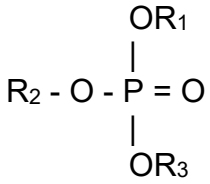
GLYPHOSATE - NOT AN ORGANOPHOSPHATE

Glyphosate, an active ingredient in Roundup® branded herbicides, is periodically referred to as an organophosphate. This contributes to the incorrect perception that glyphosate is a cholinesterase inhibitor like various well-known insecticides. As a result, some patients who ingested Roundup® brandeds herbicide have received inappropriate medical treatment which may have worsened their condition. The intent of this bulletin is to clarify the structural/biological characteristics of glyphosate and prevent improper medical care.

It has become customary to generically refer to any organic compound containing phosphorous as an “organophosphate”. However, there are actually different classes of “organic phosphate” compounds that are determined by the atoms attached to the phosphorus. The phosphorus atom of a true organophosphate is attached only to oxygen atoms[1] (Figure 1).

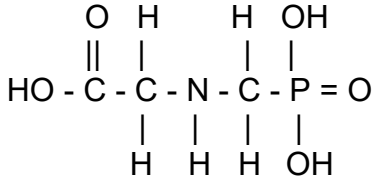
Figure 1.



where R_{1-3} are compound -specific side chains

The structure of glyphosate is different in two important respects. First, the phosphorus atom is attached to the remainder of the molecule by a carbon atom, not an oxygen (Figure 2). This classifies the glyphosate molecule as an “organophosph**on**ate”[1]. Secondly, there are no other side chains attached to the phosphorus atom. Glyphosate consists of a glycine moiety and a phosphonomethyl moiety.

Figure 2.



These distinctions are important for the following reason. The nature of the groups attached to the phosphorous determine how strongly the molecule will

interact with the enzyme cholinesterase[1]. The groups attached to the phosphorus of a true organophosphate allow it to be readily broken by cholinesterase. This interaction is responsible for the subsequent inhibition of the enzyme and disruption of normal nerve function. The phosphorus of an organophosph**on**ate such as glyphosate, on the other hand, is not as strongly attracted to the enzyme. In addition, the carbon-phosphorus bond of an organophosph**on**ate is strong and not easily broken[2]. Thus, this type of molecule would not be expected to interfere with cholinesterase and normal nerve function.

Studies in rats and dogs have confirmed that glyphosate does not inhibit cholinesterase. Serum cholinesterase measurements performed in human patients who have swallowed glyphosate are within normal limits. Furthermore, these patients do not exhibit the classical symptoms seen after excessive organophosphate exposure. This is additional clinical evidence that glyphosate does not inhibit cholinesterase.

Distinguishing between true organophosphates and organophosph**on**ates is critical when treating patients exposed to either type of chemical. Administration of atropine and PAM (2-Pralidoxime) is standard treatment in cases involving organophosphates exposure, but these drugs are not necessary for an organophosph**on**ate like glyphosate[3]. In fact, atropine and PAM are also toxic [4,5], and the unnecessary administration of these drugs could put the patient at additional risk.

In summary, glyphosate is **NOT** an organophosphate compound. Generic reference to glyphosate as an organophosphate perpetuates the misconception that it inhibits cholinesterase. This should be avoided to prevent inappropriate and possibly dangerous medical treatment.

REFERENCES

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The following organophosphate insecticides are abstracted from US EPA's list of pesticides grouped for tolerance reassessments, as published in the Federal Register: August 4, 1997 (Volume 62, Number 149) page 42019 - 30. Glyphosate is not included.

Pesticide	Chemical Class
Group 1 Pesticides	
Cadusafos	organophosphorus
2,2-Dichlorovinyl dimethyl phosphate(Dichlorvos).	organophosphorus
Acephate	organophosphorus
Chlorpyrifos	organophosphorus
Chlorpyrifos methyl	organophosphorus
Coumaphos	organophosphorus
Diazinon	organophosphorus
Dimethoate including its oxygen analog	organophosphorus
Dimethyl phosphate of 3-hydorxy-N,N-dimethyl-cis-crotonamide(Dicrotophos).	organophosphorus
Ethion..	organophosphorus
Ethoprop	organophosphorus
Ethyl 3-methyl-4-(methylthio) phenyl(1-methylethyl)phosphoramidate(Fenamiphos).	organophosphorus
Fenitrothion	organophosphorus
Malathion	organophosphorus
Methamidophos	organophosphorus
Methidathion	organophosphorus
Methyl 3-[dimethoxy phosphinyl)oxy]butenoate, alpha and beta isomers(Mevinphos).	organophosphorus
N-(Mercaptomethyl) phthalimide S-(O,O-dimethyl phosphorodithioate) and its oxygen analog(Phosmet).	organophosphorus
Naled	organophosphorus
O,O-Dimethyl O-(4-nitro-m-tolyl)phosphorothioate(Fenthion).	organophosphorus
O,O-Dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-ylmethyl]phosphorodithioate (Azinphos-methyl).	organophosphorus
O,O-Diethyl S-[2-(ethylthio)ethyl]phosphorodithioate(Disulfoton).	organophosphorus
O-Ethyl S-phenyl ethylphosphonodithioate(Fonofos).	organophosphorus
O-[2-(1,1-Dimethylethyl)-5-primidinyl] O-ethyl-O-(1-methylethyl phosphorothioate(Phostebupirim).	organophosphorus
Parathion (methyl and ethyl)	organophosphorus
Phorate	organophosphorus
Phosphorothioic acid, O,O-diethyl O-(1,2,2,2-tetrachloroethyl) ester(Chlorethoxyfos).	organophosphorus
Pirimiphos methyl	organophosphorus
Profenofos.	organophosphorus
Propetamphos	organophosphorus

S,S,S-Tributyl phosphorotrithioate(DEF)..... organophosphorus
S-(O,O-Diisopropyl phosphorodithioate) of.....organophosphorus
N-(2-mercaptoethyl)benzenesulfonamide
(Bensulide).
S-[2-(Ethylsulfinyl)ethyl] O,O-dimethyl .....organophosphorus
phosphorothioate(Oxydemeton methyl).
Terbufos ..... organophosphorus