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Selection of Derivatisation Agents for Chlorophenols Determination with Multicriteria Decision Analysis

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ABSTRACT

The paper shows very systematic method of selection of derivatisation agents for a given group of analytes. In this study 8 derivatisation agents are assessed for their capability to derivatise 8 chlorophenols. Multicriteria decision analysis is used to combine many objectives of derivatisation agents selection into single, easy to be interpreted numerical value. Three basic analyses were performed to obtain rankings with the aims to assess derivatisation reaction, chromatographic separation of derivatised analytes and greenness of derivatisation agents. The first assessment showed acetic anhydride to be the most favourable alternative, the second one indicated N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) - chlorotrimethylsilane (TMCS) mixture to give the best separation and the third proved heptafluorobutyrylimidazole (HFBI) to be the greenest agent. Fourth, comprehensive assessment showed BSTFA:TMCS to have the best total performance. Multicriteria decision

analysis can be successfully applied in analytical procedure multi-objective optimisation, at the stage of derivatisation agent selection.

Keywords: method optimization; TOPSIS; multicriteria decision making; gas chromatography; derivatisation; chlorophenols

1. Introduction

The eighth principle of Green Chemistry states that unnecessary derivatisation should be minimised or avoided whenever possible since it requires additional reagents and can generate wastes [1]. The term derivatisation is referred to chemical reactions performed to obtain analyte derivatives that can be isolated, separated and detected more easily than target compounds. Even though avoiding derivatisation reactions is advisable, the use of simple microreactions is eminently justified when enables, for instance, the sensitive determination of analytes of concern present at ultra-trace levels in environmental compartments. Notwithstanding, the chemicals used in derivatisation reactions can significantly differ in terms of environmental, health and safety (EHS) concerns, so this information should be carefully considered for appropriate selection of derivatisation agents [2].

Chlorophenols (CPs) are toxic, mutagenic and carcinogenic substances that have been used in the chemical and pharmaceutical industry and agriculture. As a consequence of their widespread use and recalcitrance to biodegradation, chlorinated phenols are widespread pollutants in the environment. Apart from their release to the environment as a consequence of their anthropogenic uses, CPs can also be formed during water disinfection (by chlorination) and biodegradation of herbicides such as 2,4-dichlorophenoxyacetic acid or 2,4,5-trichlorophenoxyacetic acid [3–5]. Several CPs have been classified as priority pollutants by the US Environmental Protection Agency [6], and a maximum admissible

concentration has been set by the European Union at 0.5 μg L^{-1} for total phenols and 0.1 μg L^{-1} for individual compounds in water, respectively [7]. Thus, a number of methodologies have been described in the literature for determination of CPs involving mainly chromatographic techniques with different detectors [7]. CPs can be determined by liquid chromatography, although they show low resolution and can be affected by the sample matrix. Alternatively, CPs can be determined by gas chromatography. In this case, derivatisation of CPs prior to their determination is recommended in order to increase analytes' volatility, to improve the chromatographic characteristics of analytes and/or to increase the detector sensitivity. Different derivatisation reactions have been reported in the literature for CPs, mainly based on acylation and silylation reactions [8–10]. Metrological aspects are usually considered when choosing derivatisation agents for CPs, whereas the EHS issues of derivatising agents are commonly overlooked.

Choosing the best solution is sometimes a difficult decision problem, especially if we take into consideration many alternatives, many criteria, even contradictory ones, or there is also a need to involve decision makers' preferences. In these cases making a proper, objective decision may be impossible. Therefore, it may be a good idea to use some aid of Multicriteria Decision Analysis (MCDA). MCDA is a group of methods based on mathematical algorithms which are able to formalise decision problem. They allow to analyse the problem with a reference to various points of view, i.e. technical aspects, quality, environmental aspects, security and safety, delays, ethics, economy [11]. Additionally, these methods provide assessment which includes the decision makers' preferences by giving a proper weight values to each criteria. The most popular MCDA methods are TOPSIS (Technique for Order of Preference by Similarity to Ideal Solution), AHP (Analytic Hierarchy Process), PROMETHEE (Preference Ranking Organization Method for Enrichment Evaluations), ELECTRE (Elimination and Choice Expressing the Reality), and MAUT (Multi-Attribute

Utility Theory). MCDA methods are successfully used to solve complex problems in many areas such as management, business, engineering, science and other areas of human activity [12]. Utilization of MCDA methods in chemical sciences is rather scarce, however there are some studies where they are used. For instance, TOPSIS and AHP have been used in chemicals selection (solvents and derivatisation agents) [2,13–15], whereas AHP, TOPSIS and PROMETHEE have been used for chemical processes selection (analytical procedures, chemical processes, and process conditions) [16–23].The basic concept of TOPSIS is selection of alternative, which have the shortest distance from the positive ideal solution in a geometrical sense. This tool assumes that each attribute has a monotonically increasing or decreasing utility. Therefore its algorithm provides to allocate the ideal and negative ideal solutions, what finally leads to obtain the ranking of alternatives and choice of the best option. It should be highlighted that there is a great deal of variation in the experimental conditions used for determination of CPs after derivatisation. Thus, aspects such as the type of sample, the concentration levels of CPs, or even if the analytical method of choice involves simultaneous or sequential derivatisation and extraction steps, can influence to a large extent the experimental conditions required to perform derivatisation reactions.

The mixture of N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) and chlorotrimethylsilane (TMCS) (99:1) has been used in several works for derivatisation of CPs. For instance, BSTFA:TMCS was used to derivatise 50 phenolic compounds (including 14 CPs) present in wastewater [24]. The sample preparation procedure was based on solid-phase extraction and derivatisation was performed with 100 µL of BSTFA:TMCS at 60 ºC for 2 h. In another study, 50 µL of CPs solution was derivatised with 50 µL of this mixture in 15 s at room temperature [25]. This study was aimed at the optimisation of electrospray ionization in mass spectrometry and sample preparation methods were not involved. Another study showed that BSTFA:TMCS derivatisation mixture can be preferentially applied in more polar solvents like

acetone than in dichloromethane or hexane due to the slower reaction rates in nonpolar solvents that in fact are commonly used for analytical extractions [26].

Acetic anhydride is one of the most commonly applied derivatisation agents to derivatise CPs. It has been used to simultaneously derivatise and extract CPs by dispersive liquid-liquid microextraction [27]. Thus, 50 µL of acetic anhydride was added to the sample together with a mixture of 0.5 mL of acetone (disperser solvent) and 10 µL of chlorobenzene (extractant solvent). The simultaneous extraction/derivatisation procedure was performed in a short time (<3 min) and presumably at room temperature [27]. Acetic anhydride was also used as derivatising agent in a simultaneous ultrasound assisted dispersive liquid-liquid microextraction/aqueous acetylation under basic conditions derivatisation procedure to the simultaneous determination of CPs and chloroanisoles in wine samples. The optimised procedure involved a volume of 65 µL of acetic anhydride per sample together with 180 µL of tetrachloroethene (extractant solvent) at 60 ºC [28]. In another procedure described for determination of cork-taint compounds by GC-MS, 200 µL of acetic anhydride was applied for derivatisation of CPs under basic conditions (pH 11) and, subsequently, extraction of acetylated analytes was performed by dispersive liquid-liquid microextraction [29]. Acetic anhydride was also used to derivatise phenolic compounds in water samples directly. A volume of 400 µL of derivatisation agent, 55 ºC of reaction temperature and 20 min were established as optimal conditions [30].

As regards BSTFA, the fourth choice in the ranking, it is said that poor resolution is obtained if excess of reagent is not removed [31]. In case of our experiments no excess of BSTFA was removed, so it may potentially deteriorate its performance in terms of peak areas and overall chromatogram quality. BSTFA has been used for derivatisation of CPs present in urine samples at 80 ºC for 1 h after enzymatic hydrolysis and solid-phase extraction [32]. Another procedure involved the application of BSTFA for the simultaneous derivatisation (silylation)

and dispersive liquid-liquid microextraction with a derivatisation/extraction time of ~5 min at the room temperature [33].

All above-mentioned examples show that derivatisation reactions are applied in a variety of ways in combination with different sample preparation techniques. What is more, it is hard to select one optimal set of conditions of performing derivatisation reaction. The aim of the study is to perform a comprehensive assessment of derivatisation agents that are applied for CPs determination. Based on different groups of criteria, namely derivatisation reaction effectiveness, quality of chromatogram and greenness of the agents themselves, it is aimed to create derivatisation agents rankings. This study represents the first work aimed at the selection of derivatisation agents for CPs determination from several alternatives through a more holistic approach. The selection procedure is not sample preparation type specific.

2. Materials and Methods

2.1.Chemicals

The analytical standards were purchased from Sigma Aldrich (Germany): 2,4-dichlorophenol (2,4-DCP), 2,6-dichlorophenol (2,6-DCP), 2,4,6-trichlorophenol (2,4,6- TCP), 2,3,4-trichlorophenol (2,3,4-TCP), 2,4,5-trichlorophenol (2,4,5-TCP), 2,3,4,5-tetrachlorophenol (2,3,4,5-TeCP), 2,3,4,6-tetrachlorophenol (2,3,4,6-TeCP), pentachlorophenol (PCP) as well heptane (anhydrous, 99%). Acetic anhydride was purchased from Sigma-Aldrich (Germany). A stock standard solution of CPs was prepared in heptane with concentration level of 1 µg mL^{-1} for each of analytes.

All derivatisation agents - acetic anhydride, ethyl chloroformate, N-heptafluorobutyrylimidazole (HFBI), hexamethyldisilazane (HMDS), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), N,O-bis(trimethylsilyl)acetamide (BSA), chlorotrimethylsilane (TMCS) and BSTFA:TMCS (99:1) were purchased from Sigma-

Aldrich (Germany). Deuterated naphthalene (Sigma-Aldrich, Germany) was applied as internal standard. Internal standard was used mainly to compensate the stability of mass spectrometer operation.

2.2.Derivatisation of CPs

A number of derivatisation agents typically used for CPs determination, namely acylating agents (acetic anhydride, ethyl chloroformate, N-heptafluorobutyrylimidazole (HFBI)) and silylating agents (hexamethyldisilazane (HMDS), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), N,O-bis(trimethylsilyl)acetamide (BSA), chlorotrimethylsilane (TMCS) and BSTFA:TMCS (99:1)), have been assessed in this work. All of these derivatisation agents are commonly applied in various sample preparation techniques before final determination of CPs and other phenolic compounds with gas chromatography.

The derivatisation procedure was as follows: 100 µL of 1.0 µg mL^{-1} working solution of eight (8) CPs in heptane was placed in the glass chromatographic vial with 250 µL glass insert. After that, 40 µL of 2.0 µg mL^{-1} solution of deuterated naphthalene in methanol as an internal standard (IS) was added. Such IS is selected intentionally, in order not to undergo derivatisation reaction, but to overcome the reproducibility of GC injections and stability of MS signal. Each derivatisation agent was added as purchased in the amount of 10 µL. The solution was vortexed for 1 min and the reaction was carried out for 10 min at room temperature without any enhancement. After that, the mixture was immediately injected into the GC-MS system.

2.3.Chromatographic conditions

The analysis of CPs derivatives was performed by using Agilent Technologies Gas Chromatograph 7890A coupled with Agilent Technologies Mass Spectrometer 5975C.

Separation of analytes took place on Agilent Technologies chromatographic column DB5-MS (30m, id: 0,25mm, film thickness: 0.25µm, 95% PDMS, 5% phenyl groups) with 2 m of fused silica pre-column. Helium 6.0 was used as carrier gas with a constant flow equal to 1 mL min^{-1}. 1 µL of sample was injected in a splitless mode. GC oven temperature program was as follows: 100 °C for 5 min, then an increase of 10 °Cmin^{-1} to reach 280°C that was held for 10min. Transfer line temperature was set at 280°C. The temperature of ion source in mass spectrometer was set at 250 °C, while the temperature of quadrupole at 150 °C. CPs derivatives were analysed by GC-MS in SCAN mode.

2.4.TOPSIS

TOPSIS is one of the expert systems included in the MCDA methods. It was developed by Hwang and Yoon in 1981 [34]. Its aim is ranking of available alternatives, or in other words, selecting the best option among all of them. TOPSIS mathematical model allows finding a winner by choosing the alternative that simultaneously has the shortest distance from the positive ideal solution and at the same time the farthest distance from the negative ideal solution.

General steps for all MCDA methods are presented elsewhere [35]. Initially, the main aim of the analysis should be defined. In the present case the evaluation concerns choosing the best derivatising agent for CPs determination. Then, criteria and alternatives are established. Criteria represent groups of parameters that are able to describe each available option (alternative) and concurrently make the assessment and arrangement possible. Bearing in mind sustainable development, criteria are divided into three main groups describing different points of view: greenness, derivatisation effectiveness and chromatographic quality. This idea is summarised in **Table 1**.

The properties and safety data for derivatisation agents were taken from material safety data sheets (MSDS) for the respective compounds. Detailed descriptions of greenness parameters are provided elsewhere [2]. Derivatisation effectiveness and chromatographic quality parameters were determined by performing chromatographic experiments (for 8 CPs). Alternatives are examples of derivatisation agents typically used in CPs determination, as described in section 2.2.

To apply one of the MCDA methods, all of the factors describing possible options must be numerical or easily transformable into calculable units [21]. According to this requirement, hazard (H) and precautionary (P) statements as well as signal word and special hazards arising from the substance or mixture/hazardous decomposition products were transformed into numerical values. Hazard and precautionary statements were transformed to penalty points based on 10 point scale, as described previously [2]. Therefore, values for signal wording information have been determined in accordance with the pattern: “none” – 0 points, “warning” - 1 point, “danger” – 4 points [2]. This approach was also used in transformation of “special hazards arising from the substance or mixture/hazardous decomposition products” in combination with the analytical eco-scale approach [36]. Thus, points for signal wording were multiplied by the number of labelling pictograms. Additionally, compounds marked with a (+) indication (hydrogen fluoride and hydrogen cyanides), were given extra 10 points due to hazard properties associated with lethal effects [2]. If there are more than one hazardous compound formed during fire or decomposition, then their points are summed up.

Next step of evaluation using MCDA method was giving a proper weight of each criterion. The choice of the best solution was carried out in four stages. First, a separate analysis according to three points of view, namely greenness, derivatisation effectiveness, and chromatogram quality was conducted. Then ranking by all criteria was performed. Weighting

of greenness criteria was based on an approach proposed in previous research [2]. Given values of weight are presented in **Table 2**.

In case of derivatisation effectiveness, responses ratio for analytes and internal standard, as well as relative standard deviations (RSD) for every of 8 analytes were measured. Their weights (for each CPs) were characterised as having the same importance. The weights for assessment according to all CPs' chromatographic quality, including retention time of last eluting compound and peaks' symmetry described by tailing factor and overall chromatogram quality, were established and are presented in the **Table 3**.

The last step was application of TOPSIS. In general, the input data are the matrix consisting of *n* alternatives which are described by *m* criteria. The algorithm of TOPSIS can be described in several steps as follows:

1. Construction of normalised decision matrix

$$r_{ij} = x_{ij} \div \sqrt{\sum x_{ij}^2}, \quad \mathrm{i} = 1, 2, \ldots, \mathrm{m} \text{ and } \mathrm{j} = 1, 2, \ldots, \mathrm{n} \quad (1)$$

Where x_{ij} and r_{ij} are original and normalised scores in decision matrix, respectively.

2. Construction of the weighted normalised decision matrix

$$v_{ij} = r_{ij} \times w_j, \quad \mathrm{i} = 1, 2, \ldots, \mathrm{m} \text{ and } \mathrm{j} = 1, 2, .., \mathrm{n} \quad (2)$$

Where w_j is the weight of the criterion j and $\sum_{j=1}^{n} w_j = 1$

3. Determination of positive ideal (A^*) and negative ideal (A^-) solutions

$$A^* = \left\{\left(max_i v_{ij} | j \in C_b\right), \left(min_i v_{ij} | j \in C_c\right)\right\} = \{v_i^* | j = 1, 2, \ldots, m\} \quad (3)$$

$$A^- = \left\{\left(min_i v_{ij} | j \in C_b\right), \left(max_i v_{ij} | j \in C_c\right)\right\} = \left\{v_j^* | j = 1, 2, \ldots, m\right\} \quad (4)$$

4. Calculation of the separation measures for each alternative

$$S_i^* = \sqrt{\sum_{j=1}^{m} \left(v_{ij} - v_j^*\right)^2} \quad \mathrm{j} = 1, 2, \ldots, \mathrm{m} \quad (5)$$

$$S_i^- = \sqrt{\sum_{j=1}^{m} \left(v_{ij} - v_j^-\right)^2} \quad \mathrm{j} = 1, 2, \ldots, \mathrm{m} \quad (6)$$

5. Calculation of the relative closeness to the ideal solution

$$C_i^* = \frac{S_i^-}{S_i^* + S_i^-}, \quad \mathrm{i} = 1, 2, \ldots, \mathrm{m} \text{ and } 0 < \mathrm{C_i^*} < 1 \quad (7)$$

6. Arrangement of scenarios in order of closest to ideal to furthest from ideal - creation of a ranking

The alternative with $\mathrm{C_i^*}$ closest to 1 is the best preference among the possible options.

Above, only basic information about TOPSIS algorithm is presented. For more details please refer to the articles describing its fundamentals. All the calculations involving TOPSIS application for CPs derivatisation agents assessment included in this study were performed in Excel program (Microsoft 2010).

3. Results and Discussion

The chemical structures of selected CPs is shown in **Figure 1**, whereas acyl and silyl derivatives formed by reaction of CPs with the above mentioned derivatisation agents are shown in **Figure 2**. The application of derivatisation agents (alternatives) that show minimal environment, health and safety issues and give rise to a quantitative conversion of CPs in a reduced reaction time and without additional energy consumption are clearly the preferable solution. Rankings of the 8 alternative derivatisation agents were performed according to different groups of criteria. Initially, no derivatisation option was considered as an alternative but no chromatographic peaks were obtained for CPs in given chromatographic conditions.

As it is preselection of derivatisation agents, we do not aim to work in optimised derivatisation reaction conditions but in constant conditions for every agent. It is not feasible to select derivatisation agents' optimal reaction conditions before selection of the agent itself.

The optimisation of derivatisation reaction conditions is one of the next steps in procedure development. In fact, as shown in the introduction, sometimes optimised derivatisation conditions differ strongly, even for single given agent and analyte(s).

3.1.Ranking by chromatographic quality

The first ranking was performed with chromatogram quality criteria being input data. Retention time of last eluting analyte - PCP was a measure of chromatographic run time, symmetry factor of 2,3,4,6-TeCP was selected to represent tailing of the derivatised CPs. To avoid excess of criteria this peak was selected as all of them give very similar results. Last criterion is strictly arbitrary and reflects the easiness of analyst to read the chromatogram. In other words, chromatogram with many artificial peaks was assessed as being low quality. Here, arbitrary five point scale was used.

Table 4 shows ranking results within above-described criteria. The best alternative within these criteria was the mixture of BSTFA:TMCS (99:1). This alternative was characterised by best performance in terms of peak symmetry, and its chromatogram contained no many artificial peaks, with score 4 out of 5. The retention time of PCP with this alternative was moderate (17.5 min), as in case of all other silylating agents. The second rank was occupied by acetic anhydride with an easy to interpret chromatogram (4 points) and good symmetry of peaks. The retention time of PCP was 16.9 min, what was the second best result, being HFBI characterised by a shorter chromatographic run time (PCP retention time of 14.4 min). In fact, HFBI occupied the third rank position with very good symmetry of peaks and moderate easiness (3) of chromatogram reading. The values of similarities to ideal solution of three first alternatives did not differ significantly. This means that three best derivatisation agents perform rather similarly, within these criteria. The next ranks were obtained by other silylating agents. In general, their chromatograms were easy to be interpreted but the peaks

were strongly tailing. Last place was occupied by ethyl chloroformate, as PCP had the longest retention time (18.5 min), peaks were not symmetric and the chromatogram was rather hard to be interpreted (2 out of 5 points).

3.2.Ranking by derivatisation effectiveness

The ranking of derivatisation effectiveness was performed considering two types of criteria. The first group of criteria were the ratios of peak areas for every analyte to internal standard, what reflects the reaction efficiency and the possibility to obtain good sensitivity. The second group of criteria was relative standard deviations (n = 3) of ratios of peak areas of analytes and internal standard of all CPs. This group of criteria reflects repeatability of derivatisation reaction and the possibility to obtain precise results.

Table 4 presents the results for above mentioned criteria. The first rank for these criteria ranking was obtained by acetic anhydride. It is characterised by large peak areas (the best for 4 out of 8 CPs) and good precision (the best for only 1 analyte). The second rank was for BSTFA:TMCS (99:1) mixture and the reason for obtaining high rank was excellent precision (the best for 6 out of 8 analytes) and good performance for peak areas. The next positions in the ranking were obtained by other silylating agents. The lowest ranks were obtained by ethyl chloroformate and HFBI. HFBI was characterised by poor precision (the poorest for 4 out of 8 analytes) and poor peak areas (the poorest for 3 out of 8 analytes). Similarly, ethyl chloroformate performance was poor in terms of precision (the poorest for 3 out of 8 analytes) and weak performance in terms of peak areas.

3.3.Ranking by greenness

Table 4 presents the results of ranking by greenness criteria. The weights to criteria were assigned according to derivatisation agents selection guide [2], with the difference that the

criterion of carcinogenicity was not included in the assessment as all the agents are classified as not carcinogenic. As a result, 0.05 of total weight originally assigned to carcinogenicity criterion was transferred to “precautionary statements” weight, which was therefore 0.25 instead of 0.2. The mixture of BSTFA:TMCS (99:1) was treated in this ranking as a compound with mixed properties – 0.99 of BSTFA properties and 0.01 of TMCS properties.

HFBI was first rank, mainly because it had neither hazard nor precautionary statements. The next ranks were obtained by silylating agents. The last ranks were obtained by acetic anhydride, HMDS and ethyl chloroformate. These derivatisation agents are labelled with many hazard statements and they cause problems with handling what is expressed by many precautionary labels. To our best knowledge, no other studies deal with assessment of derivatisation agents in terms of their greenness for a particular group of analytes.

3.4.Comprehensive ranking

It is clear that consideration of different assessment criteria results in completely different rankings. Therefore, it is beneficial to perform ranking with all criteria at the same time. As the main goal of derivatisation agent selection is to obtain good analytical performance and greenness we investigate how the results change for variable weights with no dominant group of criteria. **Figure 3** shows the ranking results for such weights applied. BSTFA:TMCS (99:1) is the first rank for different combinations of weights for derivatisation efficiency and chromatogram quality if the weight for greenness does not exceed 40 %. At this value of weight for greenness criteria no matter what are the weights for two other groups of criteria HFBI is the first rank.

The most often mentioned advantage of silylation agents over methylation and acetylation ones is that they produce derivatives of higher masses, which is especially important in case of analytes of low molecular weight. In this way the risk of losses by evaporation during

sample preparation is minimised, which is likely to be observed in case of methyl esters or acetates of low molecular weight analytes. In addition, in case of silyl derivatives, characteristic fragmentation pattern is observed, which facilitates the identification and also characteristic ions for SIM may be easily selected. Silylation agents, especially BSTFA, are also recognised as those reacting with analytes fast and quantitatively under mild conditions [26]. Additionally, it has been also emphasized in some studies that byproducts of the reaction of analytes with BSTFA/TMCS and excess of this agent elute early in the chromatogram (far from derivatised analytes), which simplifies the evaluation of obtained results [37]. This has been also observed in our study – considering chromatogram quality BSTFA/TMCS has been ranked as the best alternative. Some authors also indicate that alkylation and acylation reagents (in contrast to silylation ones) are not applicable to all phenols relevant in environmental analysis [38]. On the other hand, BSTFA is rather expensive, which is probably the reason why acetic anhydride is applied for chlorophenols determination in water in majority of reported studies. Interestingly, in EPA methods for such a purpose, pentafluorobenzyl bromide is advised.

4. Conclusions

The selection of derivatisation agent is seldom taken into consideration during procedure development. The presented study shows a comprehensive method for the selection of derivatisation agent for CPs for further optimization. The rankings give strongly different results if different ranking criteria are considered. Thus, derivatisation agents that stand out from the rest of alternatives within one ranking are poorly assessed when different criteria are considered. Therefore, a comprehensive assessment of derivatisation agents considering many criteria is strongly recommended. Regarding derivatisation agents applied to CPs

determination, the best peak areas and precisions were reached by acetic anhydride, the best symmetry of peaks and overall chromatogram quality was obtained with BSTFA:TMCS mixture, while the greenest alternative was HFBI. If all criteria are considered together BSTFA:TMCS mixture is the best alternative.

Application of TOPSIS allows considering many criteria during selection process and is easy to be applied algorithm. It allows users to pick criteria that are relevant to the optimisation process and by application of weights can assign relative importance to criteria. This makes the presented approach very flexible.

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References

[1] P. Anastas, N. Eghbali, Green chemistry: Principles and practice, Chem. Soc. Rev. 39 (2010) 301–312.

[2] M. Tobiszewski, J. Namieśnik, F. Pena-Pereira, A derivatisation agent selection guide, Green Chem. 19 (2017) 5911–5922.

[3] T. Ge, J. Han, Y. Qi, X. Gu, L. Ma, C. Zhang, et al., The toxic effects of chlorophenols and associated mechanisms in fish, Aquat. Toxicol. 184 (2017) 78–93.

[4] A.O. Olaniran, E.O. Igbinosa, Chlorophenols and other related derivatives of environmental concern: Properties, distribution and microbial degradation processes, Chemosphere. 83 (2011) 1297–1306.

394 [5] M. Czaplicka, Sources and transformations of chlorophenols in the natural
395 environment, Sci. Total Environ. 322 (2004) 21–39.
396 [6] Agency for Toxic Substances & Disease Registry (ATSDR), Priority List of
397 Hazardous Substances, (2013). http://www.atsdr.cdc.gov/SPL/.
398 [7] P. De Morais, T. Stoichev, M.C.P. Basto, M.T.S.D. Vasconcelos, Extraction and
399 preconcentration techniques for chromatographic determination of chlorophenols in
400 environmental and food samples, Talanta. 89 (2012) 1–11.
401 [8] F. Orata, Derivatization Reactions and Reagents for Gas Chromatography Analysis, in:
402 M. Ali Mohd (Ed.), Adv. Gas Chromatogr. - Prog. Agric. Biomed. Ind. Appl., InTech,
403 2007.
404 [9] V.G. Zaikin, J.M. Halket, Derivatization in mass spectrometry — 2 . Acylation, Eur. J.
405 Mass Spectrom. 9 (2003) 421–434.
406 [10] J.M. Halket, V.G. Zaikin, Derivatization in mass spectrometry — 1 . Silylation, Eur. J.
407 Mass Spectrom. 9 (2003) 1–21.
408 [11] J. Figueira, S. Greco, M. Ehrgott, Multiple criteria decision analysis: State of the art
409 surveys, Springer-Verlag, New York, USA, 2005.
410 [12] A. Mardani, A. Jusoh, K.M.D. Nor, Z. Khalifah, N. Zakwan, A. Valipour, Multiple
411 criteria decision-making techniques and their applications - A review of the literature
412 from 2000 to 2014, Econ. Res. Istraz. 28 (2015) 516–571.
413 [13] M. Tobiszewski, S. Tsakovski, V. Simeonov, J. Namiesnik, F. Pena-Pereira, A solvent
414 selection guide based on chemometrics and multicriteria decision analysis, Green
415 Chem. 17 (2015) 4773–4785.
416 [14] P. Bigus, J. Namieśnik, M. Tobiszewski, Application of multicriteria decision analysis
417 in solvent type optimization for chlorophenols determination with a dispersive liquid-
418 liquid microextraction, J. Chromatogr. A. 1446 (2016) 21–26.

419 [15] S. Perez-Vega, S. Peter, I. Salmeron-Ochoa, A. Nieva-De La Hidalga, P.N. Sharratt,
420 Analytical hierarchy processes (AHP) for the selection of solvents in early stages of
421 pharmaceutical process development, Process Saf. Environ. Prot. 89 (2011) 261–267.
422 [16] J. Serna, E.N. Díaz Martinez, P.C. Narváez Rincón, M. Camargo, D. Gálvez, Á.
423 Orjuela, Multi-criteria decision analysis for the selection of sustainable chemical
424 process routes during early design stages, Chem. Eng. Res. Des. 113 (2016) 28–49.
425 [17] C. Li, X. Zhang, S. Zhang, K. Suzuki, Environmentally conscious design of chemical
426 processes and products: Multi-optimization method, Chem. Eng. Res. Des. 87 (2009)
427 233–243.
428 [18] M. Tobiszewski, A. Orłowski, Multicriteria decision analysis in ranking of analytical
429 procedures for aldrin determination in water, J. Chromatogr. A. 1387 (2015) 116–122.
430 [19] D. Xu, L. Lv, J. Ren, W. Shen, S. Wei, L. Dong, Life cycle sustainability assessment
431 of chemical processes: A vector-based three-dimensional algorithm coupled with AHP,
432 Ind. Eng. Chem. Res. 56 (2017) 11216–11227.
433 [20] R. Jędrkiewicz, A. Orłowski, J. Namieśnik, M. Tobiszewski, Green analytical
434 chemistry introduction to chloropropanols determination at no economic and analytical
435 performance costs?, Talanta. 147 (2016) 282–288.
436 [21] R. Jędrkiewicz, S. Tsakovski, A. Lavenu, J. Namieśnik, M. Tobiszewski,
437 Simultaneous grouping and ranking with combination of SOM and TOPSIS for
438 selection of preferable analytical procedure for furan determination in food, Talanta.
439 178 (2018) 928–933.
440 [22] M. Cinelli, S.R. Coles, M.N. Nadagouda, J. Błaszczyński, R. Słowiński, R.S. Varma,
441 et al., Robustness analysis of a green chemistry-based model for the classification of
442 silver nanoparticles synthesis processes, J. Clean. Prod. 162 (2017) 938–948.
443 [23] P. Bigus, J. Namieśnik, M. Tobiszewski, Implementation of multicriteria decision

analysis in design of experiment for dispersive liquid-liquid microextraction optimization for chlorophenols determination, J. Chromatogr. A. 1553 (2018) 25–31.

[24] W. Zhong, D. Wang, X. Xu, B. Wang, Q. Luo, S. Senthil Kumaran, et al., A gas chromatography/mass spectrometry method for the simultaneous analysis of 50 phenols in wastewater using deconvolution technology, Chinese Sci. Bull. 56 (2011) 275–284.

[25] R.-Y. Hsu, J.-H. Liao, H.-W. Tien, G.-R. Her, Gas chromatography electrospray ionization mass spectrometry analysis of trimethylsilyl derivatives, J. Mass Spectrom. 51 (2016) 883–888.

[26] D. Li, J. Park, J.-R. Oh, Silyl derivatization of alkylphenols, chlorophenols, and bisphenol a for simultaneous GC/MS determination, Anal. Chem. 73 (2001) 3089–3095.

[27] N. Fattahi, Y. Assadi, M.R. Milani Hosseini, E.Z. Jahromi, Determination of chlorophenols in water samples using simultaneous dispersive liquid-liquid microextraction and derivatization followed by gas chromatography-electron-capture detection, J. Chromatogr. A. 1157 (2007) 23–29.

[28] C. Pizarro, C. Sáenz-González, N. Pérez-del-Notario, J.M. González-Sáiz, Development of an ultrasound-assisted emulsification-microextraction method for the determination of the main compounds causing cork taint in wines, J. Chromatogr. A. 1229 (2012) 63–71.

[29] N. Campillo, P. Viñas, J.I. Cacho, R. Peñalver, M. Hernández-Córdoba, Evaluation of dispersive liquid-liquid microextraction for the simultaneous determination of chlorophenols and haloanisoles in wines and cork stoppers using gas chromatography-mass spectrometry, J. Chromatogr. A. 1217 (2010) 7323–7330.

[30] Y.J. Yu, S. Zhong, G.Y. Su, H.L. Liu, X.L. Dai, R.J. Wang, et al., Trace analysis of phenolic compounds in water by in situ acetylation coupled with purge and trap-

GC/MS, Anal. Methods. 4 (2012) 2156–2161.

[31] C. Basheer, H.K. Lee, Analysis of endocrine disrupting alkylphenols, chlorophenols and bisphenol-A using hollow fiber-protected liquid-phase microextraction coupled with injection port-derivatization gas chromatography-mass spectrometry, J. Chromatogr. A. 1057 (2004) 163–169.

[32] L. Schmidt, T. Göen, Simultaneous determination of the full chlorophenol spectrum in human urine using gas chromatography with tandem mass spectrometry, Anal. Chim. Acta. 965 (2017) 123–130.

[33] M. Saraji, H. Ghambari, Suitability of dispersive liquid-liquid microextraction for the in situ silylation of chlorophenols in water samples before gas chromatography with mass spectrometry, J. Sep. Sci. 38 (2015) 3552–3559.

[34] C.L. Hwang, K.P. Yoon, Multiple Attribute Decision Making: Methods and Applications, Springer-Verlag, New York, USA, 1981.

[35] M. Bystrzanowska, M. Tobiszewski, How can analysts use multicriteria decision analysis?, TrAC - Trends Anal. Chem. 105 (2018) 98–105.

[36] A. Gałuszka, Z.M. Migaszewski, P. Konieczka, J. Namieśnik, Analytical Eco-Scale for assessing the greenness of analytical procedures, TrAC Trends Anal. Chem. 37 (2012) 61–72.

[37] Á. Kovács, A. Kende, M. Mörtl, G. Volk, T. Rikker, K. Torkos, Determination of phenols and chlorophenols as trimethylsilyl derivatives using gas chromatography–mass spectrometry, J. Chromatogr. A. 1194 (2008) 139–142.

[38] Á. Kovács, M. Mörtl, A. Kende, Development and optimization of a method for the analysis of phenols and chlorophenols from aqueous samples by gas chromatography–mass spectrometry, after solid-phase extraction and trimethylsilylation, Microchem. J. 99 (2011) 125–131.

Figures with captions

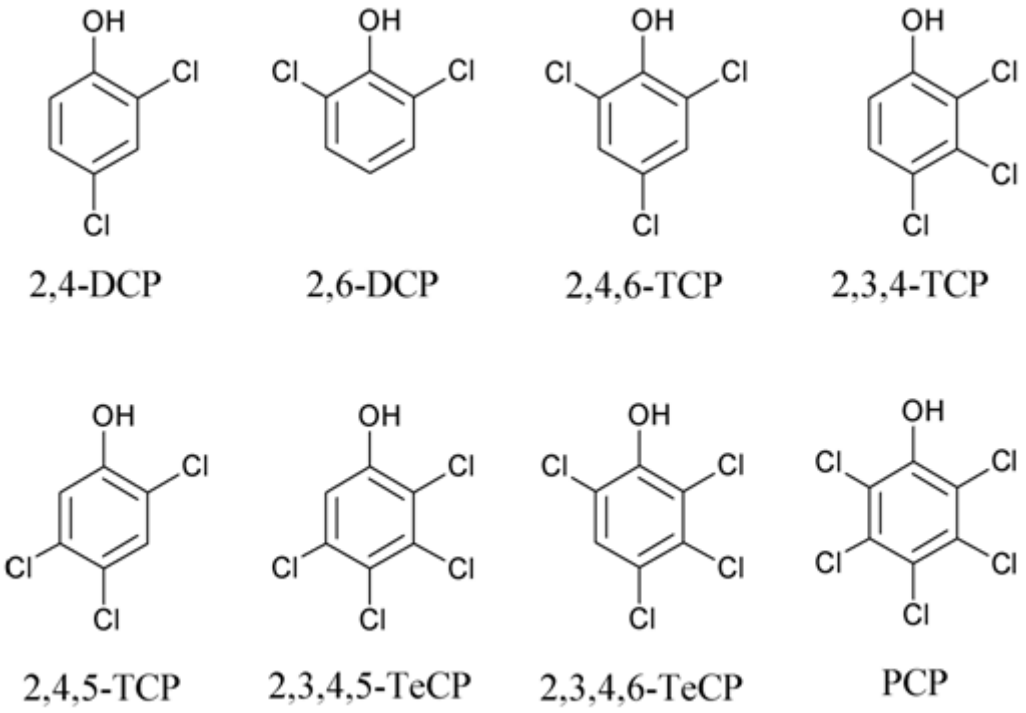

Figure 1. Chemical structures of the eight CPs.

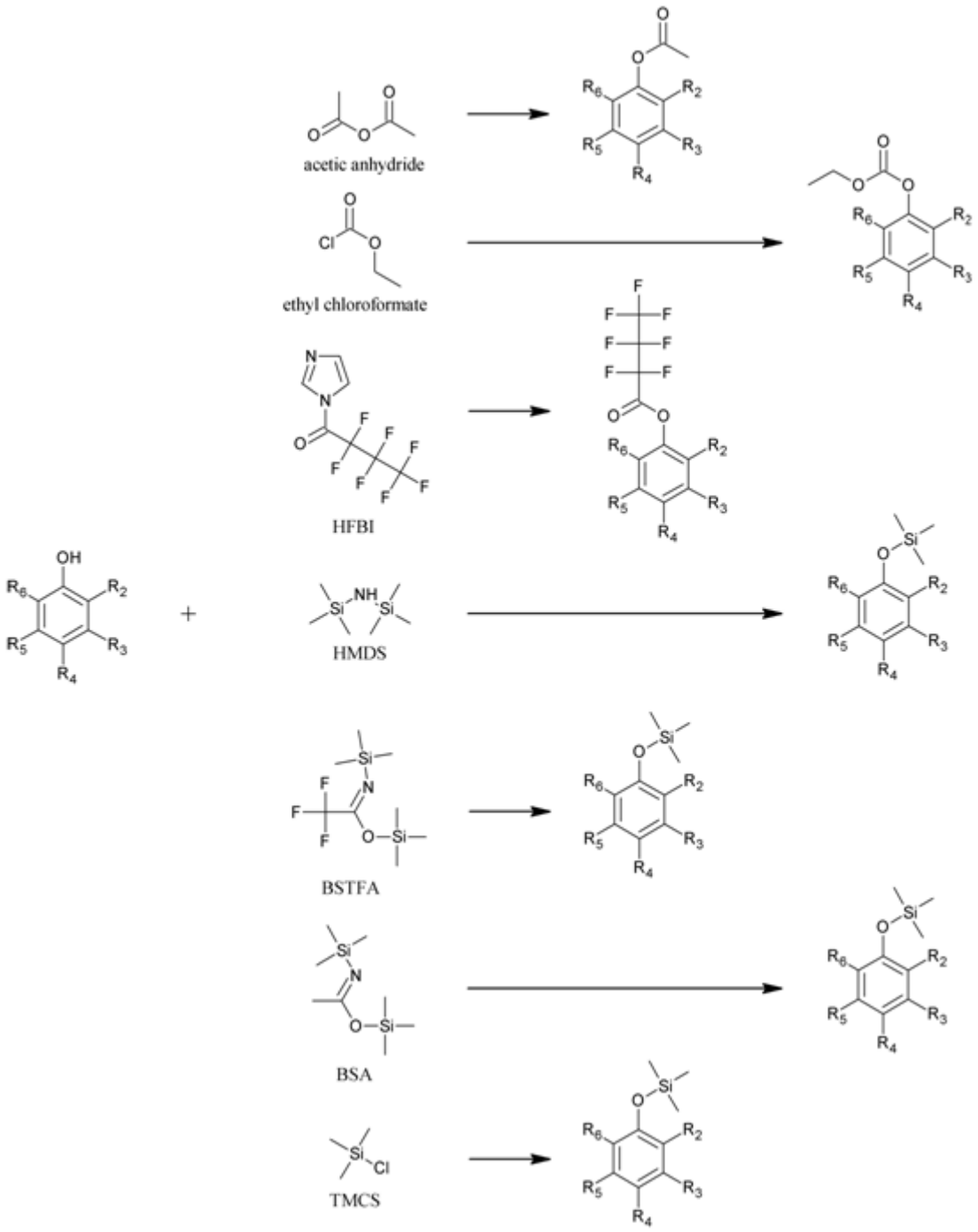

Figure 2. Derivatisation products obtained by reaction of CPs (R_i=H, Cl) with acetic anhydride, ethyl chloroformate, HFBI, HMDS, BSTFA, BSA and TMCS.

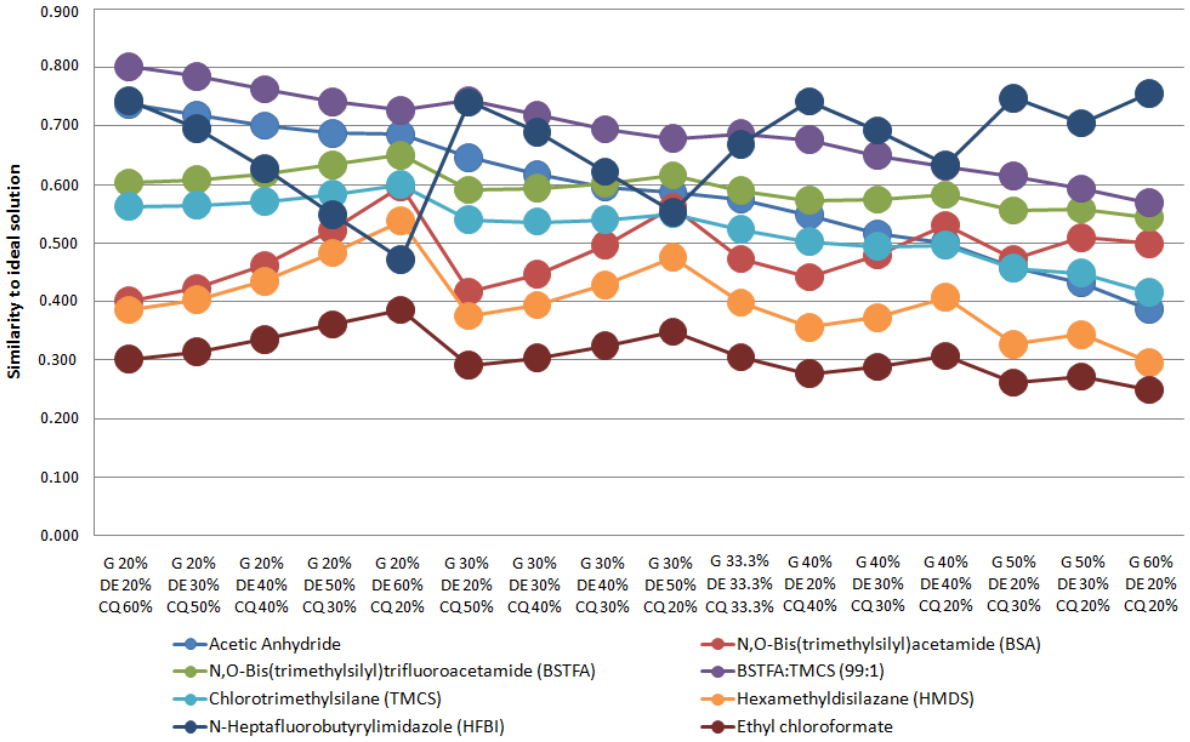

Figure 3. The results of rankings for changing weights of criteria. G- Greenness, DE – Derivatisation efficiency, CQ – chromatogram quality.

Table 1

Criteria for TOPSIS analysis and its classification.

Greenness parameters	**Derivatisation effectiveness parameters**	**Chromatographic quality parameters**
• Boiling point • Flash point • Vapour pressure • log K_{OW} • log K_{OC} • log BCF • Total removal wastewater treatment (%) • Persistence time (h)	• Responses ratio • RSD	• Retention time of last eluting compound • Symmetry of all peaks • Easiness to obtain information from chromatogram – number of artificial peaks within range of elution of analytes

- Hazard statements (H)
- Precautionary statements (P)
- Signal word
- Special hazards arising from the substance or mixture/Hazardous decomposition products

Table 2

Weighting of criteria in case of green approach [2].

Criterion	**Weight**
Boiling point	0.025
Flash point	0.025
Vapour pressure	0.025
$\log K_{OW}$	0.025
$\log K_{OC}$	0.025
logBCF	0.025
Total removal by wastewater treatment (%)	0.025
Persistence time	0.025
Hazard statements (H)	0.25
Precautionary statements (P)	0.25
Signal Word	0.2
Special hazards arising from the substance or mixture/Hazardous decomposition products	0.1

Table 3

Weighting of criteria for comprehensive ranking of derivatization agents.

Chromatogram quality		**Derivatisation effectiveness**		**Greenness**	
Criteria	**Weight**	**Criteria**	**Weight**	**Criteria**	**Weight**
Retention time of last eluting compound	0.13(3)	Responses ratio		Boiling point	0.005
Tailing factor for 2,3,4,6-TTCP	0.13(3)	2,6-DCP		Flash point	0.005
Overall chromatogram quality	0.13(3)	2,4-DCP		Vapour pressure	0.005
		2,4,6-TCP	0.025	logKow	0.005
		2,4,5-TCP		logKoc	0.005
		2,3,4-TCP		logBCF	0.005
		2,3,4,6-TTCP		Total removal by wastewater treatment (%)	0.005
		2,3,4,5-TTCP		Persistence time	0.005
		PCP		Hazard statements (H)	0.05
		RSD		Precautionary statements (P)	0.05
		2,6-DCP		Signal Word	0.04
		2,4-DCP		Special hazards arising from the substance or mixture/Hazardous decomposition products	0.02
		2,4,6-TCP	0.025		
		2,4,5-TCP			
		2,3,4-TCP			
		2,3,4,6-TTCP			
		2,3,4,5-TTCP			
		PCP			

Table 4

Ranking results according to different criteria.

Ranking for chromatogram quality criteria		Ranking for derivatisation effectiveness criteria		Ranking for greenness criteria	
Derivatisation agent	**Similarity to ideal solution**	**Derivatisation agent**	**Similarity to ideal solution**	**Derivatisation agent**	**Similarity to ideal solution**
BSTFA:TMCS (99:1)	0.855	Acetic Anhydride	0.812	HFBI	0.793
Acetic Anhydride	0.832	BSTFA:TMCS (99:1)	0.757	BSTFA	0.530
HFBI	0.773	BSA	0.724	BSTFA:TMCS (99:1)	0.529
BSTFA	0.608	BSTFA	0.696	BSA	0.510
TMCS	0.573	TMCS	0.655	TMCS	0.367
BSA	0.382	HMDS	0.643	Acetic Anhydride	0.310
HMDS	0.382	Ethyl chloroformate	0.430	HMDS	0.238
Ethyl chloroformate	0.300	HFBI	0.316	Ethyl chloroformate	0.230