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Use of Capsaicin for Nonlethal Technology

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Abstract

Hot peppers have been used as a seasoning for food, because of both the characteristic flavor and the peculiar feature of pungent sensation. In the same way, it has been used as cosmetics and in other forms such as topical stimulants and body creams. Nonetheless, this chapter shows a not-so-common application of pepper's properties, like the so-called pepper spray for defense technology. According to the premise that the action of the police officer must be adapted to each situation, it is necessary to prepare him for the gradual and proportional use of force, avoiding excesses and even lethal resources. In this way, pepper spray is a resource that can place police action within this premise. The main aspects of pepper spraying technology are discussed and the main concepts related to use, hazards, solution formulations and capsaicinoids quantification tests are pointed out. The advance showed here is around the use of capsaicinoids to extract raw material instead of OC to produce pepper spray solutions. The absence of oils and resin is the main point, as nonflammability is achieved much easier and avoids the use of hazardous organic solvents. The chemical analyses by GC-MS/FID applied to quantify the capsaicinoids, with capsaicin and dihydrocapsaicin together, are demonstrated and can be reproducible for the quality control of this product.

Keywords: pepper spray, nonlethal technology, capsaicinoids, capsaicin

1. Introduction

The Article XII in the Declaration of the Rights of Man and of the Citizen—France—1789, declares that “*The guarantee of the rights of man and of the citizen necessitates a public force; this force is thus instituted for the advantage of all and not for the particular utility of those in whom it is trusted*”.¹ The exercise of police work in civic security is very complex and thorough; it requires, at the same time, the application of the law to those who do not want to comply with it and requires the correct, just and necessary application of force to maintain law and order. If, on the one hand, the violation of the law is not correct, the same law provides that this citizen must be treated by the State according to the citizen protective premises of that law [1].

The State, through the Police, has to act with legality and attention to the protection of the human person; in other words, “police solutions” to violations of the law

¹ Declaration of the Rights of Man and of the Citizen—France—1791.

must not incur excesses by law enforcement officers. In order to adjust the conduct of law enforcement officers, there is a need to prepare to use force gradually, according to the premise that police action should suit each situation—considering that most police cases do not involve the use of lethal weapons—so, the police response must include nonlethal solutions [2].

The gradual use of force is an internationally recognized concept, which aims to point out the best way, in terms of containment, during police assistance [3]. Resisting the use of nonlethal technologies means exposing public security professionals to irreparable excesses and errors, due to their effects.

Among the nonlethal solutions for the use of force (in response to police incidents) are disabling agents that do not require physical contact between the police and the lawbreaker (for example, pepper spray), with the advantage of maintaining the offender at a safe distance and unable to harm others, including himself and the police officer.

We must be aware of the growing issue of police officers who are injured during police duties. There is great public attention, fully justified and correct, regarding the excessive actions that can result from the confrontation between citizens and police officers, with a primary focus on avoiding lethality in these situations. However, it is important to understand that the State, through its agents, vulnerability is also not desirable, that is, the impediment to the use of lethal actions could be compensated by the access to nonlethal solutions, more immediate equipment, as previously said, the pepper spray is an example.

Still with respect to the vulnerability of the police, there is the attack of animals (usually dogs), against police officers or third parties; it also strongly indicates the use of pepper spray as a nonlethal solution. There are reports of criminals who train dogs to attack police officers, or even police dogs; such a condition would be mitigated with the use of pepper spray.

2. Pepper spray

Usually, hot peppers are used as a seasoning for food, because of both the characteristic flavor and the peculiar feature of pungent sensation. In the same traditional way, they have also been used as cosmetics and in other forms such as topical stimulants and body creams. Nonetheless, this chapter shows a not-so-common application of hot pepper's properties, like the so-called pepper spray for defense technology. Since the 1970s, pepper spray is used as a nonlethal defense solution by law enforcement forces and civilians around the world [4].

The irritating effect—when the solution contained in the spray is sprayed on the face—allows for disabling the opponent by providing some advantage in self-defense (or third party), crowd controlling, and dispersing civilian disturbances. The immediate and involuntary closure of the eyelids and lacrimation were the main expected effects. Burning eyes, cough, nasal discharge, difficulty breathing, burning in the mouth, and other reactions occur within seconds of exposure. Those pain effects, together with the psychological (or moral) reflexes, cause temporary disability, thereby allowing police officers to avoid the opponent's resistance or even counteracts. The temporary incapacitation lasts for about 10–15 min and, after a few hours, the individual self-regains full capacity without any permanent effect, in other words, without irreversible harm. These properties take the pepper spray for defense as a nonlethal defense technology, an alternative to lethal force.

There are cases of serious injuries from the use of pepper spray, like the situations reported were the mechanical damage to the eye by the high-pressure aerosol jet applied directly to the eye [5], but this can be avoided through training and

respecting the safe distance for application. Use in closed spaces, or “in door” uses, is dangerous too, because the spray can asphyxiate in closed spaces, for no other reason other than the aerosol taking the place of breathable air. Several authors have studied the permanent injury cases with the use of pepper sprays (when used improperly), and the most important permanent injury is cornea damage, followed by pulmonary injury cases [6–10]. Nevertheless, in general, the reported cases of death always involve adverse circumstances, due to either the environment or the individual, or even both, which leads to death for reasons other than the single effect of the irritant. The inverse problem is dangerous too, because the inefficiency of the incapacitating properties of the spray solution leads the law agents at risk [11]. Both injuries and inefficiency should be considered when developing pepper spray solutions. The challenge is to find the best formulation that is efficient without causing damage.

Although there are several types of hot pepper extracts, the most widely used irritant agent in the production of pepper sprays is the oleoresin capsicum (OC) [12]. OC is a viscous liquid extracted from the hot peppers fruit (*Capsicum*), which contains more than a hundred different types of substances, consisting of complex mixtures, mainly of lipophilic molecules, and does not have a simple chemical formula [13].

Oleoresin can be just a colorant red type (paprika), colorant and pungency type (red pepper), or high pungent type (capsicum). With regard to industrial production, the capsicum OC pepper spray type has been the most supplied to police forces.

The nonivamide (pelargonic acid vanillylamide or PAVA) is a surrogate substance and some manufacturers use it instead of OC or capsicum extracts. This irritant can be found in some pepper extracts at lower concentrations; however, PAVA can be synthetically made, at low costs, and used alone or together with OC in some formulations. PAVA is much less irritating and its effect is felt much later than capsaicin.

Notwithstanding, there are formulation improvements by the application of another irritant capsaicin content that presents more homogeneous composition and can be more effortlessly controlled than OC. This irritant is an alternative type of pepper extract named natural capsaicin (N.Cap) [14] that engenders high-quality sprays. In practice, the irritant effect is not so different from OC but have a better-defined chemical composition and other advantages. The first advantage point is the absence of red dyes plus the characteristic seasoning smell of the OC, and the second point is the absence of oils and resins making possible the totally nonflammable solution formulation. Therefore, the N.Cap spray solutions cause just pungent effects and nothing else.

The N.Cap can be purchased from manufacturers that supply common pepper extracts to the pharmaceutical market. The product presents a white crystalline coarse powder with the presence of flat-shaped flakes. The irritant content requirement meets a minimum of 95% capsaicin plus dihydrocapsaicin. The remaining 5% consists of the extraction residues at pharmaceutical levels and by other capsaicinoids. Furthermore, it meets maximum drying loss of 1%, maximum ignition residue of 1%, and residual solvent (methanol) max 3000 ppm (USP-467). It has a melting range of 57–66°C. Metal content is <10.0 ppm and arsenic <2.0 ppm.

3. The chemical composition of OC

The chemical composition of OC depends on several factors—the species of plant, the extraction method, the season of the year in which the crop is harvested,

and the region of the plant where it is cultivated—as well as processing way and production. All of these and a lot of other factors contribute to make it difficult to standardize the concentration of irritating agent in pepper spray solutions, thereby leading to a wide range of capsaicin amounts contained in different commercial products and also in separate lots from the same supplier.

Since they produce the desired irritant effect, the capsaicinoids are the most important substances present in the OC used in pepper spray solutions. Other substances such as phenols, acids, alcohols, aldehydes, carotenes, esters, oils, and resins are also present in the OC, but cause a little or no irritant effect compared to capsaicinoids. It should be noted that oils and resin compounds are potentially flammable, and they become undesirable by increasing the flammability of the spray solution. If the spray solution has flammable properties, a jet of flame can be produced if there is an ignition source in the path of the spray jet.

Furthermore, the OC normally has a strong spice smell, a striking reddish brown color, and has hydrophobic characteristics, thereby requiring organic solvents (or even emulsions) for its complete dissolution. All these features mentioned are undesirable in pepper spray technology.

The OC extraction has wide types of processes, and the most simple is the extraction through ground powder fruits. Organic solvents like hexane, ether, alcohols, acetates, and ethylene dichloride are common extraction liquid phase media. In general, the extractions pass by two or three times, removing and replacing with pure solvent at each time. Other simple extractions consist basically to macerate the fruit with olive oil or other seed oils, but the impurity is high and the standardization is far from ideal to use as a raw material for pepper sprays. Modern processes of extractions are advanced Soxhlet extraction, microwave-assisted extraction, supercritical fluid extraction, ultrasound-assisted extraction, and pressurized liquid extraction. All they are more suitable for better-controlled extractions. However, these methods are very expensive and greatly increase the production costs [13].

The concentration of capsaicinoids in OC, in general, shows variations from 1 to 10%, depending on the type of fruit, solvent, process, and so on. Some types of OC capsicum have an approximate concentration range of 3–6% of capsaicinoids, but some Indian suppliers may have OC with 20% of capsaicinoids [15]. Of course, this large amount of concentrations and side substances present in the OC leads to a difficult standardization of raw material for the pepper spray proposal [12].

4. Capsaicinoids

The substances so-called capsaicinoids can be represented, in a simple way, by the binding of a vanillylamide group with fatty acids as a principal characteristic molecular structure, where the fatty chain would have 9–11 carbon atoms. The capsicum fruits synthesize the capsaicinoids in the placenta-fruit region, close to the tissue adjacent to the seeds. This type of metabolite is unique to *Capsicum* genus. Although little data exist on this compound's biosynthesis, there are reports that the principal two pathways are phenylpropanoid and fatty acid metabolism [16]. The amount of capsaicinoids in the pepper fruit reaches the maximum concentration in about 2 or 3 months of natural fruit development, and after the deceleration initiated by the action of the peroxidase enzymes, the concentration decreases generating secondary compounds. Certainly, the concentration in the fruit varies with the plant species, cultivation conditions, soil, place, seasonality, and so on.

From the point of irritant effect, the capsaicin is the main substance in the midst of capsaicinoids compounds, followed by dihydrocapsaicin. The total capsaicinoids content in the fruits has a typical concentration range of 0.1–1.0% on a dry basis [17],

but it is not a rule and some species have lowest concentration like 0.003% and others have a far high concentration like 1.86% [18]. In general, the capsaicin and dihydrocapsaicin together correspond to ~90% of the total capsaicinoids present in the ready fruit. The typical distribution is 60–70% capsaicin, 20–30% dihydrocapsaicin, 3–7% nordihydrocapsaicin, ~1% homocapsaicin, and ~ 1% homodihydrocapsaicin. However, this is not true in all cases; once, for example, there is evidence that the degree of fruit maturation and incidence of sunlight in the cultivation area, temperatures, and water availability are important factors in the accumulation and proportion of capsaicinoids in the fruit [19]. **Table 1** shows the name, chemical structure, and molecular formula of the major capsaicinoids.

Unfortunately, there are associations between OC and the molecular capsaicin formula in some pepper spray technicians media, thereby leading to erroneous perception that OC and capsaicin are synonymous with the same substance. Nevertheless, the molecular formula $C_{18}H_{27}NO_3$ is not the OC formula but only the capsaicin molecular formula, which is contained in OC.

4.1 The biological action of capsaicinoids

The biological action of capsaicinoids is complex and multi-targeted mechanisms. The action involves, above all, the activation of peripheral nerve receptors

Homolog name	Chemical structure	Molecular formula	CAS
Capsaicin		$C_{18}H_{27}NO_3$	404-86-4
Dihydrocapsaicin		$C_{18}H_{29}NO_3$	19408-84-5
Nordihydrocapsaicin		$C_{17}H_{27}NO_3$	28789-35-7
Homocapsaicin		$C_{19}H_{29}NO_3$	58493-48-4
Homodihydrocapsaicin		$C_{19}H_{31}NO_3$	20279-06-5
Nonivamide (PAVA)		$C_{17}H_{27}NO_3$	2444-46-4

Table 1.
Name, chemical structure, molecular formula, and CAS number of the major capsaicinoids.

in the mucous membranes, by interactions of the capsaicinoids with the vanilloid transient receptor potential type-1 cation channels (TRPV1). These receptors are normally activated by temperatures between 37 and 45°C when opening the calcium channels and induce reflexes of burn sensation. However, when TRPV1 binds with the capsaicinoids, it causes these channels to open below 37°C and the burn sensation occurs at normal body temperature. This is why capsaicinoids are linked to the sensation of heat [20].

Furthermore, the interactions of the TRPV1 with capsaicin are strictly related to pain by nociceptor activation and the release of substance-P. Nociceptor is a nervous sensory receptor responsible for pain mechanisms in the human body [21]. Prolonged contact may cause nerve endings to be desensitized; however, it does not lead to a permanent desensitization state and can be reversed by discontinuing contact.

The capsaicin and dihydrocapsaicin content in the pepper spray solution is determinant for the irritant properties and the disabling effect of the spray. Thus, to evaluate the effectiveness of the disabling properties of the spray, the capsaicinoids concentration in the solution can be measured, particularly the capsaicin together with dihydrocapsaicin [14]. Obviously, the limits to this concentration must take into account the toxicity and security against injury. So, some connections among the concentration and the irritant effect must be evaluated.

The Scoville test, whose unit of measure is SHU, is a known form of evaluating the effect of pungency or blazing of the peppers. This method was developed in 1912 by Wilbor Scoville [22] giving a five-level scale for pungency: nonpungent (0–700 SHU), low pungency (700–3000 SHU), moderate pungency (3000–25,000 SHU), high pungency (25,000–70,000 SHU), and very high pungency (>80,000 SHU). However, the Scoville method is a taste organoleptic method made by a dilution series of the pepper extracts. It makes subjective responses and unreproducible results. Qualitative and quantitative information can be precisely obtained by modern instrumental chemical methods with many advantages [12, 23].

5. Toxicology of capsaicin

Since the peppers are largely used as a food, through several forms and quantities around the world for centuries, it is not expected that it is a poison. The individual consumption of capsaicin in India may be around 7–120 mg/day. In Northeast Thailand, the individual consumption may be 26 g of (jaew) pepper per meal [24]. The main concern with the use of pepper spray is with the possible toxic properties of the solution. Another important aspect is the observation of the tactical way of use, which involves the amount of solution applied, environment conditions, closed spaces and psychological state of the aggressor; all of these characteristics must be well studied in action using pepper spray.

Previous study shows that the toxic level of 60-kg human consumption of capsaicin corresponds to consumption of 1.94 kg of dry weight of capsicum fruit. Obviously, there is no person who can consume this amount of dry pepper at once; due to the pain and pungent sensation, it prevents over consumption [25].

There is no consensus in the literature for the acceptable dose of capsaicin for oral, skin, and eyes human contact. The studies are commonly connected with lethal doses values (LD_{50}), which means a quantity limit that kills 50%, at least, of the population studied. This kind of test programs normally uses rats or mouse to access results. Rabbits, dogs, and guinea pig are common too. It is sustained by a presumption that these animals have a close correlation with human responses to capsaicin [26].

An oral LD₅₀ value was reported at range of 60–75 mg/kg (Swiss male albino mice). On the other hand, another experiment with the same mice type and procedure, just changing the solution vehicle, showed LD₅₀ at 190 mg/kg [25]. Another work reports male mice with LD₅₀ values of 118.8 mg/kg and for female mice of 97.4 mg/kg [27]. The U.S. National Library of Medicine—National Center for Biotechnology Information—reports 47.2 mg/kg for mouse. OSHA or NIOSH has reported no occupational exposure limits for capsaicin or OC. As can be seen in these short examples above, there is not a single value to use to computation and derive secure concentrations of spray solutions to manufactories.

Some inhalation response studies showed no evidences that inhalation of capsaicum oleoresin spray causes respiratory compromise [28]. An investigation made with the concern on the respiratory effects of OC concludes that the exposure did not result in abnormal hypoxemia or hypoventilation. This experiment was made by aerosol delivery exposure box with a hood for the subject attached to one end of the exposure box. The aerosol was 5.5% OC (with 0.92% of capsaicinoids) solution with isopropyl alcohol as carrier agent and isobutane/propane as propellant [29]. These types of studs are more conclusive and can take better access for more suitable results to manufactories.

The ocular contact with capsaicin is the primary incapacitation response. Furthermore, the hydrophobic properties of capsaicin (and capsaicinoids) allow them to penetrate the eye tissue, accessing the terminal nervous and, consequently, causing pain and great lacrimation response. The use of contact lenses can lead to an increase in the duration of the effect, due to the accumulation under the lens. In these cases, care should be taken to remove the lens as soon as possible.

6. Experimental

The quantification of capsaicin in pepper spray can be made by GC-MS/FID [14]. This experimental result presented here aims to exemplify the quantitative and qualitative analysis of the samples of the commercial Brazilian pepper spray. About 500 µl of solution sample was weighed on an analytical balance and the contents were solubilized with HPLC grade acetone and transferred quantitatively to a 1 ml volumetric flask. The solution was swollen and an aliquot was conducted for analysis by gas chromatography.

A model GC-2010 equipped with a mass spectrometer GCMS-QP2010 Ultra and an automatic sampler AOC-5000 (Shimadzu) was used. The chromatographic separation was performed using RTx-5MS capillary column (Restek) with a stationary phase containing 5% phenylmethyl and 95% polydimethylsiloxane (30 m × 0.25 mm × 0.25 µm of film). The temperatures of the injector and the transfer line of the mass spectrometer were 300°C. The samples were injected with a split ratio of 1:50. The oven temperature program followed the following conditions: 50°C (2 min), heating rate from 10°C/min to 300°C (2 min). Helium was used as the carrier gas in a flow rate of 1.2 ml/min. The mass spectrometer was operated in electron impact ionization mode, with acquisition in the scan mode with m/z between 50 and 500.

To identify the compounds, a comparison of the spectra with the NIST library was carried out. Only substances whose similarity was greater than 80% were considered, compared with data from the library. **Figure 1** shows the chromatogram result with the solvent around 7.2 min and capsaicin and dihydrocapsaicin peak around 24 min.

With the purpose of quantifying, the capsaicin and dihydrocapsaicin are integrated together and the calibration curve was made by this result against

Figure 1.

GC-FID chromatogram of capsaicin and dihydrocapsaicin peaks with retention time around 24 min.

standard solutions made with Sigma-Aldrich Capsaicin (purity capsaicin: 61.1%, dihydrocapsaicin: 31.2% LOT#: LRAA9221 09 September 2015). The regression coefficient R^2 was 0.999 and uncertainty was 0.9%. The subsequent dilution was satisfactory by the statistical linear fit results. In this way, it is possible to quantify the capsaicinoids, that is, capsaicin and dihydrocapsaicin together, on the pepper spray solution.

7. NMR analyses

Nuclear magnetic resonance (NMR) is a powerful analytical tool for identification and quantification of capsaicinoids in raw materials for pepper spray solutions. Its ability to analyze samples with minimum pre-treatment allows a safe analysis that preserves the original characteristics. In the specific case of organic molecules, their sensitivity is increased by the detection of the isotope ^1H . Thus, the ability of NMR to evaluate the quality control of the nonlethal arms industry becomes clear.

In order to verify the N.Cap content, a sample of 26.4 mg was weighed and solubilized in 600 μl of CDCl_3 in a 5-mm NMR tube. The analysis was performed at 25°C using glass capillary for the quantification of the maleic acid present in the solution with 100 mmol of D_2O . The broad band inverse (BBI) probe inserted into Bruker Avance III 11.75 T equipment was used. The simple pulse sequence used was zg. The spectra were processed with 0.3 Hz line broadening and zero filling.

Figure 2 shows the graphical results, and the relative chemical shift integration of hydrogens of capsaicin and dihydrocapsaicin are presented. All the signals of the main chemical groups present in the sample were identified through the NMR analyses. Groups 1 from capsaicin and 2 from dihydrocapsaicin (amplified in **Figure 2**) can be used for relative integration of the signals. In addition to being unobstructed, they had a higher signal-to-noise ratio due to having six hydrogens contributing to the integration of each signal. Thus, it was possible to verify the proportion of these compounds among themselves present in the mixture. This led to the proportion of 33% dihydrocapsaicin (minority) and 66% capsaicin (majority), the latter being twice the concentration of the former.

The ^1H NMR technique proved efficient in the identification and relative quantification of the components present in the mixture of pepper derivatives. The spectra were acquired quickly and with a simple sample preparation step.

Figure 2.
¹H NMR identification and relative quantification of the components present in the N.Cap.

The analyses allowed a broad view of the absence of other compounds, even if minority, thereby proving the purity of the material and absence of degradation products. On the other hand, the presence of other components could be identified concomitantly in a mixture of higher complexity. Thus, this work suggests that ¹H NMR can be used as a quality control tool in the nonlethal industry.

8. Conclusion

The main aspects of pepper spraying technology were discussed and the main concepts related to use, hazardous, solution formulations and quantification tests were pointed out. This technology is relatively recent, and a wide field of research is not addressed yet. The advance showed here is around the use of capsaicinoids to extract raw material N.Cap instead of OC to produce pepper spray. The absence of oils and resin is the main point, as nonflammability is achieved much more easily and without the use of hazardous organic solvents. Chemical analyses by GC-MS/FID applied to quantify capsaicinoids (capsaicin and dihydrocapsaicin together) have been demonstrated and can be reproducible for the quality control of this product. The ¹H NMR provides information about raw material and how to access quality information and impurity with our relative concentration.

The concentration range between 0.2 and 0.3% (mass of solution) of capsaicinoids guarantees satisfactory spray efficiency, allowing the aggressor to be incapacitated without serious injury. Toxicological study preferred with human voluntaries is the way for a better evaluation of limits.

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References

- [1] Sutherland RG. Chemical and biochemical non-lethal weapons: Political and technical aspects. SIPRI Policy Paper. 2008;**23**:1-40
- [2] NATO. NATO Policy on Non-Lethal Weapons [Online]. 2008. Available: https://www.nato.int/cps/en/natohq/official_texts_27417.htm?selectedLocale=en [Accessed: 19 March 2020]
- [3] Office of the United Nations High Commissioner for Human Rights (OHCHR). Basic Principles on the Use of Force and Firearms by Law Enforcement Officials [Online]. 1990. Available: <https://www.ohchr.org/en/professionalinterest/pages/useofforceandfirearms.aspx> [Accessed: 19 March 2020]
- [4] Olajos EJ, Stopford W. Riot Control Agents: Issues in Toxicology, Safety, and Health. USA: CRC Press; 2004. ISBN: 9780415299022
- [5] Brown L, Takeuchi D, Challoner K. Corneal abrasions associated with pepper spray exposures. The American Journal of Emergency Medicine. 2000;**18**(3):271-272
- [6] Haar RJ, Iacopino V, Ranadive N, Weiser SD, Dandu M. Health impacts of chemical irritants used for crowd control: A systematic review of the injuries and deaths caused by tear gas. BMC Public Health. 2017;**17**:831
- [7] Kearney T, Hiatt P, Birdsall E, Smollin C. Pepper spray injury severity: Ten-year case experience of a poison control system. Prehospital Emergency Care. 2014;**18**:1-6
- [8] Recer GM, Johnson TB, Gleason AK. An evaluation of the relative potential public health concern for the self-defense spray active ingredients oleoresin capsicum, o-chlorobenzylidene malononitrile, and 2-chloroacetophenone. Regulatory Toxicology and Pharmacology. 2002;**36**(1):1-11
- [9] Watson WA, Stremel KR, Westdorp EJ. Oleoresin capsicum (CAP-STUN) toxicity from aerosol exposure. Annals of Pharmacotherapy. 1996;**30**:733-735
- [10] Granfield J, Onnen J, Petty CS. Pepper spray and in-custody deaths. RCMP Gazette. 1994;**56**(11):12-17
- [11] Broadstock M. What Is the Safety of “Pepper Spray”. Vol. 1. Christchurch: NZHTA Tech Brief Series; 2002
- [12] Reilly CA, Crouch DJ, Yost GS, Fatah AA. Determination of capsaicin, dihydrocapsaicin, and nonivamide in self-defense weapons by liquid chromatography–mass spectrometry and liquid chromatography–tandem mass spectrometry. Journal of Chromatography A. 2001;**912**:256-267
- [13] Lalanne GM, Álvarez AJH, Fernández MJ, Azuara E. Oleoresins from *Capsicum* spp.: Extraction methods and bioactivity. Food and Bioprocess Technology. 2017;**76**:51-76
- [14] Junior NO, Padulla V, Flores I, Annuniação D, Neiva M, Brant V. Evaluation of natural capsaicin (N.Cap) in pepper spray by GC-MS/FID, NMR and HPLC as an alternative to the use of oleoresin capsicum (OC). Human Factors and Mechanical Engineering for Defense and Safety. 2019;**3**. Article number 8
- [15] Govindarajan VS, Salzer UJ. Capsicum—Production, technology, chemistry, and quality—Part II. Processed products, standards, world production and trade. C R C Critical Reviews in Food Science and Nutrition. 1986;**23**:207-288

- [16] Reyes ML. Chemical and pharmacological aspects of capsaicin. *Molecules*. 2011;**16**:1253-1270
- [17] Antonio AS, Wiedemann LSM, Veiga Junior VF. Food pungency: The evolution of methods for capsaicinoid analysis. *Food Analytical Methods*. 2019;**12**:1327-1345
- [18] Govindarajan VS, Salzer UJ. Capsicum—Production, technology, chemistry, and quality—Part II. Processed products, standards, world production and trade. C R C Critical Reviews in Food Science and Nutrition. 1985;**22**:109-176
- [19] Zamora AG, Campos ES, Ortega JGL, Morales RP, Ortiz JCR, Hernández JLG. Characterization of different capsicum varieties by evaluation of their capsaicinoids content by high performance liquid chromatography, determination of pungency and effect of high temperature. *Molecules*. 2013;**18**:13471-13486
- [20] Simonsen HT. Short commentary: Capsaicin—The hot and spicy diet turned mild and effective by glycosylation. *Biochemistry Insights*. 2009;**2**:47-49
- [21] Chung M-K, Campbell JN. Review: Use of capsaicin to treat pain - Mechanistic and therapeutic considerations. *Pharmaceuticals*. 2016;**9**:66
- [22] Scoville WL. Note on capsicums. *The Journal of the American Pharmaceutical Association*. 1912;**1**:453-454
- [23] Othman ZAA, Ahmed YBH, Habila MA, Ghafar AA. Determination of capsaicin and dihydrocapsaicin in capsicum fruit samples using high performance liquid chromatography. *Molecules*. 2011;**16**:8919-8929
- [24] García-Casal MN, Peña-Rosas JP, Gómez-Malavé H. Sauces, spices, and condiments: Definitions, potential benefits, consumption patterns, and global markets. *Annals of the New York Academy of Sciences*. 2016;**1379**(1):3-16
- [25] Glinsukon T, Stitmunnaithum V, Tosulkao C, Buranawuti T, Tangkrisanavinot V. Acute toxicity of capsaicin in several animal species. *Toxicol*. 1980;**18**:215-220
- [26] W. J. Jr. Final report on the safety assessment of *Capsicum annuum* extract, *Capsicum annuum* fruit extract, *Capsicum annuum* resin, *Capsicum annuum* fruit powder, *Capsicum frutescens* fruit, *Capsicum frutescens* fruit extract, *Capsicum frutescens* resin, and Capsaicin. *International Journal of Toxicology*. 2007;**26**:3-10
- [27] Saito A, Yamamoto M. Acute oral toxicity of capsaicin in mice and rats. *The Journal of Toxicological Sciences*. 1996;**21**:195-200
- [28] Fuller RW. Pharmacology of inhaled capsaicin in humans. *Respiratory Medicine*. 1991;**85**:31-34
- [29] Chan TC, Vilke GM, Clausen J, Clark RF, Schmidt P, Snowden T, et al. The effect of oleoresin capsicum “pepper” spray inhalation on respiratory function. *Journal of Forensic Sciences*. 2002;**47**:299-304