IA GRANJA: Revista de Ciencias de la Vida

pISSN:1390-3799; eISSN:1390-8596

http://doi.org/10.17163/lgr.n36.2022.10

#### Scientific paper/ Artículo científico

FOOD SCIENCE



0

# RISKS OF CHEMICAL CONTAMINATION IN MILK AND ITS DERIVATIVES

### RIESGOS DE CONTAMINACIÓN QUÍMICA EN LECHE Y SUS DERIVADOS

Sixto Reyna\* and José Arteaga

Veterinary Department, Veterinary Medicine Career, Universidad Técnica de Manabí, Zip Code 130103, Portoviejo, Ecuador.

\*Corresponding author: sixto.reyna@utm.edu.ec

Received on November 10th, 2020. Accepted, after review, on October 19th, 2021.

#### Abstract

Milk is a complete and balanced food that, along with its derivatives, represent important components of a healthy diet for the population, since they provide proteins, lipids, carbohydrates, vitamins, minerals and bioactive compounds. However, these foods are susceptible to contamination by a wide variety of chemical products, whose presence beyond certain established legal limits determines a chronic intake of small doses of these compounds. By accumulating in the body, and depending on their toxicity, they have the potential to cause serious affections in various organs and systems, constituting a major public health problem. This review seeks to describe the entry of chemical contaminants (aflatoxins, veterinary drug residues, dioxins, polychlorinated biphenyls, dioxin analogues, disinfectants and detergents) into the food chain, as well as the potential effects on consumer health, the Maximum Residue Limits of these contaminants established for bovine milk and the most frequent methods used for their detection. On this basis, measures are proposed to avoid this type of contamination in dairy products, whose quality is closely related to the conditions of the surrounding environment, associated with anthropogenic activities, agricultural practices, animal production and processing conditions.

Keywords: Foods, Bovine, Milk, Safety, Toxicity

#### Resumen

La leche es un alimento completo y equilibrado que, junto a sus derivados, son componentes importantes de una dieta saludable en amplios sectores de la población, pues suministran proteínas, lípidos, hidratos de carbono, vitaminas, minerales y compuestos bioactivos. Sin embargo, estos alimentos son susceptibles de contaminación a partir de una amplia variedad de productos químicos, cuya presencia más allá de ciertos límites legalmente establecidos, determina una ingesta crónica de pequeñas dosis de estos compuestos. Al acumularse en el organismo, y en función de su toxicidad, tienen el potencial de ocasionar severas afecciones en diversos órganos y sistemas, constituyendo un importante

problema de salud pública. Esta revisión busca describir el ingreso de contaminantes químicos (aflatoxinas, residuos de fármacos veterinarios, dioxinas, bifenilos policlorados, análogos a las dioxinas, desinfectantes y detergentes) a la cadena alimenticia, así como los potenciales efectos sobre la salud del consumidor, los Límites Máximos de Residuos de estos contaminantes establecidos para la leche bovina y los métodos más frecuentes utilizados para su detección. En base a esto, se plantean medidas tendentes a evitar este tipo de contaminación en productos lácteos, cuya calidad está estrechamente relacionada con las condiciones del medio circundante, que a su vez se asocia con actividades antropogénicas, prácticas agrícolas, de producción animal y condiciones de procesamiento.

Palabras clave: Alimentos, Bovino, Leche, Inocuidad, Toxicidad

Suggested citation: Reyna, S. and Arteaga, J. (2022). Risks of chemical contamination in milk and its derivatives. *La Granja: Revista de Ciencias de la Vida.* [Early Access] http://doi.org/10.17163/ lgr.n36.2022.10.

Orcid IDs:

Sixto Reyna: http://orcid.org/0000-0002-3950-9993 José Arteaga: http://orcid.org/0000-0002-2929-0940

## **1** Introduction

Milk is a white liquid secreted by breasts of mammals to feed their offspring (RAE, 2019). With an estimated production of 522 million metric tons in 2019, bovine milk is the most consumed by the population (85%), although in some regions there is significant consumption of buffalo milk (11%) and other ruminants (3.9%) (Kalyankar et al., 2016; STA-TISTA, 2020). In all latitudes, dairy products are susceptible to chemical contamination (OMS, 2018; Dimitrieska et al., 2016), which occurs through soils, agricultural practices, dairy production practices and processing (Nguyen and Flint, 2020; Priyanka et al., 2017), becoming an important problem for public health due to 1) several of the chemical agents are highly stable, so are incorporated into the food chain even when their use has been banned for decades, 2) are not susceptible to decrease after the application of physical, chemical or biological treatments of milk, contaminating dairy products, 3) the lipophilic nature of several contaminants determines a cumulative effect on the animal organism and its presence in dairy fat 4) chronic exposure to these pollutants has the potential to severely impair the health of the population (Akhtar and Ahad, 2017; Ismail et al., 2019). Therefore, the set of contaminants in milk and its derivatives will be reviewed in relation to their structural characteristics, in aspects such as their entry into the animal organism, the mechanisms by which they exert harmful effects on health after chronic consumption of dairy

products with concentrations of chemical agents at levels above the maximum residue limits (MRLs) allowed in bovine milk, and which are described in this review. Finally, the aim is also to mention the main methods used for its detection and propose strategies to prevent and control chemical contamination of dairy products.

## 2 Chemical contaminants

#### 2.1 Aflatoxins

Aflatoxins (AF) are widely distributed mycotoxins, which after contaminating crops and entering the food chain affect animal health and productivity and food safety in the population by presenting toxic, mutagenic, teratogenic, carcinogenic and immunosuppressive effects (OMS, 2018; Dimitrieska et al., 2016; Ayar et al., 2007).

Although more than twenty types of AF have been reported (Nguyen and Flint, 2020), AFB1, AFB2, AFG1 and AFG2 are the main mycotoxins related to dairy contamination. AFB1 and AFG1 differ structurally from AFB2 and AFG2 with an additional dual link. On the other hand, AFG have a furan ring, while AFB have a lactone ring. Depending on their degree of toxicity and carcinogenicity, the following order is found: AFB1 > AFG1 > AFB2 > AFG2, whose structures are shown in Figure 1 (AE-COSAN, 2015).



Figure 1. Molecular structure of B and G aflatoxins (AECOSAN, 2015)

LA GRANJA: *Revista de Ciencias de la Vida* Universidad Politécnica Salesiana, Ecuador.

Aflatoxin B1 (AFB1) is produced by fungi, particularly *Aspergillus flavus* and *Aspergillus parasiticus* (Van der Fels-Kler and Camenzuli, 2016; Duarte et al., 2013). *A. flavus* colonizes mainly the aerial parts of the plants, being found in stored foods such as peanuts, corn and cotton seeds. *A. parasiticus* is found mainly in the soil and has a similar distribution to *A. flavus*, but is rarely seen in maize (Van Asselt et al., 2016; IARC, 2002). Although temperature and humidity are the main factors affecting the presence of AF in food, international transport of agricultural products determines that no region of the planet is free from it (IARC, 2002).

In the liver tissue of ruminants, AFB1 is metabolized to aflatoxin M1 (AFM1), which is secreted into urine, feces and milk, mainly within 48 hours of contaminated food consumption, reducing to undetectable levels 96 hours later (Marchese et al., 2018; Nguyen and Flint, 2020). Transfer rates from AFB1 to AFM1 in milk have been estimated from 0.3% to 6.2% (Vaz et al., 2020), being maize and other contaminated concentrated foods the main sources of AFM1 in raw milk (Fink, 2008), which in turn is the main introducer of this aflatoxin in the human diet (Dimitrieska et al., 2016; Duarte et al., 2013; Vaz et al., 2020). AFM1 is hardly affected by pasteurization (Neagu et al., 2009), found in pasteurized milk (Van Asselt et al., 2016), ultra-pasteurized milk (UHT) (Duarte et al., 2013), cheese (Urbán et al., 2009) and yogurt (Rahimirad et al., 2014).

Although a tolerable daily intake (TDI) has not been specified for AFM1, the European Union has established its MRL at 0.05  $\mu$ g/L for raw milk, pasteurized milk, and milk used in the manufacture of dairy products, and 0.025  $\mu$ g/L for infant formula and diet foods; whereas in the United States, China and Brazil the MRL for AFM1 in milk is 0.5  $\mu$ g/L. Although maximum AF levels are regulated in more than 80 countries, there is no international equality (Nguyen and Flint, 2020; Akbar et al., 2019; Vaz et al., 2020; Rahimirad et al., 2014).

Due to the stability, toxicity and MRL allowed for AF, particularly AFM1, their quantification is extremely important. In this sense, enzyme-linked immunosorbent assay (ELISA) is commonly used for screening purposes, while high-performance liquid chromatography (HPLC) with fluorescence detection or mass spectroscopy is frequently used for the identification and quantification of AF in food (Vaz et al., 2020; Rahimirad et al., 2014).

Crop rotation, prevention of infestations and grain deterioration, the use of resistant seed varieties, low moisture crops, the promotion of dehydration, proper storage and transport of grains and monitoring of FA in food have been considered to reduce fungal contamination and FA production in food (Van Asselt et al., 2016; IARC, 2002). Although it is impossible to completely prevent milk contamination (Ayar et al., 2007), limiting dairy cattle access to food with high concentrations of AFB1 helps prevent milk contamination (Dimitrieska et al., 2016; Ayar et al., 2007). On the other hand, the application of physical, chemical and biological methods as alternatives for reducing the milk content of AFM1 is questionable and poses an additional risk to food safety (Nguyen and Flint, 2020; Rahimirad et al., 2014).

## 2.2 Residues of veterinary drugs

#### Antibiotics

Antibiotics have been used as promoters of animal growth and disease prevention and treatment (Albright et al., 1961; Sachi et al., 2019). Noncompliance with milk withdrawal times, use of non-prescribed antibiotics, their use as food additives and a limited or non-existent monitoring system, among other factors, determine MRLs higher than legally established antibiotic residue (AR), which represents a serious threat to public health, especially of vulnerable age groups, and contributing to the emergence of microbial resistance (Priyanka et al., 2017; Albright et al., 1961; Kurjogi et al., 2019; Sachi et al., 2019). Screening and confirmatory methods are used for the detection of AR in milk, the former include bacterial growth inhibition assays, receptor binding enzyme assays and immunoassays (Navrátilová, 2008; Padol et al., 2015), while chromatographic tests are confirmatory, offering greater sensitivity, specificity and quantification of the analyte (Priyanka et al., 2017; Sachi et al., 2019).

Measures to reduce the concentration of RA in dairy products have been proposed, such as the education of the dairy farmer, strict compliance with the milk withdrawall time (Albright et al.,

1961), the use of adequate techniques for the detection of AR in dairy (Priyanka et al., 2017; Sachi et al., 2019), the suppression of antibiotics as growth promoters, the adoption of management and hygiene practices during milking and processing of milk, and the minimization of the use of antibiotics or their replacement by probiotics, immunomodulators, organic acids and food supplements (Priyanka et al., 2017; Sachi et al., 2019; Padol et al., 2015; Yang et al., 2019).

#### Anthelmintics

Anthelmintics are used to treat parasitosis of flat worms (tapeworms and trematodes) and round worms (nematodes). Depending on their chemical structure and mode of action, they are mainly classified in benzimidazoles (albendazole, fenbendazole, flubendazole, mebendazole, oxfendazole, thiabendazole, triclabendazole), tetrahydropyrimidines (levamisole, pyrantel, morantel), imidazoles (tetramisol, levamisole) and macrocyclic lactones (abamectin, doramectin, ivermectin, selamectin, moxidectin) (Romero-González et al., 2014).

Incorrect use of anthelmintics contributes to their entry into the food chain, with residues observed in milk (Romero-González et al., 2014; Cerqueira et al., 2014). In this food, the concentration of benzimidazoles is not affected by cooking, cold storage (-18 °C), baking or microwave action (Tsiboukis et al., 2013), while levamisole residues are stable during fermentation processes and heat treatment of serum, remaining in cheese (Whelan et al., 2010). In contrast to thermal treatment, macrocyclic lactones present in milk are partially degraded, which does not happen when they are present in the cream of milk (Avci and Filazi, 2020).

In several species, benzimidazoles have been related with carcinogenic, genotoxic, embryotoxic and teratogenic effects (Romero-González et al., 2014; Tsiboukis et al., 2013; Santos et al., 2019), while ivermectin presents mutagenic and teratogenic effects in several mammals, in addition to an ecotoxic effect (Santos et al., 2019; Pérez-Cogollo et al., 2018). Thus, anthelmintic residues in food represent a public health risk (Padol et al., 2015; Romero-González et al., 2014; Avcı and Filazi, 2020). Table 1 shows the permitted MRLs of various anthelmintics and antibiotics in bovine milk. Furthermore, monitoring veterinary prescriptions, observing withdrawal periods in milk production, following the application of anthelmintics and controlling and monitoring antiparasitic residues contribute to the prevention of their contamination. Chromatographic methods are the most commonly used to identify and confirm the presence of anthelmintics in milk (Cerqueira et al., 2014; Santos et al., 2019).

#### Organochlorine and organophosphate pesticides

Pesticides are "chemical compounds intended to prevent, destroy, attract, fight or control any pest, including unwanted species of plants or animals during the production, storage, transport and process of food, agricultural products or animal food that can be administered to animals for the control of ectoparasites" (FAO/OMS, 2013).

Depending on their ability to enter the food chain, bioaccumulation and toxicity, organochlorine pesticides (OCPs) and organophosphorus pesticides (OPs) stand out as contaminants in milk and milk derivatives, which, despite their progressive prohibition, still represent a risk to public health.

OCPs or chlorinated hydrocarbons are broadspectrum synthetic chemicals that include ethane derivatives such as dichlorodiphenyltrichloroethane (DDT), cyclodienes, including chlordane, aldrin, dieldrin heptachlor, endrin and toxaphene, and hexachlorocyclohexanes (HCH) as lindane (Zaragoza-Bastida et al., 2016).

The main routes of OCP contamination include inadequate management practices, such as the storage of pesticides next to food and fumigation of crops in areas close to dairy farms, causing pesticide deposition in water and food (Bedi et al., 2018), transcutaneous transmission, soil fertilization with residual sludge and the use of animal feed from countries where lindane and DDT are still used (Rusu et al., 2016; Fischer et al., 2016). High environmental stability and liposolubility determine the deposition of OCP in animal tissues especially rich in fat and milk (Zaragoza-Bastida et al., 2016; Rusu et al., 2016), being considered a persistent organic pollutant (POPs) (OMS, 2020). The mobilization of adipose tissue to maintain milk secretion, particularly in grazing-based livestock or in case of malnutrition of livestock, implies that the milk of these these pesticides (Fischer et al., 2016). animals registers an increase in the concentration of

Antimicrobial	MRLs (µg/l)
Amoxicillin	4
Benzylpenicillin	4
Ceftiofur	100
Chlortetracycline/	
oxytetracycline/	100
tetracycline	
Dihydrostreptomycin/	200
streptomycin	
Spiramycin	200
Gentamicin	200
Monensin	2
Neomycin	1500
Pyrithromycin	100
Sulphylendazole	25
Tylosin	100
Anhelmintics	MRLs (µg/l)
Albendazole	100
Doramectin	15
Eprinomectin	20
Febantel/	
Fenbendazole/	100
Oxfendazole	
Ivermectin	10
Thiobedazole	100

Despite reports of decreasing concentrations of OCP and its derivatives in relation to previous studies, probably because these compounds were banned decades ago, OCP contamination is still reported in different regions of the world, occasionally exceeding the MRLs established in raw milk, pasteurized milk, sour cream, cheese and butter. Thus, humans are exposed to these pollutants mainly through animal food (Akhtar and Ahad, 2017; Ishaq and Nawaz, 2018; Rusu et al., 2016), representing a threat to public health due to its mutagenic, teratogenic and deleterious effects on the endocrine, cardiovascular and respiratory systems. In addition, several organochlorine pesticides such as DDT, HCH, and hexachlorobenzene (HCB) are potential human carcinogens (Rusu et al., 2016).

On the other hand, organophosphate pesticides

(POF) such as dichlorvos, diazinon, dimethoate, chlorpyrifos, malathion and methylparathion have replaced OCPs with less stability and persistence. Thus, they enter the animal organism through contaminated food and water, either by inhalation, through the use of insecticides in pastures, stables and dairy factories, or through the skin after the application of ectoparasites and subsequent violation of the established withdrawal period of time (Bedi et al., 2018; Fischer et al., 2016; Fernández et al., 2010). The lipophilic nature and its ability to covalently bind to proteins determine the presence of OPS in milk and its subsequent incorporation into the food chain, being detected in pasteurized milk, raw milk and cheese (Salas et al., 2003; Al-Julaifi et al., 2015; Pagliuca et al., 2006). OPS have potential effects on human and animal health, causing excessive stimulation of acetylcholine receptors and thus muscle

weakness or paralysis, excessive secretory activity, and changes in consciousness (Bedi et al., 2018; Fernández et al., 2010). Table 2 shows milk MRLs for various organochlorine and organophosphate pesticides.

It has been proposed that the control of environmental pollution in dairy farms (Bedi et al., 2018), the improvement of storage conditions for dairy food, farmer education programs, the control of pesticide, the application of organic agriculture, the implementation of integrated pasture management methods (Rusu et al., 2016), the identification of contamination sources, the monitoring of pesticide residues in animal food and dairy products by gas chromatography (GC), liquid chromatography coupled to tandem mass spectrometers (LC/MS/MS) (Akhtar and Ahad, 2017) can help reduce the presence of these pesticides in milk and milk products.

## 2.3 Heavy metals

These are metallic and metalloid elements with a higher density compared to other metallic elements (5 g/cm<sup>3</sup> or an atomic weight between 63.5-200.6 g/mol), are widely distributed in the environment and induce systemic toxicity even at low exposure levels (Ismail et al., 2019; Mahmoudi et al., 2017; Jan et al., 2015). Although iron (Fe), zinc (Zn), nickel (Ni) and copper (Cu) have been considered in this group when found in food products beyond certain

Methods used to detect heavy metals in dairy products include capillary electrophoresis, pulse voltammetry and spectrometric methods. To prevent these elements from entering the food chain, the idea is to reduce their concentrations in the water destined for dairy cows, using adsorbent agents such as smectite, palygorskite and zeolite, as well as food monitoring, the use of safe materials for dairy processing and packaging, periodic analysis of dairy products and monitoring of water used in milk and dairy processing (Mahmoudi et al., 2017). In addition, the supply of cumin (Cuminum cyminum L.), white turmeric (Curcuma zedoaria Rosc.) and mango ginger (Curcuma mangga Val.) in dairy cow food reduces the concentration of lead in milk and increases it in feces, probably by modulating the rulimits, the most toxic heavy metals found in food are generally mercury (Hg), arsenic (As), cadmium (Cd) and lead (Pb). According to the 2011 and 1999 editions of the Codex Alimentarius Commission, the maximum permitted level of Pb and Cd in milk has been established at  $0.02 \ \mu g/ml$  and  $0.01 \ \mu g/ml$ , respectively. The European Union has set the maximum permitted level of As at  $0.1 \ \mu g/ml$ , while Indian legislation stipulates  $1.0 \ \mu g/ml$  as the maximum permissible limit for mercury in milk and milk products (Ismail et al., 2019).

Anthropogenic activities such as urbanization, industrialization, irrigation with contaminated water, the application of fertilizers containing heavy metals and non-hygienic conditions in the processing and distribution of milk determine its entry into the body, reported in samples of raw, pasteurized and powdered milk (Ismail et al., 2019; Mahmoudi et al., 2017; Jan et al., 2015). Contamination of milk and milk products with heavy metals is important to public health because they cause diseases, especially in infants and the elderly, who are the main dairy consumers (Ismail et al., 2019; Mahmoudi et al., 2017). Thus, one of the main causes of saturnism is precisely the consumption of leadcontaminated milk, whose absorption rate in children is 40% higher than in adults (Ismail et al., 2019; Harlia et al., 2018). From a pathophysiological point of view, metals stimulate the generation of reactive oxygen and nitrogen species, generating oxidative stress and impairing the cellular antioxidant system (Jan et al., 2015).

minal microbiota (Nurdin et al., 2013). In addition, a lower concentration of heavy metals has been observed in yogurt compared with raw milk, an effect attributed to fermentation processes as a result of bacterial activity (Enb et al., 2009).

# 2.4 Dioxins and polychlorinated biphenyls analogue to dioxins (PCB-AD)

These are a group of polychlorinated compounds, almost aromatic planar with similar physical and chemical structures, consisting of 75 polychlorinated dibenzo-p-dioxins (PCDD) and 135 polychlorinated dibenzofurans congeners (PCDF). Out of the dioxins (PCDD/Fs), 17 exhibit toxicological properties, and 12 show 209 polychlorinated biphenyls

Organochlorines	MRLs µg/kg
DDT	40
DDE	40
Dieldrin	6
ү-НСН	1
α- endosulfan	100
β-endosulfan	100
Endosulfan sulphate	100
Organophosphates	MRLs µg/kg
Acephate	20
Chlorpyrifos	10
Chlorpyrifos- methyl	10
Diazzinon	10
Methamidophos	10
Metidation	20
Forate	20
Pyrimifos-methyl	50

Table 2. MRLs for various organochlorines and organophosphates (Ishaq and Nawaz, 2018; Pagliuca et al., 2006).

(PCBs), and when adopting a dioxin-like planar structure they exhibit toxicological properties similar to dioxins (analogue to dioxin PCB-AD) (DO, 2011; AECOSAN, 2018).

These compounds are characterized by being highly stable in the environment, by their ubiquity, their toxicity and their ability to enter the organism through air, soil or sediments, inhalation, skin absorption and especially by contaminated food (AE-COSAN, 2018; Gallego et al., 2005). In ruminants, the intake of PCDD/Fs and PCB-AD occurs mainly during grazing, by the consumption of contaminated grass and soil particles, as well as by the consumption of silage and fodder subjected to drying processes (Bogdal et al., 2017).

Once accumulated in the organism, mainly in animal adipose tissue, gestation and lactation will mean the mobilization of these compounds, increasing their concentration in milk which, along with their derivatives, becomes a potential source of dioxins and PCB-AD for the consumer (Gallego et al., 2005; Schulz et al., 2005; Piskorska-Pliszczynska et al., 2017). Dioxins have been detected in more than 90% of samples of infant formula, butter, and other dairy products (yogurt, frozen dairy desserts, baked products containing dairy) and various types of cheese (CFIA, 2019), being a serious threat to public health. PCDD/Fs and PBC-AD have carcinogenic, teratogenic, and mutagenic effects and are associated with dermal and hematic alterations, which act as an endocrine disruptor causing reproductive, immunological, and neurological disorders (Gallego et al., 2005).

In order to prevent food intended for milkproducing animals from being contaminated by dioxins and PCB-AD, it has been proposed the identification of agricultural areas with significant presence of these compounds, as well as the identification and monitoring of feed and feed ingredients coming from these areas, the monitoring of the concentration of dioxins and PCB-AD in sewage sludge and compost used in agriculture, and the identification and control of critical feed manufacturing processes (for example, artificial drying by direct

heating) (FAO/OMS, 2018). Ingestion of dioxin and PCB contaminated soil particles can also be prevented by reduciing animal density during grazing and increasing pasture availability. Since dioxins remain in the animal organism for 30 to 60 days before they are excreted through milk, it has been proposed to transfer animals to uncontaminated soil for three months to reduce dioxins in the milk. Since milk contamination with PCB-AD has been reported following the ingestion of painting remains in stables and grazing in areas near industrial centers, these should be considered as potential sources of contamination (Gallego et al., 2005; Bogdal et al., 2017; Schulz et al., 2005).

PCDD/Fs and PCB-ADs, along with organochlorine pesticides, are the most common persistent organic pollutants (POPs) (OMS, 2020), which are released into the environment as a result of various anthropogenic activities and enter the food chain due to their capacity for transport, toxicity and persistence (Figure 2).

Detection of PCDD/Fs and PCB-AD is based on gas chromatography along with highresolution mass spectrometry (GC-HMRS). Gas chromatography-based methods are also used with tandem mass spectrometry (GC-MS/MS). Additionally, bioassay techniques have been developed as high-throughput screening methods (FAO/OMS, 2018).

## 2.5 Disinfectants and Detergents

Cleaning and disinfection are critical steps in primary production and later dairy processing, allowing the removal of milk residues and minimizing the level of bacterial contamination in milking facilities. Detergents including surfactants in their composition and disinfectants are used for this purpose with a wide range of products containing biocides such as chlorine, iodine, quaternary ammonium and chlorine dioxide (Van Asselt et al., 2016; Fis-



Although chlorine residues in milk degrade rapidly, without presenting a health risk (Fischer et al., 2016; Šalomskienė et al., 2013), chlorine contact with organic matter results in milk containing residues of contaminants that are not intentionally added, such as trichloromethane (TCM) or chloroform (Siobhan et al., 2012). Other disinfectants such as chlorine dioxide generate by-products whose intake inhibits the absorption of iodine (Van Asselt et al., 2016), while quaternary ammonia is stable in milk, negatively affecting the health of consumers and inhibiting milk fermentation and cheese processing (Siobhan et al., 2012). The MRL for disinfectants and detergents in milk and other foods has been estimated at 0.1 mg/kg (DO, 2014). On the other hand, the high intake of iodine from its residues in milk can lead to disorders in thyroid function, mainly in children (Fischer et al., 2016).

Due to the wide variety of disinfecting products, several analytical techniques have been described for their detection in food, including simple colorimetric tests, potentiometer with ion selective electrodes, thin layer chromatography and liquid and gas chromatography. For the quantification and detection of chlorates, perchlorates, and quaternary ammonium in milk and dairy products, chromatography-tandem mass spectrometry is used (Fischer et al., 2016).



Figure 2. Entry of Persistent Organic Pollutants (POPs) into the food chain

# 3 Conclusions

Milk is a source of nutrients for a significant number of the population. However, anthropogenic activities aimed at improving animal productivity and dairy processing cause a risk of chemical contamination of these products. Due to the ubiquity of these pollutants and their effects after their chronic intake through milk and dairy products, maximum residual limits have been established for most of these compounds, and it is necessary to prevent, or at least minimize, and monitor the concentration of chemical contaminants in dairy products, using appropriate screening techniques and contributing to the food security of the population.

# References

- AECOSAN (2015). Alfatoxinas. Agencia Española de Consumo, Seguridad Alimentaria y Nutrición. Online: https://bit.ly/342IthQ.
- AECOSAN (2018). Contaminantes orgánicos persistentes (pops) y otros contaminantes (melamina, bisfenoles). Technical report, Agencia Española de Consumo, Seguridad Alimentaria y Nutrición. Online:https://bit.ly/33VLswx.
- Akbar, N., Nasir, M., Naeem, N., Ahmad, M., Iqbal, S., Rashid, A., Imran, M., Aslam, T., Atif, M., and Salehi, B. (2019). Occurrence and seasonal variations of aflatoxin m1 in milk from pun-

jab, pakistan. *Toxins*, 11(10):574. Online: https://bit.ly/311GgWl.

- Akhtar, S. and Ahad, K. (2017). Pesticides residue in milk and milk products: Mini review. *Pakistan Journal of Analytical y Environmental Chemistry*, 18(1):37–45. Online: https://bit.ly/3tkzgja.
- Al-Julaifi, M., Bazalou, M., Ibrahim, A., and Ghamry, S. (2015). Quantitative determination of organophosphorus compounds in hard cheese using gas chromatography coupled with ion traptandam spectrometry. *Egyptian Journal of Chemistry and Environmental Health*, 1(1):113–133. Online: https://bit.ly/3cN7EJj.
- Albright, J., Tuckey, S., and Woods, G. (1961). Antibiotics in milk-a review. *Journal of Dairy Science*, 44(5):779–807. Online: https://bit.ly/3KeZoCb.
- Avcı, B. and Filazi, A. (2020). The effects of heat applications on macrocyclic lactone-structured antiparasitic drug residues in cows' milk. *Food Additives y Contaminants: Part A*, 37(7):1145–1155. Online: https://bit.ly/3tok3NV.
- Ayar, A., Sert, D., and Çon, A. (2007). A study on the occurrence of aflatoxin in raw milk due to feeds. *Journal of food safety*, 27(2):199–207. Online: https://bit.ly/3ndw451.
- Bedi, J., Gill, J., Kaur, P., and Aulakh, R. (2018). Pesticide residues in milk and their relationship with pesticide contamination of feedstuffs supplied to dairy cattle in punjab (india). *Journal*

https://bit.ly/33qvWrC.

- Bogdal, C., Zuüst, S., Schmid, P., Gyalpo, T., Zeberli, A., Hungerbuhler, K., and Zennegg, M. (2017). Dynamic transgenerational fate of polychlorinated biphenyls and dioxins/furans in lactating cows and their offspring. Environmental science y technology, 51(18):10536–10545. Online: https://bit.ly/3zSWlun.
- Cerqueira, M., Souza, F., Cunha, A., Picinin, L., Leite, M., Penna, C., Souza, M., and Fonseca, L. (2014). Detection of antimicrobial and anthelmintic residues in bulk tank milk from four different mesoregions of minas gerais state-brazil. Arquivo Brasileiro de Medicina Veterinária e Zootecnia, 66(2):621-625. Online: https://bit.ly/3GjHfk7.
- CFIA (2019). Dioxins and dioxin-like compounds in selected foods, ca. Technical report, Canadian Food Inspection Agency. Online: https://bit.ly/ 2S3yKSJ.
- Dimitrieska, E., Stojanovska, B., Ilievska, G., Uzunov, R., Stojković, G., Hajrulai, Z., and Jankuloski, D. (2016). Assessment of aflatoxin contamination in raw milk and feed in macedonia during 2013. Food control, 59:201-206. Online: https: //bit.ly/33bAaUn.
- DO (2011). Reglamento (ue) no. 1259/2011 de la comisión por el que se modifica el reglamento (ce) no 1881/2006 en lo relativo a los contenidos máximos de dioxinas, pcb similares a las dioxinas y pcb no similares a las dioxinas en los productos alimenticios. ref: Ue. 1 320/18. Online: https://bit.ly/335ogIK.
- DO (2014). Reglamento (ue) no 1119/2014 de la comisión que modifica el anexo iii del reglamento (ce) no 396/2005 del parlamento europeo y del consejo en lo relativo a los límites máximos de residuos de cloruro de benzalconio y cloruro de didecildimetilamonio en determinados productos. ref: L 304/43. Online: https://bit.ly/335ogIK.
- Duarte, S., Almeida, A., Teixeira, A., Pereira, A., Falcão, A., Pena, A., and Lino, C. (2013). Aflatoxin m1 in marketed milk in portugal: Assessment of human and animal exposure. Food Control, 30(2):411–417. Online: https://bit.ly/3GmNpzN.

- of Animal and Feed Sciences, 27(1):18–25. Online: Enb, A., Abou, M., Abd, N., Abou, A., and El, M. (2009). Chemical composition of raw milk and heavy metals behavior during processing of milk products. Global Veterinaria, 3(3):268-275. Online: https://bit.ly/33sxdOR.
  - FAO (2004). Code of hygienic practice for milk and milk products cac/rcp 57. Technical report, Organización de las Naciones Unidas para la Alimentación y la Agricultura. Online: https://bit. ly/3cCYqz4.
  - FAO/OMS (2008). Límites máximos de residuos (lmr) y recomendaciones sobre la gestión de riesgos (rgr) para residuos de medicamentos veterinarios en los alimentos. roma: It. comisión del codex alimentarius, ref: Cx/mrl 2-2018. Technical report, Organización de las Naciones Unidas para la Alimentación y la Agricultura / Organización Mundial de la Salud. Online: https://n9.cl/ 8uwl3.
  - FAO/OMS (2013). Food standards programme. codex alimentarius commission procedural manual. twenty-first edition. Technical report, Organización de las Naciones Unidas para la Alimentación y la Agricultura / Organización Mundial de la Salud. Online: https://bit.ly/337zzQM.
  - FAO/OMS (2018). Código de prácticas para prevenir y reducir la contaminación en los alimentos y piensos por dioxinas y bifenilos policlorados (bpc) análogos a las dioxinas, 2018. Technical report, Organización de las Naciones Unidas para la Alimentación y la Agricultura / Organización Mundial de la Salud. Online: https: //bit.ly/3i87I7n. Comisión del Codex Alimentarius, ref: CXC 62-2006.
  - Fernández, D., Mancipe, L., and Fernández, D. (2010). Intoxicación por organofosforados. Revista Med, 18(1):84-92. Online: https://bit.ly/ 3tob67g.
  - Fink, J. (2008). Mycotoxins in cattle feeds and carryover to dairy milk: A review. Food Additives and Contaminants, 25(2):172–180. Online: https://bit. ly/3fgaXL5.
  - Fischer, W., Schilter, B., Tritscher, A., and Stadler, R. (2016). Contaminants of milk and dairy products: contamination resulting from farm and dairy practices. Encyclopedia of Dairy Sciences, 2:887-97. Online: https://bit.ly/3tOdkgm.

- Gallego, M., Roy, T., Hermoso, M., Hernández, D., Soler, R., and Pérez, M. (2005). Las dioxinas en la producción animal: situación actual. *Producción animal*, 20(212):60–72. Online: https://bit.ly/ 3GnBP7P.
- Harlia, E., Rahmah, K., and Suryanto, D. (2018). Food safety of milk and dairy product of dairy cattle from heavy metal contamination. In *IOP conference series: earth and environmental science*, volume 102, page 012050. Online: https://bit.ly/ 3treiz1.
- IARC (2002). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene, volume 82. International Agency for Research on Cancer. Lyon: FR.
- Ishaq, Z. and Nawaz, M. (2018). Analysis of contaminated milk with organochlorine pesticide residues using gas chromatography. *International Journal of Food Properties*, 21(1):879–891. Online: https://bit.ly/3fo30Di.
- Ismail, A., Riaz, M., Akhtar, S., Goodwill, J., and Sun, J. (2019). Heavy metals in milk: global prevalence and health risk assessment. *Toxin Reviews*, 38(1):1–12. Online: https://bit.ly/3tlq2TH.
- Jan, A.and Azam, M., Siddiqui, K., Ali, A., Choi, I., and Haq, Q. (2015). Heavy metals and human health: mechanistic insight into toxicity and counter defense system of antioxidants. *International journal of molecular sciences*, 16(12):29592– 29630. Online: https://bit.ly/3nnyXQJ.
- Kalyankar, S., Khedar, C., Pail, A., and Deosarkar, S. (2016). *The Encyclopedia of Food and Health*, volume 3, chapter Milk: sources and composition, pages 741–747. Oxford: Academic Press.
- Kirsanov, V., Yu, V., Maslov, M., Zaikin, W., and Erzamaev, M. (2020). Influence of devices for cleaning the milk pipes of the milking units on the ecology of milk production. In *IOP conference series: earth and environmental science*, volume 422, page 012075. Online: https://bit.ly/3tl5dHU.
- Kurjogi, M., Issa, Y., Alghamdi, S., Abdelrahman, M., Satapute, P., and Jogaiah, S. (2019). Detection and determination of stability of the antibiotic residues in cow's milk. *PloS one*, 14(10):e0223475. Online: https://bit.ly/3qm3HDH.

- Mahmoudi, R., Kazeminia, M., Kaboudari, A., Pir, S., and Pakbin, B. (2017). A review of the importance, detection and controlling of heavy metal in milk and dairy products. *Malaysian Journal of Science*, 36(1):1–16. Online: https://bit.ly/ 3FosSd5.
- Marchese, S., Polo, A., Ariano, A., Velotto, S., Costantini, S., and Severino, L. (2018). Aflatoxin b1 and m1: Biological properties and their involvement in cancer development. *Toxins*, 10(6):214. Online: https://bit.ly/33rxAta.
- Merin, U., Rosenthal, I., Bernstein, S., and Popel, G. (1985). The effect of residues of detergents and detergents-sanitizers on the performance of antibiotic test and the organoleptic quality of milk. *Le Lait*, 65(649-650):163–167. Online: https://bit.ly/ 3zQNf10.
- Navrátilová, P. (2008). Screening methods used for the detection of veterinary drug residues in raw cow milk–a review. *Czech J Food Sci*, 26(6):393– 401. Online: https://bit.ly/33tbPt8.
- Neagu, D., Perrino, S., Micheli, L., Palleschi, G., and Moscone, D. (2009). Aflatoxin m1 determination and stability study in milk samples using a screen-printed 96-well electrochemical microplate. *International Dairy Journal*, 19(12):753–758. Online: https://n9.cl/wnny0.
- Nguyen, T. and Flint, S.and Palmer, J. (2020). Control of aflatoxin m1 in milk by novel methods: A review. *Food chemistry*, 311:1–370. Online: https: //bit.ly/3A6SLND.
- Nurdin, E., Putra, D., and Amelia, T. (2013). Analysis of heavy metal lead (pb) levels with aas in cow's milk by giving cumin (cuminum cyminum l.), white turmeric (curcuma zedoaria rosc.) and mango turmeric (curcuma mangga val.). *Pakistan journal of biological sciences: PJBS*, 16(21):1373– 1377. Online: https://bit.ly/3I5Xzpf.
- OMS (2018). Aflatoxins. Technical report, Organización Mundial de la Salud. Online: https://n9. cl/l4q2d.
- OMS (2020). Persistent organic pollutants (pops), international programme on chemical safety, food safety. Online: https://bit.ly/2GjBskf0.
- Padol, A., Malapure, C., Domple, V., and Kamdi, B. (2015). Occurrence, public health implications

and detection of antibacterial drug residues in cow milk. *Environment y We an International Journal of Science and Technology*, 10(2015):7–28. Online: https://bit.ly/3fiQzsv.

- Pagliuca, G., Serraino, A., Gazzotti, T., Zironi, E., Borsari, A., and Rosmini, R. (2006). Organophosphorus pesticides residues in italian raw milk. *Journal of dairy research*, 73(3):340–344. Online: https://bit.ly/3nljnoG.
- Pérez-Cogollo, L., Rodríguez-Vivas, R., Basto-Estrella, G. d. S., Reyes-Novelo, E., Martínez-Morales, I., Ojeda-Chi, M. M., and Favila, M. (2018). Toxicidad y efectos adversos de las lactonas macrocíclicas sobre los escarabajos estercoleros: una revisión. *Revista mexicana de biodiversidad*, 89(4):1293–1314. Online: https://n9.cl/2mht9.
- Piskorska-Pliszczynska, J., Maszewski, S., Mikolajczyk, S., Pajurek, M., Strucinski, P., and Olszowy, M. (2017). Elimination of dioxins in milk by dairy cows after the long-term intake of contaminated sugar beet pellets. *Food Additives y Contaminants: Part A*, 34(5):842–852. Online: https: //bit.ly/3fkcY8W.
- Priyanka, P., Sheoran, M., and Ganguly, S. (2017). Antibiotic residues in milk-a serious public health hazard. *Journal of Environment and Life Sciences*, 2(4):99–102. Online: https://bit.ly/30juPpf.
- RAE (2019). Leche, asociación de academias de la lengua española. Online: https://bit.ly/ 30eJHW600.
- Rahimirad, A., Maalekinejad, H., Ostadi, A., Yeganeh, S., and Fahimi, S. (2014). Aflatoxin m1 concentration in various dairy products: evidence for biologically reduced amount of afm1 in yoghurt. *Iranian journal of public health*, 43(8):1139 Online: https://bit.ly/3fhpupE.
- Romero-González, R., Frenich, A., and Vidal, J. (2014). Veterinary drugs residues: anthelmintics. *Encyclopedia of Food Safety*, 3:45–54. Online: https: //bit.ly/3fAt1jf.
- Rusu, L., Harja, M., Suteu, D., Dabija, A., and Favier, L. (2016). Pesticide residues contamination of milk and dairy products. a case study: Bacau district area, romania. *Journal of Environmental Protection and Ecology*, 17:1229–1241. Online: https://bit.ly/3cBgTfc.

- Sachi, S., Ferdous, J., Sikder, M., and Hussani, S. (2019). Antibiotic residues in milk: Past, present, and future. *Journal of advanced veterinary and animal research*, 6(3):315–332. Online: https://bit.ly/ 3zWaN4J.
- Salas, J., González, M., Noa, M., Pérez, N., Díaz, G., Gutiérrez, R., Zazueta, H., and Osuna, I. (2003). Organophosphorus pesticide residues in mexican commercial pasteurized milk. *Journal of agricultural and food chemistry*, 51(15):4468–4471. Online: https://n9.cl/e42wj.
- Šalomskienė, J., Mačionienė, I., Žvirdauskienė, R., and Jonkuvienė, D. (2013). Impact of the residues of detergents and disinfectants used in dairy farms on the results of inhibitor tests for raw milk. *Advances in Bioscience and Biotechnology*, 4(2):266– 272. Online: https://bit.ly/3KkT4ZV.
- Santos, P., Cruz, J. d., Santos, J. d., Mottin, V., Teixeira, M. R., and Souza, J. (2019). Ivermectin and albendazole withdrawal period in goat milk. *Revista Brasileira de Saúde e Produção Animal*, 20:1–12. Online: https://bit.ly/3ts0lAS.
- Schulz, A., Wiesmüller, T., Appuhn, H., Stehr, D., Severin, K., Landmann, D., and Kamphues, J. (2005). Dioxin concentration in milk and tissues of cows and sheep related to feed and soil contamination. *Journal of Animal Physiology and Animal Nutrition*, 89(3-6):72–78. Online: https://bit. ly/339edFF.
- Siobhan, R., David, G., Kieran, J., and Ambrose, F.and Bernadette, O. (2012). Evaluation of trichloromethane formation from chlorine-based cleaning and disinfection agents in cow's milk. *International journal of dairy technology*, 65(4):498–502. Online: https://bit.ly/3I00v6K.
- STATISTA (2020). Global cow milk production 2015 to 2019. STATISTA. Online: https://bit.ly/ 344SIYf00.
- Tsiboukis, D., Sazakli, E., Jelastopulu, E., and Leotsinidis, M. (2013). Anthelmintics residues in raw milk. assessing intake by a children population. *Polish journal of veterinary sciences*, 16(1):85–91. Online: https://bit.ly/339Yq6G.
- Urbán, G., Pérez, J., Martínez, F., Salas, J., Díaz, G., Ramírez, M., Castro, G., Vega, S., Gutiérrez, R., and Escobar, A. (2009). Niveles de aflatoxina m1

en quesos frescos producidos en diferentes zonas de méxico. *Revista de Salud Animal*, 31(2):115–121. Online: https://bit.ly/33J1jOx.

- Van Asselt, E., Van der Fels-Kler, H., Marvin, H., Van Bokhorst-van de Veen, H., and Nierop, M. (2016). Overview of food safety hazards in the european dairy supply chain. *Comprehensive Reviews in Food Science and Food Safety*, 16(1):59–75. Online: https://bit.ly/3GRUYyY.
- Van der Fels-Kler, H. and Camenzuli, L. (2016). Effects of milk yield, feed composition, and feed contamination with aflatoxin b1 on the aflatoxin m1 concentration in dairy cows' milk investigated using monte carlo simulation modelling. *To-xins*, 8(10):290. Online: https://bit.ly/3tNuefp.
- Vaz, A., Cabral, A., Rodrigues, P., and Venâncio, A. (2020). Detection methods for aflatoxin m1 in dairy products. *Microorganisms*, 8(2):246. Online: https://bit.ly/3rrc1Bc.

- Whelan, M., Chirollo, C., Furey, A., Cortesi, M., Anastasio, A., and Danaher, M. (2010). Investigation of the persistence of levamisole and oxyclozanide in milk and fate in cheese. *Journal of agricultural and food chemistry*, 58(23):12204–12209. Online: https://bit.ly/3KjeVAQ.
- Yang, W., Ke, C., Wu, W., Lee, R., and Tseng, Y. (2019). Effective treatment of bovine mastitis with intramammary infusion of angelica dahurica and rheum officinale extracts. *Evidence-Based Complementary and Alternative Medicine*, 2019:1–8. Online: https://bit.ly/351i7B3.
- Zaragoza-Bastida, A., Valladares-Carranza, B., Ortega-Santana, C., Zamora-Espinosa, J., Velázquez-Ordoñez, V., and Aparicio-Burgos, J. (2016). Implications of the use of organochlorine in the environment, and public health. *Abanico veterinario*, 6(1):43–55. Online: https://bit.ly/3Ac2jXt.