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IDENTIFICATION OF IMPACTS AND HUMAN HEALTH RISKS PRODUCED BY THE PRESENCE OF PESTICIDES IN THE ENVIRONMENT
II. HUMAN HEALTH RISKS GENERATED BY THE PRESENCE OF PESTICIDES IN PLANT PRODUCTS

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Abstract. *The risk to human health generated by the consumption of fruits and vegetables containing pesticide residues is evaluated applying the method recommended by the United State Environmental Protection Agency (USEPA), taking strawberries, apples, lettuce and potatoes for evaluation. In the case of the USEPA method, several age categories of consumers were considered, from 3 years to over 75 years in the acute case, and from 18 years to over 75 years age categories in the chronic case. The results showed that no risks to significant human health were identified. According to the results, it was found that most of the pesticides taken into account do not pose a risk to the population, except for a few cases in which the short-term and long-term evaluation values exceeded the limits at which the pesticides pose a risk to the population represented by children (especially those that have exceeded the maximum allowed residual limit).*

Keywords: acute exposure, chronic exposure, EFSA, health risk, USEPA method

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2. Impacts and risks of pesticides on human health

The impacts of pesticides on human health are highly variable. They may appear after a few days and are immediate in nature (acute effects) or may take months or years to manifest (chronic effects). In addition, certain people, such as children, pregnant women, or the elderly, may be more sensitive to the effects of pesticides than others [1, 2]. Pesticides can enter the human body through ingestion, inhalation or dermal contact, and the effects on human health due to exposure to pesticides depend not only on the degree of toxicity of the pesticides but also on the type and time of exposure [3].

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Pesticides have been associated with a multitude of human health hazards, from short-term effects such as headaches, nausea, dizziness, vomiting, skin irritation to long-term effects such as cancer, reproductive harm and disorders endocrine Chronic health effects can occur even years after minimal exposure to pesticides in the environment or in food and water, and pesticides can cause various types of cancer. Some of the most common forms include leukemia, brain, bone, breast, ovarian, prostate or liver cancer. There is also evidence that exposure to pesticides disrupts the endocrine system, the reproductive system, and the embryonic development of the fetus. Endocrine disorders can cause infertility, hormonal imbalances, behavioral disorders, and more [4, 5].

Children represent a category of population particularly sensitive to exposure to pesticides, they are particularly sensitive to the dangers associated with the use of pesticides, as their toxicity can differ quantitatively and qualitatively from that found in adults. As children's immunity and nervous systemsare in evolution, detoxification mechanisms have not fully developed, leaving them less able to resist the introduction of toxic pesticides into their systems, researchers have found that exposure to pesticides can induce asthma in children [4].

Among the major groups of pesticides, organochlorines are dangerous because of their persistence and stability. Due to the lipophilic nature of these pesticides, they accumulate in milk, meat and fish and enter the human body through the food chain and cause serious health problems [6]. Organophosphorus insecticides have very different physicochemical properties, such as polarity and water solubility. Because these substances act by inhibiting acetylcholinesterase, they also pose a risk to human health [7]. Exposure to carbamate pesticides, which act as acetylcholinesterase inhibitors, can lead to reversible neurological disorders, and some are suspected carcinogens and mutagens [4]. Triazines are among the most widely used herbicides in agriculture. Most of them are derived from s-triazine (1,3,5-triazine), but a few are based on 1,2,4-triazine. These herbicides are suspected of causing cancer and hormonal disturbances and are banned in several countries [4].

The purpose of the work is to calculate the hazard index for human health as a result of the acute and chronic exposure of some population groups, depending on age, to the action of some pesticides as a result of the consumption of some fruits and vegetables, through a method recommended by the United States Environmental Protection Agency.

2. Human health impact and risk generated by the presence of pesticides in the environment and in plant products

Food safety is an important issue for both consumers and governments. While consumers are concerned about the safety of what they eat, governments are concerned with finding ways to reduce food and disease risks [8, 9]. Several international organizations are involved in ensuring and controlling food safety worldwide: Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO), Codex Alimentarius Commission (CAC), Joint FAO/WHO Meeting on Residues of Pesticides (JMPR) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA). There are also bodies involved in ensuring food safety, especially in Europe, such as: the European Food Safety Authority (EFSA), the Directorate-General for Health and Consumer Protection of the European Commission (DGSANCO) [10].

2.1. Steps in risk analysis

The US Environmental Protection Agency (EPA) defines health risk as "*the probability of adverse effects on human health or ecological systems resulting from exposure to an environmental stressor"* [11, 12]. A stressor is any physical, chemical or biological entity that can induce an adverse response. Stressors can negatively affect natural resources and entire ecosystems, as well as the environment with which they interact [11, 13].

In general, the health risk depends on the following three [12, 14]:

- the amount of substance present in the environment (e.g. in soil, water, air) or in plant products (vegetables, fruits);
- how long a person is exposed;
- the toxicity of the chemical.

Exposure to pesticides can be acute or chronic, professional and extra-professional, deliberate or following an accident [15]. The ways of pesticide penetration into the body can be either through ingestion, inhalation or skin absorption. Concerning the ingestion of food containing pesticide residues, the most vulnerable are babies, followed by children, pregnant women, the elderly, adults [16] (Figure 1).

Babies represent the most vulnerable category because their enzymatic activity and therefore their ability to break down chemical compounds are lower compared to adults. Children consume more food than adults, leading to relatively higher exposures to certain compounds, and they also have a different physiology than adults. Children have been found to be more sensitive and vulnerable to certain compounds, while for some compounds there is no difference between the sensitivity of children and adults [1, 17].

The necessary stages in human health risk estimation are: hazard identification, dose-response assessment, exposure assessment and risk characterization [11] (Figure 2).

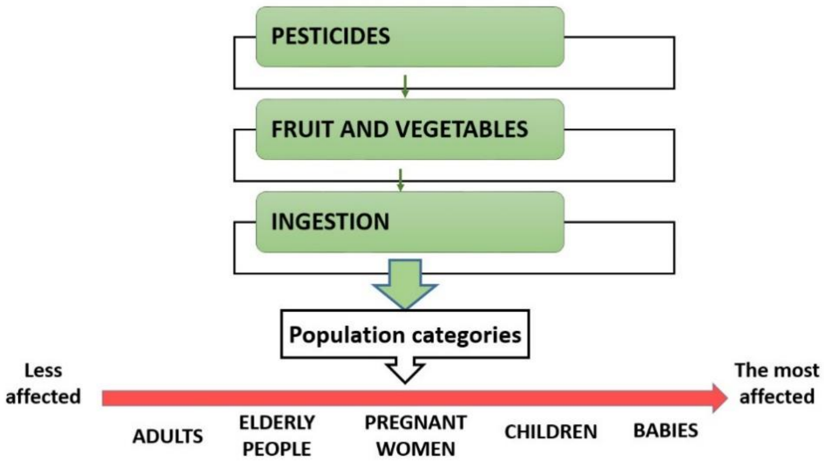


Fig. 1. Population categories affected by the ingestion of plant products containing pesticide residues

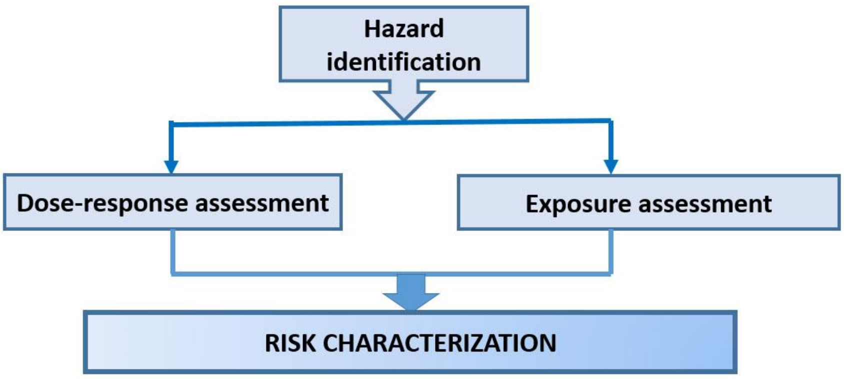


Fig. 2. Steps in human health risk assessment (adapted upon USEPA [11])

1. Hazards identification - consists in finding the possible threats that come from the activity carried out, identifying the factors that can generate the appearance of risks, as well as the properties of substances that can present a potential danger. There are some key components of hazard identification:

Toxicokinetics take into account the manner in which the body absorbs, distributes, metabolizes, and eliminates chemicals.

Toxicodynamics focuses on the effects that chemicals have on the human body. A key component of hazard characterization involves evaluating the weight of evidence for a chemical's potential to cause adverse effects on human health.

2. Dose-response assessment **-** in this stage, the degree and routes of exposure, duration or frequency of exposure are determined. The dose-response relationship (which can refer to dose, concentration, other specific exposure conditions) correlates the amount and type of exposure with the probability and severity of adverse effects on human health.

3. Exposure assessment **-** is the process of measuring or estimating the extent, frequency and duration of human exposure to pesticides. Exposure assessment considers both the route of exposure (the course an agent takes from the source to the contact person(s)) and the route of exposure (the means by which the agent enters the body.

4. Characterization of the risk – in this stage, the results of the exposure estimation are compared with the results of the estimation of the degree of exposure.

After going through the four stages in estimating the risks to human health, a series of measures are taken to reduce the identified risks. If the risk assessment provides information about potential risks to human health including their identification, risk management consists in the actions taken following the risk assessment, taking into account the following information.

- *scientific factors* provide the basis for risk assessment, including information from toxicology, chemistry, epidemiology, ecology and statistics;

- *economic factors* inform the manager about the cost of risks and the benefits of their reduction, the costs of risk reduction or the remedial options;

- *social factors* such as income level, community values, land use, health care availability, lifestyle and psychological state of affected populations can affect the susceptibility of an individual or a defining group to the risks of a particular stressor.

- *technological factors* include feasibility, impact and range of risk management options.

- *political factors* are based on interactions between branches of the federal government, with other federal, state, and local government entities, and even with foreign governments; these may vary from practices defined by Agency policy and from political administrations through inquiries from members of Congress, special interest groups, or interested citizens.

2.2. Interpretation and characterization of human health risks generated by the presence of pesticides in vegetable products

Risk characterization is the 4th stage of the human health risk assessment. Its objective is to review and incorporate information from the previous stages of risk assessment and express a general conclusion about the risk [18]. During risk characterization, the results of risk assessment should reveal the presence or absence of risks. Also, information about risk magnitude and uncertainties are considered [11]. Each component of the risk assessment (dose-response assessment, exposure assessment) has an individual risk characterization to carry forward findings, assumptions and uncertainties. These individual risk characterizations offer the required data base to report a complete risk characterization [19].

Principles of good risk characterization [11, 12]:

Transparency - the characterization must fully and explicitly present the risk assessment methods, assumptions, logic, rationale, uncertainties.

Clarity - the data from the risk assessment must be easily understood by readers both inside and outside the risk assessment process. Documents should be concise, and use easy-to-understand tables, graphs and equations.

Consistency - the risk assessment should be conducted and presented in a manner consistent with the country's environmental protection agency policy and consistent with other risk characterizations of similar scope developed under agency programs.

Reasonableness - the risk assessment must be based on sound judgment, with methods and assumptions compatible with the current state of science and communicated in a complete and appropriate manner.

2.3. Maximum Residue Level (MRL) approach for pesticides in plant products

Maximum residue limit (MRL) means " *the maximum concentration of a residue that is legally permitted or recognized as acceptable in or on a food or agricultural product or in a type of animal feed* " [20].

In order to ensure a high level of consumer protection, Regulation (EC) No. 396 (2005) establishes "the maximum permissible limits (MRL) for more than 500 pesticides covering 370 food products/food groups. For pesticides not explicitly mentioned in MRL legislation, a maximum permissible limit of 0.01 mg/kg is applied" [21]. Maximum residue level databases provide comprehensive information on statutory and non-statutory MRLs applicable to pesticides in foodstuffs following the introduction of Regulation (EC) No. 396 (2005).

There are two types of MRLs that can apply to food sold in the European Union [21, 22]:

1. Statutory MRLs established in accordance with Regulation (EC) 396/2005, which entered into force on 1 September 2008. Where MRLs are established, all those involved in the marketing of food or feed within The EU must comply with th8ese requirements. Annex 1 of the regulation lists the food and feed products for which maximum limits can be set. Annexes 2, 3a and 3b contain the applicable MRLs. Regulation (EC) No. 396 (2005) aims to establish MRLs for all active substances in pesticides which, when used, produce an identifiable residue.

2. Non-statutory MRL codes. They are established by the Codex Alimentarius Commission, an international body that aims to protect consumer health and ensure fair trade practices in international food trade. Code MRLs are non-regulated levels. These are used as guidance on acceptable levels, but are only relevant if they apply to a product for which limited MRLs are not established by the European Commission [23].

Chemical MRLs represent the highest residue levels expected to be detected in food when pesticides are used in accordance with authorized agricultural practices. These agricultural practices are called good agricultural practices (GAP) and are defined as the pattern of use derived from efficacy studies that determines the lowest effective rate of the specific pesticide combination. The usage pattern includes the application rate and the interval between the last application and harvest, also known as the pre-harvest interval (PHI). A minimum number of field trials are required to set MRLs. In the European Union (EU), eight field trials are required over at least two seasons in both the northern and southern part of the EU for major crops and four field trials per region for crops minor. Supervised studies should reflect the variability of residues that may occur in normal agricultural practice when a pesticide is used in critical Good Agricultural Practices (GAP) [24]. Critical GAP criteria refer to the conditions under which the maximum application rate of the pesticide formulation and the minimum PHI are used. The GAP for each country and region must be different, but there is an initiative of the GLOBALGAP organization that aims to establish a standard for good agricultural practice (GMP) with different product applications able to suit the entire global agriculture. The organization already operates in over 100 countries worldwide [10].

3. Methods for identifying risks to human health due to the presence of pesticides in vegetable products

Risk assessment of the impact of pesticides on human health is not an easy process due to differences in exposure periods and levels, type of pesticide (in terms of toxicity), mixtures used, geographical features and weather conditions in agricultural areas where pesticides are applied. Given that human health risk is a function of pesticide toxicity and exposure, a greater risk would be expected to occur from high exposure to a moderately toxic pesticide than from low exposure to a potent pesticide toxic [25].

In terms of risk to human health, the exposure time of humans to pesticides should be assessed, in the case of acute or short-term exposure, the absorption of pesticide residues in food consumed over a short period, usually within one meal, is estimated or of a day. Chronic or long-term exposure assessment aims to quantify the intake of pesticides by consumers over a long period of time [25].

The ratio of the pesticide's average daily dose (ADI) to the corresponding reference dose (RfD) indicates whether consumers are exposed to pesticide residues that may pose a health risk. If the exposure by consumption is less than or equal to the toxicological reference values, a risk to the health of the consumer can be excluded with a high probability [26]. However, possible negative health outcomes cannot be completely excluded if exposure exceeds toxicological reference values [21].

Adverse effects on human health can be:

- *acute* results from short-term exposure;
- *sub-chronic* - exposure greater than a few days, but not more than a year;
- *chronic* - the result of exposure over a period of more than a year, or over a lifetime.

Short-term effects (acute risks) include headaches, dizziness, nausea, discomfort, skin and eye irritation etc. Chronic risks include cancer, diabetes, leukemia, asthma [1].

A variety of methods and appropriate software are applied for risk assessment, some recommended by the European Food Safety Authority (EFSA), others by the United States Environmental Protection Agency [11, 12].

3.1. Human health risk assessment by quantitative analysis of USEPA

Human health risk assessment is the process of estimating the nature and likelihood of adverse health effects from short-term or lifetime exposure to certain chemicals. USEPA proposed quantitative human health risk assessment analysis based on answers to the following questions [12]:

- what kind of health problems occur when pesticides are present in the environment?
- what is the probability that people will have health problems when exposed to different levels of pesticides?
- is there a level below which certain substances do not pose a risk to human health?
- which pesticides are people exposed to and for how long?

- are there legal limits for pesticide residues in food that protect human health?

- are people likely to be more sensitive or exposed to pesticides due to age, genetics, health, gender, job, what they eat?

The application of this method follows the 4 stages of risk assessment.

1. Identification of hazards includes: identifying the possible threats arising from the activity of spraying plant products with pesticides; identifying the factors that can generate risk and the properties of pesticides that can present a potential danger to human health. At this stage, it is identified whether the pesticides are carcinogenic, mutagenic or neurotoxic. Information on the characteristics of pesticides can be found at international organizations such as: JMPR, WHO - International Agency for Research on Cancer (IARC), European Union database and IRIS - Integrated Risk Information System database.

2. Dose-response assessment: means the determination of the degree and routes of exposure to pesticides, and the duration or frequency of exposure to pesticides. People are exposed to pesticides both during their manufacture, during application to agricultural crops, when plant products are harvested and consumed. Exposure to pesticide residues is assumed to be five orders of magnitude greater than other routes of exposure. Fruits and vegetables are frequently eaten raw or semi-processed and may contain a higher amount of pesticide residues compared to other foods [27]. Since human exposure to pesticides can be acute or chronic, occupational or non-occupational, deliberate or accidental, a distinction has to be made. In the case of occupational exposure, people involved in the manufacture of pesticides, those who transport and apply pesticides are normally considered to be the most exposed group due to the nature of their work and are therefore at the highest risk of possible acute poisoning. In some situations, exposure to pesticides can occur due to accidental chemical spills, leaks, or faulty spraying equipment. Workers' exposure increases when instructions on how to use pesticides are not heeded, and especially when they ignore rules about the use of personal protective equipment and hygiene practices, such as washing hands after handling pesticides or before eat [25].

3. Exposure assessment: can be influenced by several factors: weather conditions, type of pesticide formulation, those in liquid form are prone to splashing and occasionally spillage, lead to direct skin contact or indirect skin contact through contamination of clothing. Solids can generate dust while being loaded into application equipment, resulting in face and eye exposure and also respiratory hazards. The type of packaging can also affect the size of cans, bottles or other liquid containers can affect the potential for leakage and splashing. In addition, the frequency and duration of pesticide handling, both seasonally and over a lifetime, affect exposure. In particular, the exposure of a farmer who applies a pesticide once a year is lower than that of a commercial applicator who normally applies a pesticide for several consecutive days or weeks in a season [25]. Exposure estimation is carried out by determining the average daily dose calculated by population category expressed in mg/kg/day (Eq. 1):

$$\textit{Average daily dose} = \textit{pesticide residual concentration x consumption rate/body weight} \quad (1)$$

Certain pesticides could present an acute hazard, in which case the establishment of an acute reference dose - ARfD for all compounds is considered. ARfD is an estimate of the amount of a substance in food (mg/kg/body) that can be ingested in a short period of time (during a meal, a day), without the consumer being subject to risks significant for his health [28]. Analysis of chronic exposure to pesticides involves determining the estimated amount of food (mg/kg/body/day) that can be consumed without significant health risks throughout life. This represents the acceptable daily intake (ADI) [29]. In the analysis of chronic exposure to pesticides, the acceptable daily dose (ADI) is established, which represents the estimated amount of food that can be consumed without significant risk to health throughout life. It is expressed in mg/kg/body/day [29].

4. Risk characterization

It is the stage whose purpose is to compare the exposure estimation results with the exposure estimation results.

● *Hazard coefficient*

To assess the risk to human health, it is necessary to determine the hazard coefficient (HQ), which represents the ratio between the average daily dose (ADD) and the corresponding reference dose, which can be calculated using Eqs. (2) or (3), as appropriate [29].

For short-term exposure (Eq. 2):

$$aHQ = \frac{\mathrm{ADD}}{\mathrm{ARfD}} \quad (2)$$

For long-term exposure (Eq. 3):

$$cHQ = \frac{\mathrm{ADD}}{\mathrm{ADI}} \quad (3)$$

Risk magnitude can be interpreted depending on the HQ values, according to Table 1.

Exposure to two or more pesticides can lead to cumulative effects. By adding the hazard coefficients, the hazard index is determined. The hazard index is a measure of the potential risk of adverse effects on human health for a mixture of substances. The hazard index can be calculated by Eq. (4).

$$HI = \sum_{n=1}^{i} HQn \tag{4}$$

Table 1. Interpretation of hazard ratios

Hazard coefficient	*Interpretation*
HQ < 1	unlikely adverse effects
HQ>1	probable adverse effects
HQ>10	high chronic risk

● *Hazard Index (HI)*

3.2. Pesticide residue consumption model (PRIMo) developed by the European Commission for Food Safety (EFSA)

In 2006, the European Food Safety Authority (EFSA) developed a risk assessment tool in the form of an Excel document (EFSA PRIMo - Pesticide Residue Consumption Model) for the examination of approximately 90,000 temporary maximum residue levels of some chemical substances according to the criteria set out in Article 24 of Regulation (EC) No 365 (2005).

The purpose of the model is to estimate short-term (acute) and long-term (chronic) exposure to pesticide residues, for different groups of consumers (children, adults, elderly) and to compare these values with toxicological reference values, if possible thus identifying potential risks for consumers. In 2007, the model was revised (EFSA PRIMo version 2) including additional features that allowed more calculations in accordance with the internationally agreed risk assessment methodology of the Joint Meeting on Pesticide Residues [30].

Exposure calculations using the PRIMo model version 2 are based on food consumption data for the crops/food commodities listed in Annex I of Regulation (EC) No. 396/2005. This consumption data was provided by 14 EU Member States for use in pesticide risk assessment. The spreadsheet for entering the input values (ie the residue concentrations to be assessed) has been structured in such a way as to be compatible with the food classification set out in Annex I to Regulation (EC) No. 396, 2005), which was in force in 2007.

The PRIMo model is intended to [30]:

- support risk assessors in conducting risk assessments in a transparent manner;
- provide risk managers with the relevant information necessary for making risk management decisions regarding the establishment or modification of legal

limits and risk management decisions that must be made within the application of the maximum residue level;

• be easy to handle, based on standard tools (Excel) that do not require specific IT expertise of the user;

• perform risk assessments in a standardized way required for EU-wide regulatory questions and also allow flexibility to calculate non-standard risk assessment scenarios.

For risk calculation there are necessary the following data: concentrations of pesticide residues in vegetables and fruits, ARfD and ADI values for each identified pesticide. In long-term (chronic) risk assessment, calculated exposure values are compared to the acceptable daily intake (ADI) value which is the maximum allowable amount of a chemical that can be consumed over a long period of time without causing adverse health effects. For short-term (acute) risk assessment, the acute reference dose (ARfD) is used to identify possible risks to consumer health. The ARfD value represents the concentration of a chemical that can be ingested in a short period of time (one meal, one day) without producing considerable risks.

3.2.1. Calculation of acute exposure

For the calculation of short-term exposure, the estimated international short-term consumption (IESTI) is calculated, and four different situations are distinguished for the calculation of the IESTI value, each with a specific mathematical method [31, 32]:

Case 1:

The concentration of residues in composite samples from residue studies corresponds more or less to the residue in a portion (meal size) of the product, (unit weight is <25 g) (Eq. 5):

$$IESTI = LP \times (HR\ or\ HR\text{-}P)] / bw \tag{5}$$

where: *IESTI* – estimated short-term international consumption; *LP* = highest reported portion (97.5% of consumption data) (kg/day); *HR* = maximum level of residues in composite samples from the consumption portion, found in residue studies (mg/kg); *HR-P* = maximum residue level, if crop processing is taken into account (mg/kg); *bw* = body weight;

Case 2:

Some of the fruit or vegetables may contain a higher amount of residue than the composite samples from the residue studies (unit weight > 25 g). A variability factor is therefore introduced (a standard factor or based on available data on residues in separate pieces of fruit or vegetables).

Case 2a

This refers to unit weights that are less than the largest part (LP) (Eq. 6).

$$IESTI = [\{U \times (HR\ or\ HR\text{-}P) \times v\} + \{(LP - U) \times (HR\ or\ HR\text{-}P)\}]/bw \qquad (6)$$

where: U = unit weight of portion consumed (g), provided by the country from which the LP was reported; v - variability factor.

If sufficient separate-unit residual data are available to obtain a separate-unit *HR*, this value should be entered into the first part of the equation without the variability factor. The *HR* value derived from composite samples should then be used in the second part.

Case 2b

In case of the unit weight greater than the largest portion, it is applied Eq. (7).

$$IESTI = LP \times (HR\ or\ HR\text{-}P)] \times v/bw \qquad (7)$$

If sufficient separate-unit residue data are available to obtain a separate-unit HR, this value should be entered into the equation without the variability factor.

Case 3

This refers to processed products that have been combined or mixed; the *STMR-P* value represents the highest residue concentration (Eq. 8).

$$IESTI = LP \times STMR\text{-}P/bw \qquad (8)$$

where: *STMR-P* = median residue of supervised study, in which crop processing is taken into account (mg/kg);

Short-term exposure was calculated for all consumer groups for which food consumption data were presented in the development of the PRIMo model. If an *ARfD* value was established for the active substance in question, the exposures calculated for the highest measured residue were expressed as a percentage of the *ARfD* (Eq. 9).

$$\%\ ARfD = IESTI/ARfD \times 100 \qquad (9)$$

3.2.2. Calculation of chronic exposure

Chronic or long-term exposure assessment consists of calculating the expected exposure value of an individual over his entire lifetime. EFSA calculated the long-term exposure with a deterministic model, analogous to the calculation of the theoretical maximum daily dose [31]. Calculation formula for TMDI (Eq. 10):

$$TMDI = \sum MRLi \times Fi \tag{10}$$

where: *TMDI* = theoretical maximum daily consumption; *MRLi* = maximum residual level of a certain product (mg/kg); *Fi* = corresponding national consumption of the product in question per person (kg/day).

If the *TMDI* is found to exceed the *ADI* value of one or more diets, the IEDI value (international estimate of daily) is determined in which the processing data is included and the STMR (median) is considered as the residue level instead of the maximum level of residues (Eqs. 11-12).

$$IEDI = \sum STMRi \times Ei \times Pi \times Fi \tag{11}$$

where:*IEDI* = international estimated daily consumption; *STMRi* = median level of residues at the level of a supervised study of a certain product (mg/kg); *Ei* = the factor for the edible product separated from the respective product; *Pi* = processing factor of the respective product; *Fi* = the corresponding national consumption for the product in question per person;

$$\%\,ADI = [TMDI/(ADI \times 100)] \times 100 \tag{12}$$

The results of both short-term and long-term exposure estimation are expressed as a percentage of *ARfD* or *ADI*, as appropriate, and can be interpreted as follows:

- If the values expressed as % *ARfD* and % *ADI* are < 100 %, then pesticide residues do not pose a risk;

- If the values expressed as % *ARfD* and % *ADI* are > 100 %, then the pesticide residues pose a risk to human health.

4. Case study: Identification of risks to human health generated by the presence of pesticides in plant products through quantitative analysis (USEPA method)

4.1. Input data

To calculate the risk to human health, a series of input data is required: the residual concentration of the pesticides identified in fruits and vegetables, the consumption rate for each fruit or vegetable in the acute case, the age categories for which the risk is calculated (children, adolescents, adults, elderly people, people over 75 years of age), reference dose for both short-term exposure (*ARfD*) [33]. These data are presented in Tables 2 - 5. The evaluation was carried out according to the procedure described in the section 5. The data on the concentration of pesticides in vegetable products were taken from the public *Report on the national plan for monitoring pesticide residues in fruits, vegetables and cereals, from domestic production*, since 2016 issued by the National Phytosanitary Authority [35].

Table 2. Input data required for risk calculation*

Fruits vegetables	***Pesticides***	***Pesticide concentration (mg/kg)***	***MRL (mg/kg)***	***ARfD (mg/kg/ /body)***	***ADI (mg/kg/body/ /day***
Strawberries – Iasi area, Romania	Tebuconazole	0.183	0.02	0.03	0.03
	Dimethoate	0.432	0.02	0.01	0.001
	Azoxystrobin	0.122	10	not applicable *ADI*-0.2 is taken into account	0.2
	Propiconazole	0.037	0.05	0.3	0.04
	Chlorothalonil	0.43	4	0.6	0.6
	Penconazole	0.021	0.5	0.5	0.03
Apples – Dâmbovița area, Romania	Dimethoate	0.454	0.02	0.01	0.001
	Carbendazim	0.253	0.2	0.02	0.02
Salad dale	Chlorothalonil	15,435	0.01	0.6	0.6
	Tebuconazole	0.018	0.5	0.03	0.03
	Iprodione	0.118	25	not applicable ADI 0.06 is taken into account	0.06
Potatoes - Olt	Carbendazim	1,241	0.1	0.02	0.02
	Methyl Thiophanate	1,377	0.1	0.2	0.08
	Chlorpyrifos-methyl	0.021	0.05	0.1	0.01

*MRL- the maximum permissible limit established by the legislation of the European Union * from Minut et al. [34] under the terms and conditions of the Creative Commons Attribution (CC BY) license*

Table 3. Population/age categories considered [36]

Age	***Weight (kg)***
3- 10 years	23.1
10-14 years	43.4
14-18 years	61.3
18-65 years	73.9
65-75 years	76
>75 years	71.2

Table 4. Consumption rates of strawberries, apples, lettuce and potatoes according to the age categories of the population considered [31, 32]

Age categories	***Consumption rate (acute case) g/pers.***			
	Strawberries	***apples***	***Salad***	***Potatoes***
3-10 years	126.67	134.74	75	194.98
10-14 years	203.60	156.23	140.22	186.29
14-18 years	203.60	156.23	140.22	186.29
18-65 years	235.90	184.46	124.69	185.40
65-75 years	320.00	191.81	105.74	176.11
>75 years	30	172.91	129.25	167.25

Table 5. Consumption rates of strawberries, apples, lettuce and potatoes according to the age categories of the population considered [31, 32]

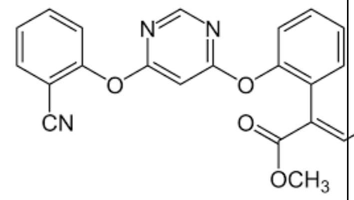
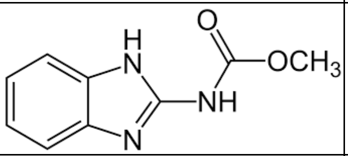
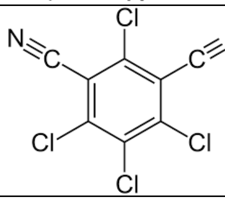
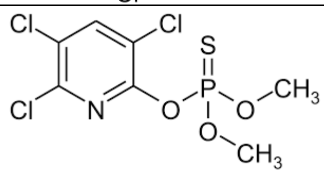
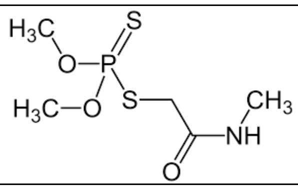
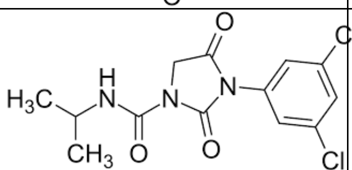
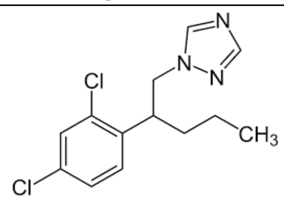
Age categories	***Consumption rate (chronic case) g/pers.***			
	Strawberries	***apples***	***Salad***	***Potatoes***
18-65 years	54.76	69.03	30.77	82.14
65-75 years	114.29	77.64	27.19	91.20
>75 years	4.29	65.87	33.85	78.90

4.2. Identification of hazards

According to ANF [35], the samples of tested vegetables and fruits are taken from supermarkets, silos and markets. In the case of strawberries, 6 types of pesticides were identified: chlorothalonil, dimethoate, penconazole, propiconazole, tebuconazole, azoxystrobin. Two of these pesticides were observed to exceed the maximum permissible limit, namely chlorothalonil and azoxystrobin. In the case of apples, 2 pesticides were found: dimethoate, carbendazim, both exceeding the maximum permissible limit. The pesticides identified in the lettuce were: chlorothalonil with an extremely high concentration of 15.435 mg/kg, against the MRL value of 0.01 (mg/kg), tebuconazole and iprodione. In the case of potatoes, three types of pesticides were identified: carbendazim, thiophanate methyl and chlorpyrifos-methyl. Two of these pesticides were observed to exceed the maximum permissible limit namely carbendazim and methyl thiophanate (Table 2).

Each type of pesticide identified in the fruits and vegetables considered for risk estimation is briefly described in Table 6 together with the effects associated with each pesticide identified (Table 7) according to literature data.

Table 6. Characteristics of pesticides identified in strawberries, apples, lettuce and potatoes

Trade name	***Active substance***	***Chemical structure***	***Group of chemical compounds***	***Use***
Ortiva	**Azoxystrobin 250g/L**		strobilurins	fungicide Strobilurine
	Carbendazim		benzimidazole	fungicide
Well done 500	**Chlorothalonil 500g/L**		chloronitriles	fungicide
RELDAN	**Chlorpyrifos-methyl 225 g/L**		organophosphate	insecticid, acaricide
Novadim Progress	**Dimethoate 400g/L**		organophosphate	insecticide and acaricide
	Iprodione		dicarboximides	fungicide
Topas 100 EC	**Penconazole 100g/L**		triazoles	fungicide

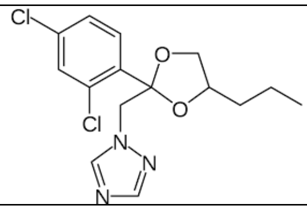
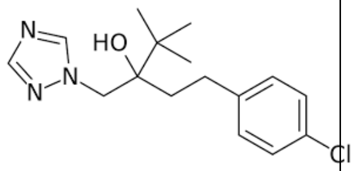
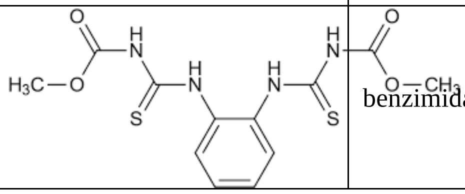
Tilt 250	**Propiconazole 250g/L**		triazoles	fungicide
Tebucur	**Tebuconazole 250g/L**		triazoles	fungicide
Thiophanate methyl 500	**Thiophanate metil 500g/L**		benzimidazole	fungicide

Table 7. Long-term effects associated with identified pesticides [37]

Pesticides	***Health problems associated with pesticides***		
	Carcinogenic	***Mutagenic***	***Neurotoxic***
Azoxystrobin	no	no	no
Carbendazim	no	yes	no
Chlorothalonil	Cf. IARC possibly carcinogenic	no	no
Chlorpyrifos-methyl	no	no	yes
Dimethoate	no	no	no
Iprodione	no	no	no
Penconazole	no	no	no
Propiconazole	no	no	no
Tebuconazole	no	no	no
Methyl thiophanate	no	yes	no

IARC- International Agency for Research on Cancer

4.3. Dose-response assessment

The assessment of the dose-response relationship is carried out by determining the average daily dose which is calculated for each pesticide using Eq. (2) results in Table 8.

4.4. Exposure assessment

At this stage, the reference dose established for each pesticide is taken into account, in the case of short-term exposure - ARfD, respectively ADI - in the case of long-term exposure [15]. ARfD and ADI values can be found in Table 2.

Table 8. Dose response assessment

average daily dose aDD, mg/kg/day.10^3 **Pesticide**	***Children 3 - 10 years***	***Adolescents 10 - 14 years***	***Adolescents 14 - 18 years***	***People 18 - 65 years***	***People 65 - 75 years***	***People >75 years:***
Strawberries, short-term (acute) exposure						
Tebuconazole	1.0034	0.8585	0.60781	0.5842	0.7705	0.0077
Dimethoate	2.3688	2.0266	1.4348	1.3790	1.8189	1.9415
Azoxistrobin	0.8804	0.5723	0.4052	0.3894	0.5137	0.0514
Propiconazole	0.2029	0.1735	0.1229	0.1181	0.1558	0.0156
Chlorotalonil	2.3579	2.0172	1.4281	1.3726	1.8105	0.1812
Penconazole	0.1152	0.0985	0.0695	0.0671	0.0884	0.0088
Apples, short-term (acute) exposure						
Dimethoate	2.6481	1.6342	1.1570	1.1332	1.1458	1.1025
Carbendazim	1.4757	0.9108	0.6448	0.6315	0.6385	0.6144
Salad, short-term (acute) exposure						
Chlorotalonil	50.1130	49.8680	35.3060	26.0430	21.4740	28.0190
Tebuconazole	0.0584	0.0582	0.0417	0.0304	0.02504	0.03268
Iprodione	0.3831	0.7163	0.2699	0.1999	0.1642	0.2140
Potatoes, short-term (acute) exposure						
Carbendazim	10.4740	53.2680	3.7713	3.1134	2.8756	2.9151
Thiophanate-methyl	11.6220	5.9106	4.1846	3.4546	3.1908	3.2345
Chlorpyrifos-methyl	0.1772	0.0902	0.0638	0.0527	0.0487	0.0493
Strawberries, long-term (chronic) exposure						
Tebuconazole				0.1356	0.2752	0.0125
Dimethoate				0.3201	6.4964	0.0297
Azoxistrobin				0.0940	0.1835	0.0084
Propiconazole				0.0274	0.5564	0.0025
Chlorotalonil				0.3186	0.6466	0.0029
Penconazole				0.0156	0.0316	0.0014
Apples, long-term (chronic) exposure						
Dimethoate				0.0424	0.4637	0.4200
Carbendazim				0.2363	0.2584	0.2340
Salad, long-term (chronic) exposure						
Chlorotalonil				6.4267	5.5220	7.3381
Tebuconazole				0.0749	0.0064	0.0086
Iprodione				0.4913	0.0422	0.0561
Potatoes, long-term (chronic) exposure						
Carbendazim				1.3793	1.4892	1.3752
Thiophanate-methyl				1.5306	1.6524	1.5259
Chlorpyrifos-methyl				0.0233	0.0252	0.0024

4.5. Risk characterization

At this stage, the risk can be determined by calculating the hazard coefficient (HQ) according to Eqs. (3 - 4), followed by the calculation of the hazard index (HI) based on Eq. (5), resulting in Table 9.

Table 9. The hazard coefficient (HQ) calculated according to Eqs. (3 - 4)

HQ / *Pesticide*	*Children 3 - 10 years*	*Adolescents 10 - 14 years*	*Adolescents 14 - 18 years*	*People 18 - 65 years*	*People 65 - 75 years*	*People >75 years:*
Strawberries, short-term (acute) exposure						
Tebuconazole	0.0334	0.0286	0.0202	0.0194	0.0256	0.0025
Dimethoate	0.2368	0.2026	0.1434	0.1379	0.1818	0.1941
Azoxistrobin	0.0044	0.0028	0.0020	0.0019	0.0025	0.0002
Propiconazole	0.0006	0.0005	0.0004	0.0003	0.0005	0.00005
Chlorotalonil	0.0039	0.0033	0.0023	0.0022	0.0030	0.0003
Penconazole	0.00023	0.00019	0.00013	0.0001	0.00017	0.000017
aHI	0.279	0.238	0.168	0.162	0.213	0.197
Apples, short-term (acute) exposure						
Dimethoate	0.2648	0.1634	0.1157	0.1133	0.1145	0.1102
Carbendazim	0.0737	0.0455	0.0322	0.0315	0.031	0.030
aHI	0.338	0.0455	0.147	0.144	0.146	0.140
Salad, short-term (acute) exposure						
Chlorotalonil	0.0835	0.831	0.0588	0.0434	0.0357	0.0466
Tebuconazole	0.0019	0.0019	0.0013	0.0010	0.0008	0.0010
Iprodione	0.0063	0.0119	0.0044	0.0033	0.0027	0.0035
aHI	0.091	0.0969	0.064	0.0477	0.039	0.0511
Potatoes, short-term (acute) exposure						
Carbendazim	0.5237	0.2663	0.1885	0.1556	0.1437	0.1457
Thiophanate-methyl	0.058	0.0295	0.0209	0.0172	0.0159	0.0161
Chlorpyrifos-methyl	0.0017	0.0009	0.0006	0.0005	0.00048	0.00049
aHI	0.583	0.296	0.21	0.173	0.160	0.162
Strawberries, long-term (chronic) exposure						
Tebuconazole				0.00452	0.0091	0.0004
Dimethoate				0.3201	0.649	0.029
Azoxistrobin				0.0004	0.0009	0.00004
Propiconazole				0.0006	0.0013	0.00006
Chlorotalonil				0.0212	0.00431	0.0019
Penconazole				0.0005	0.0010	0.00004
cHI				0.347	0.705	0.031
Apples, long-term (chronic) exposure						
Dimethoate				0.424	0.464	0.42
Carbendazim				0.0118	0.0129	0.0117
cHI				0.435	0.476	0.431
Salad, long-term (chronic) exposure						
Chlorotalonil				0.4284	0.368	0.489

Tebuconazole				0.0002	0.00002	0.0028
Iprodione				0.0008	0.0007	0.0009
				0.429	0.369	0.491
Potatoes, long-term (chronic) exposure						
Carbendazim				0.0689	0.0744	0.0190
Thiophanate-methyl				0.0191	0.0206	0.0190
Chlorpyrifos-methyl				0.0023	0.0025	0.0023
cHI				0.0903	0.0975	0.0891

4.6. Interpretation of results

The results of the human health risk assessment using the USEPA method in both acute and chronic cases are presented below:

4.6.1. The acute case

- **The case of strawberries**

After carrying out the necessary calculations to identify the risks to human health, in the case of strawberries, it can be observed that no pesticide poses a risk for any age category, with hazard coefficients having values lower than 1, even if the residual concentrations of some pesticides exceeded the maximum allowed residual limit (for example dimethoate which had a value of 0.432 mg/kg compared to the maximum allowed residual limit of 0.02 mg/kg). The values of the hazard coefficient related to dimethoate show a significant value for all age categories taken into account, with the highest value of 0.236 for children aged between 3 and 10 years. Also, tebuconazole exceeded the maximum allowed residual limit with a value of 0.183 mg/kg compared to what is allowed, i.e. 0.02 mg/kg, the hazard coefficients having a more significant value associated to the rest of the pesticides in strawberries, but not higher than the dimethoate values.

- **The case of apples**

In the case of apples, after carrying out the necessary calculations to identify the risks to human health, it was found that no pesticide poses a risk, the values of the hazard coefficients being below the value of 1. Both dimethoate and carbendazim exceeded the maximum residual limit allowed have values of 0.454 mg/kg, respectively 0.253 mg/kg. The values of the hazard coefficients calculated for dimethoate have more significant values compared to carbendazim for all categories, with the highest value of 0.264 for children between 3-10 years.

- **The case of the salad**

3 pesticides were identified in lettuce: chlorothalonil, tebuconazole, iprodione and only chlorothalonil exceeded the maximum allowed residual limit of 0.01 mg/kg, having a concentration of 15.435 mg/kg in lettuce. Following the calculations performed to identify the risks, in the case of lettuce it can be observed that the values of the hazard coefficients are values lower than 1, which means, according to their interpretation, that no pesticide poses a risk. The pesticide that exceeded the maximum allowed residual limit, namely chlorothalonil, has more significant hazard coefficient values compared to the other pesticides for all age categories, with the highest value of 0.08 for children between 3 – 10 years old.

- **The case of potatoes**

According to the calculations made to identify the risks to human health, in the case of potatoes it was found that no pesticide presents a risk, all the values of the hazard coefficients being lower than 1, but nevertheless the pesticides that have exceeded the maximum allowed residual limit have higher values significant compared to the rest of the pesticides. The pesticide carbendazim has a concentration of 1.24 mg/kg in potatoes, compared to the maximum allowed residual limit of 0.1 mg/kg, and after calculating the hazard coefficients for all categories, for the category of children aged between 3 - 10 years, the hazard coefficient has the highest value of 0.52 compared to the others.

4.6.2. The chronic case

- **The case of strawberries**

After carrying out the calculations regarding the identification of risks in the chronic case, it was found that no pesticide poses a risk, the hazard coefficients having values lower than 1, but it can be observed that the hazard coefficient values calculated for the dimethoate pesticide present significant values compared to the other calculated hazard coefficients, with the highest value of 0.65 for people aged 65 - 75 years.

- **The case of apples**

After carrying out the calculations regarding the identification of risks, it can be observed that in the case of apples, no pesticide poses a risk, all the values of the hazard coefficients being lower than 1, but it can be noted that dimethoate, which presented a concentration well above the maximum allowed residual limit shows more significant values for all age categories, but with the highest value for people aged 65 - 75 years of 0.47.

- **The case of the salad**

Of the three pesticides found in salad, only chlorothalonil displayed a concentration of 15.435 mg/kg compared to the maximum residual limit allowed of 0.01 mg/kg. Therefore, the hazard coefficients calculated for chlorothalonil have significant values for all age categories compared to the other pesticides, with the highest value of 0.49 for people older than 75 years. However, the values of the hazard ratios are less than 1, which means that no pesticide poses a risk.

- **The case of potatoes**

In the case of potatoes, three pesticides were identified. Two of them having concentrations of 1.241 mg/kg for carbendazim, respectively 1.377 mg/kg for thiophant methyl, exceed the maximum allowed residual limit of 0.1 mg/kg. The values of the hazard coefficients are lower than 1, but for the pesticide carbendazim, the most significant values corresponding to the hazard coefficients were obtained, with the highest value for the population category 65 - 75 years of 0.075.

Conclusions

The development of society implicitly led to the development of the pesticide industry, necessary for the elimination of pests present in agricultural crops. In addition to the benefits they bring, they can pose risks to human health, as the population can be exposed to pesticides through inhalation, dermal contact or ingestion. The effects of pesticides on human health are highly variable, they can appear after a few days and be immediate in nature (acute effects) or take months or years to manifest (chronic effects) and some people may be more sensitive to the effects of pesticides than others.

The evaluation of the risk to human health goes through a series of stages and by using the calculation methods the risks to human health due to exposure to pesticides can be identified and thus a series of measures can be taken to reduce the identified risks.

In order to identify the risks to human health, we took into account both fruits and vegetables, in which up to six pesticide residues were found, some exceeding the maximum allowed residual limits. This was performed by applying the USEPA method and the results showed that the pesticides found did not pose any risks on human health, but in the acute case it was observed that children aged between 3 - 10 years are more prone to risk, and in the chronic case it is observed that the people prone to risk are those aged between 65 - 75 years.

Following the application of the USEPA method we can conclude that if the concentration of the pesticide in the respective fruit/vegetable is higher, the higher the probability of the occurrence of the risk. As a result of food consumption by the human population during a day/week/ month differs, pesticide concentrations can accumulate and inevitably lead to the appearance of effects either in the short term or over a longer period of time.

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