

# Acute glyphosate herbicide poisoning

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# Classification of Toxic Substance

- Target organ : Liver, kidney, hematopoietic system
- Usage : Pesticide, solvent, food additive
- Source : Exogenous (Animal or Plant toxins) or Endogenous
- Effect : Cancer, Mutation, liver injury, Kidney
- Physical state : Gas, liquid, dust
- Origin
  - Toxin: a poisonous substance produced by living cells or organisms
  - Toxicants are typically introduced into the environment by human activity.

# Toxicant vs. Toxin

A toxicant is any toxic substance. In popular usage, the term is often used to denote substances made by humans or introduced into the environment by human activity, in contrast to toxins, which are toxicants produced naturally by a living organism.

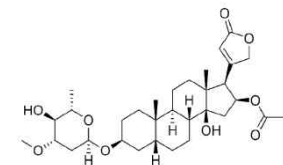
## Toxicants

- Drugs
- Pesticides
- Herbicides
- Solvents
- Plasticizer
- Endocrine disrupters



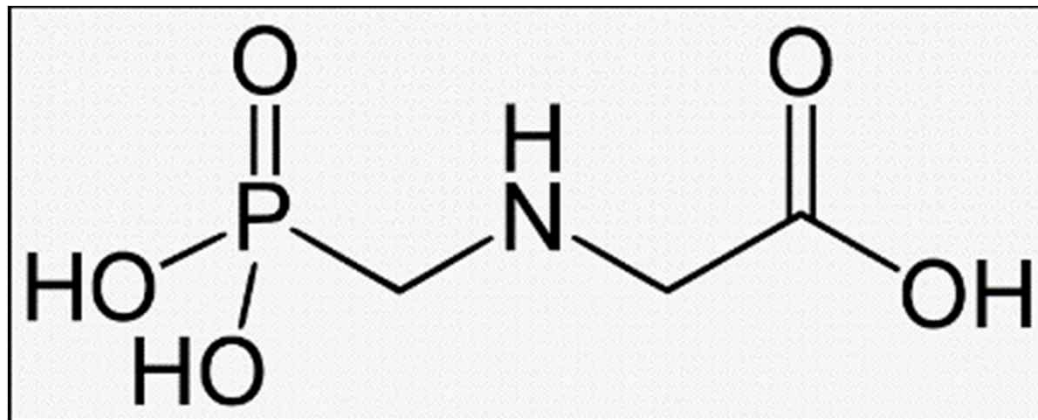
## Toxin

- Toxins produced by plants
  - oleandrin: Oleander (*Nerium indicum*)
  - grayanotoxins: Rhododendron
- Toxins produce by animals
  - gcorpion toxin
  - venom
  - tetrodotoxin
- Toxins produce by microorganism
  - aflatoxin
  - trichothecens



# Organic phosphorus

- Active ingredients: Bensulide, Butamifos, Bialaphos, anilofos, Glufosinate, Fosamine, **Glyphosate**
- Glyphosate
  - A broad-spectrum, non-selective systemic herbicide.
  - LD50 in the rat 5,600 mg/kg
- Accessory ingredients: Surfactant, Ammonium, Isopropylamine, Potassium



# Glyphosate in Korea

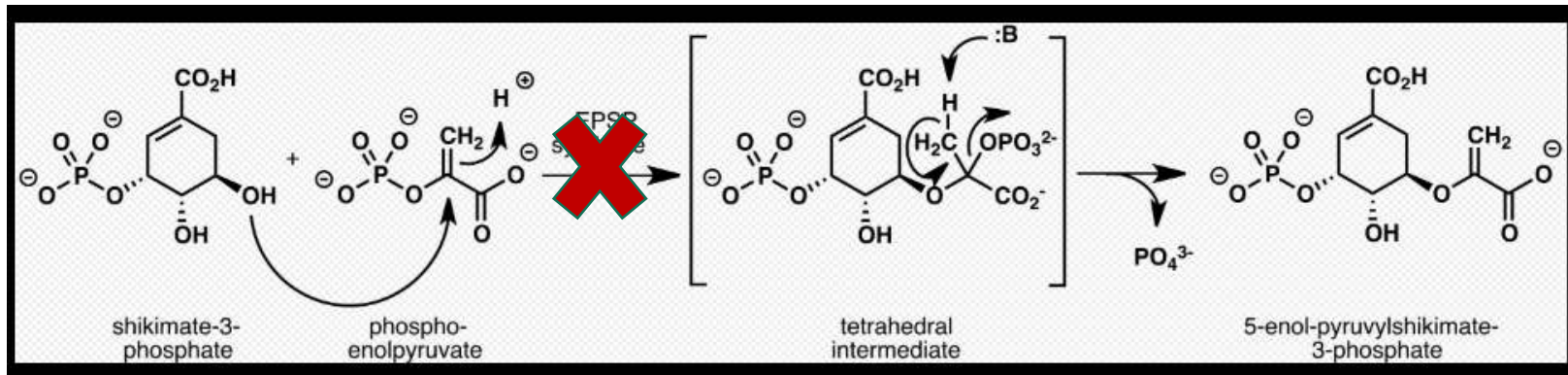
- 근사미, 라운드엿, 근자비, 글라신골드, 성보글라신, 이비엠글라신, 풀마타, 풀오버, 아리스타글라신, 아리글라신, 선문뉴글라신, 지심왕, 몬산토 클래식, 글라신파워





# Pharmacology

- A nonselective postemergence herbicide
- Interferes with the shikimate pathway



- The mechanism of toxicity of glyphosate-containing herbicides to humans is not adequately described.

# Mechanism of toxicity

- Corrosive -> Direct GI tract injury
- Multisystem effects, non-specific
- Glyphosate salts
  - Ammonium: Metabolic acidosis -> Severe organ damage
  - Isopropylamine:
    - Rat LD<sub>50</sub> 111-820 mg/kg
    - CNS depression
    - Severe organ damage
  - Potassium: Hyperkalemia
  - Trimesium: Cardiac arrest
- Surfactant effect (Usually polyoxyethyleneamine: POEA)
  - Corrosive
  - Large volume at a risk of hypotension, mental deterioration, respiratory failure, and arrhythmia
  - $\geq 8 \text{ mL}$

Kamijo, Yoshito, Michiko Takai, and Tetsuya Sakamoto. "A multicenter retrospective survey of poisoning after ingestion of herbicides containing glyphosate potassium salt or other glyphosate salts in Japan." *Clinical toxicology* 54.2 (2016): 147-151.

Seok, Su-Jin, et al. "Surfactant volume is an essential element in human toxicity in acute glyphosate herbicide intoxication." *Clinical Toxicology* 49.10 (2011): 892-899.

# Pharmacokinetics and Toxicokinetics

- Does not penetrate the skin
- Up to 40% of an oral dose is absorbed in rats
- The peak glyphosate plasma concentration occurs within 2 hours of ingestion
- Does not readily cross the placenta
- Elimination half-life of less than 4 hours



# Pathophysiology

- Disruptions of oxidative phosphorylation impairing normal cellular function
    - limiting energy supply
  - Direct toxicity to cell membranes
    - Interferes with normal cellular processes
- Multiorgan toxicity
- Hypotension, dysrhythmia, liver and kidney injuries, pulmonary toxicity
- > Irreversible cellular toxicity and death

# Clinical manifestation

- GI sx: most common
  - Abdominal pain, nausea, vomiting, diarrhea
  - Severe poisoning: inflammation, ulceration, infarction of the gut wall
  - GI burns and necrosis
- Multi-organ failure
  - 12 to 72 hours
- If IV -> hemolysis
- If IM -> rhabdomyolysis
- Proposed risk factors for death
  - Large exposure, delayed presentation to hospital, elevated glyphosate concentration, and increasing age

# Diagnostic testing

- Diagnosed on the basis of a history of exposure and clinical findings
- Higher plasma glyphosate concentration -> More severe poisoning
- >734 mg/L predicted death in one study
- Evaluate for
  - Metabolic acidosis, Electrolyte imbalance, Target organ damage
  - Upper airway and upper GI for corrosive injury

# Management -1

- Maintain airway and ventilation support
- Intravenous fluid replacement
  - Hypotension due to hypovolemia
  - Renal excretion of unchanged glyphosate
- Vasopressor if needed
- Routine supportive care
  - Electrolyte, ICU care

# Management -2

- Gastric lavage: should not be routinely performed
- Activated charcoal: only if ingested within one hour
- Renal replacement therapy
  - Not routinely applied
  - Recommend in severe poisoning
- No antidotes


# Management -3

- Lipid emulsion
  - 20 % lipid emulsion product
    - < 100 *ml of glyphosate* -> IV 20 mL/H for ingested
    - ≥ 100 *ml of glyphosate* -> IV Loading 500 ml over 2-3 hr and 1000ml over 24 hr
  - Lower incidence of hypotension and arrhythmia


Gil, Hyo-Wook, et al. "Effect of intravenous lipid emulsion in patients with acute glyphosate intoxication." *Clinical Toxicology* 51.8 (2013): 767-771.

<https://www.e-gen.or.kr/toxinfo/main.do>


[NEMC](#) [E-Gen](#) [중독정보](#) [교육](#) [응급의료모니터링](#) [로그인](#) [회원가입](#) [고객센터](#) [사이트맵](#) [ENG](#) [통합검색](#)


[중독정보관리 시스템 소개](#) [응급 해독제](#) [중독물질 분석](#)

**거점병원**






**중독분석실**




**해독제 요청**

해독제 요청은 응급실에서 급성중독환자 치료를 담당하는 의료진만 요청할 수 있습니다. (일반인의 요청은 제한됩니다.)

요청


-  해독제 요청조회 >
-  해독제 안내 >
-  중독물질분석 요청조회 >
-  사업개요 >



**중독물질분석 요청**

중독물질분석 요청은 응급실에서 급성중독환자 치료를 담당하는 의료진만 요청할 수 있습니다. (일반인의 요청은 제한됩니다.)

요청



## 중독분석실 시료분석 결과보고서

- 분석내용 : Glyphosate
- 접수번호 : 2018-0109
- 의뢰기관 : 연세대학교 원주세브란스 기독병원
- 분석기관 : 국립과학수사연구원 원주분석실

### 1. 보고내용 : 혈액에서 glyphosate가 검출됨

#### 2. 일정 :

- 분석접수 일시 : 2018.05.10 12:00
- 중간보고 일시 : 2018.05.10 14:07
- 최종보고 일시 : 2018.05.10 18:49

#### 3. 개요

2018.05.07 18:30 근사미 음독하여 내원

##### 3-1. 분석대상

혈액	( 20 ) mL	소변	( ) mL
위세척액	( ) mL	중독물질	( )
(환자노출 독성물질)			

##### 3-2. 분석기기

GC/MS       LC/MS       LC/Q-TOF       GC/Orbitrap  
 기타 : ( )

#### 4. 분석결과

05.09 06:00 채취 혈액에서 glyphosate 0.99 mg/L

18:00 채취 혈액에서 glyphosate 0.71 mg/L

05.10 00:00 채취 혈액에서 glyphosate 0.72 mg/L 이 검출됨





감사합니다.