of the pathogens (four main pathogens viz. *Escherichia*, *Acinetobacter*, *Pseudomonas* and *Bacillus*) can be removed when the bacterial count was less than 105 CFU/mL.

Zhang et al. [83] synthesized magnetic nanoparticle coated with Cu doped MgO through a hydrophilic carbon layer (Fe_3O_4@C@MgO-Cu). They found its potential application as disinfectant in water purification by examining the antibacterial activity of the Fe_3O_4@C@MgO-Cu composite toward Gram-negative *Escherichia coli* and Gram-positive *Staphylococcus aureus*.

Zhang et al. [84] synthesized magnetic poly-N,N′-[(4,5-dihydroxy-1,2-phenylene)bis(methylene)]bisacrylamide) (POHABA)-based core-shell nanostructure on the Fe_3O_4 core surface (Fe3O4@POHABA). The magnetic nanocomposite, Fe_3O_4@POHABA can be used in domestic water treatment against bacterial pathogens.

Rana et al. [85] synthesized ferromagnetic Ni-doped ZnO nanoparticles and applied as an antibacterial agent to control the growth of bacterial pathogens. They found the as synthesized material to be very effective against water related bacteria such as *E. coli* and *V. cholera*.

Magnetic materials used	**Pharmaceuticals present in water**	**Processes involved for decontamination**	**References**
Nano zero-valent iron (nZVI)	Carbamazepine	Adsorption, chemical degradation (Fenton oxidation)	[71]
Nano zero-valent iron (nZVI) and PEG and zeolite supported nZVI	Amoxicillin, ampicillin	Adsorption	[72]
Zero valent iron (ZVI)	Carbamazepine	Chemical degradation	[73]
	Diazepam	Chemical degradation	[74]
Maghemite (Fe_2O_3) core confined in a silica porous layer	Atenolol, gemfibrozil, and sulfamethoxazole	Adsorption	[75]
MFe_2O_4 (M = Fe, Mn, Co, Zn)	Tetracycline, oxytetracycline, and chlortetracycline	Adsorbent	[76]
$MnFe_2O_4$/(activated carbon)AC	Sulfamethoxazole	Adsorption	[77]
$MgFe_2O_4/\gamma\text{-}Fe_2O_3$	Minocycline	Adsorption	[78]
Fe_3O_4 MNPs in ultrasound (US)/H_2O_2 system		Sono-degradation	[79]
Fe_3O_4@α-MnO_2 microspheres	Ciprofloxacin	Catalytic degradation	[80]
Fe-ZnO	Diclofenac	Photocatalytic degradation	[81]

Table 2. Magnetic nanomaterials used for removal of pharmaceuticals.

Shukla et al. [86] synthesized the iron oxide nanoparticles coated with chitosan oligosaccharide and used for the removal of pathogenic protozoan cysts, entamoeba cyst (which causes amebiasis) from water. They found that *E. histolytica* can be efficiently captured using the magnetic nanoparticles from contaminated water.

Zhang et al. [87] synthesized Fe_3O_4 nanoparticles surrounded with polyethylenimine-derived corona and found to be efficient in capturing the pathogens and heavy metals.

Zhan et al. [88] synthesized the amine-functionalized magnetic nanoparticle (Fe_3O_4-SiO_2-NH_2) and used for rapid removal of pathogenic bacteria and viruses. The magnetic materials can be effectively used to capture a wide range of pathogens including various bacteria such as *S. aureus*, *E. coli* O157:H7, *P. aeuginosa*, *Salmonella*, and *B. subtilis*.

Park et al. [89] developed a novel magnetic hybrid colloid (MHC) decorated with varying sized Ag nanoparticles. The MHC was prepared as a cluster of superparamagnetic Fe_3O_4 coated with silica shell. The MHC decorated with the Ag nanoparticle of 30 nm size (Ag30@MHC) exhibited the highest antimicrobial efficacy toward *E. coli* CN13 (6-log reduction) and the bacteriophage MS2 (2–3 log reduction).

4. Magnetic water treatment

Magnetic water treatment (MWT) is a new technique which is promising in environmental remediation in addition to its increased application in the area of medicine, agriculture and industrial process. The water molecules acquire unique physicochemical characteristics under the influence of the magnetic fields (MFs). It is a non-chemical method and the water molecules undergo change from their cluster of many loosely bound water molecules into very small, uniform and hexagonally organized clusters of molecules under the magnetic treatment [90]. These features of the magnetized water prevent the polluting agents to enter in to its cluster and also make their easy passage through the cells of plant as well as of animals. Moreover, the MFs have antimicrobial activity on water. Therefore, the magnetized water molecules depict as bio-friendly and eco-friendly compounds to environmental management as well as to plant and animal cells.

5. Sustainability of magnetic nanoparticles

While taking sustainability in to consideration there are various factors over which it depends. Important factors include environmental impact on use of MNPs, toxicity associated with the MNPs, reusability, reactivity, adsorption capacity, biocompatibility, stability, etc. For example, uncoated nanoparticles are associated with some toxicity while coating can help them to make non-toxic. Similarly, their regeneration and reusability are the main factors for making them technically more viable and economically sustainable materials for commercial uses.

6. Conclusions

In this chapter the removal of water pollutants by using magnetic materials of zero valent iron, magnetite (Fe_3O_4), maghemite (γ-Fe_2O_3) as adsorbent, photocatalyst and coagulants have been described. The MNPs have been used in removal of water pollutants through their various surface functionalities (e.g., coating with polyphenols, amino acids, sugars, alkaloids, terpenoids, proteins, carbonyl, carboxyl, carbon, polysaccharides, and semiconductors) with desired size and shapes, and magnetic behavior. Looking in to the fast development of magnetic materials in different technological and scientific fields, magnetic nanomaterials appear to be extremely promising for water and wastewater treatment. The waste water treatment methods using these materials are fast, non-toxic, and eco-friendly as compared to the available physic-chemical treatments which make it attractive for materializing commercially. Their magnetic nature makes them attractive for waste water treatment because of their easy separation from aqueous medium after purification and can be reused in repeated treatment cycles. However, research for bulk production, controlling morphology, optimizing surface functionality and their stability, and biocompatibility should be essentially considered prior to commercial application from laboratory scale. Moreover, further studies needs to be addressed to detail mechanism of magnetic nanomaterials in water treatment. The magnetic nanoparticles and their composites with their high surface to volume ratio offer more surfaces for chemical as well as physical adsorption and thus show high reactivity which gives the prospects of using these materials in large scale removal of emerging water pollutants.

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Chapter 5

EPs Antibiotics: Photodecomposition and Biocarbon Adsorption

Nilce Ortiz

Additional information is available at the end of the chapter

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Abstract

The emerging pollutants (EPs) are considered a global monitoring challenge, present in the environment in very reduced concentrations, and the proper methods for sampling and analysis are still in development. Many published types of research considering the EPs identification only depend on the analytical methodology and a more efficient higher number of EPs. The quantitative determination of the prioritized EPs in water needs advanced and ultra-sensitive instrumental techniques applied in water, water-suspended matter, soil, and biota. The regulatory framework of the water-quality parameters does not often include the microplastics, EPs, and their metabolites; especially, the groundwater water-quality monitoring and control are urgent but not yet achieved. The EPs sources in water are the sewage, industrial, and agricultural waste discard, and the UN estimated that the wastewater produced annually is about 1500 km^3, about six times more water than existing in all rivers of the word. In 2015, in China, which has a fast-growing economy, the water is a scarce resource with just 8% of the world's fresh water to meet the water needs of the 22% of the world's population.

Keywords: emerging pollutants, biocarbon, biochar, antibiotics, solar, photodecomposition

1. Introduction

In the world, about 33% of the industrial wastewater and 70% of the household sewage are untreated and directly discharged into rivers and lakes, while 80% of China cities have no sewage treatment facilities and water supplies in 90% of the cities, the water being contaminated [1]. There are 20 classes of categorized EPs accordingly with their origin; the prominent categories are pharmaceuticals (urban and protein production), pesticides (agriculture), disinfection by-products (urban and industry), wood preservation, and industrial chemical manufacturing. Different types of EPs show different properties as the organic substances divided in PBT for persistent bioaccumulative and toxic substances as POPs and persistent organic compounds. The EPs with more polarity are the pesticides, pharmaceuticals, and industrial chemicals. The inorganic compounds as poisonous metals are also found in polluted waters and finally the newly developed particulate contaminants as nanoparticles and microplastics [2].

The EPs monitoring and control are a huge problem, and the solution represents a significant challenge in sampling procedures and analytical techniques. The monitoring procedures do not cover all EPs with a potential concern being the highly known hazardous controlled, and the newly discovered contaminants as nanomaterials and microplastics are virtually analytically nonexistent. In the study, the EPs presence and toxicity are studied using bioindication; the most common organism is the *Gammarus pulex* as a model invertebrate from water and sediment.

The properties such as absorption behaviors of pharmaceuticals, for example, can vary vastly in different soil types on ionized and nonionized form, affecting the interaction of soil. Little information is available about the EPs dynamics in the water column, sediments, and the accumulation in the aquatic food chain and the loads from the agro-environment through diffuse pollution or from urban and industrial areas [3, 4].

The EPs decomposition products detection includes enantiomeric distribution of chiral compounds found in the environment, and their possible toxicological differences between enantiomers that are of concern. Such information for the risk assessment analysis is also considered [3].

Worldwide, the regulatory framework is under development to control the production and the discharge of the EPs into water resources, a complex set of regulations governing the production, commercialization, and emission to control the EPs presence in the environment and the drinking water (quality standards and monitoring specification). The European Union (EU) has a regulation plan to register, evaluate, authorize, and restrict the use of almost all EPs substances manufactured or imported to EU.

The agricultural activity is one of the most critical contributors to diffuse pollution in Europe, and such emissions are predicted to increase in the future. The agriculture activity is considered an essential business for regulating the chemical EPs use and emission discharge into the environment. Some research projects are under development, trying to treat, decompose, and remove those pollutants from the water resources.

The emerging pollutants are considered the potentially toxic chemicals present in low concentrations and many environmental compartments. They include pesticides, biocides, pharmaceuticals, industrial chemicals, and personal care products. The common entrance of these compounds in surface water resources is via untreated sewage discharge, the effluents of wastewater treatment plants (WWTPs), and from agricultural, urban, and street runoff. The organic pollutant water inputs usually occur continuously in low dosages or as peaks trigged by emission or runoff events. Such a behavior is particularly harmful to antibiotics environmental contamination, providing the optimized conditions for microorganism adaptation and increase in resistance.

The concept of chemical activity helps to understand the EPs environmental fate, distribution, quantification, and prediction of the ecological partitioning theory of the chemicals in aquatic systems as water column, sediment (mostly organic matter), and biota (lipids and proteins). It addresses single compound or mixtures reaching the equilibrium. The chemical activity relies on partition coefficients which are only available as experimental values. There are some models calculating partition coefficients from octanol–water systems (Kow-based models), and they were used for decades to estimate the concentration in different compartments.

Nowadays, the relationship of the polyparameters linear-free energy is used to calculate the partition coefficients of biological and nonbiological matrices including lipids and different proteins [4, 5]. The model helps to describe the diffusion and partitioning processes and estimate when an environmental compartment acts as an EPs source or a sink for a single contaminant or a multi-compartment system.

2. EPs photodecomposition

Two of the main topics of growing concern in analytical chemistry are the development of green water treatment. TiO_2 has emerged as a promising photocatalyst for environmental cleanup applications; they have efficiently decomposed and removed a variety of pollutants promoting the generation of OH radicals using oxidation reactions with in situ active oxygen generated upon light irradiation. In water purification, photodegradation of contaminants in real water samples has become an important topic of research in the recent years.

There are some studies using electrocoagulation process to decompose EPs compounds. The process is an electrochemical introducing coagulants and removing suspended solids, colloidal material, and metals as well as other dissolved solids from water and wastewater eliminating pollutants, pesticides, and radionuclides. A direct current is applied, and one electrode is soluble into a solution which finally precipitates as oxides or hydroxides.

The environmental chemistry is the base for many treatment technologies of these pollutants, and the application of the adsorption process is one of the most used techniques. The results and comparison of different treatment technologies usually consider the initial concentration and the final concentration. The adsorbent materials are graphene oxide, clay mineral and biochar, nanocrystalline mineral, and arsenite using an enhanced coagulation process [6, 7]. The pharmaceuticals used iron chemical reduction reaction, and the advanced oxidation performed by ozone/UV also was used. The pharmaceuticals uses iron chemical reduction reaction, and the advanced oxidation performed by ozone /UV. The study of micropollutants biodegradation uses also a membrane.

The most common material used for EPs adsorption is the activated carbon (AC) with high porosity and surface area, and the use of AC shows the removal percentage higher than 90% for a wide variety of compounds bringing the residual concentration below the regulation limit. Other materials need more contact time for the same results. The advanced wastewater reclamation plant often uses the AC [5]. Many authors point out the high importance of the AC origin, depending on the initial crystalline structure of the biomass, the AC obtained from wood, vine, and olive waste, and coal showed the removal percentage always higher than 80% for antibiotics.

There are some adsorbents used for pharmaceutical removal as biochar, clay minerals, zeolites, Fe-Mn-binary oxide, graphene oxide, alumina, nanoscale iron, molecularly imprinted polymer, and carbon nanotubes [5, 8].

The phase extraction uses organic phase to remove organic contaminants, and the use of membrane technology is for pharmaceuticals removal from polluted waters. The bases of the membrane technology are the hydrostatic pressure to remove suspended solids, and solutes with a high molecular weight also classified as ultrafiltration, nanofiltration, microfiltration, forward osmosis, and reverse osmosis. The high removal percentages are obtained for forward and reverse osmosis with the removal percentages usually more than 95%.

The biological processes in conventional activated sludge decompose only the natural pharmaceutical compounds like caffeine, dichlorofenac, and trimethoprim. The advanced oxidation processes provide higher removal percentages associated with the hydroxyl radical production with removal percentages always higher than 96% including the sonochemical decomposition. The solar photo Fenton process obtains the removal percentage of 95–97.5% in just 20 min of reaction.

Many published results indicate that the degradation of EPs using a single treatment is not likely the best approach to treat and remove EPs from water, and the use of a combined technology can overcome deficiencies of individual technologies and be able to ply in complex mixtures of contaminants. The advanced oxidation processes are at present the most efficient degradation processed for EPs contamination.

The results of the kinetics studies of photodecomposition and biocarbon sorption provide valuable insights about the kinetics models: pseudo-first-order (Eq. (1)), pseudo-second-order (Eq. (2)), and intraparticle (Eq. (3)) with the determination of photodecomposition and adsorption rates on pseudo-first-order equation [9, 10].

$$\log(q_e - q_t) = \log(q_e) - \frac{K_1}{2.303}t \tag{1}$$

where K_1 is the pseudo-first-order rate (min^{-1}) and qe (mgg^{-1}) refers to the experimental adsorbed mass at equilibrium. The plotting of the calculated values of ln (qe-qt) for t (time) and the calculation of K_1 were used the slope values of the line equation.

Pseudo-second order equation:

$$\frac{t}{q_t} = \frac{1}{K_2} + \frac{1}{q_e}t \tag{2}$$

where K_2 ($g.mg^{-1}.min^{-1}$) is the kinetics adsorption rate, plotting the t/qt for t (min), and the calculation predicted the adsorption capacity qe (mg g^{-1}) and the integrated adsorption rate K_2 with the slope and the intercept of the line equation, respectively.

Intraparticle equation:

$$\log(q_t) = \log(K_{id}) + a\log(t) \tag{3}$$

The use of the experimental results allows performing the kinetics calculations [11–13], using Eqs. (1)–(3). The pseudo-first-order equation represents a logarithm of the reactant species and the reaction time; larger K_1 indicates a fast reactant consumption and small time to complete the reaction; the R^2 values obtained for the pseudo-first equation indicate a lower correspondence between the results and the theory. Some published results show the solar photodecomposition processes with goethite as pseudo-first-order kinetics with $K = 0.26 \times 10^{-2}$ min^{-1}. Usually, the photodecomposition experimental results indicated a lower correlation with pseudo-first-order, sometimes just one K_1 value; all results showed a better correspondence with the pseudo-second order.

Considering the pseudo-second-order reaction, the sum of the exponents in the equation rate is equal to two for the plotted reactant concentrations with time. The pseudo-second-order response depends on the initial content, of the two different reactants A and B combining in a single elementary step. Before the rate, where A decreases, they can be expressed using the differential equation, and the linear equation can be rearranged, integrated, and followed where the slope value is K_2. The pseudo-second order showed better correspondence with the experimental results corroborating with many published results for biocarbon adsorption and amoxicillin (AMX) removal treatments. The interparticle reaction usually points out the slow step of the adsorption reaction.

The use of integrated processes as solar/TiO_2 photodecomposition followed by adsorption has many advantages as an excellent potential for photocatalysis with the application of solar treatment chambers and possible self-cleaning surfaces. However, the practical applications and continuous use demand solutions to kinetics problems, and they may rise as the adsorbent-reduced surface area, TiO_2 oxidation surface, and solid low stability due to long-term use and the potential oxide mass production. The amoxicillin degradation with solar/TiO_2 anatase proceeds about three times faster than with ultraviolet (UV) lamp [14, 15]. The explanation of the disproportional improvement oxidation rates is the difference between the small spectrum irradiance of UV band and the broad spectrum of visible solar light. The intensity of radiation spectrum grows with an increasing wavelength from 300 to 500 nm. The combination of solar photodecomposition and the adsorption process is efficient and low cost.

3. The antibiotics photodecomposition products

The electrospray ionization mass spectrometry (ESI-MS) analytical technique measures the EPs methylene blue (MB) photodecomposition. Before the photodecomposition reaction, the methylene blue compound was m/z 284 (**Figure 1(a)**), and after 1 day of photodecomposition, there are several peaks (**Figure 1(b)**). Those peaks were MB fragment degradation compounds with m/z values of 109, 129, and 165. Those peaks have the relative intensity of 37.3, 44.2, and 40.5% considering the original MB peak of 100% with m/z 284 (**Figure 1(a)**).

The EPs dye photosensitization process involves the dye initial electronic excitation D to D* induced by hν incident radiation energy which ejects one electron in the semiconductor (SC) conduction band [8, 16, 17]. The emitted electron reacts with the environment oxygen oxidizing the radial D^{*o}, and the total process results in colorless products, Eq. (6).

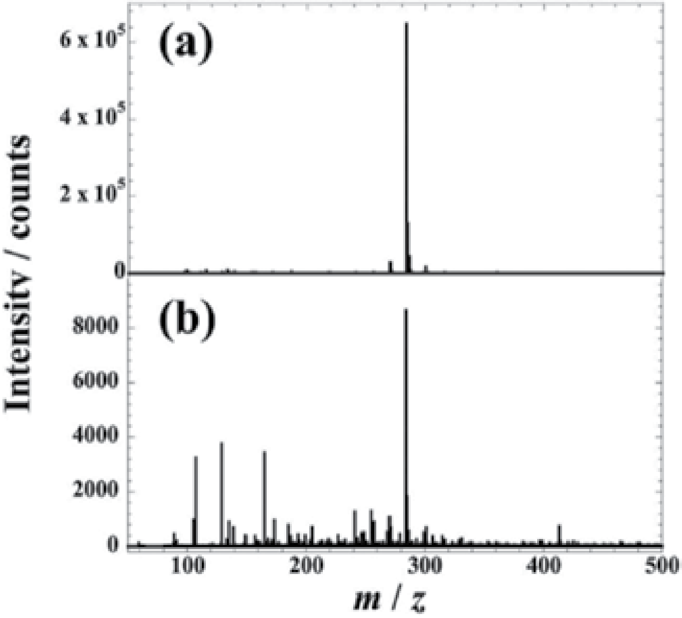

Figure 1. ESI-MS spectra of methylene blue photodecomposition (a) before and (b) after degradation of 1 day (adapted from Kobzi et al. [27]) [8].

The study provides some example of dye sensitization, and the photosensitized bleaching occurring under visible light and an aerated aqueous dispersion of TiO_2. The light absorbed by the dye alone was able to promote its rapid and complete photobleaching. The photonic efficiency η for the visible photobleaching of the MB is already known, and it is a function of the incident radiation wavelength. The spectrum η versus λ plot was similar in shape to the diffuse reflectance spectrum (DRS) of the MB adsorbed on TiO_2 with a peak at 665 nm which is the wavelength of the maximum adsorption for MB.

By contrast, the dye photolysis involves the electronically excited state of the dye which is either unstable and quenched by ambient O_2 to produce singlet oxygen which oxidizes the dye. Considering only the equation, it is not surprising if the rate of dye bleaching due to photolysis is often unchanged in the absence of the semiconductor. When the photolysis and photosensitization are examined, the presence of SC enhances the production of the bleached product.

$$D + hv'' \rightarrow D^{*} (+O_2) \rightarrow \text{Bleached products} \quad (4)$$

The rapid and irreversible reduction of the photogenerated holes by glycerol followed the reduction reaction and the molar absorptivity of 4.7000 M^{-1} cm^{-1} at 620 nm. The glycerol behaves as an SED which is also present in the ink film. The MB photocatalytic process runs as follows:

The use of photocatalyst indicator (paiis) helps to measure the electron generation efficiency of the $TiO_{2,}$ changing from blue redox dye Resazurin (Rz) to pink Resorufin (Rf). The Rz as the MB adsorbs little in the UVA region. The elimination of the photogenerated holes by the glycerol, which acts as an SED, followed the reduction reaction.

Photocatalyzed MB redox reaction:

$$\text{Glycerol} + \text{Rz} \xrightarrow[h\nu <= \text{Ebg}]{\text{SC}} \text{Glyceraldehydes} + \text{Rf (reduction reaction)} \tag{5}$$

$$\text{Glycerol} + \text{MB} \xrightarrow[h\nu <= \text{Ebg}]{\text{SC}} \text{Glyceraldehydes} + \text{LMB (reduction reaction)} \tag{6}$$

The colorless species identified as Leuco methylene blue (LMB) is readily re-oxidized to MB by ambient O_2 and has to be produced and maintained in anaerobic conditions to be stable, **Figure 2**. This environmental condition also ensures that the traditional dye-sensitized bleaching reaction cannot occur [19, 20].

The MB is excited under the red region of the light source and received electrons to the excited MB which produces an anion which abstracts a proton from water to provide LMB; the LMB is very readily re-oxidized back to MB if there is any oxygen in the solution [9, 10, 21]. The CG results showed no change in the MB concentration for the first few minutes of reaction, but if the reaction progresses, efficiently all molecules of MB will be converted to LMB. Subsequently, the visual observation indicates that the intense blue color of the solution starts to disappear as the reaction progresses as an effect of the photoreduction of the MB to LMB at the adsorption band of MB. Experimental results indicated the irradiation of the MB at 365 nm in the absence, and the presence of glycerol electron donor occurs, and the MB rapidly photobleached via an oxidative route with LMB primary production in 15 min. The air presence also quickly reduced the LMB to MB, gaining 92% of the original color.

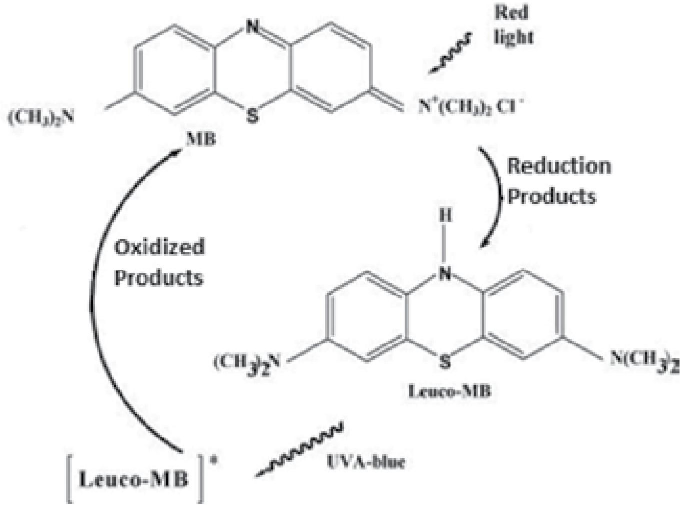

Figure 2. Scheme for photodecomposition mechanism of MB and the Leuco MB (LMB) production [9, 10].

The photocatalytic dye bleaching process using the λ = 617 nm is much slower than the reaction mediated by TiO_2 and λ = 365 nm light. The MB/glycerol has the potential as the dye-based test for UV presence, and visible absorbing photocatalytic materials provided by photocatalyst test.

The redox potential for the reduction of MB at pH 7 to LMB is 0.011 v, whereas for oxygen it depends on electron transference and how many are present. For 4e-, O_2/H_2O (0.815 v) and for 1 electron O_2/O_2- (−0.33 v). It is not obvious that an SC is capable of reducing MB to LMB and also will be able to reduce O_2. The oxi-reduction indicator dyes are important to visualize the redox chemistry and measure the dye environmental oxidation/reduction.

The environmental antibiotics resistance to widely used medical and veterinary medicine is a serious problem and poses a significant threat to the health of humans and livestock infected with resistant bacterial strains. The alarming fact is that resistant genes can be mobilized between various environmental compartments and transferred into the food chain. The conventional processes associated with sewage treatment, hydrolysis, biodegradation, and sorption are ineffective for the removal of many antibiotics, and thus the photodegradation may be the predominant transformation pathway for antibiotics deactivation in the environment.

The UV spectra of amoxicillin (AMX) and the amoxicillin decomposition products (ADPs) as ADP1,2, ADP4,5, and ADP8,9 consisted of two peaks at λ = 230 and 275 nm, similar with AMX. This effect is due to the para-substituted phenolic group, which do not change in the AMX and ADPs skeleton (**Figures 3** and **4**) and is the primary contributor to the observed UV spectra. Those peaks enable a quantitative calculation of these ADPs in the environment based on the assumption that the UV RF is relatively similar for AMX and its ADPs at λ = 230 nm.

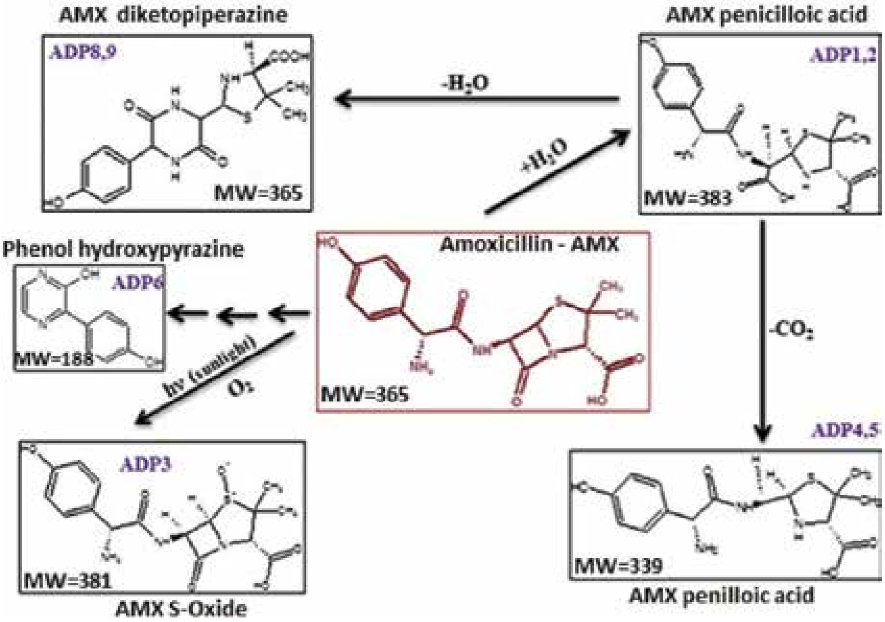

Figure 3. Suggested photodegradation pathway of amoxicillin in an aqueous medium (adapted from Gozlan et al., 2010) [7].

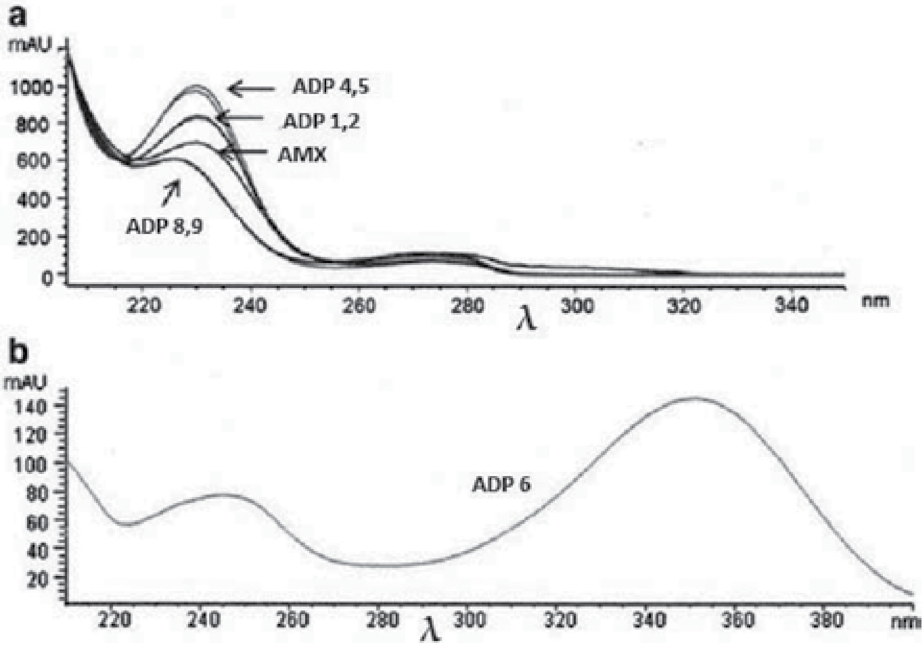

Figure 4. UV spectra of (a) amoxicillin and degradation products ADP1,2, ADP4,5, and ADP8,9 and (b) the degradation product ADP6 [11].

On the other hand, the compound ADP¨6 has conjugated double bonds (**Figure 3**), and thus, its UV spectrum consists of two different peaks at λ = 240 and 250 nm. The calculation and quantification of ADP could not be in the environment due to the incompatibility of the AMX and ADP6 UV spectrum at λ = 230 nm.

The confirmation of the proposed AMX DP structures was by comparison of the H NMR spectra of the AMX and those of purified ADP. **Figure 4** presents the degradation schematics of the AMX to its ADPs, the products ADP1,2, ADP4,5, and ADP8,9 are epimers, and preparative purification was carried out separately for each.

The penicilloic acid epimers (ADP4,5) are rapidly isomerized and become stable at an isomer ratio of 3:2, so the NMR spectra could not be obtained separately, **Table 1**. The isomers spectrum showed that H in the AMX spectrum is δ = 5.44 ppm, consisting of two hydrogen atoms, which shift to a higher field and become H-6a and H6b δ = 5.18 and 4.46 ppm, the ADP3 and ADP 8,9.

In recent years, the water-quality monitoring results indicated the presence of antibiotics and antibiotics residues in aquatic environments in many countries, including Europe, North America, and Asia. In addition, the antibiotic-resistant bacteria have become a serious problem worldwide, caused by the excessive use and incorrect discharge of antibiotics into the environment.

The use of ampicillin (AMP) is worldwide, as an essential antibiotic but this organic molecule rapidly decomposes in water containing bivalent cations as Ca^{2+} and Mg^{2+} and their

Hydrogen	AMX	ADP1	ADP2	ADP3	ADP4	ADP5	ADP6	ADP7	ADP8
CH_3	136	0.95	1.33	1.20	1.37	1.26		131	1.28
	1.37	1.53	1.39	1.57	1.53	1.62		1.65	1.66
H-4	4.09	3.97	3.67	4.31	4.00	4.09		3.69	3.69
H-17	5.07	5.18	5.10	4.99	5.09	5.09		4.91	4.95
H-2	5.44	5.17	5.37	5.25	4.95	5.05		5.17	5.15
H-6a	5.44	5.18	4.46	5.90	3.54	3.70		3.90	4.39
H-6b					3.87	3.83			
H-21,23	6.92	6.96	6.96	6.94	6.96	6.96	6.81	6.82	6.82
H-20,24	7.31	7.40	7.40	7.31	7.35	7.35	8.13	7.18	7.18
ADP6							7.24		
ADP6							7.45		

Table 1. The RMN results for amoxicillin photodecomposition and byproducts [11].

detection in the environment is difficult. The development of analytical technique allows the identification and quantification of the ampicillin and ampicillin degradation by-products as 2-hydroxy-3-phenylpyrazine (HPP) in the environment. The results indicate their presence in 42–79% of the monitored rivers and household ponds but they were not detected in aquaculture ponds. In these locations, the HPP concentrations were in the range of 1.3–413.3 ngL^{-1}.The research results indicate the HPP presence as a promising marker for AMP presence and other β-lactam antibiotics with AMP substructure into the environment [22, 24, 25] (**Figures 5** and **6**).

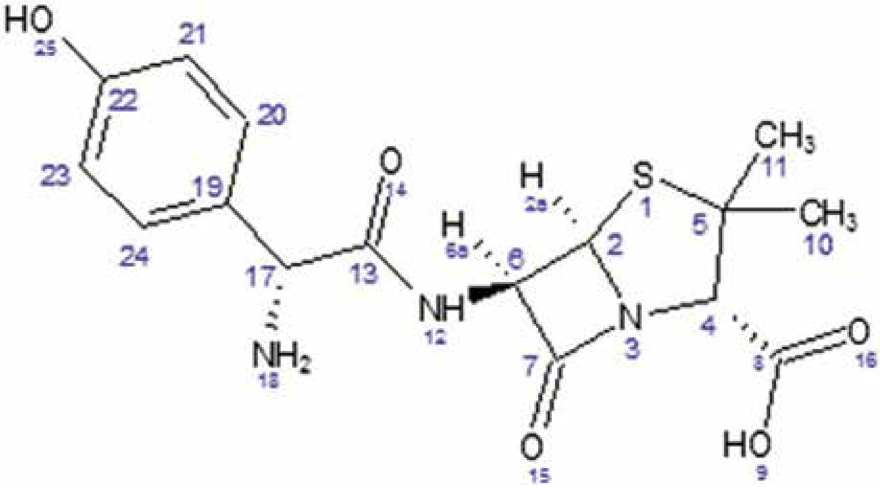

Figure 5. Amoxicillin chemical structure.

The β-lactams antibiotics such as ampicillin, penicillins, cephalosporins, and oxicephalosporins inhibit biosynthesis of the bacterial cell wall by acylating and thereby inactivating transpeptidases. The antibacterial activity depends on the β-lactams rings, and some complex

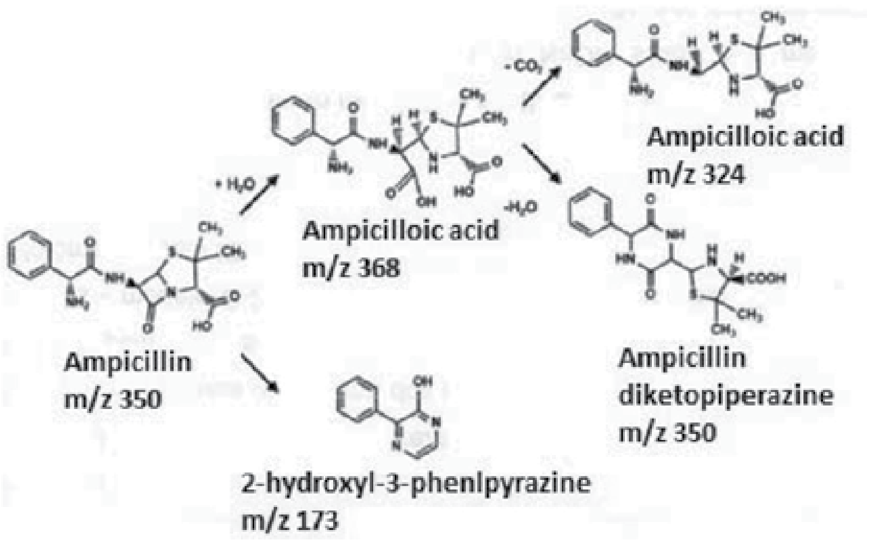

Figure 6. The photodecomposition scheme for ampicillin and its by-products.

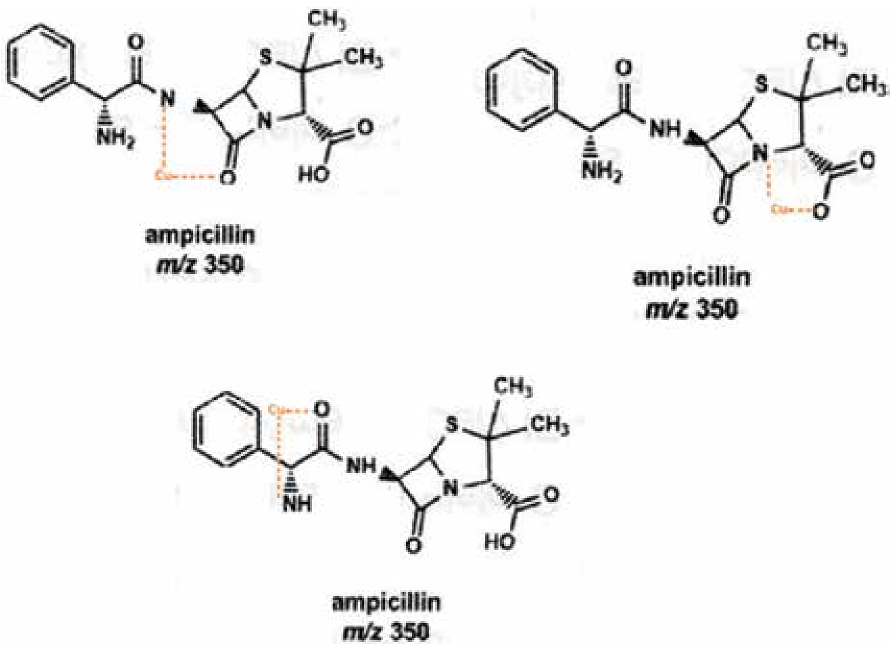

Figure 7. The complex formation with Cu-ampicillin chemical structure as a complex ligand.

compounds are responsible for their deactivation. There are several possible sites of the coordination for the metal ions on penicillin. The nitrogen and the double oxygen bonding are the most probable [13, 24, 26].

The amoxicillin and many antibiotics can act as a complex ligand with several possible sites for metal ions like Cu (II), Zn (II), and Cd(II) for coordination on penicillin. In the study, the kinetics and thermodynamics calculations are easy to find and how the neighboring group affects the probable complexation sites, of metals and the C=O of the antibiotic β-lactamic group and the NH amido penicillin group. The two most probable structures are shown in **Figure 7**. They are not excluding each other. For cephalexin and Cu^{2+}, the interaction takes place through the side chain, the same as expected for ampicillin structure.

The metal ligand binary constants at temperature 37°C and ionic strength for ampicillin and Co^{2+} are = 3.12, for Ni^{2+} = 3.66, for Cu^{2+} = 4.79 and for Zn^{2+} = 2.98. Usually, the complex constants with Cooper are more stable [14, 23].

4. Binary and ternary antibiotics mixture

The TiO_2 is steady, inexpensive photocatalyst, and widely applied for removal and decompose organic pollutants. However, the poor selectivity of the TiO_2 is not conducive to remove high toxic contaminants from mixed solution, mostly in the presence of other pollutants [15, 16]. Some studies use tetracycline (TC) as a molecular template and the TiO_2 fly ash cenospheres as a supporter, the synthesis of the molecularly imprinted photocatalyst (MIP). Such a material possesses the specific recognition ability toward tetracycline (TC) using surface-imprinting technology and the photo-induced method. The cenospheres hollow spherical structure has the diameter from 90 to 120 μm, and the degradation process of photocatalytic activity of MIP with 20 mgL^{-1} of TC under visible light radiation reached the photodegradation rate of 77%. Also, MIP showed the TC-selective recognition and promoted the photodegradation of TC in the ternary solutions containing TC, oxytetracycline (Oxy), and ciprofloxacin (CIP). The coefficients of selectivity of degradation from TC, Oxy, and CIP were 1.67 and 1.25, respectively. The photodegradation mechanism of TC analyzed by mass spectrum (MS) indicated the TC decomposition step by step, resulting in CO_2, H_2O, and other gases.

A large number of antibiotics and their residues lead to the environmental emergence as a threat to indigenous microbial populations. The tetracycline (TC) ranks second in the global production and use. In spite of its consumption, environmental TC residues are very low (μgL^{-1} or nanogram L^{-1}), but they are resilient, and the TC residues may cause a series of ecological environmental and human health effects, such as promoting the resistant bacteria. The photocatalytic with solar energy is green technology and capable of decomposing the organic pollutant to a nontoxic compound.

The molecular imprinting is a versatile and straightforward method for the preparation of robust materials which can recognize the specific target in secondary and tertiary systems. Then, stability, the ease of development, and low cost make the molecularly imprinted particularly attractive. Two or more antibiotics always coexist in the polluted aquatic environment. Thus, it is essential and meaningful to discuss the multicomponent antibiotics solution.

Published works related a variety of antibiotics in polluted soil and water environment. Therefore, it is of great significance to explore the ecological risk of the combined exposure to various antibiotics. The mixture of different types of antibiotics may lead to varying joint effects on the bacteria's, synergistic, additive, and some antagonistic effects.

Some published works indicate that antibiotics mixtures present synergetic effects and others antagonistic effects. The presence of sulfonamides (SA), as potentiator effects (SAP), and tetracycline's (TC) was investigated for binary and tertiary mixture toxicity. The mixtures of SA-SAP and SA-SAP-TC presented a synergetic impact on bacteria tests, while SA-TC and SAP-TC showed antagonistic effects. The TC presence in ternary mixtures altered the toxic ratio of SA and SAP, which lead to the various joint effects of the ternary mixtures on different bacteria populations.

5. The biocarbon: adsorbent uses

Since the beginning, the powder biocarbon in Brazil was considered a worthless material, always related to airborne pollution, infant and slavery condition work, and work-related disease. Nowadays, a group of researchers is trying to restore the biocarbon industrial use as an essential additive for agroindustry on soil amendment with possibility of enhancing the organic matter and water content retention.

The biocarbon (biochar) has been used to increase the amount of organic matter in the agricultural soil. There are many benefits in this application, resulting in improved soil fertility, nutrient content, water retention, better physical structure, and improved microbial activity. Intense agricultural operation tends to reduce the amount of organic matter present in the soil.

The application of biocarbon can be decisive in the semi-arid region of the northeast region with low rainwater retention, and such water source is scarce and used in a short period of the year. Soon, the agriculturists of these areas will be able to produce the own bio-carbon utilizing the agriculture biomass.

The biocarbon organic matter composition allows its use as a slow-release fertilizer such as adsorbent properties promoting the addition, retaining and the release of nutrients. The addition of some plastic agents like stack gel and bentonite clay helps the nutrient releasing rate control during the pellets formation. The biocarbon is a renewable organic matter source and provides phosphate and nitrate from wastewater adsorption treatment with nutrient retention for further agriculture use as slow-release fertilizer.

Biocarbon produced in a high-temperature pyrolysis application on heavy metals retention such as cadmium and zinc is studied. In some cases, it has been used in the recovery of soils with different levels of cadmium, zinc, and leads contaminated by the mining industry, reducing the concentration of toxic metals in plants such as beans.

Biocarbon as an alternative adsorption matrix for water treatment and emerging pollutants removal has been confirmed. The biocarbon usually shows better environmental results in comparison with activated carbon, and also in many cases, it provides better potential energy supplied for lignocellulosic materials.

The biochar has various environmental applications like pollutant removal, carbon sequestration, and soil amendment. It has unique properties which makes it an efficient, cost-effective, and environmentally friendly material for contaminant removal. The different physical–chemical properties of the surface are microporosity and pH that can maximize its efficiency to various environmental applications. The research updates related to the pollutants interaction with surface functional groups of biochar and the effect of the parameters variability in biochar attribute to specific pollutants removal, involved mechanisms, and efficiency for these removals.

Emerging pollutants (EPs) include agrochemicals, antibiotics, polycyclic aromatic hydrocarbons (PAHS), polychlorinated biphenyls (PCBs), volatile organic compound (VOC), aromatic dyes, toxic metals, ammonia, nitrate, phosphate, sulfite from aqueous, gaseous, and solid phases. There is also the possibility of the biochar-tailoring properties to improve their removal efficiency for organic–inorganic contaminants [20]. The soil application not only remediates but improves soil properties as water-holding capacity, O2 content, and moisture level.

The removal of aromatic dyes, for example, rhodamine, methyl violet, and methyl blue by anionic biochar, is mainly involved in electrostatic attraction/repulsion interactions [17, 18, 25]. In these sorption mechanisms, highly polar biochar pyrolyzed at = <400°C contained aromatic Pi-configuration and electron donor and acceptor functional groups [20]. These π electron-rich biochar functional groups (-Ve) have electron donor-acceptor interactions with π electron-deficient (+Ve) organic dyes. Hence, these interactions have resulted in an electrostatic repulsion and promoted pollutant adsorption via H-bonding between biochar and apolar dyes [26].

Crop residues as peanut, canola, soybean straw, rice hull, and so on derived biochar at a temperature of <400°C contained more O- and H-bearing functional groups. Thus, such a material exhibited a higher sorption capacity for apolar methyl violet and methylene blue due to pH change through biochar amendment [17, 24]. At higher pH, the net negative charge on biochar surface (due to dissociation of phenolic OH groups) increased the electrostatic interactions with methyl violet, whereas at lower pH, the π-π electron donor-acceptor interactions increased, thus improving the H-bonding for methylene blue sorption.

At zero point charge (ZPC), biochar does not have any surface charge, and it develops surface charge dependent on pH. The pH below the biochar ZPC (8.17, 8.52 and 8.79) comprised positive charge and sorbs less methylene blue. Whereas the pH higher of the biochars ZPC comprise negative surface charge increasing the methylene blue adsorption due high electrostatic attractions.

Likewise, the sorption of polar antibiotics sulfamethazine (SMZ) by hardwood/softwood-derived biochars (produced at 300–700°C has pH-dependent interactions. At higher pH, H bonding occurs between anionic SMZ and COOH or OH group biochar. At lower and neutral pH, the π-π electron donor-acceptor interactions and cation exchange are dominant mechanisms between biochar and SMZ [23, 26]. These studies confirmed that pH is the most crucial factor for biochar interactions with polar organic pollutants.

The integrated process of photodecomposition followed by adsorption study includes the adsorption isotherms, performing the calculations of Langmuir, Freundlich, and Redlich-Peterson (R-P) isotherms, Eqs. (7)–(9), respectively. The Langmuir isotherm adsorption assumes an ideal solid surface composed by a series of distinct sites capable of binding the adsorbate in a molecular coverage; the chemical reaction between the adsorbate molecule and the surface is a pseudo-second-order reaction. The Freundlich isotherm is empirical but widely used, and the value of n is a measure of the adsorption intensity higher than 1, where the adsorption processes are more favorable. The Redlich-Peterson (R-P) is more accurate than the Langmuir and Freundlich due the "g" value equal to 1. Usually, the R-P is by Langmuir and Freundlich isotherm equations; such observed behaviors were also studied. The error calculation will help to point out better isotherm adjustment

$$\mathrm{Ce/qe} = 1/\mathrm{Q}_0\,\mathrm{b} + \mathrm{Ce/Q}_0, \tag{7}$$

$$\mathrm{logqe} = \mathrm{logKf} + 1/\mathrm{n}\ \mathrm{logCe} \tag{8}$$

$$\ln\left(\mathrm{Ce/qe}\right) = \mathrm{g}\ \mathrm{lnCe} - \mathrm{lnKr} \tag{9}$$

where Ce = equilibrium concentration (mgL^{-1}), qe = the amount adsorbed at equilibrium ($\mathrm{mg.g}^{-1}$), Q_0 and b are Langmuir constants, Q_0 indicates the adsorption capacity of the material, and b indicates the energy of adsorption. Kf and n are Freundlich constants. Kf indicates the adsorption capacity of the material and n indicates the efficiency of adsorption. Kr and g are Redlich-Peterson constants; Kr indicates the adsorption capacity and "g" is the exponent between 0 and 1.

The RL values were in the interval from 0 to 1, with favorable adsorption accordingly with Langmuir isotherm. The Freundlich isotherm constant n was also in the range of $2 < n < 10$; the indication of the agreement with Freundlich model with equal adsorption heating and Redlich-Peterson parameters were also promising.

6. Conclusion

The emerging pollutants are considered potentially toxic chemicals present in low concentrations and many environmental compartments. They include pesticides, biocides, pharmaceuticals, industrial chemicals, and personal care products. The common entrance of these compounds in surface water resources is via untreated sewage discharge, the effluents of wastewater treatment plants (WWTPs), and from agricultural, urban, and street runoff. The organic pollutant water inputs usually occur continuously in low dosages or as peaks trigged by emission or runoff events. Such a behavior is particularly harmful to antibiotics environmental contamination, providing the optimized conditions for microorganism adaptation and increase in resistance. The concept of chemical activity helps to understand the EPs environmental fate, distribution, quantification, and prediction of the ecological partitioning theory of the chemicals in aquatic systems as water column, sediment (mostly organic matter), and biota (lipids and proteins) address single compound or mixtures reaching the equilibrium. The chemical activity relies on partition coefficients which are only available as experimental values. TiO_2 has emerged as a promising photocatalyst for environmental cleanup applications; they have efficiently decomposed and removed a variety of pollutants, promoting the generation of OH radicals using oxidation reactions with in situ active oxygen generated upon light irradiation. In water purification, photodegradation of contaminants in real water samples has become an important topic of research in recent years. The results of the kinetics studies of photodecomposition and carbon sorption provide valuable insights about the kinetics models: pseudo-first-order (Eq. (1)), pseudo-second-order (Eq. (2)), and intraparticle with the determination of photodecomposition and adsorption rates. The ESI-MS analytical technique allows the measurement of the EPs methylene blue photodecomposition. Before the photodecomposition reaction, the methylene blue compound was only m/z 284, and after 1 day of photodecomposition, there are several peaks.

The UV spectra of amoxicillin (AMX) and the amoxicillin decomposition products (ADPs) as ADP1,2, ADP4,5, and ADP8,9 consisted of two peaks at $\lambda = 230$ and 275 nm, similar with AMX. This effect is due to the para-substituted phenolic group, which do not change in the AMX and ADPs skeleton and is the primary contributor to the observed UV spectra. The development of analytical technique allows the identification and quantification of the ampicillin and ampicillin degradation by-products as 2-hydroxy-3-phenylpyrazine (HPP) in the environment. The results indicate their presence in 42–79% of the monitored rivers and household ponds. In these locations, the HPP concentrations were in the range of 1.3–413.3 $ngL^{-1.}$. The amoxicillin and many antibiotics can act as a complex ligand with several possible sites for metal ions like Cu (II), Zn (II), and Cd (II) for coordination on penicillin. The kinetics and thermodynamics calculations indicate neighboring group effects of the probable complexation sites, of metals and the C=O of the antibiotic β-lactamic group and the NH amido penicillin group. Published works related to a variety of antibiotics in polluted soil and water environment. Therefore, it is of great significance to explore the ecological risk of the combined exposure to various antibiotics. The mixture of different types of antibiotics may lead to varying joint effects on the bacteria, synergistic, additive, and some antagonistic effects. The biocarbon acts as an alternative adsorption matrix for water treatment and emerging pollutants removal, usually showing better environmental results in comparison with activated carbon, and also in many cases, it provides better potential energy supplied for lignocellulosic materials.

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