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Assessment of safety margins of exposure to non-genotoxic chemical substances in food

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ABSTRACT

The concept of Food Safety Margin (FSM) was introduced in microbiological risk analysis as an alternative approach to risk characterization within the informed-risk decision-making process. Its aim was to verify compliance with food safety objectives by assessing the effects of uncertainties. This paper describes the fundamentals and develop a new formulation of safety margins to verify compliance with food safety goals in relation to exposure to non-genotoxic chemical hazards. Both classical and probabilistic metrics were used to compare a given exposure to an estimated daily intake (EDI) with a given safety goal, the acceptable daily intake (ADI). The safety margins of these metrics were assessed in the exposure of peaches to organophosphorus pesticides. The pesticides considered were Azinphos-methyl, Chlorpyrifos, Diazinon, Dimethoate, Methamidophos, Parathion-methyl and Phosmet. The concentrations were obtained from the USDA pesticide database. The study period included the 11 years in which peaches were analysed from 1994 to 2014. The results show the importance of using the effect of uncertainty instead of mean values for risk characterization and that not only safety margins increased during this period but also that uncertainty was reduced. In general, large safety margins were observed in the period studied and few situations were found in which exposure was outside the safety limits.

1. Introduction

The consumption of potentially harmful contaminants remains a real problem that can cause human illness and significant economic losses in both developed and non-developed countries. Both chemical and biological contaminants are the most frequent hazards in food. In fact, the 2014 report on the management of food alerts in Spain showed that chemical hazards were detected in 54.63% of the notifications, while biological hazards were identified in 28.35% (AECOSAN, 2014).

Humans are exposed to a wide variety of chemical hazards throughout their lives via environmental pollution of the air, water, soil and food. Chemical substances play an important role in food as they can be intentionally added as additives to prolong shelf-life or as flavouring to make food tastier. Although chemicals such as pesticides are not intentionally added, they are sometimes present in the final product. For example, the EFSA's report on pesticide residues in food (2013) shows that the concentration of pesticides in 97.4% of samples originating in the EU fell within the legal limits, i.e. the MRL (Maximum Residue Level); 54.6% were free of detectable residues, while 1.5% of the samples clearly exceeded it (EFSA, 2015). Similar results were published by the USDA pesticide data programme, in which over 41% of the samples tested had no detectable pesticide residue (USDA, 2016a). Of the cases detected (59%), more than 99% had residues below the tolerances established by the MRL. The data also indicated the disquieting presence of multiple pesticides, in fact, the samples tested during 2014 showed that only 14.8% contained 1 pesticide, and the remaining 43.7% contained more than 1 pesticide, while 12.7% had two, 1% had nine and in an extreme case, 0.01% of the samples had 17 different pesticides. (USDA, 2016a). High concentrations of pesticides in food beyond the MRL can jeopardize consumer health if they are higher than the safety limit, i.e. the ADI (Admissible Daily Intake) in the non-genotoxic chemical hazard framework.

In order to preserve consumer safety, in recent decades risk

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assessment, risk management and risk communication have been formalised and incorporated into a process known as *risk analysis*. This has been gradually introduced as a tool to support decision-making processes in food management policies aimed at improving food safety in the global framework, where food safety principles must follow ALARA criteria (Doménech & Martorell, 2016). This new focus has enabled a change from a hazard-based approach to a risk-based approach (FAO/WHO, 2005; CAC, 2007).

Risk assessment provides a systematic means of assessing, both qualitatively and quantitatively, the probability of the occurrence and the severity of known or potentially adverse health effects in a given population, based on hazard identification, hazard characterization, exposure assessment and risk characterization. The results obtained through risk assessment are the foundations of risk management policies, whose aim is to weigh policy alternatives and propose appropriate prevention and control options (CAC, 2007).

In the context of quantitative microbiological risk assessment, the food safety margin (FSM) was introduced as a new risk characterization metric to verify compliance with food safety objectives (FSO), addressing the effect of uncertainties. In this way, FSM is able to support microbiological risk management in the risk-informed decision-making framework (Doménech & Martorell, 2016). Its classical approach is intended to be used to measure the Euclidean distance between exposure, FSO, and a safety threshold, which has to be preserved in order to guarantee an appropriate level of protection (ALOP). Alternatively, the probabilistic approach permits estimation of the probability that exposure does not violate the corresponding safety limit, or, complementarily, estimates the exceedance probability and its uncertainty. This approach fits the realistic formulation of the condition for verification of the safety threshold, particularly for microbiological hazards, in compliance with the FSO. Having a quantitative measure of FSM permit us to assess whether the margin between exposure and the safety threshold is big enough and to estimate the increase or decrease of the margin after changes in food chain conditions, i.e. comparing the safety margin before and after the change.

The objective of this paper is thus to describe the fundamentals and to develop a new formulation to measure the margin between exposure to non-genotoxic chemical hazards, or Estimated Daily Intake (EDI) and the safety limit or Admissible Daily Intake (ADI). Both classical and probabilistic metrics are proposed to provide verification of the compliance of food safety goals in relation to exposure to non-genotoxic chemical hazards and assess the effects of random uncertainties. In a case study, these metrics were applied to measure the safety margins of exposure to organophosphorus pesticides in peaches.

2. Risk assessment of non-genotoxic chemicals, addressing uncertainty

Risk assessment of chemical hazards in food, e.g. non-genotoxic chemicals, can generally be described as characterizing the potential hazards and the associated risks to life and health resulting from the exposure of humans to chemicals present in food over a specified period (FAO/WHO, 2009). This assessment consists of four steps: hazard identification, hazard characterization, exposure assessment and risk characterization.

Risk assessment must include the appropriate uncertainty characterization and treatment (CAC, 2013; Dorne & Fink-Gremmels, 2013; IPCS, 2008; WHO, 2014). Uncertainty can be categorized as either “random” or “epistemic” (Doménech & Martorell, 2016). The former reflects our inability to predict random observable events and represents the true heterogeneity of the population, which is a consequence of both biological and physical systems and is irreducible by further measurements, so that it is often referred to as “variability”. Epistemic uncertainty represents our lack of knowledge, which is often divided into three main categories: completeness, model and parameter uncertainty (Martorell et al., 2014). Random uncertainty is the only type of uncertainty considered in this paper.

According to (Martorell et al., 2014), the treatment of uncertainties in risk assessment depends on the type of uncertainty. Uncertainty assessment is a type of treatment for random uncertainty, which is often based on a probabilistic approach to uncertainty formulation and propagation by a standard Monte Carlo method.

2.1. Hazard identification

This stage consists of identifying possible chemical hazards and taking into account the possibility of adverse health effects. With this aim the available data on toxicity, analyses and observations in humans or domestic animals are considered to decide whether a chemical should be considered a hazard.

2.2. Hazard characterization

Hazard characterization describes the relationship between the administered dose of a chemical and the adverse health effect that it produces (FAO/WHO, 2009). These effects can range from mild eye irritation and nausea to serious chronic diseases, such as cancer. The description of the dose-response, which quantifies the relationship between the amount of exposure to a chemical and the extent of toxic injury or disease, is different for non-genotoxic and genotoxic carcinogens. Those acting via genetic alteration are called *genotoxic carcinogens* and contrast with non-genotoxic carcinogens, which do not damage DNA but act as tumour promoters. Non-genotoxic carcinogens usually affect only one organ and because of the nature of their indirect action mechanism have an action threshold (Leeuwen & Vermeire, 2007). The exact action mechanism of non-genotoxic carcinogens has as yet only been partially elucidated, but the end result is usually increased proliferation in specific tissues caused by excessive secretion of hormones, or by injury, or can be receptor-mediated (e.g. peroxisome proliferation).

Considering pesticides as a type of non-genotoxic chemical hazard, the ADI represents the threshold value, which is a reference limit for risk characterization in relation to food safety goals. The ADI is the amount of a chemical to which a person can be exposed daily for a long period without suffering harmful effects (WHO, 2004). It is determined by applying safety factors such as uncertainty data to the highest dose in human or animal studies, which has been shown not to cause toxicity. The WHO (2014) provides guidance on evaluating and expressing uncertainty in hazard characterization and establishes an ADI that guarantees the appropriate level of protection for humans.

2.3. Exposure assessment

Exposure assessment is defined as the qualitative or quantitative evaluation of the likely intake of chemical agents via food, as well as exposure from other sources if relevant (FAO/WHO, 2006). More recently, the EFSA (2011) defined the same concept as a combination of the data on concentrations, i.e. level and frequency of a chemical substance present in food and on the quantity of those foods consumed. Exposure assessment must include uncertainty assessment. The IPCS (2008) provides guidance on uncertainty treatment in chemical exposure assessment.