Aluminium phosphide - draft revised Poisons Information
Monograph for peer review

CHEMICAL SUBSTANCES

1. NAME

1.1 Substance

Aluminium Phosphide

1.2 Group

1.3 Synonyms

Celphos, Quickphos, Alphos, Synfume, Chemfume, Phostoxin, Phostek, Delicia

1.4 Identification numbers

1.4.1 CAS number

20859-73-8

1.4.2 Other numbers

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2. SUMMARY

2.1 Main risks and target organs

Cardiovascular system is the major system affected and severe hypotension is a major risk.

2.2 Summary of clinical effects

Vomiting, abdominal pain, loose motions, restlessness are seen. Cardiovascular complications include thready pulse, tachycardia, tachypnoea, acidosis, marked hypotension.

Other common complications of aluminium phosphide poisoning include haemorrhage, acute renal failure, disseminated intravascular coagulation and arrhythmias

Patients remain mentally clear till cerebral anoxia due to shock supervenes resulting in drowsiness, delirium and coma.

Several ECG changes ranging from ST segment elevation/depression, PR and QRS interval prolongation, complete heart block to ectopics and fibrillation have been observed. Reversible myocardial injury has also been reported.
2.3 Diagnosis

The following factors alone or in combination would help in the diagnosis.
1. Positive history of ingestion
2. Symptoms compatible with aluminium phosphide ingestion
3. Chemical test for phosphine positive in gastric aspirate and breath

The breath of patients who have ingested aluminium phosphide has a characteristic garlic-like odour. Conformation of diagnosis is based on the patient's history and a positive result (blackening) on tests of the patient's breath with paper moistened with fresh silver nitrate solution or by chemical analysis of blood or gastric acid for phosphine.

2.4 First-aid measures and management principles

Gastric lavage is important in the initial stage.
The management principles aim to sustain life with appropriate resuscitation measures until phosphine is excreted from the body.
The main principles are –
1. Carry out methods to absorb phosphine through GI tract.
2. Steps to reduce organ toxicity
3. Steps to enhance phosphine excretion
4. Supportive measures

3. PHYSICO-CHEMICAL PROPERTIES

3.1 Origin of the substance

This is a synthetic substance.

3.2 Chemical structure

AIP (aluminium phosphide)

3.3 Physical properties

3.3.1 Colour
Dark grey or dark yellow crystals.

3.3.2 State/Form
Solid - crystalline

3.3.3 Description
Formulated as a greenish grey tablet of 3 gm which in presence of moisture or HC1 releases phosphine:

\[ \text{AIP} + 3\text{H}_2\text{O} = \text{Al(OH)}_3 + \text{PH}_3 \]
\[ \text{AIP} + 3\text{HC}_1 = \text{AlC}_13 + \text{PH}_3 \]

The residue, Al (OH)3 is non-toxic

3.4 Hazardous characteristics

The tablet has typical odour of garlic.
4. USES/CIRCUMSTANCES OF POISONING

4.1 Uses

4.1.1 Uses

4.1.2 Description

Grain fumigant

4.2 High risk circumstance of poisoning

Self poisoning is common. Rarely accidental poisoning is seen in grain freight trades.

4.3 Occupationally exposed populations

Farmers while using the fumigant, but poisoning is rare.

5. ROUTES OF ENTRY

5.1 Oral

Common route

5.2 Inhalation

Rare route

5.3 Dermal

Not relevant

5.4 Eye

Not relevant

5.5 Parenteral

Not relevant

5.6 Others

Not relevant

6. KINETICS

6.1 Absorption by route of exposure

In the stomach phosphine is released which is responsible for toxicity.

6.2 Distribution by route of exposure

6.3 Biological half-life by route of exposure
6.4 Metabolism

6.5 Elimination by route of exposure

7. TOXICOLOGY

7.1 Mode of Action

The exact mechanism is not known. It is suggested to produce non-competitive inhibition of the cytochrome oxidase of mitochondria, blocking the electron transfer chain and oxidative phosphorylation producing an energy crisis in the cells. (Cherfuka W et al. 1976)

Recently Chugh et al. found inhibition of catalase and induction of SOD in humans leading to free radicals stress brought out lipid peroxidation and protein denaturation of cell membrane leading to hypoxic cell damage.

7.2 Toxicity

7.2.1 Human data

7.2.1.1 Adults

1/4th tablet is lethal.
Cardiotoxicity (Toxic chemical myocarditis is manifested as depressed left ventricular ejection fraction, ECG changes varying from ST segment elevation/depression, PR prolongation, broad QRS complexes, and right or left bundle branch block, supraventricular ectopics or fibrillation.
(Mathur A, et al. 1999)

Biochemical changes include rise in AST, CPK-MB and LDH. Histopathology shows myocytolysis, multiple areas of necrosis, congestion.
(Karanth S & Nayyar V. 2005)

7.2.1.2 Children
Toxicity, biochemical changes and histopathological changes are similar to adults.

7.2.2 Relevant animal data

LD50 mice (Inhalation of fumes)
Rat: 0.68gm/m3 - 65-75 min. exposure.
1.47gm/m3 - 35-50 min. exposure
Cat: 25ppm (2-4hrs daily during 3 days)

7.2.3 Relevant in vitro data
Data not available

7.2.4 Workplace standards
Data not available for aluminium phosphide.
For phosphine: TLV: 0.3 ppm as TWA; 1 ppm as STEL. EU OEL: 0.1 ppm and 0.14 mg/m³ as TWA; 0.2 ppm and 0.28 mg/m³ as STEL (WHO/ICSC 2006)

7.2.5 Acceptable daily intake (ADI) and other guideline levels
Data not available

7.3 Carcinogenicity
Not known

7.4 Teratogenicity
Not known

7.5 Mutagenicity
Not known

7.6 Interactions
Not known

8. TOXICOLOGICAL ANALYSES AND BIOMEDICAL INVESTIGATIONS

8.1 Material sampling plan

8.1.1 Sampling and specimen collection
8.1.1.1 Toxicological analyses
Gastric lavage - test for phosphine.
8.1.1.2 Biomedical analyses
8.1.1.3 Arterial blood gas analysis
8.1.1.4 Haematological analyses
8.1.1.5 Other (unspecified) analyses

8.1.2 Storage of laboratory samples and specimens
8.1.2.1 Toxicological analyses
Send immediately to laboratory after properly covering the sample.
8.1.2.2 Biomedical analyses
8.1.2.3 Arterial blood gas analysis
8.1.2.4 Haematological analyses
8.1.2.5 Other (unspecified) analyses

8.1.3 Transport of laboratory samples and specimens
8.1.3.1 Toxicological analyses
8.1.3.2 Biomedical analyses
8.1.3.3 Arterial blood gas analysis
8.1.3.4 Haematological analyses
8.1.3.5 Other (unspecified) analyses

8.2 Toxicological analyses and Their Interpretation
8.2.1 Tests on toxic ingredient(s) of material
8.2.1.1 Simple Qualitative Test(s)
Determine the phosphine liberated by acid treatment, measure by GLC.
8.2.1.2 Advanced Qualitative Confirmation Test(s)
Determine the phosphine liberated by acid treatment, measure by GLC.
8.2.1.3 Simple Quantitative method(s)
8.2.1.4 Advanced Quantitative method(s)

8.2.2 Tests for biological specimens
8.2.2.1 Simple Qualitative test(s)
Heat the lavage at 50 degree C for 15-20 minutes and place a silver nitrate
impregnated filter paper (0.1M) on the mouth of flask. On drying the paper
turns black indicating the presence of phosphine.

8.2.2.2 Advanced Qualitative confirmation Test(s)

8.2.2.3 Simple Quantitative Method(s)

8.2.2.4 Advanced Quantitative Method(s)

8.2.2.5 Other Dedicated Method(s)

8.3 Biomedical investigations and their interpretation

8.3.1 Biochemical analysis

8.3.1.1 Blood, plasma or serum

8.3.1.2 Urine

8.3.1.3 Other fluids

8.3.2 Arterial blood gas analyses

8.3.3 Haematological analyses

8.3.4 Interpretation of biomedical investigations

8.4 Other biomedical (diagnostic) investigations and their interpretation

8.5 Overall Interpretation of all toxicological analyses and toxicological
investigations

8.6 References

9. CLINICAL EFFECTS

9.1 Acute poisoning

9.1.1 Ingestion

This is the most common mode of poisoning.

Vomiting, abdominal pain, loose motions, restlessness are seen.
Cardiovascular complications include thready pulse, tachycardia,
tachypnoea, acidosis, marked hypotension. ECG changes can be seen.
Other common complications of aluminium phosphide poisoning
include haemorrhage, acute renal failure, disseminated intravascular
coagulation and arrhythmias.

Patients remain mentally clear till cerebral anoxia due to shock
supervenes resulting in drowsiness, delirium and coma.

9.1.2 Inhalation

Rarely inhalation of phosphine (PH₃) can occur.

9.1.3 Skin exposure
Not relevant

9.1.4 Eye contact
Not relevant

9.1.5 Parenteral exposure
Not relevant
9.1.6 Other

9.2 Chronic poisoning

9.2.1 Ingestion
Not relevant

9.2.2 Inhalation
Not relevant

9.2.3 Skin exposure
Not relevant

9.2.4 Eye contact
Not relevant

9.2.5 Parenteral exposure
Not relevant

9.2.6 Other
Chronic poisoning not seen.

9.3 Course, prognosis, cause of death
Features of hepatotoxicity usually develop 72 hours after poisoning. Death due to acute hepatocellular toxicity and fulminant hepatic failure has also been reported in acute poisoning. Cardiovascular changes and respiratory system changes (ARDS) can also lead to death.

9.4 Systematic description of clinical effects

9.4.1 Cardiovascular
Various changes in ECG ST segment elevation/depression, PR and QRS interval prolongation, complete heart block to ectopics and fibrillation have been observed. Reversible myocardial injury has also been reported, biochemical, histopathological changes in heart, hypotension and shock.

9.4.2 Respiratory
Acute respiratory distress syndrome (ARDS) and exudative plural effusions can develop. A possible explanation for the exudative pleural effusion might be that when aluminium phosphide comes in contact with moisture, it releases phosphine ($PH_3$) gas which is absorbed by simple diffusion. This phosphine gas due to non competitive inhibition of cytochrome oxidase system of mitochondria or damage by free radicals causes global hypoxia. This global hypoxia leads to an increase in capillary permeability that could lead to pleural effusion.

Furthermore, this phosphine gas is eliminated through the lungs, hence due to high concentration in the respiratory alveoli, it is responsible for direct alveolar damage. This alveolar damage (acute lung injury) causes ARDS. Studies in the
past have shown increased levels of inflammatory markers (cytokines and interleukins) in ARDS which increase the capillary permeability. This combined effect of increase in capillary permeability due to global hypoxia and ARDS could be responsible for the exudative effusion seen predominantly in the pleural cavity and not in other serous cavities.

(Suman RL & Savani M 1999)

9.4.3 Neurological

9.4.3.1 CNS
Restlessness, drowsiness and delirium, all due to shock and acidosis

9.4.3.2 Peripheral nervous system
No data available

9.4.3.3 Autonomic nervous system
No data available

9.4.3.4 Skeletal and smooth muscle
No data available

9.4.4 Gastrointestinal
Vomiting, abdominal pain can occur initially.

9.4.5 Hepatic
Death due to acute hepatocellular toxicity and fulminant hepatic failure has also been reported in acute poisoning.

Features of hepatotoxicity usually develop 72 hours after poisoning. During this time the patient may not have any gastrointestinal system problem at all.

Initially the patient would have icterus and soft, non-tender hepatomegaly. Investigations would reveal alteration of liver enzymes. Abdominal ultrasonography may reveal hepatomegaly with increased echotexture with areas of sparing and ascites (Karanth S & Nayyar V. 2005).

9.4.6 Urinary

9.4.6.1 Renal
Acute renal failure due to shock could occur (Chugh SN 1998).

9.4.6.2 Others

9.4.7 Endocrine and reproductive systems
No data available
9.4.8 Dermatological
Nil

9.4.9 Eye, ears, nose, throat: local effects
Nil

9.4.10 Haematological
Haemoconcentration

9.4.11 Immunological
Nil

9.4.12 Metabolic
9.4.12.1 Acid-base disturbances
Metabolic acidosis occurs.

9.4.12.2 Fluid and electrolyte disturbances

9.4.12.3 Others

9.4.13 Allergic reactions
Nil

9.4.14 Other clinical effects
Oedema

9.4.15 Special risks
Cardiotoxicity
Hypotension
ARDS

9.5 Others

10. MANAGEMENT -

10.1 General principles
Supportive treatment mainly gastric lavage, vasoactive substances.

10.2 Life supportive procedures and symptomatic treatment
The following conditions should be anticipated and supportive measures should be tailor made according to the individual’s condition.
1. Hypoxia- blood gas monitoring should be done.

2. Shock - blood pressure should be maintained above 70 mmHg using IV fluids. Low dose dopamine (4-6ug/kg/min) and intravenous hydrocortisone (200-400mg after 4-6 hours) have been found to be effective. (Chugh SN 1998)

3. Arrhythmias- conventional drugs such as digoxin, xylocaine are ineffective. Atropine is not useful in bradyarrhythmias. Magnesium sulphate has been effective in both tachy and bradyarrhythmias due to its membrane stabilizing effect (Chugh SN 1998).

4. Metabolic acidosis- moderate to severe metabolic acidosis can be seen

5. ARDS- 100% O2 can be delivered via a face mask. Mechanical respiratory support and positive end-expiratory pressure therapy is given for haemodynamically unstable patients.

Magnesium sulphate has been shown to reduce organ toxicity produced by PH₃ mediated oxidative injury. The antioxidative, antihypoxic and antiarrhythmic properties all come into play in the management of aluminium phosphide toxicity (Chugh SN 1998).

10.3 Decontamination

Gastric lavage with saline or sodium bicarbonate or potassium permanganate (1:1000) (Chugh SN 1998).

10.4 Enhanced Elimination

Phosphine is excreted through the breath and urine, therefore, adequate hydration and renal perfusion by low dose dopamine 4-6 microg/kg/min must be maintained. Diuretics are not useful in the presence of profound shock. However, if blood pressure is stable around 80 mmHg, the frusemide (20 mg IV) may be tried.

10.5 Antidote treatment

10.5.1 Adults

Nil

10.5.2 Children

Nil

10.6 Management discussion

No specific antidote available. The treatment with Magnesium sulphate is not correlated with serum magnesium levels. Early treatment of shock and magnesium therapy results in better prognosis.
11. ILLUSTRATIVE CASES

11.1 Case reports from literature

CASE REPORTS:

1. A 25 years old male was admitted to the medical intensive care unit 4 hours after ingestion of a tablet of Celphos (aluminium phosphide). He had a fight with his relatives prior to that. He was restless, irritable, drowsy, and poorly responding to simple verbal commands. He had cold clammy skin, non-palpable pulses, respiratory rate 14/min, BP 60 mmHg systolic, and peripheral cyanosis. Cardiac examination revealed tachycardia, normal first and second heart sounds and left ventricular third heart sound. Chest examination showed bilateral normal vesicular breathing with no added sound. Investigations revealed: haemoglobin 8.5 g%, TLC 7,900/ mm³, blood urea 96 mg%, and normal chest x-ray. Arterial blood gas analysis revealed severe metabolic acidosis with blood pH 6.91, PaO₂ 98. In view of hypotension, an urgent ECG was done which revealed incomplete RBBB and generalized ST-T changes.

Subsequent ECG showed idioventricular rhythm and complete RBBB. Serum Mg++ could not be done. Thus a diagnosis of toxic myocarditis was made. He was managed with intravenous fluids, MgSO₄, sodium bicarbonate, and inotropic support. Dialysis could not be done due to haemodynamic instability. Patient developed cardiac arrest on the same day and could not be revived. The ALP on contact with water liberates phosphine gas ALP + 3H₂ Al(OH)₃ + PH₃. Phosphine inhibits cytochrome oxidase and thereby hampers cellular oxygen utilization. The average time interval between poisoning and death is 3 hours with a range of 1-48 hours. As many as 95% of fatalities occur within first 24 hours. Common causes of death are ventricular fibrillation, ARDS, hepatic failure, acidosis, and dyselectrolytaemia. Our patient presented with anteroinferior wall ischaemia with incomplete RBBB which progressed to idioventricular rhythm, complete RBBB, and T-wave flattening simulating myocardial ischaemia. These changes were due to toxic injury to myocardium. Various ECG changes such as atrial arrhythmias, ventricular arrhythmia, ST-T changes, AV dissociation, bundle blocks, etc., have been described in ALP poisoning. No specific antidote is available as yet. MgSO₄ and corticosteroids have been used. However, there is no hard data to support their use.

Recently animal studies have shown xanthinol nicotinate to reduce mortality secondary to ALP poisoning. Thus, our case amply illustrates the importance of immediate ECG recording in every case of ALP poisoning to diagnose myocardial involvement in order to formulate early treatment strategies. (Ranga GS et al. 2004)

2. A 21 years housewife consumed a phosphorus-based rodenticide six days prior to admission into our ICU. Following the ingestion no immediate first-aid was administered. Twenty-four hours later she developed vomiting and abdominal pain for which she was taken to a peripheral hospital where she received primary care in the form of a stomach wash and some other symptomatic therapy before being discharged. Forty-eight hours after the alleged ingestion she again developed intractable vomiting and thus was shifted back to the same hospital where she was admitted this time. On the sixth day after the incident in view of worsening of her sensorium she was referred to our institution. She reached the ICU in shock (with a blood pressure of 80 systolic, pulse rate of 160/minute and cold peripheries), febrile (temperature 100.6°F.) and O₂ on saturation 95% on room air. Systemic examination was normal except for the presence of a decreased Glasgow Coma Scale (GCS) of 7/15 (Eye
opening 1, Verbal response 1, Motor response 5). Investigations on admission revealed an acute hepatitis-like picture with a total bilirubin 6.1mg%, ALT 826U/L, AST 389U/ L and prolonged prothrombin time of greater than two minutes. Serum ammonia was also elevated to 46.2 mcg/dl. Arterial blood gases revealed well compensated metabolic acidosis. Sonographic imaging revealed fatty liver with minimal ascites. Thus a diagnosis of acute fulminant hepatic failure secondary to toxic hepatitis following a rodenticide poisoning was made. Accordingly she was started on antihypertensive measures, low-dose dopamine and other symptomatic measures. Infective causes of acute hepatitis including malaria, leptospira and other viral markers were negative. Through the next forty-eight hours the patient showed gradual worsening of her sensorium which dropped to a GCS of 4/15 by day three of admission (ninth day following the alleged ingestion of poison). She continued to be in this state till the fifth day following admission (eleventh day after the alleged ingestion), when further worsening of her sensorium was noted. By now she had also developed haemodynamic instability requiring increasing levels of inotropic support. On the following day she had an episode of bradycardia followed by a ventricular fibrillation. She was resuscitated and placed on mechanical ventilation. However through the course of the day, she worsened and expired at 6 PM that day. A post-mortem liver biopsy was done which showed collapsed reticulin framework with fibrosis between the hepatocytes showing a bubbly and vacuolated cytoplasm suggestive of an acute fulminant hepatitis. (Karanth S & Nayyar V. 2005)

3. A 25 years housewife presented with alleged history of ingestion of an unknown quantity of a rodenticide, Ratol (containing 3% yellow phosphorus) mixed with alcohol about five days prior to admission. There were no symptoms immediately following the ingestion. However she confessed to having taken the poison four days after the incident. Following primary care in a nearby hospital she was referred to our institution. Examination revealed her to be icteric, with normal vitals and presence of a soft, non-tender hepatomegaly. Investigations at the time of admission revealed a picture of acute hepatitis with total bilirubin of 7.8mg%, direct bilirubin of 3 mg%, ALT 1055U/L, AST 824U/L, alkaline phosphatase 13 U/L and a prolonged PT of over two minutes. An abdominal ultrasonography revealed hepatomegaly with diffuse increase in echotexture of liver with areas of sparing associated with ascites. Through her stay in the hospital initially there was increasing icterus that was noticed which was also supported by a biochemical evidence showing increasing total bilirubin till about the seventh day of admission, following which there was a gradual decline in the serum bilirubin levels. However all through this period there was a steady decrease in, serum ALT and AST levels associated with an improvement in the prothrombin time suggesting improving hepatic function. smear for MP was repeatedly negative. Hepatotropic viral markers were also negative. Patient was administered vitamin-K for three days along with other symptomatic measures. She was admitted in the hospital for a period of two weeks and later discharged. At the time of discharge her liver function tests read as follows: Total bilirubin 3.5mg%, ALT 245U/L, AST 136U/L and prothrombin time 22.3 seconds. (Karanth S & Nayyar V. 2005)

12. ADDITIONAL INFORMATION

12.1 Specific preventive measures
These include-
- Availability of single tablet pack encased in hard plastic material with spikes.
- By restricting the free sale of the chemical
- Social awareness regarding handling of the substance and its lethality.
- Some emetic substance may be added in it.
13. REFERENCES


Chugh SN (1998) Aluminium Phosphide in Lall SB, Essentials of Clinical Toxicology, New Delhi, Narosa Publishing House pp 41-46


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14. AUTHOR(S), REVIEWER(S), DATE(S) (INCLUDING UPDATES), COMPLETE ADDRESSES

First Draft:
   Dr S. Lall
   New Delhi Poisons Centre
   August 1993

Revision:
   Prof. Ravindra Fernando
   National Poisons Information Centre
   National Hospital of Sri Lanka
   Colombo 8
   Sri Lanka
   November 2007