Rapid monitoring of pesticides in tomatoes (*Solanum lycopersicum* L.) during pre-harvest intervals by paper spray ionization mass spectrometry

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ABSTRACT

A rapid analysis of acephate, chlorpyrifos, and cyazofamid in tomato peels during pre-harvest intervals using paper spray ionization mass spectrometry (PSI-MS) has been demonstrated. LODs of 0.01 ppm and LOQs of 0.03 ppm were achieved. Relative standard deviations were below 9%, and recoveries close to 100%. For pesticides monitoring, samples were separated into stored and field groups. Stored group contained fruits that were harvested and stored at low temperature during the pre-harvest interval, and the field group contained fruits that were on the agricultural field over the pre-harvest interval. The decrease in pesticide amounts was lower for the stored samples. At the end of the pre-harvest intervals, acephate, chlorpyrifos, and cyazofamid were determined at 0.86, 0.96, and 0.23 ppm in the stored group, and at 0.26, 0.37, and 0.09 ppm in the field group, respectively. This work demonstrates the utility of PSI–MS for performing rapid quality control of fruit harvesting.

1. Introduction

Pesticides are toxic compounds that are used in different stages of cultivation of fruits and vegetables to avoid damage by weeds, insects, fungi, bacteria, larvae, and rodents (Matthews, 2016). Since pesticides are used against living organisms, these compounds may be toxic to humans. A rising body of evidence has established the correlation between exposure to pesticides and the development of a wide range of pathologies, including diabetes mellitus, Parkinson's disease, Alzheimer's disease, autism, reproductive disorders, hypertension, leukemia, non-Hodgkin's lymphoma, ovarian cancer, and prostate cancer (Gangemi et al., 2016). One of the causes of human exposure to pesticides is the adherence of these compounds to the final product at a concentration above the allowable limit. This may occur due to irregularities in good agricultural practice, which is defined as a collection of principles to apply for on-farm production and post-production processes, resulting in safe and healthy agricultural products (FAO, 2016). An important requirement of good agricultural practice is the crop harvesting. Fruits and vegetables need to be harvested at an appropriate time called pre-harvest interval, which is the time between the pesticide application and the crop harvesting. During this period, the pesticide concentration is decreased and falls below the tolerance level established for that crop, so that consumer exposure is minimized (Hill, 2008).

In Brazil, the insecticides acephate and chlorpyrifos and the fungicide cyazofamid are widely used on tomato (*Solanum lycopersicum* L.) crops. According to the Brazilian Health Regulatory Agency, the maximum residue limit (MRL) allowable in tomato crops is 0.5 ppm for acephate and chlorpyrifos, and 0.05 ppm for cyazofamid (Anvisa, 2016). To reach the established concentrations, pre-harvest intervals of 1, 7, and 21 days for cyazofamid, acephate, and chlorpyrifos, respectively, must be employed. However, some farmers and producers irregularly harvest the tomatoes before completing the intervals and store the fruits at low temperature for further transport and sale. As this procedure affects the health of the consumers, analytical methods for monitoring the pesticide concentrations during the pre-harvest intervals are widely required.

Traditionally, pesticide determination in agricultural foodstuffs has been performed using gas chromatography coupled to mass spectrometry (GC–MS) and liquid chromatography coupled to mass spectrometry (LC–MS) (Prodhan, Alam, & Uddin, 2017). Both techniques provide reliable results with excellent analytical performance but require extensive and laborious sample preparation steps prior to instrumental analysis, consuming reagents or solvents and generating

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chemical waste. The advent of ambient mass spectrometry (AMS) techniques allowed the analysis of compounds directly from their native environment with minimal or no sample preparation (Cooks, Ouyang, Takats, & Wiseman, 2006). Desorption electrospray ionization (DESI) (Takáts, Wiseman, Gologan, & Cooks, 2004) and direct analysis in real time (DART) (Cody, Laramée, & Durst, 2005) were the first techniques developed, followed by a large number of AMS methods that have been used for direct analysis of a wide range of analytes and samples (Feider, Krieger, DeHoog, & Eberlin, 2019). Paper spray ionization (PSI) is an AMS technique in which a triangular paper is used as a substrate for generating analyte ions for MS. The sample is dropped onto the triangular paper which is moistened with a solvent. When a high voltage is applied to the paper, a spray with charged droplets is formed at the paper tip and goes towards the mass spectrometer inlet for subsequent MS analysis (Liu et al., 2010). The easy-to-use features of PSI–MS have attracted considerable attention of researchers around the world, and its relevance can be noticed by the wide range of applications that has been recently reported, such as toxicological drug screening (McKenna, Jett, Shanks, & Manicke, 2018), quantification of pesticide residues (Pereira et al., 2016), determination of benzodiazepines in beverages (de Paula, Jurisch, Piccin, & Augusti, 2018), analysis of polycyclic aromatic hydrocarbons (Basuri, Sarkar, Paramasivam, & Pradeep, 2018), coupling to portable mass spectrometers (da Silva et al., 2019), and many others.

In this work, PSI–MS was used to track the concentration of acephate, chlorpyrifos, and cyazofamid in tomatoes during the pre-harvest intervals. The samples were separated into stored (fruits at low temperature over the pre-harvest interval) and field (fruits on the agricultural field during the pre-harvest interval) groups. As most pesticides remain in the fruit peel (Kaushik, Satya, & Naik, 2009), only this part of the tomatoes was analyzed. Thus, tomato peel extracts were prepared and deposited onto the triangular paper for MS analysis, so that minimum sample preparation was required.

2. Experimental

2.1. Chemicals and materials

HPLC grade acetonitrile, methanol, formic acid, and standards were acquired from Sigma-Aldrich (São Paulo, Brazil). Ultrapure water was produced using a water purification system (Master System MS2000, Gehaka, São Paulo, Brazil) with a resistivity of 18.2 MΩ cm. Whatman #1 paper (11 μm pores) was purchased from Whatman International Ltd. (Maidstone, UK). Orthene (acephate 75% w/w, 750 g/kg, soluble powder) was acquired from Arysta Lifescience, Lorsban (chlorpyrifos 48% w/v, 480 g/L, emulsifiable concentrate) from Dow AgroSciences, and Ranman (cyazofamid 34.5% w/v, 400 g/L, suspension concentrate) from ISK Biosciences (all from São Paulo, Brazil). The pesticide working solutions were prepared by adding 4 g of Orthene in 3 L of water, 15 mL of Lorsban in 3 L of water, and 0.75 mL of Ranman in 3 L of water, according to the specifications of the product labels. Tomatoes (*Solanum lycopersicum* L.) were cultivated on the Horticulture Sector of the School of Agronomy of the Federal University of Goiás (Goiânia, Brazil).

2.2. Field experiment

The pesticides were applied to the crops when the tomatoes reached sufficient physiological maturity, that is, when the fruits showed higher intensity of red color in the peel. Thus, after 3 months of cultivation, acephate (Orthene), chlorpyrifos (Lorsban), and cyazofamid (Ranman) were sprayed onto the whole area of the tomato plant (18 plants for each pesticide). Untreated plants were used as control. For harvesting, the tomatoes were divided into two groups: field and stored. The field group was harvested at the beginning (Day 0, shortly after pesticide application), middle (Day 3 and 10 for acephate and chlorpyrifos,

respectively) and end (Day 7, 21, and 1 for acephate, chlorpyrifos, and cyazofamid, respectively) of the pre-harvest intervals. The stored group was harvested at the beginning of the pre-harvest interval and the fruits were stored at 4 °C. The remaining pre-harvest interval of the stored group occurred under low-temperature storage.

2.3. Sample preparation

Three fruits from each group (field and stored) were taken and sampled on the days mentioned above. The tomatoes were manually peeled using a knife. The whole peel of each tomato was added to a 15-mL polypropylene centrifuge tube and manually homogenized using a glass rod. Then, 5 mL of water (for samples containing acephate) or acetonitrile (for samples containing chlorpyrifos and cyazofamid) were added, and the tube was vortexed for 3 min. This mixture was vacuum filtered, and the extract was used for PSI–MS analysis. Extracts from tomato peels containing no pesticides were used as blanks for analytical performance tests.

2.4. Paper spray ionization mass spectrometry

The PSI parameters were used according to previously published procedures (Mendes, Pereira, Ferreira, Chaves, & Vaz, 2017; Pereira, Rodrigues, Chaves, & Vaz, 2018). The paper was cut into an equilateral triangle shape (1 cm sides) and held by a metal clip connected to the voltage source of the mass spectrometer. The paper tip was positioned approximately 4 mm from the mass spectrometer inlet. The extract (15 μL) was deposited onto the paper, and the voltage source was turned on. A volume of 15 μL of methanoic acid (0.1% formic acid) was used as spray solvent. For semi-quantitative analysis, the intensity of the MS/MS product ion was employed and summed at 1 min of the total ion current. Mass spectra were obtained using a Thermo Scientific LCQ Fleet ion trap mass spectrometer (San Jose, CA). The optimized instrumental parameters were: positive ionization mode; spray voltage: 4.0 kV; capillary temperature: 275 °C; capillary voltage: 10 V; tube lens: 50 V; collision energy: 15 eV (acephate), 18 eV (cyazofamid) and 20 eV (chlorpyrifos). Spectra were processed using the Xcalibur Analysis software package (Version 2.0, Service Release 2, Thermo Electron Corporation).

2.5. Analytical performance

Calibration curves, limits of detection (LODs), limits of quantification (LOQs), recoveries, and relative standard deviations (RSDs) were evaluated to determine the analytical performance of PSI–MS. For calibration curves, the pesticides were dissolved in the extracts and aliquots were diluted in the same matrix to obtain concentrations of 0.03, 0.1, 0.5, 1, 5, 10, and 20 ppm. The analyses were performed in triplicate. The LODs and LOQs were calculated by the equations $3s_B/m$ and $10s_B/m$, respectively, where s_B is the standard deviation of 10 blank measurements and m is the slope of the calibration curve. The recovery test was performed by fortifying the samples with 0.3, 3, and 15 ppm and was calculated by the equation $[(AC - OC)/NC] \times 100$, where AC is the analyzed concentration, OC is the original concentration (amount of analyte in the sample before fortification), and NC is the nominal concentration. The RSDs were determined at 0.3, 3, and 15 ppm, and were calculated by the equation $(SD/AC) \times 100$, where SD is the standard deviation. For the recovery and RSD tests, 5 measurements for each concentration were performed. Finally, PSI–MS was used to determine the amount of acephate, chlorpyrifos, and cyazofamid in tomato peels from the stored and field samples. Differences between samples were verified using the Tukey test (Sisvar 5.6) based on a probability level of 5%.
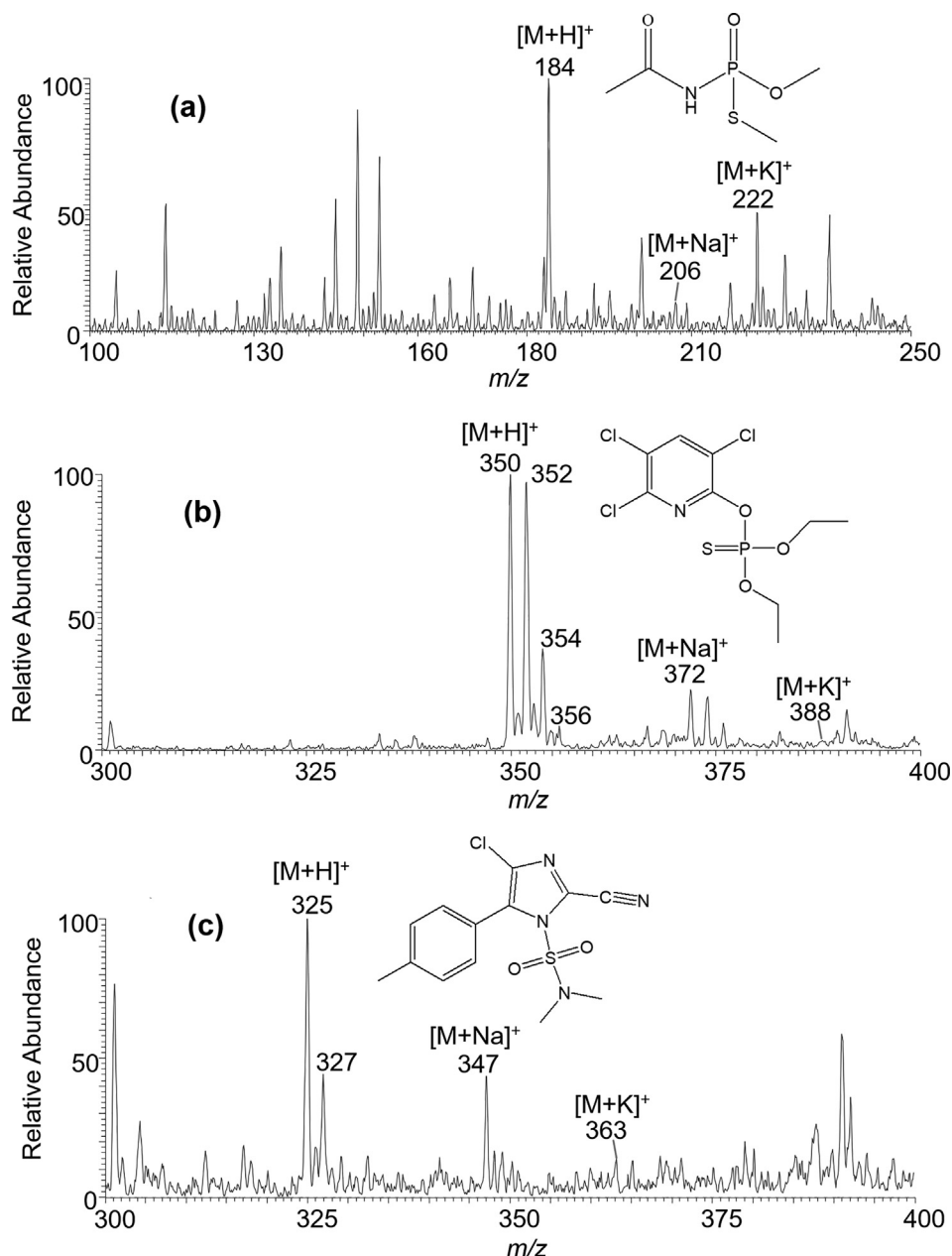
Fig. 1. PSI(+) mass spectrum of tomato peel extract with 10 ppm of (a) acephate, (b) chlorpyrifos and (c) cyazofamid.

3. Results and discussion

3.1. Qualitative analysis

An initial experiment was performed to determine the signal intensities of protonated or metal-cationized pesticides to use in subsequent analyses. Tomato peel extracts containing pesticides at 10 ppm were analyzed by PSI(+)–MS. As shown in Fig. 1a, the protonated acephate $[M+H]^+$ at m/z 184 was more intense than the metal cation ions ($[M+Na]^+$ and $[M+K]^+$). In the same way, Fig. 1b shows a strong ion signal for protonated chlorpyrifos $[M+H]^+$ at m/z 350. The set of characteristic isotopic cluster peaks at m/z 350, 352, 354, and 356 is consistent with the presence of three chlorine atoms. In Fig. 1c, the cyazofamid mass spectrum illustrates a sharp peak of $[M+H]^+$ at m/z 325. The ion at m/z 327 is an isotopologue with ^{37}Cl isotope. Therefore, the protonated pesticides were used as precursor ions for MS/MS and subsequent analyses.

3.2. Method validation

Usually, quantitative analyses by MS are performed using internal standards to avoid errors that may occur due to ion suppression caused by matrix components (Stokvis, Rosing, & Beijnen, 2005). Deuterated compounds are widely used as internal standards, but they can be very expensive or unavailable. The effort to find satisfactory analytical results without using internal standards has been demonstrated in several works using ambient MS techniques (Mendes et al., 2017; Pereira et al., 2018; Wang et al., 2019; Zhou, Lee, Kim, & Zare, 2016). Here, we carried out all quantitative analyses without internal standard with the aim of contributing to the attempts to obtain satisfactory results in a cheaper and less demanding way. Thus, the term semi-quantitative is more appropriate and therefore we used it throughout the manuscript. MS/MS of the analyte ions was used for semi-quantification since it can increase the chemical specificity as well as improve the sensitivity by the elimination of chemical noise in direct analysis of complex mixtures (Cooks, Busch, & Glish, 1983).

Table 1

MS/MS transitions, calibration equations, R^2 values, LODs and LOQs obtained for acephate, chlorpyrifos, and cyazofamid in tomato peel extracts by PSI–MS.

Pesticide	MS/MS	Calibration equation	R^2	LOD[a]	LOQ[a]
Acephate	m/z 184 → 143	$y = 6.2789x + 0.0862$	0.9996	0.01	0.03
Chlorpyrifos	m/z 350 → 322	$y = 6.4737x + 0.0955$	0.9995	0.01	0.03
Cyazofamid	m/z 325 → 261	$y = 5.1425x + 0.0042$	0.9986	0.01	0.03

[a] ppm

The MS/MS transitions, calibration equations, R^2 values, LODs, and LOQs are presented in Table 1. The transition of m/z 184 → 143 for acephate refers to the loss of an amide group (C_2H_5NO) and addition of H_2O (Hayama, Yoshida, Todoroki, Nohta, & Yamaguchi, 2008). The fragment at m/z 322 for chlorpyrifos is relative to the loss of an ethylene group (C_2H_4) (Taylor, Melton, Sharp, & Watson, 2013). The m/z 325 → 261 transition for cyazofamid may be due to the loss of SO_2 (Blasco, Vazquez-Roig, Onghena, Masia, & Picó, 2011). The MS/MS spectra are shown in Fig. S1. The calibration curves (Fig. S2) were determined by monitoring the product ions according to the pesticide concentrations in the extracts. The R^2 values for all pesticides were above 0.99. The LODs and LOQs were determined as 0.01 and 0.03 ppm, respectively, for all compounds. These values are within a range of concentration often reported for LODs and LOQs in pesticide analysis by LC–MS (Fu et al., 2017; Machado, Gérez, Pistón, Heinzen, & Cesio, 2017; Morais, Collins, & Jardim, 2018). In addition, the LOD and LOQ values were below the maximum residue limits (MRLs) for the pesticides in tomato, which are 0.5 ppm for acephate and chlorpyrifos, and 0.05 ppm for cyazofamid, according to the Brazilian Health Regulatory Agency.

To ensure the precision of the PSI method, the RSDs at three different concentrations were determined under repeatability of five measurements for each concentration (Table 2). Values ranged from 2.5 to 9.0%, which are consistent with a high-precision method (variation should be below 20%) for pesticide analysis according to the Brazilian Ministry of Agriculture, Livestock and Food Supply.

Table 2 also shows results from the recovery test for the three pesticides, which ranged from 90 to 98%. These results are similar to those reported by previous works using PSI–MS (Mendes et al., 2017; Yu et al., 2018). Furthermore, the results are consistent with LC–MS results. Han et al. (2013) analyzed chlorpyrifos in tomatoes by LC–MS using washing, peeling, homogenization, simmering, and sterilization as sample preparation, and reported a recovery of 95%. Also, Xu et al. (2017) demonstrated recovery values ranging from 85 to 108% for cyazofamid in tomato samples by LC–MS using homogenization, vortexing, centrifugation, collection of supernatant, and filtration as sample preparation.

Table 2

RSDs and recoveries obtained from the analysis of acephate, chlorpyrifos, and cyazofamid in tomato peel extract by PSI–MS.

Pesticide	Concentration (ppm)	RSD[a] (%)	Recovery[a] (%)
Acephate	0.3	4.4	96.9 ± 4.3
	3	7.4	97.1 ± 7.2
	15	3.5	97.2 ± 3.4
Chlorpyrifos	0.3	5.0	94.7 ± 4.7
	3	2.5	95.1 ± 2.5
	15	9.0	93.5 ± 8.4
Cyazofamid	0.3	5.3	90.5 ± 4.8
	3	6.6	94.0 ± 6.2
	15	7.5	98.0 ± 7.4

[a] Five measurements for each concentration.

Table 3

Concentrations of pesticides in tomato peels from field and stored groups at the beginning, middle, and end of the pre-harvest intervals.

Pesticide	Group	Concentration (ppm)*		
Acephate		Day 0	Day 3	Day 7
	Field	6.67[aA] ± 1.13	1.48[bB] ± 0.27	0.26[bD] ± 0.05
	Stored	6.67[aA] ± 1.13	1.45[bB] ± 0.12	0.86[bC] ± 0.08
Chlorpyrifos		Day 0	Day 10	Day 21
	Field	17.11[aA] ± 1.08	3.65[bC] ± 0.63	0.37[cE] ± 0.08
	Stored	17.11[aA] ± 1.08	8.79[bB] ± 0.46	0.96[cC] ± 0.25
Cyazofamid		Day 0	Day 1	–
	Field	0.38[aA] ± 0.04	0.09[bC] ± 0.05	–
	Stored	0.38[aA] ± 0.04	0.23[bB] ± 0.02	–

Different lowercase letters in each line and different capital letters in each column indicate significant differences in the concentrations (Tukey test at 5% of probability level).

* Three measurements for each sample.

3.3. Pesticide monitoring during pre-harvest intervals

The pesticide concentrations in tomato peels at the beginning, middle, and end of the pre-harvest intervals are presented in Table 3. The pesticide contents were evaluated for the field and stored groups. Concentrations of all pesticides decreased over the days for both groups. Acephate contents were detected at 6.67 ppm on Day 0. No significant difference in concentrations was achieved in the field (1.48 ppm) and stored (1.45 ppm) groups on Day 3. However, a lower concentration was detected in the field samples (0.26 ppm) compared to the stored group (0.86 ppm) on Day 7. As the MRL for acephate in tomato is 0.5 ppm, the fruits from the field group at the end of the pre-harvest interval showed acceptable pesticide levels, but the stored group showed values above allowed levels. On the other hand, 17.11 ppm of chlorpyrifos was found on Day 0. On Day 10, 3.65 ppm was detected in the field group, and 8.79 ppm was found in the stored group. On Day 21, the field samples showed 0.37 ppm, below the MRL value for chlorpyrifos (0.5 ppm), whereas the stored group presented 0.96 ppm, which may represent risk to human health. Besides, it was found 0.38 ppm of cyazofamid on Day 0. On Day 1, 0.09 ppm was found in the field group, and 0.23 ppm in the stored group. Both the concentrations were above the MRL value (0.05 ppm) determined for cyazofamid in tomatoes, although the field group was only slightly above.

As the discussion above was based on Brazilian MRL values, it is also important to compare the results with MRLs from different regulatory agencies, such as the Food and Agriculture Organization of United Nations (FAO) and the European Union (EU). As shown in Table S1, the Brazilian MRLs are lower, except for acephate and chlorpyrifos compared to the EU. By checking the concentrations of the pesticides on the last day of the pre-harvest interval (Table 3), it can be verified that the acephate and chlorpyrifos contents were above the MRL established by EU (0.01 ppm for acephate and 0.1 ppm for chlorpyrifos), and the cyazofamid concentration from the stored group was slightly above the MRL determined by FAO (0.2 ppm).

All the results mentioned above show the importance of respecting the pre-harvest intervals for each pesticide. Improper harvesting and marketing of fruits and vegetables may lead to contamination with pesticide residues at concentrations that pose a risk to human health (Quarcoo, Bonsi, & Tackie, 2014). Storing the fruits at low temperature before the appropriate pre-harvest interval may decrease the pesticide concentrations. Nevertheless, the decrease is slow, and the pesticide levels may be above the established MRLs. Fruits stored at low temperature are not under adequate conditions for decreasing pesticide concentrations as they usually are in the field before harvest. In addition, as we analyzed the pesticides only on the tomato peel, the reason for a decrease in the concentration of these compounds may be due to their penetration of the peel and migration into the tomato. As we

showed in a recent report (Pereira et al., 2019), pesticides can diffuse into fruits with a high content of water. The diffusion is influenced by the high polarity of the pesticide, which promotes transport to the high water-content interior of the fruit. Pesticide penetration into the inner region of fruits stored at low temperature (Dore, Molinu, Venditti, & D'Hallewin, 2009) appears to have a slower rate than fruits under room temperature (Taira, Tokai, Kaneko, Katano, & Kawamura-Konishi, 2015). Other factors that may have influenced the decrease in the concentrations of the pesticides are rainfall washing, photolysis, microbial degradation, and volatilization (Stoytcheva, 2011).

As shown in this work, PSI–MS is a viable technique for monitoring pesticide concentration during pre-harvest intervals in tomatoes. The easy-to-use and less demanding PSI provides rapid quality control of fruit harvesting, which is traditionally accomplished by more complex, expensive, and demanding techniques, such as GC and LC coupled to a detector. Furthermore, the analytical performance of PSI–MS has been widely validated and compared with GC or LC methods (Bartella et al., 2019; Keating, Minges, Randell, & Glish, 2018; Michely, Meyer, & Maurer, 2017; Yu et al., 2018), and satisfactory correlations have been demonstrated.

4. Conclusions

Paper spray ionization mass spectrometry (PSI–MS) was used for rapid determination of acephate, chlorpyrifos, and cyazofamid in tomato peel extracts. Calibration curves with $R^2 > 0.99$ were achieved for all pesticides. LODs and LOQs for all three pesticides were 0.01 and 0.03 ppm, respectively, which are below the maximum residue limits for the pesticides in tomatoes. Relative standard deviations ranged from 2.5 to 9%, and recoveries from 90 to 98%. To monitor the pesticide concentrations during the pre-harvest intervals, the fruits were separated into field and stored groups. The pesticide concentrations were evaluated at the beginning, middle, and end of the pre-harvest intervals, and the concentrations of all pesticides decreased over the course of the days. The field group showed a decrease of 96% for acephate, 98% for chlorpyrifos, and 76% for cyazofamid. In the stored group, decreases of 87% for acephate, 94% for chlorpyrifos, and 39% for cyazofamid were observed. The lower decrease in the pesticide concentrations of the stored samples compared to the field samples during the pre-harvest intervals demonstrates the importance of adopting appropriate harvesting protocols in order to avoid damage to consumer health. These results demonstrate that PSI–MS can be used as an alternative technique for monitoring pesticide concentrations in agricultural foodstuffs during pre-harvest intervals, with the advantages of being simpler, faster, and cheaper than traditional techniques. It is not suggested that the current PSI–MS method will replace conventional chromatography methods for quantitative analysis; rather, it is simply expected that preliminary screening should be facilitated using a faster and cheaper method.

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.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https:// doi.org/10.1016/j.foodchem.2019.125938.

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