Chapter

Role of the Microbiome as the First Metal Detoxification Mechanism

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Abstract

Exposure to environmental toxins in water, soil and air are increasing with health effects, mainly in older ages and physiological states (childhood and pregnancy). The role of the microbiota has been widely studied with effects on the maintenance of health but this is only possible with a diet that promotes it. The traditional Mexican diet is rich in fiber, which has prebiotic effects and has found a higher excretion of arsenic and fluoride in adolescents who maintained a diet high in fiber derived from traditional foods. After several descriptive studies in the state of Guanajuato, since 2004, first with arsenic in drinking water in population of several communities, in 2015, it is achieved through an intervention study with a supplementation of several vitamins and minerals in population adolescent, a greater urinary arsenic and fluoride excretion, as well as a greater consumption of traditional foods such as beans, bananas, orange and quelites. Food is key to maintain a function of the microbiota, so its review and study should be encouraged.

Keywords: microbiome, traditional Mexican diet, soluble fiber, arsenic, fluoride

1. Introduction

Exposure to toxins in the environment, soil and air increase the effects on the health of the population in all ages and physiological states of higher priority such as childhood and pregnancy [1]. The role of the microbiota has been extensively studied with effects on health maintenance, but this is only possible with a diet that promotes its development, growth and maintenance of key bacteria [2]. An adequate diet (complete, varied, balanced, sufficient and safe) generates intestinal health by preserving the microbiota [3]. Among the key nutrients, it is known that soluble fibers function as a prebiotic for bacteria. The fructoligosaccharides represents one kind of these soluble fibers and are found in food such as banana, bean, onion, garlic, etc., that are part of the traditional Mexican diet [4]. After several descriptive studies in the state of Guanajuato, since 2004, first with arsenic in drinking water in population of several communities, in 2015, it is achieved through an intervention study with a supplementation of several vitamins and minerals in population adolescent, a greater urinary arsenic and fluoride excretion, as well as a greater consumption of traditional foods such as beans, bananas, orange and quelites [5–7]. The traditional Mexican diet composed for quelites, legumes (beans, lentils), a wide variety of fruits and vegetables are rich in flavonoids, vitamins (A, B, C, D, E) have been associated prebiotic effect and a greater excretion of metals. Monroy-Torres, et al found more excretion for fluoride and arsenic in adolescents who maintained these foods in their diet during the study [7]. Knowing the food transition and its impact on the changes in the microbiota is part of a research subline of Environmental Nutrition and Food Security [8].

The contamination of the main environmental resources, necessary to preserve the life of any human being are water, soil and air, which have a deterioration in quantity and quality integrating the presence of various pollutants with their corresponding health risks. Current evidence has integrated and recognized the main toxins present in water, soil, air and therefore in food, with important implications for the health of people at different stages of life, are lead, cadmium, mercury and arsenic [9, 10].

Lead, for many years, is part of the compounds of gasoline and to date is still used in pottery despite the existence of a rule that prohibits it for Mexico and in many countries. Low doses begin to generate problems especially in childhood and when there is anemia or poor nutrition, its toxicity is exacerbated. Sweets have been a source of lead exposure and also some lead-based paints. Pregnant women and children are more susceptible to lead exposure due to their high bioavailability at the gastrointestinal level and its permeability of the blood-brain barrier [11].

Cadmium compounds not only are present in batteries and cigarette smoke, but also food could represent a source of exposure to this metal. Cadmium is used in the manufacture of rechargeable batteries (composition based on nickel and cadmium) whose main problem is that everything containing cadmium is reusable or recyclable being household waste one of the most frequent routes of exposure, so that its exposure has increased and ascending during the twentieth century. One concern is the low dose of this metal to generate kidney damage, bone damage and fractures, although this also varies according to the population group [10, 11].

With respect to mercury, this metal mainly causes deterioration and neurological damage and the main source of exposure of people is the consumption of fish contaminated with methylmercury, as well as dental amalgams that in rural communities remain the main option, given their durability. Due to the exposure of mercury orally through the consumption of fish, food alerts have been generated to avoid or minimize its exposure in pregnant women mainly, since the nervous system develops throughout fetal life, so it is vital to alert the population and avoid the consumption of large fish such as tuna, shark and swordfish [9, 12].

Arsenic is a metalloid present at different concentration in water tables. The toxicity of arsenic depends of its valence states and its organic or inorganic form. Organic As is considered less toxic than inorganic, as it is easier to excrete, this can be found mainly in shellfish and some cereals. Inorganic As is most toxic in its trivalent form that can chemically combine with sulfhydryl groups, these functional groups form intermolecular and intramolecular bridges in proteins and their structure and biological function depend accordingly [1, 12].

El To address in this chapter, with utmost importance, we consider a summary of these four toxic heavy metals since little is known about their interactions and role of the microbiota, in the chemical reactions of oxide-reduction or those that apply for their detoxification of the organism. The health effects will depend on the toxic route of entry, dose and exposure time, as well as the nutritional status of each person. One of the main causes of contamination of food by these metals is that the land and water in which they are contaminated with these environmental toxins and this coupled with the fact that they can also be contaminated in processes of their subsequent industrialization and apart from this. The process generates foods with poor null nutrient content (fiber, vitamins and minerals) and also have more additives and preservatives [9, 10]. Reason for achieving a correct diet that is complete, varied, balanced, sufficient, adequate and safe, has become a challenge, especially safety, defined "that the usual consumption of a diet or food does not involve health risks because it is free of pathogenic microorganisms, toxins and contaminants and is consumed in moderation" [3], whose definition we can affirm is difficult to achieve in the toxicological aspect [1].

Recently, the study of intestinal microbiota has increased significantly, because important protective and metabolic functions have been associated. On this regards, intestinal microbiota competes for nutrients, space and receptors with pathogenic microorganisms, as well as stimulating the production of antimicrobial peptides and immunoglobulins. The microbiota converts many complex substances such as starches, cellulose, pectin and gums into metabolites that are easily absorbed by the host, it also ferments another non-digestible residues from the diet, synthesizes some vitamins and is also involved in the absorption of ions [13, 14].

There are several probiotic bacteria that have been administered gastrointestinally to sequester toxins present in food, such as a 250 g yogurt with *1010 CFU* of *Lactobacillus rhamnosus* supplemented with probiotics to reduce exposure to metals in pregnant women and children with elevated blood lead levels in a study conducted in Tanzania, changes in blood metal levels were evaluated and children's gut microbiomes were analyzed, finding a protective effect against additional increases in mercury (3.2 nmol/L; P 0.035) and arsenic (2.3 nmol/L; P 0.011), only in women, but not in children [1, 2]. One of the reasons for these differences can be explained by the physiological immaturity of children as well as the stage of growth that are most vulnerable them; In the case of women where benefit was observed, it is explained why it is known that women have an efficiency in the excretion of metals, unlike men [1, 2, 15]. On the other hand, as regards Cadmium, it has been observed in women in the menopause stage, differences in metal metabolism and excretion as well as greater absorption of cadmium orally in women with anemia and osteoporis, causing kidney damage, osteoporosis and osteomalacia [15]. As women, in the menopause period should be more monitored being that is when there is a deterioration in nutritional status such as anemia exacerbating increased exposure to lead, for example.

Respect of lifestyle change, nutrition plays an important role in maintain the microbiota; poor quality diets are rich in refined grains and added sugars, salt, unhealthy fats and foods of animal origin; and low in whole grains, fruits, vegetables, legumes, fish and nuts are the main causes of poor microbiome. Processed red meats are associated with an increase in cardiovascular diseases and strokes. However, for our population, the relationship between these variables was not conclusive [16].

Gut microbiota is composed of bacteria, fungi, archaea, viruses and protozoa. Some of the functions of gut microbiota are metabolism and the development of the nervous system and immune system [17]. Furthermore, alterations in microbiota, a process known as dysbiosis, have been associated with the development of obesity and diseases such as diabetes, inflammatory bowel disease and even neoplasms such as colon cancer. Some factors that cause intestinal dysbiosis are antibiotics, alcohol consumption, infection of pathogenic microorganisms and diet [18], this last one can favor the proliferation of specific phyla of bacteria in the gut [19]. Likewise, gut dysbiosis has been associated to exposure to heavy metals as cadmium and mercury [20, 21], halogenated compounds such as fluoride and metalloids such as arsenic, these last two contaminants of water for human consumption [22]. On the other hand, the role of the microbiota in the detoxification of xenobiotics [23], arsenic [24] and heavy metals [25], has been little studied. In the case of heavy metals, it has been observed that probiotics, especially lactic acid bacteria (LAB), could contribute to their elimination, because these kinds of bacteria have a high affinity for heavy metals [26]. Therefore, a diet that favors the proliferation of LAB could be used as the natural detoxification of the organism in populations exposed to environmental pollutants. In this chapter, we review the role of diet in the gut microbiota and its possible use for the natural detoxification of the organism.

2. Toxicokinetics and heavy metal toxicodynamics

Of the most important aspects to consider in heavy metal poisoning is toxicokinetics and toxicodynamics. In this regard, the term toxicokinetics refers to the way through which toxins from the source of exposure enter the body, are distributed, biotransformed and eliminated [27]. On the other hand, toxicodynamics studies the mechanisms at the cellular or molecular level by which toxins cause damage [27]. These branches of toxicology are important to know because through toxicokinetics it is possible to prevent the metal from entering the bloodstream, its distribution can be modified and therapeutic measures can be taken to eliminate and reduce the toxic effects caused in the organism [28].

In this context, there are different sources of exposure to heavy metals, these sources can be natural such as water for human consumption or food of animal and plant origin mainly contaminated with arsenic, mercury or lead [29]. On the other hand, there are other sources of exposure such as the use of clay utensils or glazed earthenware that are used in Mexico to prepare food, industrial activities for the manufacture of accumulators, paints, cosmetics, medicines, thermometer manufacturing, etc., which also contribute to heavy metals being available in the environment so that they can enter the body of those exposed to them [27, 30, 31]. Of these sources of exposure, the most worrisome are natural sources such as water and food contaminated with these metals, because the population is unaware that their natural resources are contaminated and use them daily so they have a high risk of these metals that can damage your health, whether in the short, medium and/or long term [32]. In the case of the sources generated by man as a work practice, it is easier to prevent exposure by taking various hygiene and safety measures in the work environment.

From the sources of exposure, heavy metals enter the body through different routes such as oral, topical and inhalation [27]. However, the main route of entry is the oral and sometimes in the same individual heavy metals can enter through different routes; such as mercury, the most common case is when a glass thermometer containing this metal is broken and the user tries to pick it up with their hands, it will be absorbed through the skin, in addition to room temperature the mercury evaporates in its elementary form so that in this same individual mercury vapors enter by inhalation. But if, in addition, he did not wash his hands after collecting the mercury and immediately consumes food, he can contaminate them by taking them by hand and the mercury will enter orally, although by this route practically the elemental mercury is absorbed very little [33]. In this example, it is clear how the metal can enter via different ways, which increases the amount of metal that enters the body. However, in general, for all metals it is important to consider jointly and not in isolation: the source of exposure, the amount of toxic present, the route of entry of the toxic and the time of exposure to the toxic, since these aspects influence the magnitude of the damage that metals can cause in the organism [27, 28].

From these routes of entry, the four toxicokinetic processes of absorption, distribution, biotransformation and elimination are initiated. The absorption process refers to the passage of the toxic through the route of entry into the blood, for this to happen, it is important to consider whether it is exposed to organic and inorganic compounds or to the elemental form of the metal that is contaminating either water or the food. In the case of organic compounds, they enter the bloodstream more easily because they are fat soluble and diffuse biological membranes faster and therefore their absorption rate may be higher than that of inorganic species. The species in elementary state evaporate so that when they are inhaled, they diffuse through the alveoli [34]. As for the distribution of heavy metals, it is observed that the organic forms are rapidly distributed to the central nervous system since they can easily cross the blood-brain barrier due to their liposolubility, they are also distributed to adipose tissue and other organs with higher fat content such as liver, heart and kidneys [27]. In contrast, inorganic compounds do not pass blood-brain barrier [28]. In general, metals pass placenta, and are attached to the disulfide bonds present in the keratin of the skin, hair and nails. On the other hand, lead is redistributed and deposited in bone and teeth [27].

In the biotransformation process of some heavy metals such as mercury and arsenic mainly, methylation reactions occur [27]. These occur in the liver and kidney, but various biotransformation reactions in the intestine can also be carried out through the microbiota. In this context, there is evidence at the preclinical level in cell cultures and in animal models that the microbiota performs various chemical reactions that can modify the toxicity of heavy metals; since heavy metals when distributed in the body can be concentrated in the bile and subsequently enter the enterohepatic circuit, or during their journey through the gastrointestinal system they may be susceptible to being biotransformed by the microbiota enzymes to less or more compounds toxic to the individual and even to the microbiota itself [35, 36]. This is a new issue that is changing the approach to toxicokinetics and toxicodynamics of heavy metals and other environmental toxins. For example, it has been described in murine models that the intestinal microbiota specifically the presence of bacteria such as *Faecalibacterium* can protect against acute arsenic toxicity [37]. At the preclinical level, there is a very interesting study on the intestinal microbiome of conventionally raised mice (with normal microbiomes) and of mice with mammalian microbiomes altered with antibiotics and both groups exposed to sodium arsenite. In this regard, the authors found high levels of As in urine of mice with altered mammalian microbiomes, but the levels of As in the total feces were lower in this group, compared with conventionally raised mice. They also observed that the interruption of the intestinal microbiome with antibiotics significantly modified the biotransformation of arsenic and the urinary ratio of *monomethylarsonic acid/dimethylarsinic acid* increased. Regarding the expression of carbon metabolism genes (folr2, bhmt and mthfr), they observed a downward regulation, and the levels of S-adenosyl methionine (SAM) in the liver of mice with mammalian microbiome altered with antibiotics and treated with arsenic they also decreased significantly. Finally, they concluded that altering the microbiome with antibiotics also increases the toxic effects of arsenic in mice [38]. In another study, it was observed that dietary supplementation with a galactooligosaccharide produced an increase in fecal excretion of lead, a decrease in plasma and tissue concentration of the metal in mice. This effect was not observed when the microbiota of the mice was modified with antibiotics [39]. On the other hand, the probiotic strain *Lactobacillus plantarum* CCFM8661, prevented the absorption of lead in mice by intestinal sequestration, also significantly induced bile acid synthesis, improved bile flow and bile glutathione excretion, and increased bile acid excretion in feces of mice, the outflow of bile lead and improved fecal excretion of lead. Previous antibiotic treatment eliminated the effects induced by *L. plantarum* CCFM8661 on enterohepatic circulation of bile acids and lead [40].

In another study in rodents with a probiotic strain (*Lactobacillus plantarum CCFM8610*) administered orally, significantly improved hepatic synthesis of bile acids, bile glutathione release and fecal excretion of bile acids. The biliary and fecal excretion of cadmium increased markedly after the administration of *L. plantarum CCFM8610*, which resulted in a marked reduction in Cd levels in tissues. These effects were related to the intestinal microbiota, since prior antibiotic treatment reversed the effects induced by *L. plantarum CCFM8610* on the metabolism of bile acids and cadmium [41].

Finally, heavy metals and some demethylated metabolites are eliminated primarily by urine, but they can also be eliminated by bile, feces, breast milk, skin, nails and hair [27, 28]. Once the processes of absorption, distribution, metabolism and elimination of heavy metals are analyzed, it is very important to consider the pharmacokinetic changes that can occur in the most vulnerable populations who suffer from toxic effects such as children and pregnant women (**Table 1**) [27].

Regarding the toxicodynamics of heavy metals, various toxicity mechanisms have been described, however the most important are:

a. Production of free radicals with oxidative stress generation.

b. Enzymatic inhibition in a reversible and irreversible way.

c. DNA alteration probably due to the products generated in the methylation reactions.

d. Apoptosis.

e. Decoupling oxidative phosphorylation.

These cell targets are primarily responsible for alterations and damage in various organs and systems [42]. Currently, the treatment for heavy metal poisoning is based on the administration of chelating drugs, which form a coordination link with heavy metal, favoring its elimination mainly by urine [27, 43]. However, when analyzing toxicodynamics, an important aspect to consider during treatment is to block the free radicals that are formed to prevent damage caused by the oxidation

	Lead	**Mercury**	**Arsenic**	**Reference**
Children	Oral absorption of lead is more increased compared with an adult. Deficiencies of calcium and iron increase oral absorption of lead. Children accumulate more lead in bone during the growing. A greater amount of lead is absorbed by inhalation (increased ventilatory capacity). Crosses blood-brain barrier.	Crosses blood-brain barrier.	Crosses blood-brain barrier.	[30, 31]
Pregnant woman	In pregnancy, lead is redistributed of bone into the bloodstream by increased calcium requirement. A greater amount of lead is absorbed by inhalation (increased ventilatory capacity). Crosses placenta.	Crosses placenta.	Crosses placenta.	[30, 31]

Table 1.
Most important aspects to consider in the toxicokinetics of vulnerable populations.

of lipids and proteins of the membranes and thus avoid oxidative cell stress, so that phytochemical compounds present in various foods can be effective in preventing oxidative cell damage. It has been described in the literature that heavy metals readily bind to groups -SH-, -SS-, -NH2-, -OH and -COO-, these groups are present in some endogenous antioxidants such as glutathione and exogenous acids such as acid ascorbic, so many antioxidant compounds such as flavonoids present in food can be an alternative to block the oxidative effect of heavy metals and thereby minimize or prevent oxidative damage in the population that has exposure to heavy metals [28, 44].

3. Microbiota and its composition

In recent years, the study of intestinal microbiota has increased significantly, because important protective and metabolic functions have been associated.

In this regards, intestinal microbiota compete for nutrients, space and receptors with pathogenic microorganisms, as well as stimulating the production of antimicrobial peptides and IgA antibodies; whereas in metabolic functions, the microbiota converts many complex substances such as starches, cellulose, pectins and gums into metabolites that are easily absorbed and used by the host, it also ferments another non-digestible residues from the diet, synthesizes some vitamins and is also involved in the absorption of ions (such as calcium, magnesium and iron) and energy recovery [13, 14].

The intestinal microbiota comprised about 35,000 species of microbes and includes at least six bacteria phyla, among them *Firmicutes*, *Bacteroidetes, Fusobacteria, Proteobacteria, Actinomycetes and Verrucomicrobia*; the predominant bacteria populations constituting about 90% of the total being Firmicutes and Bacteroidetes [45]. In gastrointestinal tract, there is a wide variety of bacteria that survive and have adapted to different pH conditions. In the esophagus, pH <4 is inhabited by bacterial strains from phyla *Bacteroides, Gemella, Megasphaera, Pseudomonas, Prevotella, Rothia sps., Streptococcus and Veillonella*. The phylas such as *Streptococcus, Lactobacillus, Prevotella, Enterococcus* and *Helicobacter* reside mainly in stomach (pH = 2). In small intestine (pH = 5–7), the phylas such as *Bacteroides, Clostridium, Streptococcus, Lactobacillus, g-Proteobacteria* and *Enterococcus* are found mainly (**Figure 1**). In colon (pH = 5–5.7), *Bacteroides, Clostridium, Prevotella, Porphyromonas, Eubacterium, Ruminococcus, Streptococcus, Enterobacterium, Enterococcus, Lactobacillus, Peptostreptococcus* and *Fusobacteria* are the resident phylas and finally in cecum (pH = 5–7) the phylas such as *Lachnospira, Roseburia, Butyrivibrio, Ruminococcus, Fecalibacterium* and *Fusobacteria* are found [46]. The intestinal microbiota has both a symbiotic and mutualism relationship, and also it has an important influence on the health and physiology of host. In this way, intestinal dysbiosis has been associated with a large array of human diseases such as, irritable bowel syndrome, inflammatory bowel disease, metabolic diseases (obesity and diabetes), as well as allergic and neurological diseases [47–49].

There are several factors affecting variations on intestinal microbiota, including age and diet [46, 50, 51]. It has been suggested that intestinal microbiota in healthy individuals is relatively stable when the diet remains without major changes, but with a subtle change in diet, the intestinal bacterial composition may also change and produces important alterations on the protective barrier function of the intestine. It is well known that not only the intestinal microbiota supports the protective functions of host. In addition, there is a complex cellular barrier where a variety of cells with different functions are housed, such as enterocytes, goblet cells, enteroendocrine cells, Paneth cells and intraepithelial lymphocytes; together with the mucus

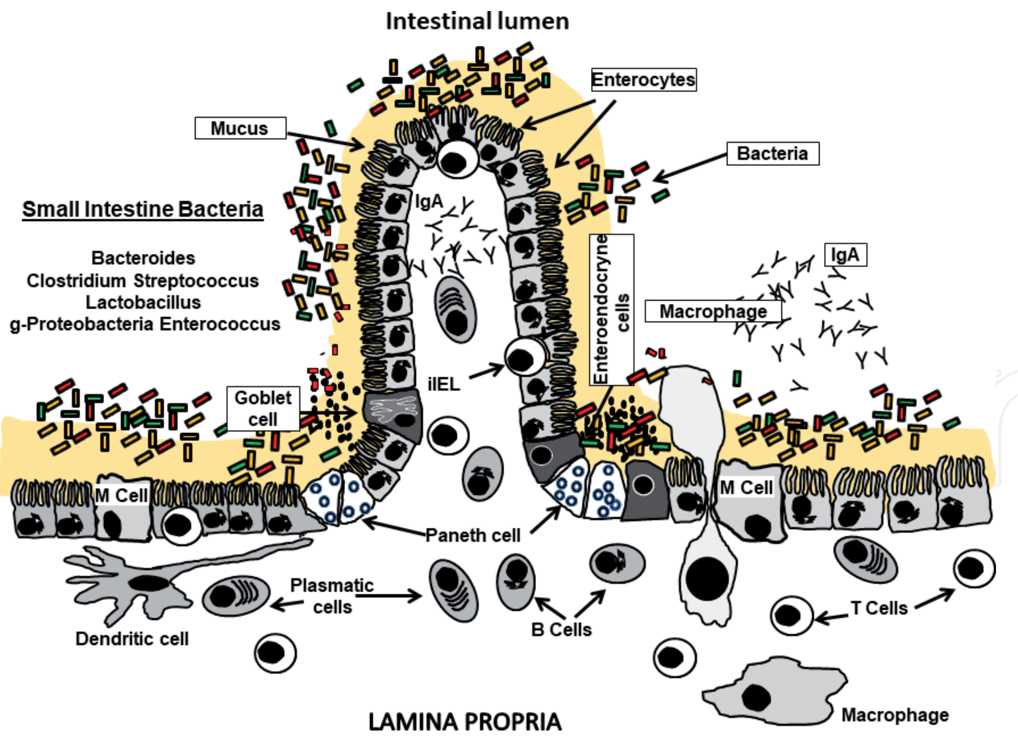

Figure 1.
The cellular composition of the complex barrier of the small intestine, where cells with different functions, such as enterocytes, goblet cells, enteroendocrine cells, Paneth cells and intraepithelial lymphocytes are the main residents. In addition, there is a layer of mucus in the intestinal lumen. Moreover, the lamina propria contains mainly T and B lymphocytes (secretory IgA plasmatic cells), macrophages and dendritic cells. It is possible to find the following bacterial phylus in the small intestine microbiota: Bacteroides, Clostridium, Streptococcus, Lactobacillus, g-Proteobacteria *and* Enterococcus *that adapt to survive at pH = 5–7. These bacteria are in constant contact with all host cells and they have several functions related to health and illness of host.*

and lamina propria (which consist of lymphocytes, macrophages and dendritic cells), the main function is to limit the translocation of bacteria or other antigens and, therefore, proinflammatory processes are avoided and controlled (**Figure 1**). However, some intestinal bacteria from microbiota could produce toxic metabolites that may damage the epithelial barrier, increasing intestinal permeability and allow the entry of bacterial products into the circulatory system [52].

On the other hand, the role of the microbiota in detoxification of xenobiotics and contaminants (pesticides and heavy metals) has been poorly studied. Nevertheless, it has been found that intestinal microbiota contributes to metabolism of xenobiotics [23] and heavy metals such as cadmium [21], mercury [20] and metalloids such as arsenic [24]. In this regards, in rats [53] and mice [54], several bacteria strains have been proposed and used as detoxifying probiotics, including mainly lactic acid bacteria. However, to date, there are no studies about the use of lactic acid bacteria as probiotics in humans. Recently, in *Drosophila melanogaster*, it has been found that use of *L. rhamnosus* has reduced both absorption and toxicity of organophosphate pesticides [55]. Also, lactic acid bacteria [56] and *Pediococcus* [57] have been used to reduce the toxic effects of aflatoxins and mycotoxin present in food, respectively. Likewise, in vitro experiments have shown the ability of lactic acid bacteria to bind and neutralize acrylamide molecules, a carcinogenic component present in some foods [58].

Since 1977, the interaction of the intestinal microbiota with the elimination of heavy metals was demonstrated. Here, elimination of mercury in feces of germ-free mice was lower, while the retention of mercury was slightly higher in organs from germ-free mice than in control mice [59]. In addition, it has been shown that oral administration of probiotics like *Lactobacillus plantarum* inhibit heavy metal cadmium (Cd) absorption by protecting the intestinal barrier upon acute and chronic Cd intoxication in mice [25]. Recently, it has been proposed that the possible mechanism of detoxification of Cd upon oral administration of *Lactobacillus plantarum* as a probiotic is through the enterohepatic cycle, increasing the metabolism of bile salts, which are conjugated with Cd and favoring its elimination in feces [40]. Similarly, the probiotic strains of *Lactobacillus rhamnosus*, *Propionibacterium freudenreichii* and *Shermanii js.* showed an effective ability to bind cadmium and lead, both in vitro and in experimental mouse model of oral heavy metal intoxication [60, 61]. Additionally, use of probiotics improved the nutritional, biochemical and physiological parameters in experimental rat model intoxicated with chromium, suggesting that probiotic bacteria neutralize the toxic effects of chromium [62]. Also, administration of *Lactobacillus plantarum* as a probiotic significantly reduced both renal and hepatic injury induced by aluminum in mice that are chronically exposed to this toxic heavy metal [63]. Recently, human gut commensal *Faecalibacterium prausnitzii* was used as probiotic in mice. Here human stool transplantation restored protection in acute arsenic toxicity in mouse models [24]. Moreover, the functions in detoxification of inorganic arsenic of arsDABC genes from obligate anaerobic bacteria *Bacteroides vulgatus*, a common resident of the human microbiota have been well characterized [64]. Interestingly, in a clinical pilot study, yogurt supplemented with probiotic was administered to pregnant women and school children living in contaminated areas of Tanzania, resulting in a significant reduction on blood levels of heavy metals such as mercury and arsenic [65].

Finally, the ability of the microbiota to metabolize drugs has been referred as Pharmacomicrobiomics [66]. Intestinal microbiota generates phase I and phase II reactions to metabolize drugs, similar to the one generated by host cells. These include hydrolysis, dealkylation, glucuronidation and others reactions [67]. Thus, it has been strongly suggested that bacteria from the intestinal microbiota produce enzymes that metabolize drugs and contribute to determine the pharmacological properties of several drugs. Some examples of drugs that are metabolized by intestinal microbiota include aminosalicylates and anthranoid laxatives; digoxin; irinotecan and non-steroidal anti-inflammatory drugs, such as rutin, diosmin and baicalin, as well as L-dopa and simvastatin, used for the treatment of Parkinson's disease [68–70].

4. Evidence in the state of Guanajuato, Mexico

Guanajuato is a Mexican state located in the middle area of the country and according to the 2015 intercensal National Population Census, Guanajuato has 5,853,677 inhabitants, representing 4.9% of the total population of the country. Guanajuato is divided into 6 socioeconomic and geographic regions with 46 municipalities [71]. Since 2005, the risks of arsenic exposure in drinking water have been studied in some rural populations belonging to the State of Guanajuato [72]. In a comparative study in children of 10 years of age on average, arsenic levels were found in hair above the norm (from <0.006 to 1.3 mg/kg) and for the control group <0.006 mg/kg of arsenic [72]; however, it was found that children with non-standard levels of arsenic in hair, referred to drinking only carafe water and not tap water, which was explained because the water used to prepare soups, broths or beans, was used tap water [73]. On the other hand, only 26% had an adequate energy intake and the consumption of protein, folic acid, zinc and fiber was low according to RDA and children used to have mainly soft drinks, fried foods and processed foods [74]. Another study was applied in 352 households (heads of family) and measuring experiences related to access to water [sufficiency, safety (safety), acceptability, availability and accessibility], 33.4% of households reported concern about not having access to water and 74.8% had no access. About 70.8% had to buy water to drink and 5.7% became ill and related it to water consumption. About 65.6% of households presented food insecurity. The correlation was significant for the level of schooling of female heads of household, the number of households with children aged 1 and 12 with the use of tap water for drinking, preparing powdered milk for children and for food at home and fresh water [70, 75], which reflects the problem of exposure to various pollutants.

4.1 Main health problems in the state of Guanajuato

Studies conducted regarding lifestyles and eating habits have found a deterioration in it, where the child and adolescent population are the first years of key life of growth and development, have a low consumption in fruit, vegetables and legumes (beans and lentils), which reflects risks of the absence of having prebiotics that allow maintaining intestinal health (microbiota) [71, 72]. Studies have shown a decrease in breastfeeding that so far during 2019 are changing these figures in Guanajuato but before that, the time of breastfeeding identified was 4.3 months in a range of not breastfeeding up to 7.3 months maximum [71, 72]. It is known that breastfeeding is the best food that promotes intestinal health and thus the microbiota. Guanajuato, as well as several regions of Mexico and in the world, has high rates of prematurity, teenage pregnancy and diabetes, which has a strong component with lifestyles and if we combine environmental pollution problems, we will face an obvious risk. For the first known biotransformation mechanism is the microbiota, but studies are still scarce [72, 73].

Regarding the stage of pregnancy, a study found reports of 26% of the mothers who reported a consumption of soda at least twice a week and preferred to buy already processed foods than prepared at home. The consumption of fruit, vegetables, legumes, cereals and tubers were low. This reflects problems of access to food and with its food insecurity, in addition to worrying about not having enough access to water, and in the last 3 months, 50% of households experienced water shortages. Most households used tap water to prepare milk for the children, as well as for personal hygiene. About 25% of the interviews reported that water availability has decreased in their homes, while the cost of water has increased [74].

4.2 Dietary and food intervention in the region

Derived from studies with arsenic and knowing its metabolism in addition to deterioration in lifestyles [74], the effect of vitamin and mineral supplementation on nutritional status and urinary excretion of arsenic in a group of 45 exposed adolescents was measured to this metal through drinking water [7], supplementation was provided daily for 4 weeks for subsequent weekly assessment of nutritional status and arsenic levels in urine and drinking water. It was observed that the basal nutritional intake was low for protein, fiber, folic acid, vitamin B2, B6, B12, E, C, selenium and iron, as well as the increase of 1 g/dL of hemoglobin in all participants, at the end of the intervention in addition to an increase in fat-free mass and decrease in the percentage of body fat; the average arsenic consumption of drinking water in participants was 96.2 ± 7.5 μg/L with a urinary excretion of arsenic in the first week of intervention [35.91 μg/g Cr (95% CI = 23.2–74.8 μg/g Cr)] resulting higher, which was statistically significant compared with baseline urinary arsenic levels [43.2 μg/g Cr (95% CI = 30.8–117.6 μg/g Cr)] ($p < 0.05$).

From several species of quelites, which are endemic plants of Mexico, its vast nutritional composition is known. A recent study, evaluated three types of quelites (purslane-*Portulaca oleracea*-;quintonil-*Amaranthus spp.- and quelite ash or green quelite-Chenopodium album*-) from Mexico, determined their nutritional composition, antioxidant capacity and physicochemical analysis finding considerable levels of carotenoids (2.85 mg/g DW) and the highest antioxidant activity. The nutritional content of iron, calcium and magnesium were higher for *quintonyl*, while for phosphorus, potassium and zinc was higher in quelite ash [75]. The ash and purslane quelite showed similar antioxidant activity but a higher level in the phenolic and flavonoid content, while the quintonil showed the presence of chlorophyll and protein concentration higher than those found in the quelite ash.

5. Conclusions

The chapter closes in a compilation of studies that reflect that despite the changes in lifestyle with a greater deterioration in healthy habits and therefore the consumption of an adequate diet (low in fruit and vegetables) and with it a low contribution in nutrients that promote the growth of the microbiota as well as in fiber which is known to have a probiotic effect, the consumption of fruit such as banana, apple and orange that is seasonal and low-cost fruit is preserved; of vegetables such as onion used as a condiment or in the preparation of most Mexican foods such as broths and sauces, as well as the consumption of beans (legume group), which are rich in antioxidants, soluble fiber rich in fructooligosaccharides.

Despite the little evidence, it is clear that the maintenance and promotion of the microbiota is to have a nutritious or adequate, varied, balanced, sufficient diet; as well as considering the alternatives of consuming fermented and probiotic-added dairy products, locally produced nutrients that are known to counteract non-toxic exposures such as those already reviewed, as is the case of prolonged exposure to arsenic, through food and drinking water, as it increases the risk of cancer, diabetes and high blood pressure, among other diseases. The typical Mexican diet is high in soluble fiber, key nutrients such as antioxidants, proteins are beans, tortilla plantain, orange, chili, quelites, showing that they co-help with a greater arsenic excretion through the urinary tract.

It is suggested to continue expanding the evidence of the combination of foods from a diet and lifestyle in general, mainly in women during the menopause period and pregnancy, due to a greater susceptibility to the development of anemia and resorption. Bone with exposure to metals such as lead or cadmium, since arsenic and fluoride are not the only contaminants that have been described in Guanajuato, the presence of lead, chromium and mercury, among the main ones, is known, and it is necessary Scale these experiences to combine nutritional treatment and drug therapy with chelators.

Conflict of interest

The authors declare none conflict interest.

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