



## ARTICLE INFO

## Open Access



Date Received:

16/05/2017;

Date Revised:

10/08/2017;

Date Published Online:

25/08/2017;

## Glyphosate: cancerous or not? Perspectives from both ends of the debate

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Glyphosate is non-selective herbicide. Studies published in the last decade, point towards glyphosate toxicity. Shikimic acid pathway for the biosynthesis of folates and aromatic amino acids is inhibited by glyphosate. Glyphosate carcinogenicity is still considered to be a controversial issue. The World Health Organizations' International Agency recently concluded that glyphosate is "probably carcinogenic to humans." Some researchers believed that glyphosate is not linked with carcinogenicity.

Glyphosate is an active substance that is widely used in pesticides. Glyphosate based pesticides are used in agriculture to combat weeds. They are typically applied before crops are sown and as a pre-harvest desiccating treatment, accelerating the ripening process. 5.8 kg active ingredient per hectare is recommended application dose [1].

Glyphosate, particularly its trademark Roundup, has been shown to have clear toxicity, both in laboratory tests and in epidemiological studies. Epidemiological studies have shown that glyphosate is absorbed through the skin and mucous membranes to produce neuromuscular symptoms. It increases the risk of abortion [2]. It has been related to chronic kidney diseases. Laboratory studies show several negative effects such as genotoxic effects, mutagenic effect, negative effects on estrogen-regulated gene expression, changes in the structure and functioning of cells and cytotoxicity in human cells [3].

It causes faster tumor development and human breast cancer cell growth. This implies that the consumption of soy products contaminated with glyphosate produces a risk of developing breast cancer [3]. Glyphosate effects on the biology and reproduction of freshwater snails have been reported as well, and as a result of this, its possible influence on the spread of mammal diseases as fascioliasis [4]. On the other hand, the exposure to this herbicide changes the susceptibility to antibiotics of some disease-producing bacteria, so in some cases these bacteria acquire greater resistance to antibiotics [5]. Glyphosate

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Hassan SA, Akhlaq F, Tayyab M, Awan AR, Firyal S, Khan WA, Saif R, Wasim M (2017). Glyphosate: cancerous or not? Perspectives from both ends of the debate Adv. Life Sci. 4(4): 108-112.

**Keywords:**

Glyphosate, Cancer, Agriculture, Health



absorbed by plants is eventually excreted by roots to the rizosphere, into the soil, where it is toxic to several beneficial fungi and bacteria, unbalancing the soil microbial community. Earthworms are also negatively affected by this herbicide [6].

In soybean crops, the application of glyphosate reduces poly-unsaturated fatty acids content and increases that of mono-unsaturated fatty acids [7]. However, it decreases mineral concentration and crop biomass production. It increases sensitivity to fungal attacks and to diseases in crops in which the herbicide is applied [8].

### **Working mechanism of glyphosate**

It is considered as a non-selective herbicide. Formation of certain proteins which are considered necessary for plant growth is inhibited by glyphosate. Chemically it is known as N-(phosphonomethyl) glycine. It is usually formulated as trimethyl sulfonium salt of glyphosate. Other ingredients are also added to the formulation. A surfactant which is polyoxyethyleneamine, is usually added to glyphosate formulations which helps the active ingredient to penetrate the plant surface. The main breakdown product or metabolite of glyphosate is amino methylphosphonic acid (AMPA).

Glyphosate inhibits Shikimic acid pathway. In microorganisms and plants, Shikimic acid pathway is very important. Glyphosate is an inhibitor (competitive) of PEP. It is found that it binds more strongly to the EPSP synthase-S3P complex. The dissociation rate for PEP is 2,300 times faster than glyphosate. When glyphosate binds with the EPSP synthase-S3P, the enzyme activity is inactivated.

### **Why glyphosate is considered as carcinogenic?**

It is a controversial issue. Some scientists are in favor of carcinogenicity of glyphosate but some scientists said that glyphosate does not lead to cancer.

### **Supporting studies**

#### ***IARC***

WHO's IARC has recently classified the under study glyphosate as a "probable human carcinogen". The evidence of carcinogenicity in humans was in support by a positive result between glyphosate exposures in 3 out of 4 studies. The panel also stated that it is genotoxic and in laboratory animals, glyphosate dose increases malignant tumors at multiple sites and not forgetting sites of kidneys and liver. There is also an evidence that tells that glyphosate might act as an estrogen mimic, which leads to breast cancer risk.

#### ***US Agricultural Health study***

Results concluded did not point out any association in glyphosate and breast cancer in the private pesticide applicators wives from North Carolina [9]. Such results need to be analyzed with caution as the control population (considering farmers and also their spouses: who had not applied glyphosate) might have chances to be exposed through contamination [10].

#### ***EPA, US***

The department has concluded the results from their screening program of endocrine disruptor concerning glyphosate alone. A major number of test results doesn't show any convincing evidence regarding the potential interaction with estrogen and thyroid pathways or androgen. Some studies include evidences regarding the endocrine disrupting effects. In animals, possible association between glyphosate



and mammary tumors is carried out by one and only one long term study. This study is seen which has used environmentally relevant concentrations of a herbicide that is glyphosate-based which then reported a clear and visible increase in the mammary tumors incidence [11]. In vitro study which used the mammary cells of humans, found out that the glyphosate, acts as an estrogen mimic which is seen to be promoting growth of mammary cells of humans. This evidence raises such concerns that glyphosate may be a chemical that has endocrine disrupting nature.

#### ***World Health Organization (WHO)***

The increased use of glyphosate in the US is correlated with increasing incidence and also death rate of many diseases and various cancers. The WHO also revised its previous assessment of glyphosate's carcinogenic potential in 2015 and relabeled it as a "probable carcinogen" [12].

#### **Non supporting studies**

##### ***Food and Agriculture Organization of the UN***

In 1986, FAO & WHO in their report on glyphosate stated that: "The chronic toxicity of glyphosate is low; the only case of significant toxicity was seen in animal bioassays where mild hepatotoxicity was observed at higher doses in mice but no evidence was reported on the carcinogenicity" and "no mutagenic activity was present in glyphosate both *in vitro* and *in vivo*" [13].

##### ***Canadian Agency for Pest Management Regulation***

The agency concluded that "Health and Welfare Canada examined glyphosate toxicology, which is considered as complete. The toxicity of glyphosate is low and no evidence was recorded regarding the development of mutations, birth defects or cancer due to glyphosate" [14].

##### ***Environmental Protection Agency (EPA)***

In 1993, the U.S. EPA stated: "Several studies on chronic toxicity/carcinogenicity resulted in findings that glyphosate was not carcinogenic" and "does not cause mutations". In June 1991, agency gave glyphosate place in the classification of the lowest cancer, "evidence of non-carcinogenicity for humans, based on the lack of convincing evidence of carcinogenicity in adequate studies" [15].

##### ***Toxicology experts***

In 2000, an international toxicology panel published an assessment of glyphosate studies. "Multiple lifetime feeding experiments have failed to prove any tumorigenic potential for glyphosate. These studies concluded that glyphosate is non-carcinogenic", "No genotoxic activity was examined in standard assays performed according to international guidelines" and on the basis of the above evaluation, glyphosate is not considered to cause heritable or somatic mutations" [16].

##### ***European Commission's Health***

A regulatory review was carried out by the ECH and after conducting this review glyphosate was re-registered. The EC review then concluded that there was "No evidence of carcinogenicity" and "Not genotoxic" [17].

##### ***Genotoxicity experts***

Two genotoxicity experts have published a review on genotoxicity, regulatory studies of glyphosate and Glyphosate Based Formulations (GBFs) in 2012. The authors observed negative results in well-conducted bacterial reversion, in vivo mammalian micronucleus and chromosomal aberration assays, which indicates that glyphosate and typical GBFs are not genotoxic in these core assays [18].

### ***Epidemiologic experts***

In 2012, a group comprising of epidemiologic experts studied the association between glyphosate and cancer outcomes by seven cohort and they have found no consistent pattern of positive associations which indicates a causal relationship between total cancer or site-specific cancer and exposure to glyphosate [19].

### ***Australian Pesticides and Veterinary Medicines Authority (APVMA)***

The APVMA currently has no data regarding any unacceptable risks of glyphosate to the environment, human health and trade. The evidence shows no genotoxicity, carcinogenicity and neurotoxicity of glyphosate [20].

### ***Glyphosate re-evaluation assessment report***

European Food Safety Authority having expertise for assessing pesticides in the European Union has organized peer review of the German assessment regarding the re-evaluation of glyphosate in 2014. According to the assessment, glyphosate was not found to be carcinogenic or neurotoxic and has no effect on fertility, reproduction and development in human.

## **Conclusion**

Some research agencies agreed with the carcinogenic potential of glyphosate and some of these believe that “glyphosate is not likely to be carcinogenic”. Further study is needed to reveal the exact relationship between cancer and glyphosate to conclude an authentic result and decision about carcinogenicity of glyphosate that whether it is carcinogenic or not.

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