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Set-off: Development of a Simulation Press and Analytical Approach to Study the Phenomenon

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One type of mass transfer between package and food is through set-off. This phenomenon is defined as the transfer of components from the external layer (printed surface) of a packaging material to the inner side (surface to come into contact with food) during storage of printed substrates in reels or stacks. The objective of this work was to build up the equipment for set-off simulation and to assess the extent of benzophenone (BP) transfer. BP is a model photoinitiator used in standard ultraviolet curable inks (non-low migration inks). For set-off simulation, the storage conditions (time, temperature and pressure) and the ink film weight are provided by EuPIA Guidelines. Ethanol 50% (v/v) as simulant and contact condition of 40°C/10 days were used. Samples were printed and cured at different speeds. The migrated BP was determined by analysing the extracts using high-performance liquid chromatography with diode-array detector. Set-off phenomenon extent was dependent on the curing. In general, the BP migrations increase as speed increased.
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Ultraviolet (UV) curable inks are mixtures made of resins or oligomers, pigments, additives, monomers and photoinitiators, which are responsible for absorbing the UV energy, forming reactive species capable of initiating a chain reaction.[1]

Although they are essential for the formulation of UV curable inks, photoinitiators can be considered an important class of migrant substances. The concern, in toxicological terms, with this type of substance started after the occurrence of two cases in Europe. One of them, in 2005, when Italian authorities warned about the presence of a substance called isopropylthioxanthone (ITX) in some batches of baby milk at levels above 250 parts per billion (ppb) and the other, in 2009, when Belgian authorities reported benzophenone (BP) and 4-methylbenzophenone concentrations in cereals of 4210 and 3729 µg/kg respectively.[2,3] These substances are commonly used as photoinitiators in UV ink compositions.

The 'Swiss Federal Department of Home Affairs' amended the 'Ordinance on Foodstuff and Utility Articles', of 2005, detailing the provisions concerning printing inks for food packaging.[4] These provisions are similar to those described in 'EuPIA Guideline on Printing Inks applied to the non-food contact surface of food packaging materials and articles'.[5] In the absence of any specific legislation in the European Union for printing inks for food packaging, EuPIA has developed its guidelines, establishing a selection scheme for packaging ink of raw materials.

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Despite all these efforts to develop guidelines in order to minimize contamination of food by photoinitiators and other components from printing inks, studies specifically involving the transfer of substances associated with the set-off phenomenon are scarce. Additionally, there are no defined standards concerning sample preparation, set-off simulation and performing tests. This is probably due to the many variables existing in the process such as the type of substrate, type of packed food, ink formulation, ink film weight, type of photoinitiator, parameters of the UV curing equipment, curing degree, storage conditions of packaging materials, analytical techniques for detecting the occurrence of the set-off phenomenon and subsequently the identification and quantification of transferred substances.

In this context, Jung *et al.*[6] carried out a study to evaluate migration by diffusion, gas-phase and set-off of two types of photoinitiators and one amine, by varying two parameters related to the process: storage time and age of the UV lamps (new and used). Liquid chromatography was used with diode array detector and fluorescence (HPLC-DAD/FLD). Cups printed with UV-curable inks were used for packaging yogurt and also ethanol 50% (v/v). It was observed that the contamination of two substances under selected conditions took place through set-off but not by diffusion or by gas phase. Additionally, the parameters related to the process (lamp age and the storage time of printed cups) could influence the potential migration of the substances.

Bentayeb *et al.*[7] detected and identified the presence of substances on the inner surface of food packaging that were transferred from the printed surface as a result of the non-visible set-off phenomenon through the ambient ionization–accurate mass spectrometry technique. A protocol has been established for identifying unknown substances using a molecular formula database for the main ions and fragments of substances in food packaging inks. The set-off was also confirmed by the analysis of extracts by gas chromatography with a mass detector (GC-MS) of the two surfaces (inner and outer) separately.

Lord *et al.*[8] developed an optical scanner for measuring the total surface area of patches of visible set-off on food contact surface of packaging. This tool provided the use of a quick and simple pass/fail test of the packaging. Furthermore, exposure techniques and analytical methods were developed to quantify individual ink components, such as photoinitiators and synergists, on the food contact surface of packaging. These ink components were extracted with solvents in different time periods at 60°C. Analytical methods (GC-MS, GC-FID, LC-UV and LC-MS) were used to measure the photoinitiators and synergists in the selected extraction solvents. It was observed that the set-off results were not the same along the length of a roll of printed film. There were no significant effects on the results after storage nor using different extraction solvents. There was also no significant influence on the results under pressure of 1.2 psi (at 40°C for 10 days).

Bentayeb *et al.*[9] carried out a study to determine if direct analysis in real time coupled to time-of-flight mass spectrometry (DART/TOF-MS) was capable of detecting photoinitiators transferred by set-off to the food contact surface of food packaging. In addition, they tried to detect, through DART/TOF-MS, other compounds from non-visible print set-off. For this, multilayer packages were used with different structures, but always containing aluminium foil in the composition to prevent contamination by other mechanisms besides the set-off. DART/TOF-MS was able to detect and identify rapidly the photoinitiators and to determine what areas contained more set-off. Matrix effects must be considered because it can lead to false conclusions.

Aznar *et al.*[10] performed a migration study with different printed multilayer structures for two food simulants using ultra performance liquid chromatography coupled to a mass spectrometer by time of flight (UPLC-QTOF-MS). They evaluated the effect of ink transfer by set-off and how it was affected by the presence of a coating that could prevent this phenomenon. The content of migrating substances was drastically reduced when a coating was applied to the outer face of the structure and particularly when a polyester film was used before the ink. However, some new migrants appeared because of a reaction between the ink and the coating.

Clemente *et al.*[11] determined the migrating volatile compounds coming from set-off phenomenon in four food simulants and investigated the use of a protective varnish (coating) to prevent the migration. Migration tests were performed on two different types of structures, one based on paper and the other on PET. The volatile compounds were analysed by GC-MS and a high number of migrants was determined. The results were evaluated using a chemometric tool, principal components analysis.

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It is possible to notice that most analytical techniques used were quite sophisticated and involved a relatively high cost of the equipment, which can be an obstacle for the industry. Currently, a potential solution for the industry to minimize the occurrence of visible set-off is visual quality control, that is, rejecting any batches of food packaging, whether plastic, paper or card, when visible set-off is detected. However, this approach is not suitable when set-off is invisible to the naked eye. In this context, an optical approach to excite and see luminescent substances was used by Bradley *et al*[12] in an attempt to establish a non-destructive test, with a clear pass/fail approach to detect invisible set-off.

Based on the aforementioned section, the purpose of this paper was to build an equipment to simulate set-off under controlled conditions as well as to evaluate this equipment efficiency by the extent of BP transfer from the external to the inner surface. For this, printed and unprinted samples (which had contact with the printed surface) were put into contact with a food simulant, which was analysed by using high-performance liquid chromatography coupled to a diode array detector (HPLC-DAD).

Storage conditions, such as time, pressure and temperature, and also the ink film weight provided by 'EuPIA Guidelines on Printing Inks applied to the non-food contact surface of food packaging materials and articles' were considered for this study.[5] BP was used because of its wide use in standard UV curable products and also because it is one of the most studied photoinitiators, as it is seen as a typical contaminant by a significant number of articles. The simulant used was ethanol 50% (v/v), and the selected contact condition (time and temperature) was 40°C for 10 days, which is set forth in legislations for food contact materials.[13,14]

The chromatographic method used was developed based on the papers published by Sanchez-Silva *et al*.[15–18] and Pastorelli *et al*.[19] who determined BP in food, food simulants and/or packaging using HPLC-DAD. Many of these studies involved previous pre-extraction steps or analyte concentration.

MATERIALS AND METHODS

Materials and chemicals

Substrate. One side Corona treated biaxially oriented polypropylene film (BOPP film) was used in this study as substrate, and it was supplied by a national manufacturer. Film grammage and thickness were 27 g/m^2 and 30 μm respectively. The polymer identification was performed by infrared spectroscopy according to ASTM E 1252-98[20] and ASTM E 573-01[21] and by differential scanning calorimetry according to ASTM D 3418-12.[22] The wetting tension of the treated surface of the BOPP film was evaluated according to ASTM D 2578,[23] and the result was 54 dyn/cm.

Printing Ink. The printing ink formulation was prepared by Siegwerk Brasil Indústria de Tintas Ltda. (São Paulo/Jandira, Brazil) and the following composition was used: Oligomer (67%), Monomer (7%), Pigment (Cyan) (15%), BP as Photoinitiator (5%), Coinitiator (5%) and Stabilizer (1%). This formulation was specifically developed for this study, and it is not commercially available.

Reagents. High-performance liquid chromatography grade ethanol (purity > 99.96%) purchased from J. T. Baker (USA) and ultrapurified water produced by Milli-Q® water purification system from Millipore (Germany) were used to prepare the ethanol 50% (v/v), which was selected as simulant for this study. HPLC grade Acetonitrile (purity > 99.99%) purchased from J. T. Baker (USA) and ultrapurified water were used as mobile phase solvents. BP (CAS 119-61-9, purity 99%) purchased from Sigma-Aldrich was used as a standard. Standard stock BP solutions were prepared by weight in acetonitrile. Working solutions were prepared by diluting the standard stock solution in ethanol 50% (v/v) used as the simulant.

Methods

Building a press for set-off simulation. The contact pressure between the test samples was simulated by using a press specifically built for this purpose. The design defined for this device considered the following contour conditions: (a) contact pressure of 80 kg/cm^2 (described in EuPIA guidelines[5]);

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(b) sample contamination under pressure by components from painted parts; (c) no contamination of the sample during the press operation; (d) eventual misalignments and/or variations of sample thickness and (e) eventual misalignments press construction, distributing the contact pressure homogeneously throughout the sample.

Based on these requirements, the following options were assessed: pneumatic, hydraulic and mechanical presses. The pneumatic alternative was selected because of the following reasons/benefits: versatility in using loads, compact size and clean operation (e.g. no external contaminants such as hydraulic oil), easy operation, operator safety and independence from a power supply to operate.

Samples printing. The samples were cut at CETEA, printed and cured at Siegwerk. An IGT printer was used, C1 type with a printing force of 250 N. For curing, the Germetec UV equipment was used, Labcura GC-150-1A/300 type. The lamp was Mercury vapor arc lamp – H type without dopant (power input 2.2 kW, irradiance 100 W/in^2).

Seventy two (72) samples were cured at speeds of 5, 10, 40 and 80 m/min (18 samples for each speed). Half of the samples were used for BP migration testing by direct immersion of the printed sample into the simulant for a direct contact situation. The other half was placed on the press for set-off simulation to be later tested for BP migration in unprinted BOPP samples.

The printed samples (used to simulate a direct contact situation) were separated from each other using an aluminium foil as shown in Figure 1a to prevent from the transfer of substances across samples. Additionally, the printed samples that were carried out for set-off simulation were separated from each other using unprinted BOPP samples as shown in Figure 1b.

Set-off simulation. To achieve a pressure of 80 kg/cm^2 (or 8000 kPa), a force about 1260 kgf was required. Furthermore, this pressure must be held for 10 days at 25°C.[5] The laboratory temperature was monitored using a digital thermohygrometer manufactured by ONSET during the period of the set-off simulation and the temperature was 22°C ± 3°C.

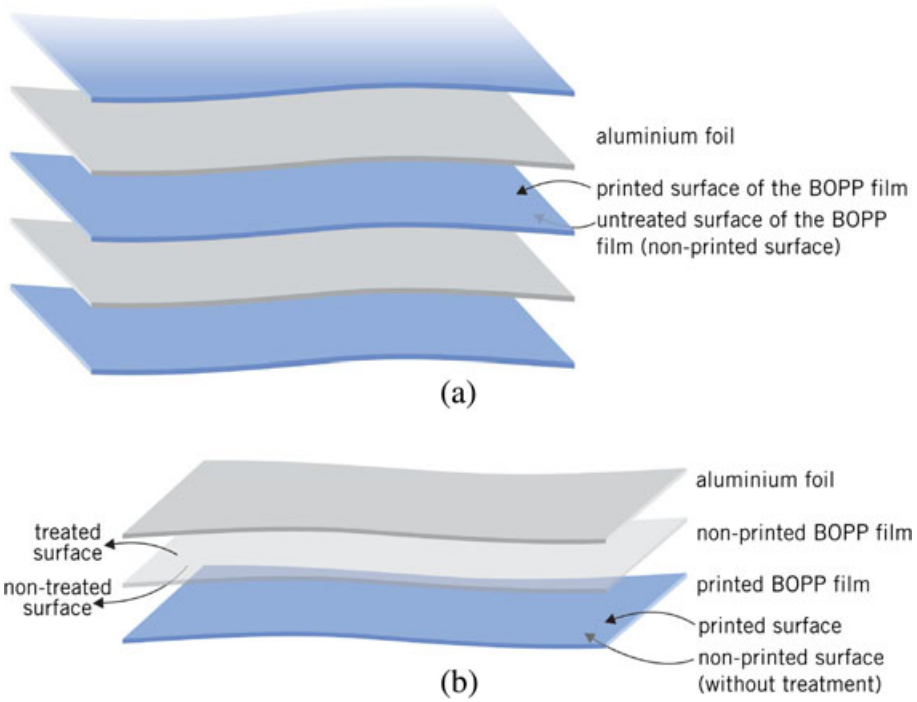

Figure 1. Samples for BP migration testing by immersion of (a) printed BOPP film (direct contact situation) and (b) unprinted BOPP film (set-off).

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The ink film was weighed for 27 samples according to Sarantópoulos *et al.*,[24] and the result was 1.57 g/m^2 (standard deviation: 0.14 g/m^2 and relative standard deviation: 8.82%). EuPIA guideline describes that the ink film weights for the flexographic, gravure and offset inks were 1–2.0 g/m^2.[5]

Specific migration. The volume of simulant used was calculated based on a ratio of 6 dm^2/kg of simulant, as provided by the Commission Regulation (EC) N° 10/2011 and Resolution RDC n. 51/2010.[13,14] The total printed sample area immersed in the simulant was 50 cm^2 and the unprinted sample area submitted to set-off simulation was 47.25 cm^2. The samples were placed in contact with the ethanol 50% (v/v) and conditioned in an oven at 40°C (±1°C) for 10 days.

Liquid chromatography coupled to a diode array detector conditions. An Agilent 1260 high-performance liquid chromatograph equipped with ZORBAX Eclipse Plus C18 (150 mm × 4.6 mm i.d. × 5 μm) column (Agilent) coupled with diode array (252 nm) was used; mobile phase 60% acetonitrile and 40% ultrapurified water, column temperature 30°C; flow rate 1.2 ml/min; stop time: 7.5 min.

After 10 days of contact at 40°C, aliquots of 10 μl of simulant were injected into the HPLC-DAD under the conditions described earlier and the quantification was performed by using external standard. Duplicate injections were made for all samples and standard solutions.

To evaluate the performance of the developed method some parameters as detection and quantification limits (LOD and LOQ respectively), linearity, repeatability, precision and recovery were determined.[25,26] LOD and LOQ were 0.009 and 0.104 mg/l respectively. A calibration curve was prepared with 11 concentration levels ranging from 0.15 to 10.0 mg/l and through linear regression, a straight line equation was obtained with a correlation coefficient >0.999. Repeatability and accuracy were determined at three concentration levels of 0.1; 0.5 and 1.0 mg/l ($n = 7$) and the relative standard deviations obtained were below 2% and 5.5% respectively. Recovery was carried out at concentrations of 0.6, 1.8 and 3.6 mg/L, therefore simulating contact conditions of 40°C for 10 days, which were used for testing the samples, and the results were 94 to 100% (results have not been published yet).

Statistical analysis. Statistical analysis was performed using software XLSTAT 2015.1.01 and the USERFRIENDLYSCIENCE R software package version 3.2.1 (2015)[27–29] for all sets of data. The results from all 72 samples were evaluated. No results were excluded, even those considered extreme (outliers).

First, normality tests were performed, followed by homocedasticity testing (assessment of variance similarity at 95% confidence level). If the data followed a typical probability distribution and also were homoscedastic, they were evaluated by ANOVA and Tukey test. If the data followed a typical probability distribution but they were not homoscedastic, Welch's ANOVA and Games–Howell tests were performed.

RESULTS AND DISCUSSION

Set-off simulation press. The equipment used to simulate set-off conditions is presented in Figure 2.

The equipment developed for this purpose was a pneumatic press powered by commercial nitrogen contained in 10 m^3 cylinder, with an initial nominal pressure of 3000 psi. This pressure passed through two pressure regulators. The first is on the cylinder (0/300 Psi ¼" NPT, code 18-013-210) that enabled pressure reduction to levels of approximately 20 kg/cm^2. This pressure was, then, applied to a second pressure regulator (1/2 NPT 17 Bar, code R73G-4AK-RSN) that was adjusted according to the required load.

Pressure was then applied to a standard pneumatic cylinder (160 × 100 mm, code RA/8160/100) via a directional valve (1/4 4/2 VIAS, code VHLA202-02) controlling the piston operation (up and down). The valve was equipped with silencing device (code T20C2800) to reduce the level of noise during operation and to control the up and down speed for a slower operation as well as to ensure operator safety. All parts described earlier were manufactured by Norgren (Birmingham, AL, USA).

At the end of the pneumatic cylinder, two circular steel plates with a diameter of 100 mm were attached. The upper plate was threaded to the end of the cylinder rod and remained firmly attached.

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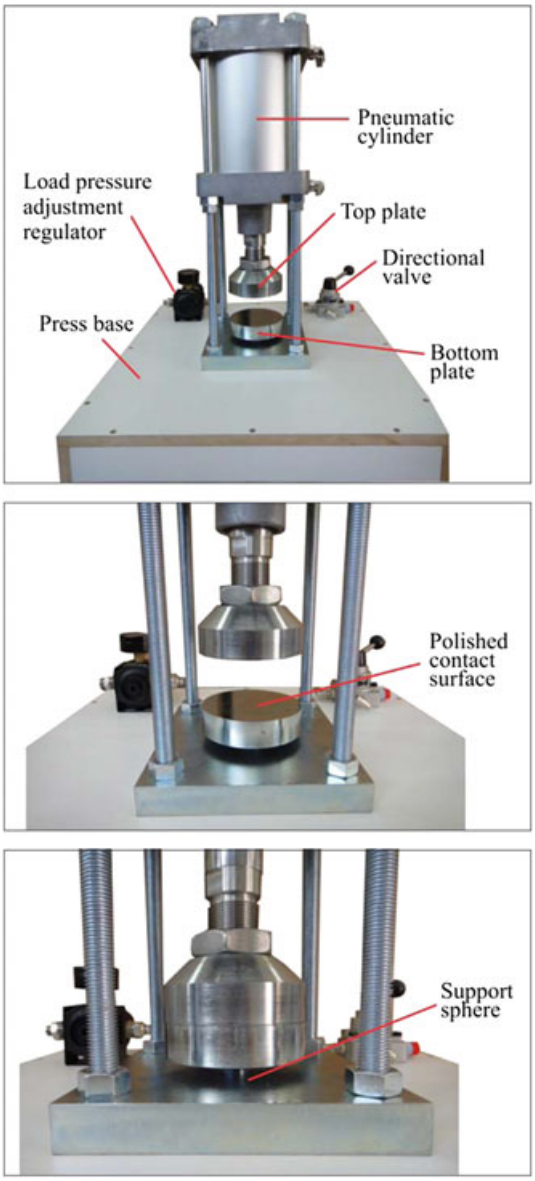

Figure 2. Set-off simulation press.

The bottom plate was supported on a steel ball, therefore creating a ball-joint type of connection which enabled its free movement to correct misalignments caused by the construction of the press and/or irregularities in the sample. The surfaces of these plates had been machined and polished to increase the contact area with the sample, and then the parts had gone through a galvanizing process for corrosion protection and assurance of required surface characteristics. This protection process was selected over the use of paint to prevent the sample from being contaminated by components from the ink that was used.

All components that were used are standardized and commercially available, except for the contact plates that were machined to the required size, according to project geometric requirements.

Before the set-off simulation, a HBM compression load cell, C2AC3 type with maximum capacity of 20 kN was used to confirm that the applied force was around 1260 kgf. The applied force had a maximum variation of 1%.

Printed samples (direct contact). Table 1 shows results from BP specific migration testing for printed samples under simulated direct contact.

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Table 1. BP specific migration testing for printed BOPP film.

	5 m/min	10 m/min	40 m/min	80 m/min
Mean[1,2] (mg/kg)	2.80 a	3.07 a,b	3.18 b	3.21 b
Standard deviation (mg/kg)	0.23	0.25	0.25	0.26
RSD (%)	8.36	8.15	7.78	8.15

[1]Mean of nine samples.
[2]Means on the same line with the same letter do not differ from each other under confidence level of 95%.
BOPP, biaxially oriented polypropylene.

For printed samples, the results from BP specific migration increased as speed increased from 5 to 80 m/min.

Non-printed samples (set-off). Table 2 shows the results from BP specific migration testing obtained for non-printed samples subjected to the set-off simulation.

For non-printed samples subjected to set-off, BP specific migration results increased as speed increased from 5 to 80 m/min.

Note that there was an extraction of this photoinitiator to the simulant. However, as expected, the results were lower than those obtained for the printed samples, which were directly immersed in ethanol 50% (v/v). Additionally, it was possible to evidence that the curing is more effective at lower speeds (5 and 10 m/min). Regardless the light source, the UV dose is inversely proportional to the speed at which the material is being irradiated. The UV dose is the total amount of energy reaching the surface of the material per unit area.

The results found for non-printed samples were above the specific migration limit established for BP, which is 0.6 mg/kg, at speeds of 10, 40 and 80 m/min.[4,13] This ink is not commercially available, and moreover, protective varnishes or lacquers are usually used on the printed surface what can, therefore, minimize the transfer of ink substances for foods or their simulants as described by Bentayeb *et al.*[9] and Clemente *et al.*[11] However, it is also necessary to check that there is no transfer of substances from these coatings for food or their simulants.

Using software XLSTAT 2015.1.01,[27] it was possible to develop a model; and the regression that achieved better adjustment ($R^2 = 96.6$) had the following equation:

$$C = 0.195 + 3.851\times10^{-2}\cdot v - 3200\times10^{-4}\cdot v^2, \quad (1)$$

where C is the concentration in mg/kg and v is the speed in m/min.

Figure 3 is the graph with all experimental points obtained in addition to the theoretical average. It can be observed that the BP migration rose up to a speed of 40 m/min and, after that, it remained constant.

This model was built considering the experimental points and therefore is valid for the conditions defined in this study (ink formulation, ink film weight, printing and curing equipment, type of lamp and its power input, pressure conditions, simulant, migration testing conditions and analytical technique used, as well as the method conditions). It should be confirmed using samples that are prepared on industrial equipment.

Table 2. BP specific migration testing obtained for non-printed BOPP film.

	5 m/min	10 m/min	40 m/min	80 m/min
Mean[1,2] (mg/kg)	0.29 a	0.69 b	1.18 c	1.21 c
Standard deviation (mg/kg)	0.03	0.07	0.08	0.16
RSD (%)	10.04	10.35	7.24	12.81

[1]Mean of nine samples.
[2]Means on the same line with the same letter do not differ from each other under confidence level of 95%.
BOPP, biaxially oriented polypropylene.

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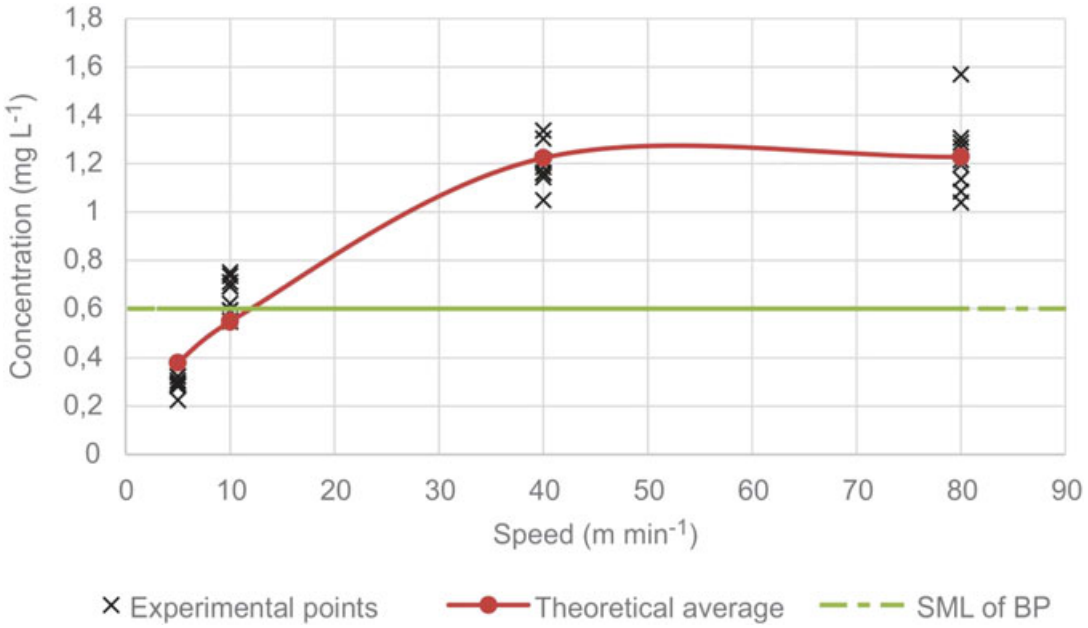

Figure 3. Graph showing concentration (mg/kg) versus speed (m/min) according to Equation 1.

The built equipment proved to be appropriate to assess the set-off. Considering its versatility, it is possible to apply different pressures to different types of materials (paper, plastic and aluminium) as described in EuPIA guidelines[5] and to develop studies with other types of formulations and photoinitiators. However, the analytical part for identifying and quantifying the substance still needs to be performed and the technique to be selected will depend on the substance of interest.

CONCLUSION

An equipment was built to simulate set-off considering the higher pressure established in EuPIA guidelines (8000 kPa), and its efficiency was tested by evaluating the extent of BP transfer from the printed surface to the non-printed side. In summary, the construction of a versatile and inexpensive device to simulate the pressures achieved both in reels and stacked sheets of different materials, enables the study of set-off phenomenon for different substances under different conditions.

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