Ecoimmunology Perspectives on Glyphosate

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Abstract

Between 2001 and 2011 more than six billion kilograms of Glyphosate Based Herbicides have been applied in the world [1]; glyphosate is now considered ubiquitous in the environment [2].

Here I explore perspectives on how as a chemical compound glyphosate can influence immunocompetence by at least three different functions: oxidative stress [3], systemic loss of bioflavonoids [4], and systemic loss of serotonin production [5].

It has been established that glyphosate affect a wide range of species beyond its botanical targets. Based on available information further research needs done looking at correlated epidemiological patterns.

Introduction

Glyphosate was originally branded as a herbicide which did not affect species other than its target due to its cited chemical action being on 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS), a key enzyme in the biosynthesis of aromatic acids and secondary metabolites. The manufacturer made the claim on the basis that EPSPS does not exist in mammalian biology therefore does not affect it.

Whilst glyphosate does act on EPSPS, in the five decades since glyphosate began being used commercially a range of research has shown the molecule exhibits several chemical properties which can be understood as part of its unintended mechanism of action.

Taking the view of ecoimmunology I scrutinize the implications of glyphosate on immunological responses across a range of species with a particular focus on the living organism being able to mount an immunological response to biotic stress.

This work focuses on three key mechanisms of action which alter immune responses of plants, mammals, and other species:

Oxidative Stress: the role of the free radical in immunological processes

Flavonoid: the role of the free radical in immunological processes

Serotonin: the role of tryptophan, serotonin and indole groups in aspects of immunity and antimicrobial peptide formation.

Methodology

The methodology of this work relies on literature review and prospective inference based on understanding the established chemical characteristics of glyphosate and situating them in contexts where theoretically, drawn from the established and practical science, we might infer probable chemical interactions

For example, we know when Reactive Oxygen Species occur, around them molecules which are in a reduced state react with molecules in their oxidized form passing on their reductive power and in turn becoming oxidized themselves. We know that the functional sites of many molecules must be in a reduced electronic state for them to be able to react with their substrates in turn allowing biological processes and electronic cascades to take place.

The effect of pro-oxidants is to challenge the biology of the organism to maintain a homeostasis through enzymic regulation. The metabolism of Reactive Oxygen Species and the complexity of the antioxidant network illustrates the inter-threaded and co-constitutional nature of the biology. Oxidation in general tends to represent the catabolic and degenerative aspect of biology; oxidative stress having been implicated in many diseases of modernity, an example being diabetes mellitus.

Drawing from peer reviewed literature which documents the effects of a molecule (i.e. that glyphosate has oxidative properties) and from a peer reviewed literature on the biology of substances which react with free radicals (i.e. the antioxidant network); through bringing together disparate bodies of work it is then possible to make prospective logical inferences in the research process.

Oxidative Stress: the role of the free radical in immunological processes

Oxidative stress is well researched and documented in relation to a wide range of illnesses and disease, amongst which immune related conditions are noted. We know that glyphosate has been demonstrated to cause oxidative stress in a variety of species including fish [6], crustaceans [7], plants [8] and humans [9, 10].

Agostini and colleagues [3] detail how oxidative stress is involved in a number of immune diseases pointing out how an excess of Reactive Oxygen Species and a deficiency of antioxidants in AIDS leads to apoptosis and virus activation.

The 'antioxidant hypothesis' proposes that antioxidant nutrients and enzymes afford protection against chronic diseases by decreasing oxidative damage. Maret [11] writes: "The antioxidant hypothesis holds that suboptimal levels of antioxidant nutrients compromise the defense against reactive oxygen species and thus constitute a risk factor for many other degenerative diseases of aging, such as cardiovascular disease, cancer, decline of the immune system, and cataracts."

Oxidative damage negatively affects compounds which have a sulfhydryl group. The amino acid cysteine and the tripeptide antioxidant enzyme glutathione both have fundamental requirements for their sulfhydryl groups to be in the reduced state for cysteine to perform its structural role in proteins. Dröge and Breitkreutz [12] document the vital operations that cysteine residues play in the immune cells. It looks like a well documented line of research examining how oxidative stress influences immunity of various species in relation with glyphosate exposure.

Results

Flavonoid: The prospective role of dietary flavinoids in immunological processes

Flavonoids are products of the secondary metabolism of plants which can be a part of the diet via consumption of edible plants. Plants produce flavonoid molecules in responses to biotic and abiotic stress in order to protect the plant against bacterial or fungal infection [13]. Glyphosate inhibits 5-enolpyruvyl shikimate 3-phosphate synthase (EPSPS), a key enzyme in the biosynthesis of aromatic acids and secondary metabolites. Blockage of this enzyme pathway results in massive accumulation of shikimate in affected plant tissues leading to a deficiency of significant end-products such as lignins, alkaloids, and flavonoids as well as a decrease in CO2 fixation and biomass production in a dose dependant manner [12].

The role which flavonoids play in immunity is complex and note worthy. Although unrecognized as an essential nutrient the levels of flavonoids in diets do have an effect on immunological function. Middleton and Kandaswami detail their effects on the function of T cells, B cells, macrophages, NK cells, basophils, mast cells, neutrophils, eosinophils, and platelets [14]. Khan et al [15] detail the flavonoids as immunomodulators in their work.

The introduction of glyphosate abolishes the occurrence of complex aromatic compounds such as flavonoids in plants. If dietary flavonoids alter the day-to-day immunological response of organisms which have them in their diet, then this loss of molecular diversity represents a vista of ecoimmunology. This space is particularly important in analysing why biotic stress (for example, aphids feeding off a plant) contributes nutritional and medical characteristics to food crops for human consumption. There is powerful evidence suggesting a line of research on how the glyphosate molecule affects the immunity of plants and humans, and the ecosystems of important immunomodulators in the diet.

Serotonin: The role of tryptophan, serotonin and indole groups in aspects of immunity and antimicrobial peptide formation.

The biology of tryptophan, serotonin and indole groups offer a particularly rich set of prospects exploring ecoimmunology. As glyphosate disrupts the enzyme EPSPS which is responsible for producing the aromatic amino acids phenylalanine, tyrosine, and tryptophan, we can infer that downstream products will be affected due to their precursors not being produced. This means that, amongst others, the serotonergic and dopaminergic compounds are unavailable to living organisms that rely on dietary sources of the essential amino acids.

Serotonin plays a special role in immunological function. Mo ssner and Lesch detail 5-HT receptors and the 5-HT transporter on immune cells suggesting four major functions for 5-HT: T cell and natural killer cell activation, delayed-type hypersensitivity responses, production of chemotactic factors, and natural immunity delivered by macrophages [16]. Afanas'eva and colleagues [17] suggest a morphogenetic role of serotonin in the critical period of the immune system development of the rat. The work by Bi and colleagues [18] illustrate the functional role which tryptophan residues play in antimicrobial peptide production; a vital part of innate immunity of hosts.

Conclusion: Taken together these lines of evidence and documentation of the mechanisms of action suggest a strong line of evidence suggesting the effect of glyphosate on immunology of a range of species.

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