Science of the Total Environment 710 (2020) 134975

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

# High-performance liquid chromatography (HPLC)-fluorescence method for determination of bisphenol A diglycidyl ether (BADGE) and its derivatives in canned foods

Mingming Guo [a], Mingfeng He [a], Jianjun Zhong [b], Qiao He [a], Balarabe B. Ismail [a], Guoying Chen [c], Donghong Liu [a,*]

[a] College of Biosystems Engineering and Food Science, National-Local Joint Engineering Laboratory of Intelligent Food Technology and Equipment, Zhejiang Key Laboratory for Agro-Food Processing, Zhejiang R & D Center for Food Technology and Equipment, Fuli Institute of Food Science, Ningbo Research Institute, Zhejiang University, Hangzhou 310058, China

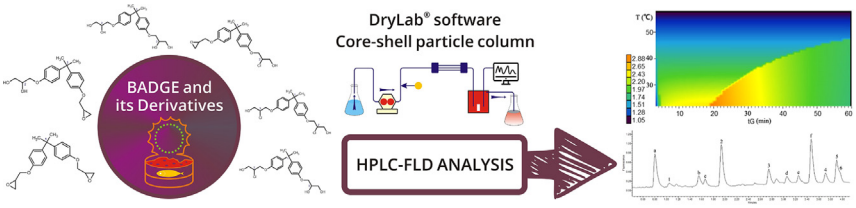
[b] School of Grain Science and Technology, Jiangsu University of Science and Technology, Zhenjiang 212000, China

[c] Agricultural Research Service, Eastern Regional Research Center, U.S. Department of Agriculture, 600 East Mermaid Lane, Wyndmoor, PA 19038, USA

## HIGHLIGHTS

- HPLC-FLD method for BADGE and its derivatives analysis with LOD of 0.01–0.20 ng/g.
- The optimization of separation conditions applying DryLab® software.
- Adequate separation in 5 min using a core–shell particle column.

## GRAPHICAL ABSTRACT




## ARTICLE INFO

*Article history:*
Received 30 August 2019
Received in revised form 9 October 2019
Accepted 12 October 2019
Available online 21 November 2019

Editor: Damia Barcelo

*Keywords:*
Bisphenol A diglycidyl ether (BADGE)
HPLC
Core–shell particle column
Canned foods

## ABSTRACT

Bisphenol A diglycidyl ether (BADGE) is used as a raw material for the production of epoxy resins and PVC organosols, which are commonly applied as inner coatings for food cans. BADGE and its derivatives can migrate from coatings to foodstuffs during processing and storage thereby creating adverse health issues. In this work, a method based on high-performance liquid chromatography (HPLC)-fluorescence detection (FLD) method was developed for the rapid determination of BADGE and its five derivatives in canned foods. Modeling software DryLab® was applied for the optimization of separation conditions. An adequate separation was achieved in 5 min including equilibration time, using a core–shell particle column; such application has not been reported so far. Also, the results showed that LOD varied from 0.01 to 0.20 ng/g, while LOQ varied from 0.03 to 0.66 ng/g, and RSD was found to be <8.64%. The analytical recoveries ranged from 70.46 to 103.44%. Excellent validation data revealed that this method is suitable for the investigation of can coating-to-food migration of BADGE and its derivatives. The HPLC-FLD method is rapid, inexpensive and highly efficient, which could be applicable for safety inspection of food contact materials involving BADGE and its derivatives.



## 1. Introduction

Bisphenol A diglycidyl ether (BADGE) is the most widely used raw material for the production of epoxy resins and PVC organosols. It is commonly applied as inner coatings for food cans to prevent metal corrosion and protect foodstuffs from metal (Grob et al., 2010; Szczepańska et al., 2018). However, during processing and

* Corresponding author at: College of Biosystems Engineering and Food Science, Zhejiang University, 866 Yuhangtang Rd., Hangzhou 310058, China.
*E-mail address:* dhliu@zju.edu.cn (D. Liu).

https://doi.org/10.1016/j.scitotenv.2019.134975
0048-9697/

storage of canned foods, BADGE and its hydrolysis and hydrochlorination derivatives have been proved migratable from can coatings to foodstuff (Fattore et al., 2015; Noureddine El Moussawi et al., 2019; Xie et al., 2015).

The toxicology of BADGE and its related products are yet to be thoroughly investigated, but they have been demonstrated to create potential adverse health issues due to their genotoxic, mutagenic and endocrine disrupting properties (Marqueno et al., 2019; Szczepańska et al., 2019; Wang et al., 2015). Consequently, specific migration limits (SMLs) of food contact material have been established by the European Union (the Commission of the European Communities, 2005). The SMLs for BADGE, BADGE·$H_2O$ and BADGE·2$H_2O$ were set at $9 \times 10^3$ ng/g in food or food simulants, while the SMLs for BADGE·HCl, BADGE·2HCl and BADGE·$H_2$-OHCl were set at $10^3$ ng/g, respectively. Therefore, this makes it necessary to develop protocols for analyzing BADGE and its derivatives in foods.

Methods for determination and quantification of BADGE and its derivatives have been well documented (Asimakopoulos et al., 2014; El-Kosasy et al., 2018a; Miguez et al., 2012). Ultra-performance liquid chromatography (UPLC) is one of the most frequently applied methods for the determination of these compounds (Cheng et al., 2017; Zhang et al., 2017; Zou et al., 2012). Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) (Chang et al., 2014; Gallart-Ayala et al., 2011) or fluorescence detection (FLD) was also employed (Alabi et al., 2014; Fischnaller et al., 2016; Xiong et al., 2018). Though UPLC-MS detector has gained reliability and accuracy advantages over other methods, it has some disadvantages as well: expensive equipment and maintenance in addition to complicated sample preparation. Comparatively, the equivalent chromatographic performance, convenience, and low cost of HPLC-FLD have tremendously increased its potential as a multi-residue method (Gallart-Ayala et al., 2010). On the other hand, HPLC coupled with diode array detector (DAD) was applied to a lesser extent (El-Kosasy et al., 2018a; El-Kosasy et al., 2018b). To the best of our knowledge, analysis of BADGE and its derivatives by HPLC-UV has been rarely discussed in previous studies. We could only refer to one study by Poustková et al. (2004) regarding the analysis of BADGE and its derivatives using HPLC-UV. Thus far, no rapid (<20 min) HPLC-FLD method for analyzing BADGE and its derivatives was reported. Based on convenient preparation, cost, and availability of HPLC instrumentation, it is vital to develop a high-throughput HPLC method to detect these compounds in complex food matrices.

Superficially porous particles, also called core–shell particles, are composed of a solid core surrounded by a thin porous shell. Compared to traditional totally porous particles, such as sub-2 mm particles, core–shell particle columns are characterized by smaller van Deemter coefficients, higher speed, and higher efficiency, but the back pressure per unit column length drops to approximately a half (Brhane et al., 2019; Horvath et al., 2019; Qamar et al., 2019).

Considerable technical skills and labour are always demanded in a trial-and-error approach for the development of HPLC methods. From the simplicity standpoint, DryLab® simulation software is used to generate retention models and predict a broad range of operating conditions, based on experimental data from a small, well-defined set of experiments. Moreover, identification of optimum separation conditions and evaluation of parameters, namely gradient time, column temperature and mobile phase composition can efficiently be facilitated by the software (Ródenas-Montano et al., 2013; Sun et al., 2015). As far as we know, DryLab® software has never been applied for developing an optimum analytical method of BADGE and its derivatives.

Due to the trace amount of BADGE and its derivatives in complex food matrices, matrix impurities would likely interfere. It is crucial to use spike-recovery approach in method development. The objective of this study was to develop a rapid HPLC-FLD method for the simultaneous determination of BADGE and its derivatives in canned foods using a modern core–shell particle column, while the experimental conditions were optimized with the aid of Drylab® software.

## 2. Methods and materials

### 2.1. Reagents

Standards of BADGE, BADGE·$H_2O$, BADGE·2$H_2O$, BADGE·HCl, BADGE·2HCl and BADGE·$H_2$OHCl were purchased from Fluka (Reinach, Switzerland). Acetonitrile (HPLC grade) was purchased from Tedia (Fairfield, Ohio, USA). Hexane and other chemicals were obtained from Sinopharm Chemical Reagent (Shanghai, China).

### 2.2. Equipment and final chromatographic conditions

HPLC was performed on a Waters 2695 module (Milford, MA, USA) coupled to a Waters 2475 fluorescence detector (FLD). A Poroshell 120 SB-C18 column (100 mm × 4.6 mm, i.d. × 2.7 μm) from Agilent (La Jolla, CA, USA) was used. The mobile phase was comprised of water (eluant A) and acetonitrile (eluant B) at 1.5 mL/min with the following program: 0–3 min, 50–72.5% B; 3–4 min, 72.5–100% B; 4–5 min, 100–50% B. The injection volume was 10 μL, and the column temperature was 30 °C. The fluorescence excitation and emission wavelengths were set at 275 and 305 nm, respectively.

### 2.3. Sample preparation

Homogenized tuna (2 g) was extracted with 10 mL of hexane for 30 min under ultrasound agitation. The extract was centrifuged at 8021 g for 10 min; the supernatant was then washed twice with 5 mL of acetonitrile. The acetonitrile extracts were evaporated to dryness at 40 °C under nitrogen. The residue was reconstituted in 1.8 mL of acetonitrile, and the resulting solution was spiked with 0.2 mL standard mixture solution (1 μg/mL BADGE, BADGE·$H_2O$, BADGE·2$H_2O$, BADGE·HCl, BADGE·2HCl and BADGE·$H_2$OHCl in acetonitrile) at 100 ng/mL each. Spiked samples were filtered through 0.45 μm syringe filters before HPLC analysis.

### 2.4. Optimization of separation condition using DryLab®

To optimize separation conditions using DryLab® (Molnár Institute, Berlin, Germany), spiked samples prepared in section 2.3 were used. The following four calibration experiments were carried out (two gradient time: $t_{G1}$ = 20 min and $t_{G2}$ = 60 min, and two-column temperatures: $T_1$ = 25 °C and $T_2$ = 55 °C for each).

Because of the extremely low concentrations of BADGE and its derivatives in canned foods and potential matrix interference, the impurity peaks with adequate signal-to-noise ratio (S/N) and close retention time to analyte compounds in food matrix also served as target peaks and included in the modeling. Specifically, a total of 12 target peaks were determined, including 6 analyte peaks and 6 impurity peaks. Peak area and retention time were used to track each peak under different chromatographic conditions, as described in our previous report (Zhong et al., 2018). The following experimental data from the four experimental runs were entered into the Drylab®: column dimensions (100 mm × 4.6 mm), particle size (2.7 μm), flow rate (1 mL/min), mobile phase composition (A: water, B: acetonitrile), linear gradient range (10–100% ACN). The retention time and peak area of the 12 target peaks in the four initial experiments were also used as input parameters for opti-

mization. Hence, a resolution map and chromatograms were predicted.

### 2.5. Further optimization

#### 2.5.1. Flow rate

The mobile phase flow rate is a crucial LC parameter. An increase in flow rate shortens run time, but elevates system pressure and decreases resolution and S/N. The elution volume, in a gradient elution system, was required to be constant during flow rate optimization, hence the flow rate was elevated to 1.5 mL/min with gradient program adjusted to 0–6.67 min: 50–100% B.

#### 2.5.2. Gradient procedure

Accelerating the increase of the organic phase in the latter stage of the gradient program was implemented, resulting in rapid elution of difficult-to-elute impurities and shortened analytical time. The gradient procedure was adjusted as 0–3 min, 50–72.5% B; and 3–4 min, 72.5–100% B.

#### 2.5.3. Equilibrium time

From the throughput point of view, the equilibrium time between consecutive injections should be as short as possible. Usually, the initial volume of the mobile phase is 5 to 10 times higher than that of the column, which is used to equilibrate the column thoroughly. However, the actual equilibrium volume can be much smaller. The equilibrium time between successive injections would significantly influence the repeatability of the retention time. Consequently, a study was performed on this parameter (0, 1, 2, 5, and 10 min). For each, the injection was repeated 6 times.

#### 2.5.4. Acquisition rates and injection volume

The influence of the detector acquisition rate (1, 2, and 5 Hz) and injection volume (2, 5 and 10 μL) on the chromatogram was investigated.

### 2.6. Method validation

#### 2.6.1. Calibration curves and linearity

Calibration curves were set up by plotting peak area versus concentration in the range 10–10000 ng/mL. Standard solutions, 10, 25, 100, 250, 1000, 2500 and 10000 ng/mL of the six analytes with duplicate injections, were evaluated for linearity.

#### 2.6.2. Limit of detection and quantitation

LODs and LOQs were calculated based on 3σ and 10σ, respectively.

#### 2.6.3. Method accuracy and precision

Fortified tuna samples at each concentration level were extracted and analyzed. Accuracy and precision were obtained from six analytes at three different concentrations (25, 100, 400 ng/g). The accuracy of the method was evaluated based on recoveries.

## 3. Results and discussion

### 3.1. Method optimization using DryLab®

Based on previous results (data not shown), Drylab® software was applied to predict the separation performance with different gradient program and column temperatures. Peak matching was conducted to identify individual peaks in the chromatogram. Impurity peaks with close retention times were picked for optimization. Retention time and resolution under different combinations of gradient program and temperature were predicted. A resolution map, of which color code represents the critical resolution ($R_s$) values, was thereby generated (see Fig. 1). The critical resolution, total analytical time and simplicity of the experimental procedure should be considered concurrently in setting an optimum separation condition.

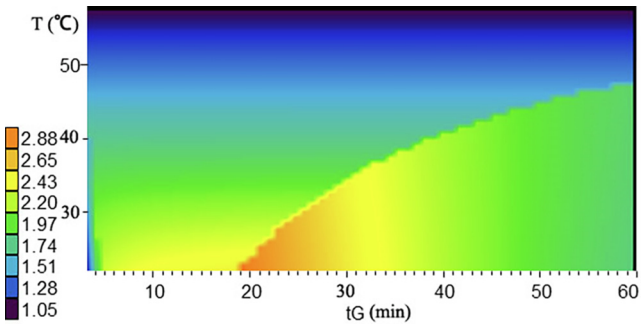



**Fig. 1.** Resolution map under varied temperature and gradient time.

Despite better resolution at lower column temperatures, the column oven can only be heated but cannot be cooled down. Hence setting the oven temperature at 30 °C is convenient for practical application. Meanwhile, 10 min of gradient time was selected based on critical resolution ($Rs$ > 1.5 criterion) and analysis time.

Further optimization can be carried out by altering the initial ACN concentration without additional experiments. As shown in Fig. 2, the first peak eluted late, so the initial mobile phase composition was adjusted, followed by modeling the separation performance with DryLab®. Finally, the initial organic phase was elevated to 50% to cut the total elution time. The software generated optimal separation conditions were 50–100% ACN gradients in 10 min at the column temperature of 30 °C; other parameters were identical to those described in Section 2.4.

The predicted and experimental chromatograms of the spiked sample under the optimized conditions were shown in Fig. 2A and B, respectively. The peaks marked a-f were target peaks, and the ones marked 1–6 were impurity peaks. Adequate separation between each target-impurity pair was achieved with excellent resolution. Meanwhile, the total elution time was 6.67 min for both experimental and predicted results. The retention times of each peak for the predicted and experimental chromatograms obtained under optimized conditions were also compared in Table 1. The resulting chromatograms showed satisfactory agreement with computer-predicted results, with retention margin <0.26 min.

### 3.2. Further optimization

The flow rate of the mobile phase is crucial in LC. In this study, the flow rate was elevated to 1.5 mL/min with the corresponding gradient program adjusted to 0–6.67 min: 50–100% B. Fig. 3 shows the chromatogram of a spiked sample under optimum conditions. Analysis time was shortened by one third without any noticeable degradation in resolution. Besides, both system pressure and S/N were within the acceptable range.

As can be seen in Fig. 3, the retention time of the last detected peak was within 4 min, suggesting that the optimization of the elution time was performed successfully. In this case, an increase in organic phase in the latter stage of the gradient elution program was accelerated, resulting in rapid elution of difficult-to-elute impurities and time-saving. The gradient procedure was adjusted accordingly: 0–3 min: 50–72.5% B, 3–4 min: 72.5–100% B. The analysis time was cut to 4 min with an adequate separation.

To improve the sample throughput, the equilibration time between consecutive injections should be minimal. A study on

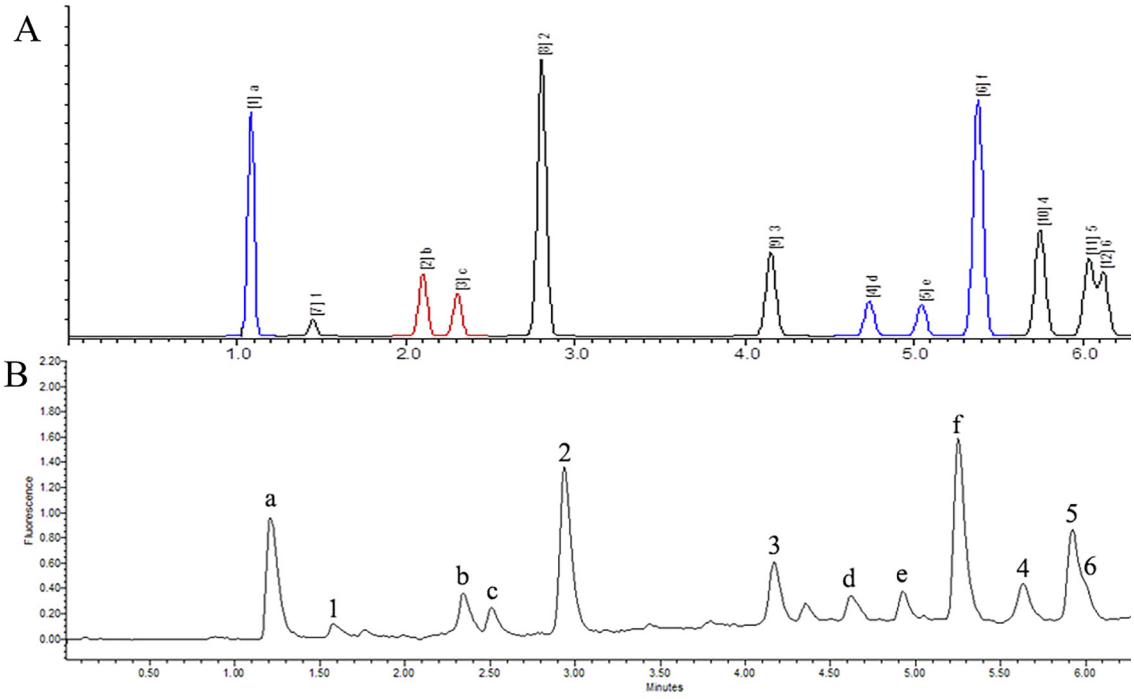



**Fig. 2.** Predicted (A) and experimental (B) chromatograms of the spiked sample under optimal conditions (gradient: 50–100% ACN, $t_G$ = 10 min, T = 30 °C, flow rate: 1 mL/min). The 12 peaks marked with numbers were those included in the optimization by DryLab.

**Table 1**
Predicted and experimental retention times of the spiked sample under optimized separation conditions.

| Peak | Predicted retention time (min) | Rs | Experimental retention time (min) | Diff.[a] (min) | Error[b] (%) |
|---|---|---|---|---|---|
| BADGE·2$H_2O$ (a) | 1.08 | 4.86 | 1.21 | 0.13 | 12.30 |
| Impurity 1 | 1.44 | 7.59 | 1.60 | 0.16 | 11.04 |
| BADGE·$H_2O$HCl (b) | 2.09 | 2.18 | 2.35 | 0.26 | 12.46 |
| BADGE·$H_2O$ (c) | 2.30 | 5.11 | 2.52 | 0.22 | 9.43 |
| Impurity 2 | 2.80 | 12.75 | 2.97 | 0.17 | 5.94 |
| Impurity 3 | 4.15 | 5.43 | 4.20 | 0.05 | 1.25 |
| BADGE·2HCl (d) | 4.73 | 2.93 | 4.64 | 0.09 | 1.94 |
| BADGE·HCl (e) | 5.04 | 3.12 | 4.96 | 0.08 | 1.69 |
| BADGE(f) | 5.38 | 3.26 | 5.28 | 0.10 | 1.77 |
| Impurity 4 | 5.74 | 2.47 | 5.67 | 0.07 | 1.25 |
| Impurity 5 | 6.03 | 0.73 | 5.95 | 0.08 | 1.27 |
| Impurity 6 | 6.12 | | 6.02 | 0.10 | 1.63 |

[a] Difference = Experimental-Predicted.
[b] Error (%): [(Experimental-Predicted)/Predicted] × 100.

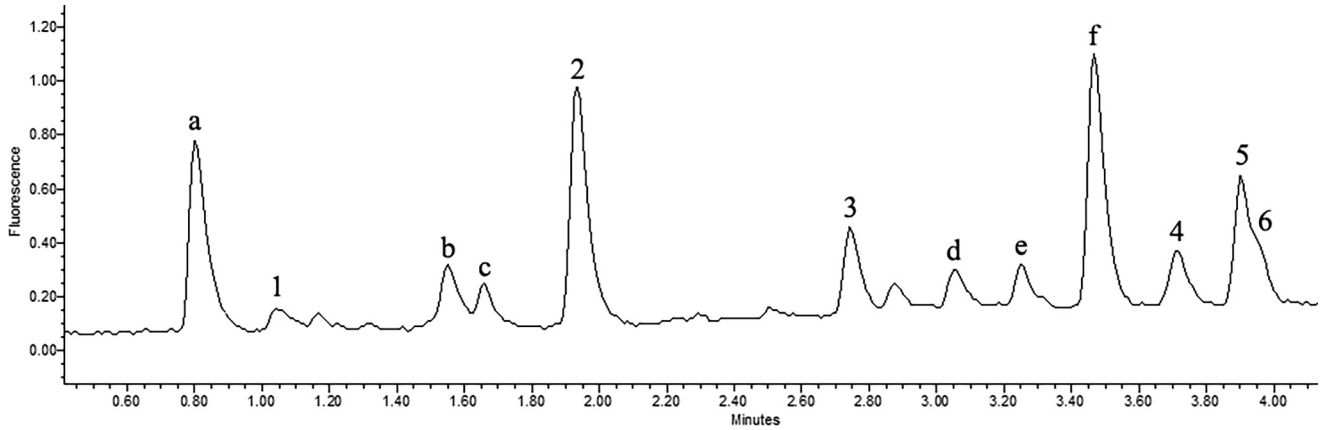



**Fig. 3.** Chromatogram of the spiked sample after optimization of flow rate.

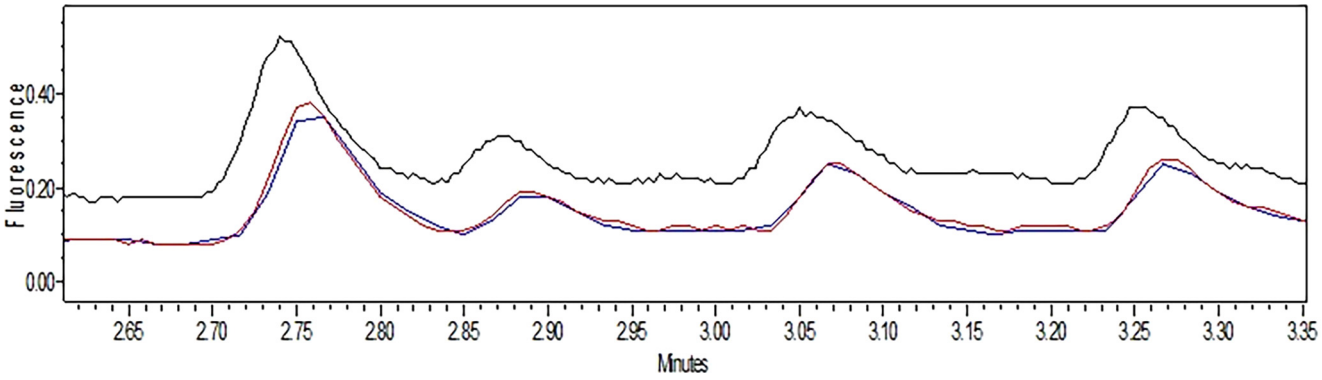



**Fig. 4.** Chromatograms of the spiked sample at different acquisition rates: 5 Hz (black), 2 Hz (red) and 1 Hz (blue). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

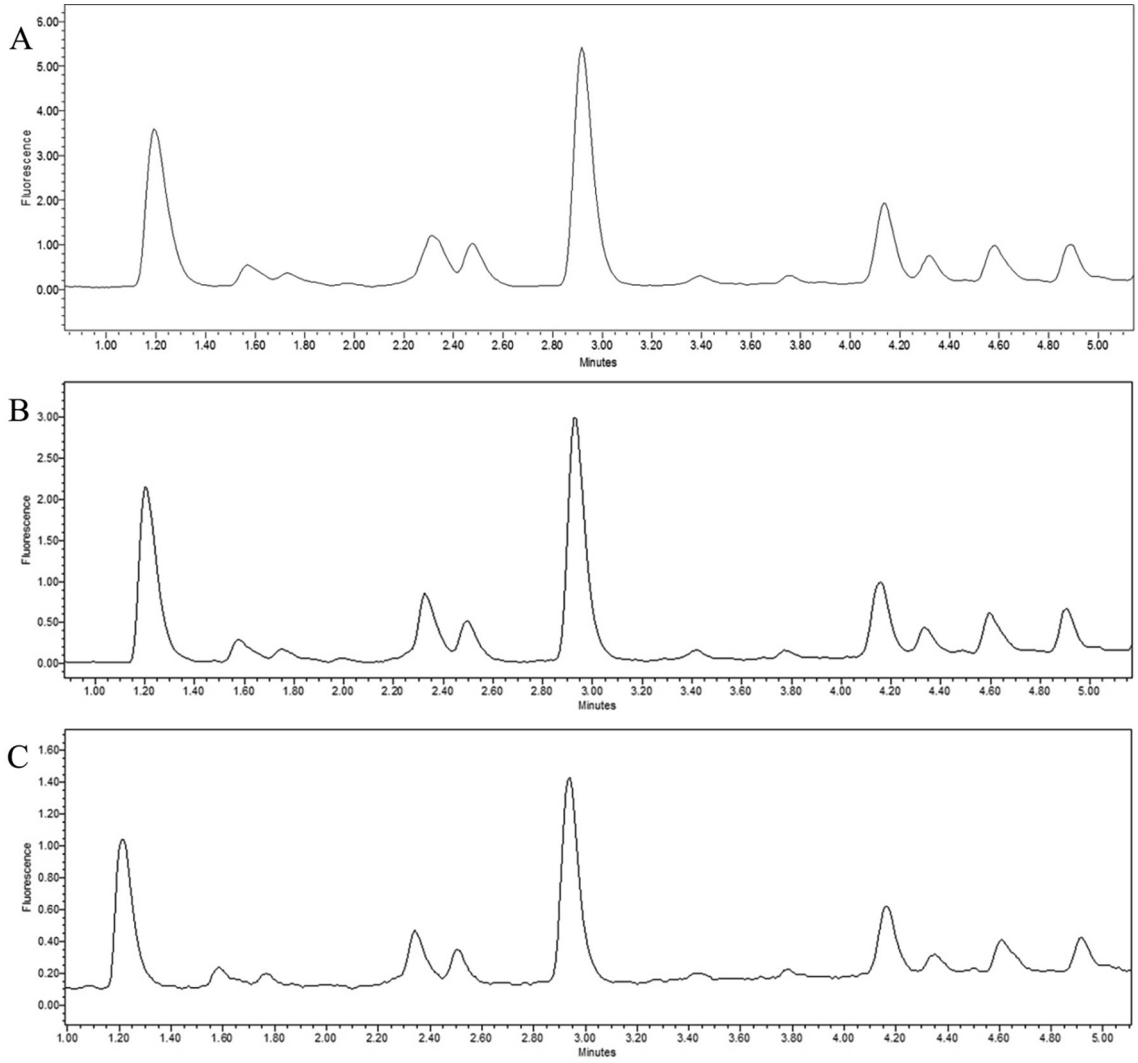



**Fig. 5.** Chromatograms of the spiked sample under different injection volumes: 10 μL (A), 5 μL (B), and 2 μL (C).

equilibration time (0, 1, 2, 5, and 10 min) was performed. The result showed that excellent repeatability of retention and resolution was achieved with 1 min of equilibration (data not shown), while inefficient equilibration resulted in reduced peak shape and resolution. As a result, the entire run took 5 min, including a 1-minute equilibration. The total runtime of HPLC-FLD in this method is shorter than those in previous reports applying fluorescence and MS methods (Xiong et al., 2018; Cheng et al., 2017).

In Fig. 4, the influence of data acquisition rate (1, 2, and 5 Hz) on the chromatogram were evaluated. For quantification purposes, at least 20 data points are required to accurately depict a peak shape (Snyder et al., 2010). At 1 Hz, insufficient data points resulted in

**Table 2**
Linear regression coefficients, LODs and LOQs of analytes.

| Analyte | Linear regression ($R^2$)[a] | LOD (ng/g) | LOQ (ng/g) |
|---|---|---|---|
| BADGE | 0.9995 | 1.03 | 3.43 |
| BADGE·$H_2O$ | 0.9998 | 1.16 | 3.86 |
| BADGE·2$H_2O$ | 0.9999 | 1.33 | 4.43 |
| BADGE·HCl | 1.0000 | 1.55 | 5.18 |
| BADGE·2HCl | 1.0000 | 1.56 | 5.18 |
| BADGE·$H_2O$HCl | 1.0000 | 1.57 | 5.24 |

[a] Calibration curves were constructed with five points ($n$ = 5) from three replicates

**Table 3**
Recoveries and repeatability (RSD, %) of the six analytes at three spiked levels.

| Analyte | Spiked (ng/g) | Recovery (%) | RSD (%) [a] |
|---|---|---|---|
| BADGE | 25 | 98.30 | 4.25 |
| | 100 | 92.68 | 3.43 |
| | 400 | 94.87 | 2.07 |
| BADGE·$H_2O$ | 25 | 93.31 | 5.73 |
| | 100 | 96.74 | 2.27 |
| | 400 | 93.88 | 3.26 |
| BADGE·2$H_2O$ | 25 | 96.32 | 6.45 |
| | 100 | 91.65 | 7.02 |
| | 400 | 94.90 | 4.42 |
| BADGE·HCl | 25 | 93.92 | 2.71 |
| | 100 | 97.19 | 3.33 |
| | 400 | 100.76 | 4.08 |
| BADGE·2HCl | 25 | 99.56 | 3.79 |
| | 100 | 98.81 | 5.10 |
| | 400 | 96.32 | 3.05 |
| BADGE·$H_2O$HCl | 25 | 92.98 | 2.64 |
| | 100 | 96.78 | 1.68 |
| | 400 | 94.72 | 4.72 |

[a] RSD% (n = 6)

missing peak height and loss of accuracy. On the other hand, 5 Hz acquisition rate resulted in significantly increased noise and degraded S/N. To ensure reasonable accuracy and S/N, a 2 Hz acquisition rate was chosen.

The effect of injection volume (2, 5 and 10 μL) on the separation was shown in Fig. 5. Larger injection volume increased sensitivity but compromised resolution. Due to the extremely low presence of BADGE and its derivatives in canned foods, a 10 μL injection was selected from a sensitivity standpoint. For samples with higher analyte presence, a smaller injection volume would be acceptable.

### 3.3. Method validation

#### 3.3.1. Calibration curves and linearity

The linear regression parameters of individual compounds are reported in Table 2. Excellent linear regression coefficients ($R^2 \geq 0.9995$) demonstrated satisfactory quantification.

#### 3.3.2. Limit of detection and limit of quantitation

LODs and LOQs of different BADGE-related compounds were listed in Table 2. The LODs ranged between 0.01 and 0.20 ng/g; LOQs ranged between 0.03 and 0.66 ng/g, respectively. These values were much lower than the limit at 1000 ng/g set by the EU Commission Regulation (EC). Moreover, these results were lower than those by HPLC-FLD in previous studies (Sun et al., 2006; Zhang et al., 2010).

#### 3.3.3. Method accuracy and precision

In Table 3, quantitative recoveries were attained between 91.65% and 100.76%. The reproducibility of the analytical procedure was also appropriate with RSD <7.02% for all analytes.

### 3.4. Comparisons with the previously reported methods

In this study, BADGE and its derivatives in canned foods were determined and validated by HPLC-FLD. In order to highlight the merits of this method, a performance comparison was conducted with other reported methods. As shown in Table 4, the proposed HPLC-FLD method provides several competitive advantages. The entire run took only 5 min which is significantly shorter than the earlier reports on HPLC-FLD methods that took 55 and 28 min, respectively (Gallart-Ayala et al., 2010; Xiong et al., 2018). It is even more rapid than UPLC-MS/MS method reported by Cheng et al.(2017). Rapid analysis reduced toxic solvent consumption, which contributes to an environment-friendly society. Furthermore, the proposed method holds the advantage of being cost-effective in instrumentation, operation, and maintenance in comparison with UPLC-MS/MS and HPLC-MS/MS methods (Cheng et al., 2017; Zou et al., 2012).

Noteworthily, the detection and quantitation limits of the proposed method are among the best, compared with other fluorescence methods (Fischnaller et al., 2016; Xiong et al., 2018). It has also proved a compelling alternative to MS/MS methods, since the values of LOD and LOQ were similar to the previous reports (Zhang et al., 2010).

**Table 4**
Comparison of reported work with the present work.

| Instrument | Column type | Runtime (min) | LOD (ppb) | LOQ (ppb) | Cost | Reference |
|---|---|---|---|---|---|---|
| UPLC-MS/MS | ACQUITY UPLC™ BEH $C_{18}$ column | 10 | 0.24–1.84 | NA | High | Zou et al., 2012 |
| UPLC-MS/MS | ACQUITY UPLC™ BEH $C_{18}$ column | 15 | 0.02–0.08 | 0.5–5 | High | Cheng et al., 2017 |
| UPLC-MS/MS | ACQUITY UPLC BEH $C_{18}$ column | 8 | 0.01–0.20 | 0.03–0.66 | High | Zhang et al., 2010 |
| HPLC-MS | Kromasil 100 $C_{18}$ column | 30 | 0.05–0.4 | NA | High | Sendon and Paseiro, 2004 |
| HPLC-MS/MS | Synergy MAX-RP | 8* | 0.5–3.1 | 1.8–10.3 | High | Miguez et al., 2012 |
| HPLC-$MS^n$ | Fused Core™ Ascentis Express $C_{18}$ | 4.5* | 0.15 Except BADGE·2HCl 8 | 0.5 Except BADGE·2HCl 2.5 | High | Gallart-Ayala et al., 2011 |
| HPLC-DAD | Synergi Hydro-RP $C_{18}$ column | 20 | 0.12–0.53 | 0.35–1.6 | Low | El-Kosasy et al., 2018a |
| HPLC-FLD | Lichrospher $C_{18}$ column | 50.5 | 0.79–3.77 | 2.75–10.92 | Low | Leepipatpiboon et al., 2005 |
| HPLC-FLD | ODS Hypersil $C_{18}$ column | 55* | 0.72–1.53 | 2.40–5.10 | Low | Gallart-Ayala et al., 2010 |
| HPLC-FLD | Nucleosil-100 $C_{18}$ column | 42 | 4.5–7.9 | 13.7–24.1 | Low | Sun et al., 2006 |
| Instrument | Column type | Runtime (min) | LOD (ppb) | LOQ (ppb) | Cost | Reference |
| HPLC-FLD | Ultrabase $C_{18}$ column | 30 | 0.4–0.5 | 1.2–1.6 | Low | Alabi et al., 2014 |
| HPLC-FLD | Kinetex $C_{18}$ column | 19 | 20.9 for BADGE, and 23.0 for BADGE·2$H_2O$ | 63.3 for BADGE and 96.6 for BADGE·2$H_2O$ | Low | Fischnaller et al., 2016 |
| HPLC-FLD | Xchrage $C_{18}$ column | 28 | 2.3 for BADGE, and 1.3 for BADGE·2$H_2O$ | 7.8 for BADGE and 3.8 for BADGE·2$H_2O$ | Low | Xiong et al., 2018 |
| HPLC-FLD | Poroshell 120 SB-$C_{18}$ column | 5 | 0.01–0.20 | 0.03–0.66 | Low | This work |

* equilibrium time not included.

## 4. Conclusions

An HPLC-FLD method was established for the rapid and simultaneous determination of BADGE and its derivatives facilitated by a modeling software DryLab®. Impurity peaks were used throughout the development process. This significantly reduced the matrix effect and enhanced analytical accuracy. Under optimized conditions, a satisfactory separation was achieved in 5 min using a core–shell particle column. To our knowledge, this is for the first time that rapid separation of BADGE and its derivatives was achieved with HPLC-FLD, gaining efficiency and cost advantages. In summary, the developed analytical method is applicable to safety inspection of food contact materials involving BADGE and its derivatives.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgment

The National Key Research and Development Program, China (grant number: 2018YFD0400700, 2016YFD0400301); the Fundamental Research Funds for the Central Universities, China (grant number: 172210181); the Key Research and Development Program of Zhejiang Province, China (grant number: 2017C02015) provided support for this study.

## References

Alabi, A., Caballero-Casero, N., Rubio, S., 2014. Quick and simple sample treatment for multiresidue analysis of bisphenols, bisphenol diglycidyl ethers and their derivatives in canned food prior to liquid chromatography and fluorescence detection. J. Chromatogr. A 1336, 23–33. https://doi.org/10.1016/j.chroma.2014.02.008.

Asimakopoulos, A.G., Wang, L., Thomaidis, N.S., Kannan, K., 2014. A multi-class bioanalytical methodology for the determination of bisphenol A diglycidyl ethers, p-hydroxybenzoic acid esters, benzophenone-type ultraviolet filters, triclosan, and triclocarban in human urine by liquid chromatography–tandem mass spectrometry. J. Chromatogr. A 1324, 141–148. https://doi.org/10.1016/j.chroma.2013.11.031.

Brhane, K.W., Qamar, S., Seidel-Morgenstern, A., 2019. Two-dimensional general rate model of liquid chromatography incorporating finite rates of adsorption-desorption kinetics and core–shell particles. Ind. Eng. Chem. Res. 58, 8296–8308. https://doi.org/10.1021/acs.iecr.9b00364.

Chang, Y., Nguyen, C., Paranjpe, V.R., Gilliland, F., Zhang, J., 2014. Analysis of bisphenol A diglycidyl ether (BADGE) and its hydrolytic metabolites in biological specimens by high-performance liquid chromatography and tandem mass spectrometry. J. Chromatogr. B 965, 33–38. https://doi.org/10.1016/j.jchromb.2014.06.005.

Cheng, Y., Nie, X.M., Wu, H.Q., Hong, Y.H., Yang, B.C., Liu, T., Zhao, D., Wang, J.F., Yao, G.H., Zhang, F., 2017. A high-throughput screening method of bisphenols, bisphenols digycidyl ethers and their derivatives in dairy products by ultra-high performance liquid chromatography-tandem mass spectrometry. Anal. Chim. Acta 950, 98–107. https://doi.org/10.1016/j.aca.2016.11.006.

El-Kosasy, A.M., Abdel-Aziz, O., Ayad, M.F., Mabrouk, O.M., 2018a. HPLC method for simultaneous determination of bisphenol-A-diglycidyl ether and some of its reaction products in canned foods using photodiode array detector. J. Chromatogr. Sci. 56, 920–932. https://doi.org/10.1093/chromsci/bmy069.

El-Kosasy, A.M., Ayad, M.F., Mabrouk, O.M., 2018b. Validated chemometrics-assisted spectrophotometric methods for simultaneous determination of bisphenol-A-diglycidyl ether and some of its reaction products in canned foods in the Egyptian market. Spectrochim. Acta A Mol. Biomol. Spectrosc. 203, 443–449. https://doi.org/10.1016/j.saa.2018.05.120.

Fattore, M., Russo, G., Barbato, F., Grumetto, L., Albrizio, S., 2015. Monitoring of bisphenols in canned tuna from Italian markets. Food Chem. Toxicol. 83, 68–75. https://doi.org/10.1016/j.fct.2015.05.010.

Fischnaller, M., Bakry, R., Bonn, G.K., 2016. A simple method for the enrichment of bisphenols using boron nitride. Food Chem. 194, 149–155. https://doi.org/10.1016/j.foodchem.2015.07.117.

Gallart-Ayala, H., Moyano, E., Galceran, M.T., 2010. Multiple-stage mass spectrometry analysis of bisphenol A diglycidyl ether, bisphenol F diglycidyl ether and their derivatives. Rapid Commun. Mass Spectrom. 24, 3469–3477. https://doi.org/10.1002/rcm.4801.

Gallart-Ayala, H., Moyano, E., Galceran, M.T., 2011. Fast liquid chromatography–tandem mass spectrometry for the analysis of bisphenol A-diglycidyl ether, bisphenol F-diglycidyl ether and their derivatives in canned food and beverages. J. Chromatogr. A 1218, 1603–1610. https://doi.org/10.1016/j.chroma.2011.01.026.

Grob, K., Camus, P., Gontard, N., Hoellinger, H., Joly, C., Macherey, A.C., Masset, D., Nesslany, F., Régnier, J.F., Riquet, A.M., Saillard, P., Ribera, D., 2010. Need for a better safety evaluation of food contact materials produced from resins. Food Control 21, 763–769. https://doi.org/10.1016/j.foodcont.2009.11.006.

Horvath, S., Gritti, F., Kormany, R., Horvath, K., 2019. Theoretical analysis of efficiency of multi-layer core-shell stationary phases in the high performance liquid chromatography of large biomolecules. Molecules 24. https://doi.org/10.3390/molecules24152849.

Leepipatpiboon, N., Sae-Khow, O., Jayanta, S., 2005. Simultaneous determination of bisphenol-A-diglycidyl ether, bisphenol-F-diglycidyl ether, and their derivatives in oil-in-water and aqueous-based canned foods by high-performance liquid chromatography with fluorescence detection. J. Chromatogr. A 1073, 331–339. https://doi.org/10.1016/j.chroma.2004.12.092.

Marqueno, A., Perez-Albaladejo, E., Flores, C., Moyano, E., Porte, C., 2019. Toxic effects of bisphenol A diglycidyl ether and derivatives in human placental cells. Environ. Pollut. 244, 513–521. https://doi.org/10.1016/j.envpol.2018.10.045.

Miguez, J., Herrero, C., Quintas, I., Rodriguez, C., Gigosos, P.G., Mariz, O.C., 2012. A LC-MS/MS method for the determination of BADGE-related and BFDGE-related compounds in canned fish food samples based on the formation of $[M + NH_4]^+$ aducts. Food Chem. 135, 1310–1315. https://doi.org/10.1016/j.foodchem.2012.05.099.

Noureddine El Moussawi, S., Ouaini, R., Matta, J., Chebib, H., Cladiere, M., Camel, V., 2019. Simultaneous migration of bisphenol compounds and trace metals in canned vegetable food. Food Chem. 288, 228–238. https://doi.org/10.1016/j.foodchem.2019.02.116.

Poustková, I., Dobiáš, J., Steiner, I., Poustka, J., Voldřich, M., 2004. Stability of bisphenol A diglycidyl ether and bisphenol F diglycidyl ether in water-based food simulants. Eur. Food Res. Technol. 219, 534–539. https://doi.org/10.1007/s00217-004-0995-1.

Qamar, S., Bashir, S., Perveen, S., Seidel-Morgenstern, A., 2019. Relations between kinetic parameters of different column models for liquid chromatography applying core-shell particles. J. Liq. Chromatogr. Rel. Technol. 42, 16–30. https://doi.org/10.1080/10826076.2019.1570522.

Ródenas-Montano, J., Carrasco-Correa, E.J., Beneito-Cambra, M., Ramis-Ramos, G., Herrero-Martínez, J.M., 2013. Determination of alcohols in essential oils by liquid chromatography with ultraviolet detection after chromogenic derivatization. J. Chromatogr. A 1296, 157–163. https://doi.org/10.1016/j.chroma.2013.04.072.

Sendon, Garcia R., Paseiro, Losada P., 2004. Determination of bisphenol A diglycidyl ether and its hydrolysis and chlorohydroxy derivatives by liquid chromatography-mass spectrometry. J. Chromatogr. A 1032, 37–43. https://doi.org/10.1016/j.chroma.2003.10.039.

Snyder, L.R., Kirkland, J.J., Dolan, J.W., 2010. Introduction to Modern Liquid Chromatography. Wiley, New York.

Sun, C., Leong, L.P., Barlow, P.J., Chan, S.H., Bloodworth, B.C., 2006. Single laboratory validation of a method for the determination of Bisphenol A, Bisphenol A diglycidyl ether and its derivatives in canned foods by reversed-phase liquid chromatography. J. Chromatogr. A 1129, 145–148. https://doi.org/10.1016/j.chroma.2006.08.018.

Sun, X.T., Tan, Q.J., Wang, S.X., Shan, J.F., Jiang, J.L., 2015. Systematic, computer-assisted development of high performance liquid chromatography for multi-component analysis. Anal. Methods 7, 5428–5435. https://doi.org/10.1039/c5ay01000d.

Szczepańska, N., Kudłak, B., Namieśnik, J., 2018. Assessing ecotoxicity and the endocrine potential of selected phthalates, BADGE and BFDGE derivatives in relation to environmentally detectable levels. Sci. Total Environ. 610–611, 854–866. https://doi.org/10.1016/j.scitotenv.2017.08.160.

Szczepańska, N., Kubica, P., Kudłak, B., Namieśnik, J., Wasik, A., 2019. Stabilities of bisphenol A diglycidyl ether, bisphenol F diglycidyl ether, and their derivatives under controlled conditions analyzed using liquid chromatography coupled with tandem mass spectrometry. Anal. Bioanal. Chem. 411, 6387–6398. https://doi.org/10.1007/s00216-019-02016-5.

The Commission of the European Communities, 2005. Commission Regulation (EC) No 1895/2005 of 18 November 2005 on the restriction of use of certain epoxy derivatives in materials and articles intended to come into contact with food. Official J. European Union.

Wang, L., Xue, J., Kannan, K., 2015. Widespread occurrence and accumulation of bisphenol A diglycidyl ether (BADGE), bisphenol F diglycidyl ether (BFDGE) and their derivatives in human blood and adipose fat. Environ. Sci. Technol. 49, 3150–3157. https://doi.org/10.1021/acs.est.5b00096.

Xie, Y., Bao, Y., Wang, H., Cheng, Y., Qian, H., Yao, W., 2015. Release of bisphenols from can coatings into canned beer in China market. J. Sci. Food Agr. 95, 764–770. https://doi.org/10.1002/jsfa.6862.

Xiong, L., Yan, P., Chu, M., Gao, Y.Q., Li, W.H., Yang, X.L., 2018. A rapid and simple HPLC-FLD screening method with QuEChERS as the sample treatment for the simultaneous monitoring of nine bisphenols in milk. Food Chem. 244, 371–377. https://doi.org/10.1016/j.foodchem.2017.10.030.

Zhang, H., Xue, M., Lu, Y., Dai, Z., Wang, H., 2010. Microwave-assisted extraction for the simultaneous determination of Novolac glycidyl ethers, bisphenol A diglycidyl ether, and its derivatives in canned food using HPLC with

fluorescence detection. J. Sep. Sci. 33, 235–243. https://doi.org/10.1002/jssc.200900564.
Zhang, J., Zhang, T., Guan, T., Ruan, P., Ren, D., Dai, W., Yu, H., Li, T., 2017. Spectroscopic and molecular modeling approaches to investigate the interaction of bisphenol A, bisphenol F and their diglycidyl ethers with PPARa. Chemosphere 180, 253–258. https://doi.org/10.1016/j.chemosphere.2017.04.034.
Zhong, J.J., Liao, N.B., Pu, Y.F., Ding, T., Xingqian Ye, X.Q., Liu, D.H., 2018. HTLC: A viable approach to fast LC of biogenic amines in food with legacy equipment. Chromatographia 81, 1097–1102. https://doi.org/10.1007/s10337-018-3539-8.
Zou, Y., Lin, S., Chen, S., Zhang, H., 2012. Determination of bisphenol A diglycidyl ether, novolac glycidyl ether and their derivatives migrated from can coatings into foodstuff by UPLC-MS/MS. Eur. Food Res. Technol. 235, 231–244. https://doi.org/10.1007/s00217-012-1734-7.