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Impact of Glyphosate on Human Health: Risks and "Needs" of its Use

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The use of pesticides in agricultural production and the resulting contamination have been a constant concern in public health, requiring varied levels of government investments and organization in implementing programs and actions on waste control, which might eliminate or minimize health risks of the Brazilian population regarding the presence of these residues in water and food. Besides, there are environmental and social impacts associated, because the use of pesticides and the strategies for their use are associated to industrial agriculture based on monocultures as a chosen economic model supported by multinational companies.

In Brazil, the pesticide market increased from $ 2 billion to over US $ 7 billion between 2001 and 2008, reaching US $ 8.5 billion in 2011. Thus, in 2009, we achieved the undesirable position of largest consumer of pesticides in the world, surpassing the mark of 1 million tons, which is equivalent to an average consumption of 5.2 Kg per capita of agricultural poison[1].

Taking into account the full range of active ingredients registered, we highlight the contribution in this market of the active ingredient in the herbicide glyphosate, [N-(phosphonomethyl)-glycine][1]. Driven by the growing diversity of use and dramatic increases in applied volumes, glyphosate and its primary metabolite aminomethyl- phosphonic acid (AMPA) have been detected in the air, soil, and water[2]. Risks to human health and the environment posed by glyphosate have been placed on the agenda of the United Nations Environment Program, the International Labour Organization, and the World Health Organization, since 1994[3].

Roundup® is the major formulation of glyphosate, which was first sold commercially by Monsanto, in 1974[2]. Glyphosate is a systemic and non-selective herbicide which is registered in Brazil since the late 70s. In Brazil, during the year of 2013, it was sold 186.000 tons of glyphosate, mainly used in transgenic soybean crops[1]. Global soybean production in 2014 was of 315.4 million metric tons (11.6 million bushels), with the U.S. (108 million metric tons), Brazil (94.5 mill. metric tons), and Argentina (56 mill. metric tons) accounting for 82% of the global harvest. Glyphosate and AMPA residues are present at relatively high, and rising levels (over 1 ppm) in a high percentage of the soybeans grown in the U.S.A., Canada, Brazil, Argentina and Paraguay, countries that account for 86.6% of the 11.6 billion bushels of soybeans produced globally in 2014, and nearly all global trade in soybeans and soybean-based animal feeds[2].The adoption of genetically engineered “Roundup®-Ready” corn, soy, canola, cotton, alfalfa, and sugar beets has made it relatively easy to control weeds without killing the crop plant. But this means that glyphosate will be present as a residue in derived foods4. Genetically engineered herbicide-tolerant crops now account for about 56 % of global glyphosate use[2].

The adoption of conservation farming techniques to improve soil structure and reduce erosion has led to an increased reliance on herbicides for weed control. One of the key herbicides used in conservation farming is glyphosate, due to its low cost and its effective control of a broad spectrum of weeds5, what stimulates the growing use of these products in agriculture.

Glyphosate prevents the growth of plants by interfering with the biosynthetic pathway of the essential aromatic amino acids needed for plant survival. It inhibits a key enzyme in the shikimate pathway: 5-enolpyruvylshikimate-3- phosphate synthase (EPSPS). Inhibition of this enzyme prevents the plant from synthesizing the aromatic amino acids phenylalanine, tyrosine, and tryptophan, which are used for the synthesis of compounds associated to plant growth regulation, cell walls, and proteins, including those involved in plant defence. However, the shikimate synthesis pathway is also present in microorganisms, and therefore, this pesticide may also disrupt microbial growth and activity in susceptible species[5].

Although glyphosate should be associated with a low toxicity[3], recent studies related to the potential toxicity of this herbicide have pointed out more evidence of the health risks (Table 1). In this sense, in 2015, the herbicide glyphosate was classified as probably carcinogenic to humans (Group 2A)[6]. A growing body of literature points to possible, adverse environmental, ecological, and human health consequences following exposure to glyphosate and/or AMPA, both alone and in combination with ingestion of genetically engineered proteins.

Environmental studies encompass possible glyphosate impacts on soil microbial communities and earthworms, monarch butterflies, crustaceans, and honeybees. Studies assessing possible risks to vertebrates and humans include evidence of rising residue levels in soybeans, cancer risk, and risk of a variety of other potential adverse impacts on development, the liver or kidney, or metabolic processes[2].

Table 1: The use of herbicide glyphosate and its potential risks to human health

	POTENTIAL RISKS TO HUMAN HEALTH
1.	Positive association between exposure to glyphosate and B cell lymphoma[7]
2.	Teratogenic effects have been demonstrated in human cell lines[8]
3.	An *in vitro* study showed that glyphosate in parts per trillion can induce human breast cancer cell proliferation[4,9]
4.	Glyphosate is a likely cause of the recent epidemic in celiac disease. Glyphosate residues are found in wheat due to the increasingly widespread practice of staging and desiccation of wheat right before harvest. Celiac patients have a shortened life span, mainly due to an increased risk to cancer, most especially non-Hodgkin's lymphoma, which has also been linked to glyphosate[4]
5.	Glyphosate is neurotoxic. Its mammalian metabolism yields two products: Aminomethylphosphonic acid (AMPA) and glyoxylate, with AMPA being at least as toxic as glyphosate. Glyoxylate is a highly reactive glycating agent, which will disrupt the function of multiple proteins in cells that are exposed. Glycation has been directly implicated in Parkinson's disease. Glyphosate has been detected in the brains of malformed piglets[4].

The meta-analysis developed by Nguyen et al.[5] has shown that much of the variation in the response of whole soil microbial biomass and respiration to glyphosate is related to the dose at which it is applied and the duration of exposure. Further, soils with pH ranging from 5.5 to 7.5 are more susceptible to reductions in both soil microbial biomass (SMB) and soil microbial respiration (SMR) following application of glyphosate than acid soils (pH < 5.5). Ultimately, the fact that management and environmental factors regulate the soil microbial response means that generalizations about the toxicity or safety of glyphosate to SMR and SMB should be qualified with details of the conditions under which glyphosate is applied[5]. This implies a rational use or not in excess.

Besides, the control model of use of allowed amounts of glyphosate needs to be changed in order to encourage alternative and sustainable practices, which must be understood as a new approach for the evolution of the field. The dominant agricultural model in Brazil, which is based on monoculture, leads to a decrease in the ecological diversity, resulting in the need for excessive use of pesticides. Moreover, it generates pest-resistant and modified seeds, that although was highly effective against some pests, became the worst enemy for country.

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