

# GLUFOSINATE

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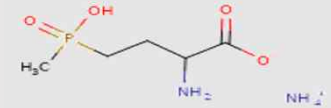
# Part 1.

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## Pharmacology



# 1. 약동학



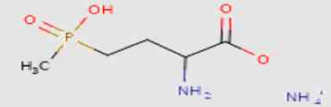
- Glufosinate Ammonium
- Non-selective herbicide
- D-,L-glufosinate enantiomer
- 바스타 : Glufosinate Ammonium 18% + 계면활성제 등 보조제
- Half -life : 9.6hrs
- Peak concentration : 1hr s4
  - 보조제와 함께 흡수될 경우 25-30% 흡수 증가
- 신장배설 90%, 배설량 97%가 24시간 이내 제거됨.



- 품목명  
글루포시네이트암모늄 액제
- 유효성분  
Glufosinate ammonium 18%
- 계통  
포스피네이트계
- 독성  
보통독성
- 포장단위  
300ml X 30병 / Box  
500ml X 20병 / Box  
1l X 12병 / Box  
5l X 4병 / Box

s4 위장관을 통한 흡수가 빨라 1시간내 혈중 최고 농도 도달  
sec, 2019-10-25

# 1. 약동학



- Fatality : 6.1~17.7% Clin Toxicol (Phila). 2012 Jun;50(5):396-402.
- 급성 경구 독성 용량 : 1.6~1.8ml/kg Toxnet.nlm.nih.gov
  - Fatal/severe outcomes : 13.9 grams (roughly 100 mL of 13.5% w/v or 75 ml of 18.5% w/v glufosinate) Clin Toxicol (Phila). 2012 Jun;50(5):396-402.

s4

**Table 1.** Demographic characteristics and clinical outcome of 131 patients with glufosinate-containing herbicide exposure in Taiwan.

Characteristics	Oral exposure (n = 115, %)	Other pathways of exposure (n = 16, %)
Calendar year of poisoning		
1993–1998	22 (19.1)	1 (6.2)
1999–2004	30 (26.1)	5 (31.3)
2005–2010	63 (54.8)	10 (62.5)
Gender (males)	80 (69.6)	10 (62.5)
Age (years; median and interquartile range)	45 (32–63)	57 (44–69)
Concentration of exposed glufosinate		
13.5 %	64 (55.7)	9 (56.3)
18.5 %	21 (18.3)	4 (25)
Unknown	30 (26.1)	3 (18.6)
Co-exposed substances		
Ethanol consumption	22 (19.1)	0 (0)
Glyphosate-surfactant herbicide	5 (4.3)	4 (25)
Benzodiazepine	2 (1.7)	0 (0)
Reason of exposure		
Intentional	98 (85.2)	0 (0)
Accidental	16 (13.9)	16 (100)
Unknown	1 (0.8)	0 (0)
<b>Severity</b>		
Asymptomatic	25 (21.7)	1 (6.3)
Mild	42 (36.5)	14 (87.5)
Moderate	15 (13.0)	1 (6.3)
Severe	26 (22.6)	0 (0)
Death	7 (6.1)	0 (0)

s4 위장관을 통한 흡수가 빨라 1시간내 혈중 최고 농도 도달  
sec, 2019-10-25

# Part 2.

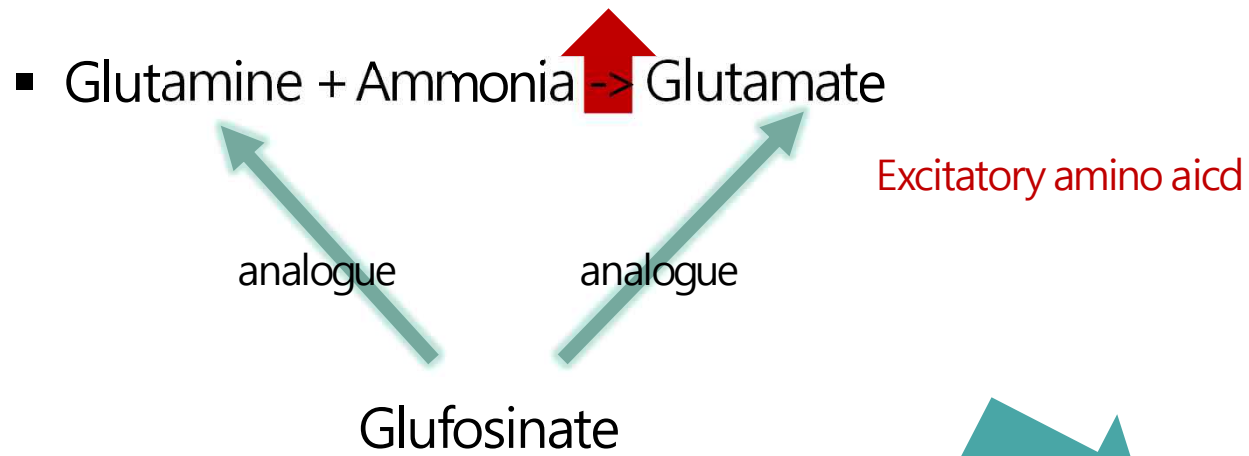
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## Pharmacokinetics and Toxicokinetics

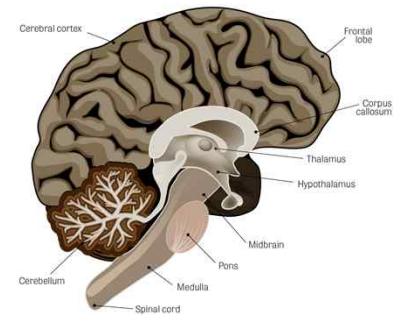




## 2. 독성학



CNS toxicity



## 2. 독성학

- 신경독성
  - Brain active transport system : 뇌로 유입되는 것으로 추정(혈액의 1/3 농도)
  - 축적되어 지연성 호흡억제 발생 가능 [Biol Pharm Bull.](#) 2003 Apr;26(4):540-3.
  - CSF 내에서 검출 안되는 시점에서도 Seizure 발생 가능 [Vet Hum Toxicol.](#) 1998 Aug;40(4):219-22.
- 소화기증상(55.7%)>신경계증상(41.7%)>심혈관계증상(37.4%)>호흡기증상(29.6%) [Clin Toxicol \(Phila\).](#) 2012 Jun;50(5):396-402.

## 2. 독성학



- 보조제 Surfactant
  - AES(Sodium polyoxyethylene alkyl ether sulfate) : 혈압 저하, 순환부전 [Toxicol Appl Pharmacol](#). 1997 Aug;145(2):409-14.
  - Genapol<sup>®</sup>, Sodium lauryl sulfate : 순환기계 독성 적을 것으로 추정
  - Propylene glycol ether

# Part 3.

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## Clinical Manifestation



### 3. 임상증상

- 음독 양에 관계 없이 발생
- 20ml 에도 사망
- 500ml 에도 합병증 없이 생존
- 초기 중독 증상
  - 계면활성제에 의한 전신 증상
  - 구강, 식도, 위 자극 증상, 오심, 구토
  - 혈압저하, 순환 부전, 사망
  - 50%: CPK, LDH, WBC 상승, Metabolic acidosis 등

### 3. 임상증상

- 순환기계 증상
  - AES 포함된 바스타 200ml 이상 음독한 경우 발생
- 중추신경계 독성
  - 과량 음독한 경우도 4~8시간 늦게 발생할 수도 있음
  - 24~48시간 이상 지속
  - 경련
  - 중추성 호흡부전 [Clin Toxicol \(Phila\)](#). 2011 Jul;49(6):510-2; author reply 513. [Clin Toxicol \(Phila\)](#). 2012 Jun;50(5):396-402.
  - 혈중 농도가 측정되지 않는 상태의 매우 적은 농도에서도 전신 경련과 같은 지연성 부작용 발생
  - 기억상실 [Neurology](#) 2006;67:914-915
  - 뇌신경마비 [J Korean Med Sci](#). 2013 Nov;28(11):1687-1689
  - 중추성 요붕증 [J Toxicol Clin Toxicol](#). 2000;38(2):153-6.

### 3. 임상증상

- Mild
  - <2hrs : Nausea, Vomiting, Diarrhea
  - <24hrs : Generalized edema, mild leukocytosis, elevated liver enzymes
- Severe
  - Initial GI upset
  - Asymptomatic latent period
  - 8~32hrs : Severe neurologic Sx
    - Seizure, coma, nystagmus, amnesia, respiratory failure
  - Upper airway, laryngeal edema : initial and latent
  - Fever, Generalized edema, elevated liver enzyme
  - Fatality : 1~3일째, surfactant -> Circulatory, respiratory failure, generalized edema, seizure, gastric mucosal injury

# Part 4.

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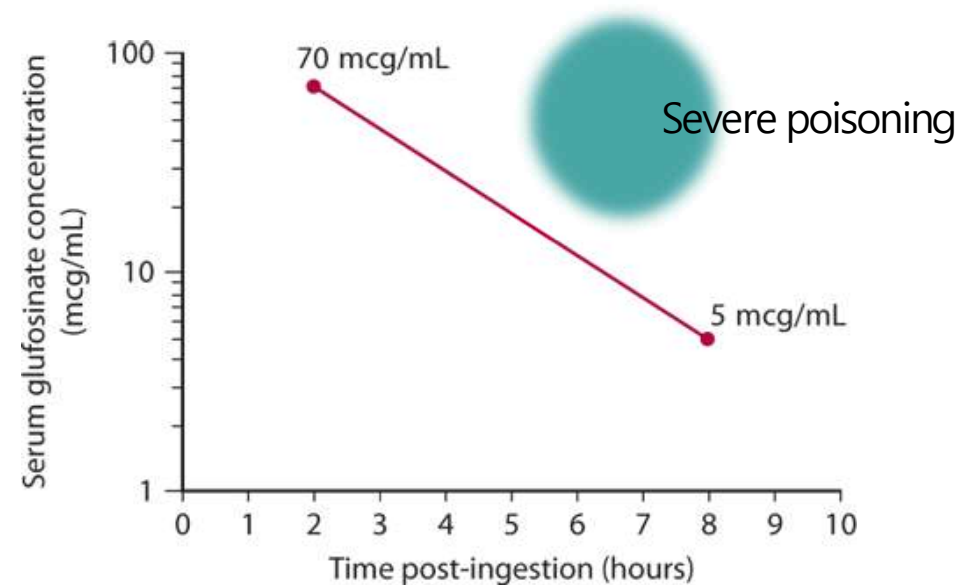
## Diagnostic Testing





## 4. 진단적 검사

- 진단 : 노출 병력
- ★ 국과수 중독물질분석 사업
- Glufosinate nomogram
- RFT, Blood gas, Electrolyte, CPK
- Metabolic acidosis : severe poisoning
- **Ammonia** : predictor of neurotoxicity [Clin Toxicol \(Phila\).](#) 2011  
Jan;49(1):48-52.



Source: L.S. Nelson, M.A. Howland, N.A. Lewin, S.W. Smith, L.R. Goldfrank, R.S. Hoffman: Goldfrank's Toxicologic Emergencies, Eleventh Edition  
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## 4. 진단적 검사

# Hyperammonemia following glufosinate-containing herbicide poisoning: A potential marker of severe neurotoxicity

Yan-chiao Mao , Jiaan-Der Wang, Dong-Zong Hung, Jou-Fang Deng & Chen-Chang Yang

Pages 48-52 | Received 11 Aug 2010, Accepted 05 Nov 2010, Published online: 03 Feb 2011

sequelae of persistent amnesia after receiving intensive care and hemodialysis. We speculated that the occurrence of hyperammonemia might at least be partially related to GS inhibition in humans. Moreover, hyperammonemia could serve as a potential marker of severe neurotoxicity, especially prolonged amnesia, following massive ingestion of GLA-containing herbicides. The possible dose-response relation between GLA exposure and serum ammonia level, however, needs more investigations.

## 4. 진단적 검사

### Initial Serum Ammonia as a Predictor of Neurologic Complications in Patients with Acute Glufosinate Poisoning

Dong Keon Lee,<sup>1</sup> Hyun Youk,<sup>1</sup> Hyun Kim,<sup>1</sup> Oh Hyun Kim,<sup>1</sup> Jin Go,<sup>1</sup> Tae Hoon Kim,<sup>2</sup> KyoungChul Cha,<sup>1</sup>  
Kang Hyun Lee,<sup>1</sup> Sung Oh Hwang,<sup>1</sup> and Yong Sung Cha<sup>✉1</sup>

The neurologic complication group (29 patients, 64.4%) comprised patients with GCS<8 (27 patients, 60.0%), seizure (23 patients, 51.1%), and amnesia (5 patients, 11.1%). Non-neurologic complications included respiratory failure (14 patients, 31.1%), intubation and ventilator care (23 patients, 51.1%), shock (2 patients, 4.4%), pneumonia (16 patients, 35.6%), acute kidney injury (10 patients, 22.2%), and death (4 patients, 8.9%). Complications of GCS<8, seizure, respiratory failure, and intubation and ventilator care appeared during latent periods within 11 hrs, 34 hrs, 14 hrs, and 48 hrs, respectively. Initial serum ammonia was a predictor of neurologic complications [odds ratio 1.039, 95% confidence interval (1.001-1.078),  $p=0.046$  and area under the curve 0.742].

## 4. 진단적 검사

### **The relationship between serum ammonia level and neurologic complications in patients with acute glufosinate ammonium poisoning: A prospective observational study**

**YS Cha<sup>1</sup>, H Kim<sup>1</sup>, Y Lee<sup>1</sup>, EH Choi<sup>2</sup>, HI Kim<sup>1</sup>, OH Kim<sup>1</sup>, K-C Cha<sup>1</sup>, KH Lee<sup>1</sup> and SO Hwang<sup>1</sup>**

tion group ( $p = 0.0085$ ) in terms of ingested amount. The peak ammonia was the only predictor for the development of neurologic complications (the optimal cutoff:  $90 \mu\text{g/dL}$ ). In patients with mental changes, the mean serum ammonia levels before and after recovery of the mental changes were statistically different ( $p = 0.0019$ ). In acute glufosinate ammonium poisoning, serial serum ammonia level measurements are needed and a serum peak ammonia level greater than  $90 \mu\text{g/dL}$  is a predictor of neurologic complications. Also, it is important to treat the hyperammonemia in acute glufosinate ammonium poisoning.

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DOI: 10.1177/0960327117715902

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# Part 5.

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## Management



## 5. 치료

### Routine resuscitation, Close observation, Supportive care

- 무증상 : 중환자실에서 48시간 이상 경과관찰 -> 지연 중독 증상 발생
- Intubation & Mechanical ventilation **유최1**
- IV Fluid : Urine output 유지
- Seizure : BDZ

### Decontamination

- 피부 : 오염된 옷 제거, 과량의 물과 비누로 세척
- 눈 : 생리 식염수 세척, 안과 협진
- 위장관 : 1시간 이내면 위세척, 수시간 이후면 활성탄 **유최2**

### Extracorporeal Removal

- 혈액투석, 혈액관류로 제거 가능
- 신장제거율이 더 높아 신장 기능 정상인 경우 필요하지 않음
- 심한 중독증상, 신기능저하시 고려

## 슬라이드 20

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유최1 신장으로 배설되니깐!!  
유리 최, 2019-10-28

유최2 -> 임상적으로 예후를 향상시키지는 debate있어서 Unprotected Airway에선 Contraindication  
유리 최, 2019-10-28

## 5. 치료

분류	음독량	치료
무증상	20~100ml	지연성 중독 작용의 발생에 대비하여 48시간 이상 증상 관찰
계면활성제 전신증상	20ml(한모금 이상)	위장관 제독 급성 폐부종/손상 - 기관삽관, 기계호흡 혈압 저하 - 혈압상승제, 혈액투석/관류
중추신경계 증상	100~500ml	경련발작 - 일반적 경련 치료 호흡곤란, 무호흡 - 예방적 기관삽관, 기계호흡 중추신경계 증상 - 보존적 치료, 조기 혈액투석/관류
기타 증상		구강, 인후두부 통증, 오심, 구토, 설사, 복통 - 대증치료 중추성 요붕증 - nasal desmopressin 부분 기억상실 - 회복이 더딤



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- Goldfrank's toxicology emergencies, 10ed
- <https://toxnet.nlm.nih.gov/>

감사합니다