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Journal of Chromatography A, 1064 (2005) 135–141
JOURNAL OF CHROMATOGRAPHY A
www.elsevier.com/locate/chroma

Subcritical water and dynamic sonication-assisted solvent extraction of fluorescent whitening agents and azo dyes in paper samples

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Received 29 October 2004; received in revised form 20 December 2004; accepted 29 December 2004

Abstract

Two low-volume solvent continuous extraction methods are applied to the extraction of paper matrices. In the methods reported here, a complex mixture of fluorescent whitening agents (FWAs) and azo dyes (AZOs) used in paper materials intended to come into contact with foodstuffs was extracted by using subcritical water extraction (SWE) and dynamic sonication-assisted solvent extraction (DSASE). Rationale for the work is based upon migration concerns of these groups of analytes from the packaging to the packaged items, thus compromising their subjective and/or objective quality. In SWE, sample was extracted in 21 min with 0.5 mL of water, whereas the DSASE method required 11 min and used 7 mL of water. DSASE was further developed by incorporating an organic modifier in order to change water polarity, thus improving extraction of moderately polar analytes. This way, modified-DSASE used a total organic volume of 0.9 mL which represents a reduction of 200 times in organic solvent consumption (200 mL versus approximately 1.0 mL) and 11 times in extraction time (2 h versus 11 min) compared to the existing methods. SWE was able to extract only 9 out of 12 test analytes with average recoveries between 10 and 25% whereas modified-DSASE succeed in extracting all the target analytes with an average recovery of 89%. Complete discussion and explanation concerning these differences are provided in the text.

Keywords: Paper analysis; Subcritical water extraction; Dynamic sonication-assisted solvent extraction; Fluorescent whitening agents; Azo dyes; Food safety

1. Introduction

The use of paper and board (P&B) as primary and secondary packaging material is prevalent in the food industry. Consumer safety is a principal aspect in food packaging and the material must accomplish a series of conditions to guaranty their safe use [1]. When analyzing such samples, a critical point is the extraction procedure, usually carried out by classical liquid or Soxhlet extraction. Recently, other methods such as pressurized liquid extraction (PLE) or supercritical fluid extraction (SFE) have been introduced [2,3].

Subcritical water extraction (SWE) is an extraction technique based on the use of water as extraction solvent at temperatures between 100 and 374 °C (water critical point: 374 °C and 217 atm; 1 atm: 101325 Pa) and at a pressure enough to keep the liquid state. Under these conditions, the dielectric constant of water (directly related to its polarity) can be lowered by increasing the temperature (ε: 80.4 at 20 °C to 27 at 250 °C), thus allowing extraction of a wide range of compounds, even non-polar *n*-alkanes ([4–6], and references cited therein).

Sonication-assisted extractions are among the easiest, cheapest and with the lowest instrumental requirements of

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doi:10.1016/j.chroma.2004.12.072

the wide range of available extraction techniques. Briefly, energy in the form of acoustic sound waves in the ultrasound region above 20 kHz is used to accelerate mass transport and mechanical removal of analytes and particles from the matrix surface by a process called cavitation. Roughly, cavitation consists in the formation and implosion of vacuum bubbles trough the liquid, thus creating microenvironments with high temperatures and pressures (estimated up to 5000 °C and 1000 atm) [7,8]. Sonication-assisted liquid extraction has been used successfully in static mode for many compounds [9–13]. When developing a sonication extraction method, care needs to be taken to avoid degradation of the analytes. Dynamic or continuous approaches can be advantageous in this respect since the analytes are removed as soon as they are extracted, and sample is exposed to fresh solvent thus promoting transfer of the analytes. Recently, a number of analytical methods based on dynamic sonication have been reported [14–18].

Azo dyestuffs (AZOs, hereafter) are widely used as colorants in consumer and industrial products, such as foods, medicines, toys, plastic, paper, etc. Azo colorants are biologically active through their metabolites since azoreduction of these compounds occurs in vivo [19,20], resulting in the release of the potentially carcinogenic aromatic amine from the colorant [21,22]. Several methods have been proposed for their analysis in water [23,24], food [25], plastic [26], or leather [27], but none of them can be directly applied to the analysis of paper samples.

Fluorescent whitening agents (FWAs) are used in the textile and paper industries and in household detergents. They absorb light in the UV range (290–400 nm) and emit visible blue light (400–480 nm), thus enhancing the optical impression of whiteness and brightness. Approximately 80% of FWAs used in paper and board formulations are based upon stilbene derivatives [28]. Toxic effects of FWAs have not yet been observed [29,30] but not all of them are authorized for use as colorants by the US Food and Drug Administration and their inclusion in P&B intended for food packaging in the European Union (EU) is under consideration due to their potential migration to the packaged items. In the scientific literature, a variety of extraction methods for their extraction in water [31–33], sludge samples [34] or sediments [35] can be found, but only two approaches involving classical large volume solid–liquid extraction have been proposed for their determination in paper-based containers [36,37].

The main aim of this work is to investigate the suitability of the proposed solvent-reduced extraction techniques for paper analysis by extracting FWAs and AZOs. The methods are optimized using experimental design and graphical analysis. The systematic use of organic solvents as modifiers in dynamic sonication-assisted solvent extraction (DSASE) is presented in order to overcome the limitations of using polar water as the extraction solvent. Fully optimized extraction method efficiency is partially validated and compared with conventional solvent extraction by Soxhlet and solid–liquid extraction techniques.

2. Experimental

2.1. Chemicals and standards

The FWAs selected for inclusion into this study are among those most commonly used by EU paper and board manufacturers. The following FWAs were investigated: bis(anilinodihydroxyethylaminotriazinyl amino) stilbene tetrasulfonate (Tetra hereafter, Ciba Geigy, Barcelona, Spain); bis(anilinodihydroxyethylaminotriazinylamino)stilbene disulfonate (RD, Robama, Barcelona, Spain); Modified Tetra (RT*, Robama); Blankophor ACR (cationic benzimidazole derivative; Color Index Fluorescence Brightener 363, ACR, Bayer Ibérica, Barcelona, Spain); Leucophor AP (anionic disulfonated stilbene brightener derivative, AP, Clariant Ibérica, Barcelona, Spain); and bis(styrylsulfonate)biphenyl (BS, Ciba Geigy). The azo dyes used in this work were selected according to their prevalence in the food-related paper industry and were: acid red 1 (CAS number 3734-67-6), acid red 114 (6459-94-5), acid yellow 17 (6359-98-4), acid orange 8 (5850-86-2), basic orange 2 (532-82-1), and Fast Garnet GBC base (97-56-3) supplied by Aldrich (Aldrich Ibérica, Madrid, Spain). Individual stock solutions (approximately 700 ng/μL) were prepared in Milli-Q water, with the only exception of Fast Garnet GBC and acid red 114, which were prepared in methanol. Standard solutions were prepared weekly by dilution of these solutions with methanol and added, at known concentrations, to the blank paper samples.

Paper samples were of non-recycled, non-surface treated liquid board triplex composed of bleached Kraft and chemothermomechanical pulp with a grammage of 267 g/m^2 and 478 μm of thickness. Spiking procedure was as follows: the appropriate amount of methanolic solutions was added to 10 g of paper samples. After an equilibration time of at least 1 h in an orbital shaker, samples were stored in the dark and allowed to equilibrate for at least 7 days at ambient temperature before use.

Except for the water, provided by a Milli-Q system (Millipore Ibérica, Madrid, Spain), all solvents used were HPLC grade or better and were supplied by Scharlab (Barcelona, Spain). Sodium dihydrogen phosphate monohydrate (analytical grade) was obtained from Panreac (Barcelona, Spain).

2.2. High-performance liquid chromatography

The HPLC system consisted of a Waters model 600 quaternary pump (Waters, MA, USA) and a Kontron model 360 autosampler (Kontron Instruments, Milan, Italy) connected in series with a Waters model 474 scanning fluorescence detector and a Waters model 2487 variable-wavelength UV detector. A PC Integration Pack (Kontron Instruments) was used for data acquisition and analysis. Separation was achieved on a 250 mm × 4.6 mm Symmetry Shield 5-μm C18 column (Waters).

Acetonitrile, methanol and Milli-Q water (10 mM Sodium dihydrogen phosphate, pH 5.0) were used as eluent solvents at a flow-rate of 1.0 mL/min. The gradient elution program was: 0–1 min: water–acetonitrile–methanol (75:15:10), then a linear gradient to 60:30:10 in 15 min held for 4 min, and a second gradient to 1:89:10 at 50 min. Then, mobile was returned to its initial composition over 1 min, and the column was equilibrated with this mixture for 15 min.

The wavelength program used to detect AZOs was as follows: initial λ 452 nm, then change to 458 nm at 8.0 min, second change to 458 nm at 25 min, third change to 370 nm at 36.0 min and final to 524 nm at 38 min, hold until the end of the run. FWAs were analyzed using fluorescence detection ($\lambda_{ex.}$: 350 nm, $\lambda_{em.}$:450 nm).

2.3. Dynamic sonication-assisted solvent extraction

The DSASE set-up used here is based upon a previously described scheme [14]. Briefly, 0.1 g of grinded spiked paper was inserted into a 0.5-mL stainless steel extraction thimble (Suprex, PA, USA) originally developed for supercritical fluid extraction. The extraction solvent was pumped trough the vessel by means of a Waters model 600E quaternary HPLC pump. The extractions were performed inside an Ultrasonic LC 130 H bath (Elma, Singer, Germany), with an output power of 120 W and a frequency of 35 kHz. To control the temperature of the bath a Tectron 3473200 heater (Selecta, Barcelona, Spain) was used.

When extraction was finished, eluent was concentrated under nitrogen stream at 50 °C to a final volume of 0.3 mL and analyzed by HPLC. Gravimetric control was applied for all the procedures.

2.4. Subcritical water extraction

SWE was performed as follows. A Kontron model 322 HPLC pump was used in the constant flow mode to pump water (Milli-Q quality, Millipore) through a 5-m stainless steel preheating coil of 1/16 in. (1 in. = 2.54 cm) connected to a 0.5 mL SFE cell (Suprex) introduced into an Hewlett Packard 5710A chromatographic oven (Hewlett Packard, CA, USA). The cell was installed to ensure upwards flow through the system. To keep water in its liquid state, pressure was controlled by using a Variflow manual variable restrictor (Suprex), which allows to variate the pressure inside the extraction cell while maintaining extraction flow thus making possible to considerate pressure as an independent factor. Grinded spiked paper (0.1 g) was introduced in the extraction cell, and clean sylanized glass wool was placed at the outlet of the vessel to prevent plugging of the frit. The outlet restrictor was closed until the pressure rises up to ∼100 atm while the GC oven reaches and equilibrates at the set point temperature. At this point, the water pump is set to the pre-defined flow and the manual restrictor is used to control the system pressure at 100 atm. When extraction is finished, water was filtered through sylanized glass wool and evaporated as explained in the previous paragraph.

2.5. Classical extraction methods

2.5.1. Soxhlet extraction

For Soxhlet extraction experiments, an aliquot of 2.5 g of grinded paper was placed in a glass Soxhlet thimble. The sample was extracted with 200 mL of methanol in a reflux for 7 h. The organic extract was then concentrated to ca. 0.5 mL gravimetrically controlled using nitrogen stream.

2.5.2. Liquid–solid extraction (LSE)

Paper sample (2.0 g) was grinded and placed into a round-bottomed extraction flask (250 mL). Methanol (200 mL) were then added to the sample and extraction is carried out for 2 h at 80 °C in the dark. After extraction is completed, extract was filtered and concentrated under nitrogen stream to give a final volume of approximately 0.3 mL (gravimetrically controlled).

3. Results and discussion

3.1. Technique optimization using factorial design

Experiments based on a fractional factorial Plackett–Burman design were first performed in order to identify significant parameters affecting both SWE and DSASE. All calculations were performed using Modde 4.0 for Windows (Umetri, Umeå, Sweden). Table 1 shows the factors selected together with their variation range for both extraction techniques. As can be seen, all parameters were continuous numerical variables, each point in the designs was replicated twice and experiments were performed in a random order. In SWE, static extraction time and temperature were the more influential variables whereas when applying DSASE dynamic flow and extraction temperature showed the biggest influence on extraction recovery.

The results were used to develop a response surface design (central composite circumscribed) to fully optimize the extraction processes. After implementing the 17 experimental trials, average recoveries were calculated from the sum of percentage recoveries from the paper spiked with the analyte

Table 1
Factors and level tested for SWE and DSASE extraction methods[a]

Factor	SWE	DSASE
Flow (mL/min)	0.5–2.0 (**0.5**)	0.2–1.0 (**0.2**/**1.0**)
Static extraction time (min)	0–20 (**20**)	0–20 (**0**)
Dynamic extraction time (min)	1–20 (**1**)	1–20 (**11**)
Extraction temperature (°C)	100–250 (**250**)	25–80 (**80**)
Extraction pressure (atm)	50–150 (**50**)	2–150 (**2**)
Extraction vessel position (cm)[b]	–	1.0–5.0 (**1.0**)

[a] Bold numbers represent optimum values found.
[b] Defined as the distance from the top of the vessel to the water–air interface.

Table 2
Comparison of the extraction techniques

Analyte	Non-sonication DSASE	SWE	LSE	Soxhlet
FWAs				
RT	81 (7) 81 (3)	23 (13)	9 (21)	–
RT*	69 (9) 70 (7)	17 (8)	14 (5)	–
ACR	62 (10) 64 (12)	25 (17)	6 (22)	5 (17)
AP	65 (8) 77 (9)	18 (10)	2 (25)	10 (21)
RD	72 (9) 83 (7)	12 (21)	12 (8)	25 (19)
BS	60 (5) 61 (6)	10 (3)	65 (7)	63 (6)
AZOs				
Acid yellow 17	71 (8) 80 (5)	13 (7)	18 (10)	18 (9)
Acid red 1	83 (4) 83 (3)	20 (11)	17 (8)	4 (22)
Acid orange 8	95 (4) 113 (5)	15 (7)	32 (11)	57 (7)
Basic orange 2	70 (9) 88 (6)	–	35 (10)	42 (7)
Fast Garnet CBC	16 (16) 15 (9)	–	2 (15)	1 (21)
Acid red 114	7 (11) 1 (11)	–	3 (13)	4 (23)

Average recoveries (RSD, %, $n = 3$).

mix. Based on the analysis of variance (ANOVA) evaluation of the design, the significance of the cross-interaction terms was found to be extremely low, demonstrating that significant factors were independent to each other. Optimum values found are shown in Table 1. Table 2 presents average results of a triplicate extraction of a 1.0 μg/g spiked sample in the optimum conditions. For comparative purposes, results obtained in LSE and Soxhlet extractions are also depicted in the Table, as well as recovery percentages obtained when extraction is conducted in the optimum DSASE conditions without sonication, which can be seen as a pseudo-PLE technique. When comparing results, it is clear that DSASE recoveries are in all cases much higher than those obtained when using SWE, LSE or Soxhlet extractions, whereas similar, although lower percentages were obtained in the non-sonication approach.

These results can be explained as follows: an extraction process can be roughly divided into four main steps: access of the extraction media to the target analytes, desorption of analytes from matrix, solubilization into the extraction solvent and final transport to the collection trap or vial. When working with paper matrices, analytes are usually incorporated inside lignin–cellulose clusters that reduce their availability for solvent interaction and thus extraction recoveries. So, as a preliminary step, clusters need to be opened in order to gain access for the extraction solvent to the target chemicals.

When using SWE, clusters can only be opened by increasing temperature or contact time, thus explaining why static extraction time has the biggest influence. However, increasing temperature decreases water dielectric constant thus reduces polar- or middle-polar-analyte extraction rate and could also provoke analyte degradation. To check the extent of the latter effect, a pressurized (approximately 100 atm) aqueous solution containing a known amount of the analytes was heated at increasing temperatures up to 250 °C and analyte integrity was controlled by chromatographic analysis every 25 °C. Significant reduction in analyte signal was found at temperatures above 125 °C, supporting analyte degradation theory.

When Soxhlet is applied, degradation phenomena occur in a similar fashion that with SWE, whereas when LSE is used combination of moderate temperature and non-facilitated extraction kinetics prevent methanol to quantitatively extract target analytes.

Better results were obtained when pseudo-PLE approach was applied, due to its combination of forced flow through the

Table 3
Modifier results

Analyte	Tetrahydrofuran (v/v)			Acetonitrile (v/v)			Methanol (v/v)			Acetone (v/v)			DSASE
	5	15	25	5	15	25	5	15	25	5	15	25	
FWAs													
RT	71	90	88	83	68	68	66	102	96	72	77	65	81
RT*	50	66	69	72	50	52	61	**85**	82	50	52	53	70
ACR	97	93	85	88	95	**110**	44	75	76	95	91	95	64
AP	70	92	89	57	72	82	39	46	41	**98**	93	72	67
RD	85	106	99	68	88	107	66	48	46	112	**116**	86	83
BS	99	**107**	100	90	95	93	103	97	82	95	101	88	61
Average	79 (7)	**92 (6)**	88 (8)	76 (9)	78 (10)	85 (8)	63 (6)	76 (8)	61 (4)	87 (5)	88 (7)	77 (8)	71 (7)
AZOs													
Acid yellow 17	93	96	91	92	**117**	111	64	69	84	101	91	80	80
Acid red 1	89	97	85	89	93	93	83	60	65	**102**	89	82	83
Acid orange 8	87	96	90	100	81	94	103	98	**118**	78	81	96	113
Basic orange 2	85	93	85	94	90	100	**102**	94	**102**	89	80	94	88
Fast Garnet CBC	8	37	8	11	**57**	26	14	37	6	26	19	8	15
Acid red 114	1	28	2	8	**65**	14	5	47	3	14	9	1	8
Average	*61 (11)*	*75 (8)*	*60 (12)*	*66 (9)*	***84 (5)***	*73 (9)*	*62 (6)*	*67 (6)*	*63 (7)*	*68 (13)*	*61 (15)*	*60 (18)*	*65 (15)*
Average[a]	89 (6)	96 (9)	88 (8)	94 (10)	95 (11)	**100 (14)**	88 (7)	80 (8)	92 (7)	93 (11)	85 (13)	88 (14)	91 (8)

Average recoveries (Average RSD, %, $n = 3$). Bold numbers represent optimum values found.
[a] Numbers in italic represent average of the first four azo dyes.

packed matrix (thus overcoming to some extent the contact problem) and moderate temperature, thus provoking cluster opening. Nevertheless, better results were obtained in the DSASE mode. The main effect of sonication can be described in terms of pure physical interactions, through the formation of cavitation bubbles, as explained in Section 1. This results in cluster destruction and accelerated mass transfer and desorption while maintaining average "mild" conditions in the bulky extraction fluid. This theory is supported by the fact that a combination of a first step at low flow (when clusters are destroyed) and a second step at a higher flow when analyte is desorbed, dissolved into the extracting flow and transported to the collection vial was found to be the optimum combination.

As was previously explained, sonication is a technique mainly influential on extraction kinetics and analyte availability, with little or no influence in the chemical solvent properties (i.e. solvating power). In the case under study, this reflects on the low extraction recoveries for the less water soluble compounds, namely BS, Fast Garnet GBC Base and acid red 114. In order to overcome this limitation, the use of organic modifiers may constitute a promising alternative, as proven for instance in SFE. So, four different organic modifiers were tested at three concentration levels (i.e. 5, 15, and 25%, v/v). Table 3 shows the results obtained in terms of average recoveries compared to plain DSASE.

The best average results were obtained for FWAs with 15% (v/v) tetrahydrofuran (THF) as the organic modifier, whereas acetonitrile at 15% (v/v) gave the best recoveries for azo derivatives, mainly due to highest improvement of extraction of low polarity analytes. When considering the whole set of compounds, THF was selected as optimum. Fig. 1 shows

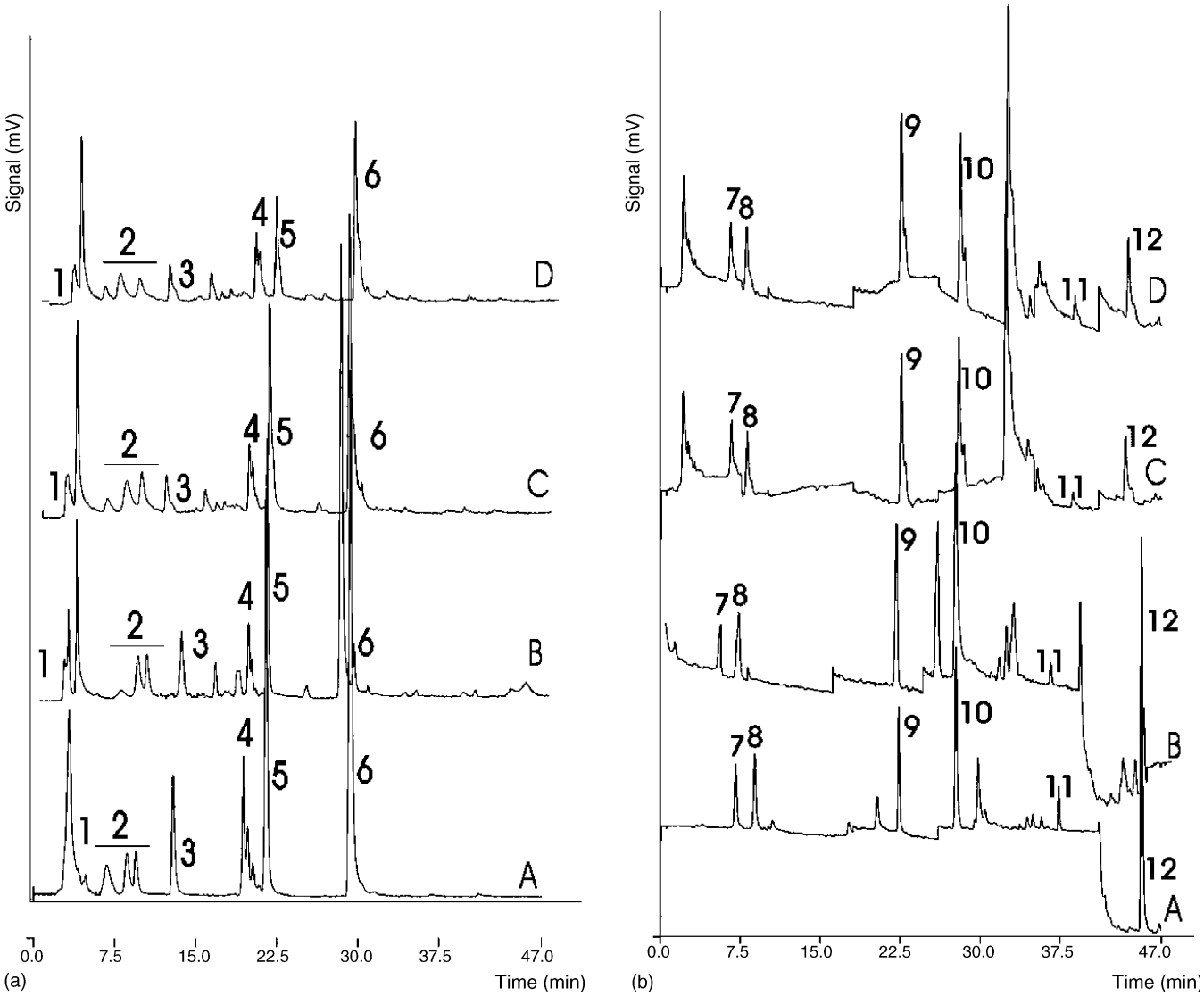

Fig. 1. Chromatograms obtained in the extraction of paper samples. (a) Fluorescent whitening agents; (b) azo dyes. Chromatogram identification: (A) standard mixture; (B) modified-DSASE; (C) DSASE; (D) pseudo-PLE. Peak identification: FWAs: (1) RT, (2) RT*, (3) ACR, (4) AP, (5) RD, (6) BS; AZOs: (7) acid yellow 17, (8) acid red 1, (9) acid orange 8, (10) basic orange 2, (11) Fast Garnet GBC Base, (12) acid red 114.

Table 4
Summary of the parameters validated for the determination of FWAs and AZOs described in the text

Figure of merit	FWAs						AZOs					
	RT	RT*	ACR	AP	RT	BS	AY 17	AR 1	AO 8	BO 2	FG GBC	AR 114
Robustness	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Linear range (μg/g)	0.3–20	1.8–20	1.8–20	1.8–20	0.3–20	0.1–20	0.3–33	1.8–33	0.3–33	0.3–33	1.8–20	0.3–33
Repeatability (%RSD)[a]												
Low level	5	7	8	7	8	6	7	8	9	10	13	15
High level	3	7	9	7	6	4	5	6	8	8	11	10
Intermediate precision (%RSD)[a]												
Low level	5	8	7	6	6	8	7	6	11	9	18	14
High level	4	6	9	7	8	3	6	7	10	9	15	9
Capability of detection (μg/g)[b]	0.05	0.20	0.21	0.32	0.07	0.01	0.30	0.20	0.09	0.08	0.40	0.08

[a] Low level: 0.5 μg/g; high level: 5.0 μg/g.
[b] ($\alpha = 0.05$; $\beta = 0.05$; $K = 3$).

typical chromatograms obtained at the 0.5 μg/g spiking level. For comparison purposes chromatograms corresponding to pseudo-PLE extraction and standard mixture have been also included in the Figure.

3.2. Analytical performance

To calculate the robustness (i.e. insensitivity of the analytical method to minor changes in environmental and procedural variables) [38] of the method, a Plackett–Burman experimental design was conducted, including the relevant factors at values representing ±10% of their optimum values. The weight of the effective changes was calculated at the α 0.05 significance level. No change was found to be relevant, so the method is robust with the only exception of Fast Garnet GBC which was influenced by both dynamic flow and extraction temperature.

To evaluate the linear range of the method two sets of 10 spiked samples in the range from 0.01 to 33 μg/g were prepared and extracted under the optimum conditions. Table 4 shows the results obtained. In order to determine the precision two sets containing six groups of three paper samples were spiked at two concentration levels. Groups were analyzed in six different days and the analysis of the variance was used to evaluate the precision. Table 4 shows the results obtained. Repeatability is the precision under most similar conditions whereas reproducibility represents precision under more variable conditions (i.e. different laboratories, equipment, operators or enlarged time span). Since only one factor (change of day) has been introduced in this work, the term intermediate precision is used instead of reproducibility [38].

Capability of detection was calculated as defined by both IUPAC and ISO 11843 [39–41] from the slope of the calibration curve used to determine the method linear range. Then, capability of detection was calculated for three replicates with a probability of false positive (α) equal to 0.05 and a probability of false negative (β) of 0.05. From the results obtained, it can be concluded that the proposed method gives comparable analytical features than those reported in the scientific literature.

4. Conclusions

A method based on DSASE has been developed and partially validated for the determination of FWAs and AZOs in paper matrices, resulting in a reduction in analysis time by a factor of 11 and in the consumption of organic solvent by a factor of 200. The introduction of an organic modifier in the DSASE approach has been proven to be highly effective in increasing extraction of less polar chemicals. The proposed method has been advantageously compared with classical liquid and Soxhlet extraction in terms of recovery and precision.

As it is, the main drawback of the proposed methodology is the need of the evaporation step, which is time consuming and can lead to recovery losses through analyte degradation. So, it is clear that further work needs to be focused on the development of an on-line approach which can overcome this problem. Another interesting field of development includes the investigation on other factors known to have influence on the sonication process, which are ultrasonic bath volume, geometry, and filling, or variable sonication frequency.

Acknowledgements

This work was financed by the Spanish Project CAL 01-084-INIA, which is part of the Plan Nacional de Alimentación, Spain. The authors would like to thank Ciba-Geigy, Clariant Ibérica, Robama, and Bayer Ibérica for providing the FWA standards. R.B. gratefully acknowledges the Spanish Ministry of Science and Technology for personal funding through the Ramón y Cajal program.

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