



# Current Status of Acute Aluminum Phosphide Poisoning in Iran: A Brief Review

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## Abstract

Aluminum phosphide (AIP) (known as "rice tablet" in Iran), is an insecticide and rodenticide used to protect stored crops from pests. This pesticide is highly toxic to humans and has been the cause of many accidental and intentional poisonings, worldwide. Due to the high incidence of acute AIP poisoning and its mortality in Iran, the authorities banned sale and distribution of AIP tablets in 2007. The aim of this review is to evaluate the current status of acute AIP poisoning in Iran. The results shows that despite the prohibition of AIP tablets, the frequency of AIP acute poisonings is high in Iran. AIP tablet is considered as one of the most important tools for suicidal poisonings. The mortality rate of AIP poisoning is estimated at 27% in Iran. This type of poisoning has been reported mostly in men aged between 20 -30 years and in the form of oral consumption. Considering the prevalence of AIP poisoning in the country due to poor legislation, it is suggested to take legal measures to limit the distribution and sale of AIP tablets in the black markets.

**Keywords:** Aluminum Phosphide; Rice Tablet; Poisoning; Iran

## Abbreviations

AIP: Aluminum Phosphide; DIC: Disseminated Intravascular Coagulation; LMO: Legal Medicine Organization; BE: Base Excess; EF: Ejection Fraction.

## Introduction

Aluminum phosphide (AIP) is a cheap, effective and broad spectrum insecticide and rodenticide in developing countries such as India, Iran, Iraq, Sri Lanka and Turkey [1,2]. It is commonly used to protect stored grains and tobacco leaves and during their transportation without impact on seed viability and residue in the crops [1,2]. Contact of AIP tablets with water, moisture or dilute gastric acid releases

colorless, flammable and toxic phosphine gas (PH<sub>3</sub>), which is known to be the main cause of toxicity of this pesticide [3].

AIP poisoning may be occurred due to accidental or suicidal ingestion of AIP and inhalation of released PH<sub>3</sub> gas [1]. AIP is a highly toxic agent for humans and no suitable antidote is available [2,3]. Its poisoning has a high mortality (with mean mortality rate: 50-70%) [3]. Following the ingestion of AIP, phosphine gas is generated and rapidly absorbed throughout the gastrointestinal tract and reaches the blood circulation and the liver by portal vein. In inhalation exposure, PH<sub>3</sub> is rapidly absorbed through lungs and most of the PH<sub>3</sub> is excreted unchanged in expired air, while the residual quantity is oxidized to phosphite and hypophosphite ions which are excreted in urine [1,2].

Phosphine acts as a respiratory poison and blocks the enzyme cytochrome C oxidase as a result of which mitochondrial oxidative phosphorylation and can lead to a blockage of mitochondrial electron transport chain. It also disturbs the mitochondrial integrity, inhibits oxidative respiration and causes a severe reduction in mitochondrial membrane potential and finally cell death. Mitochondrial cytochrome C oxidase inhibition may also lead to pulmonary and cardiac toxicity. It is also known to inhibit protein synthesis and enzymatic activity, particularly in the mitochondria of lung and myocardiocytes [1,2,4].

Phosphine is responsible for the denaturation of oxyhaemoglobin and converts it to methaemoglobin and heme chrome species [1]. PH<sub>3</sub> is known to induce oxidative damage in brain, lung and liver [1,2]. AIP causes organ damage due to cellular hypoxia and leads to a high superoxide dismutase activity and low catalase levels that result in formation of a high level of free radicals and accelerate lipid peroxidation. These alterations result in damage to cellular membrane, ionic barrier disruption and nucleic acid damage [1,2].

Phosphine gas is a cytotoxic agent affects heart, lungs, kidneys and gastrointestinal tract. Acute AIP poisoning in oral exposure causes anorexia, nausea, restlessness, abdominal pain, gastrointestinal hemorrhages, bradycardia, palpitation, pulmonary edema, cyanosis, tachypnea, hypotension, metabolic acidosis, shock and atrial and ventricular dysrhythmia. Other effects include serum electrolytes disturbances (hypomagnesaemia or hypermagnesaemia, hypo or hypernatremia, hypokalemia), blood sugar changes (hyper or hypoglycemia), methemoglobinemia, hepatitis, acute tubular necrosis and disseminated intravascular coagulation (DIC) [1,2].

The inhalation of PH<sub>3</sub> causes cough, chest tightness, headache, numbness, lethargy, anorexia, pulmonary edema, garlic-like odor in breath, cold sweats, tremors, convulsions, delirium, coma and death due to respiratory and cardiac arrest [1,2].

That mortality has been occurred due to cardiogenic shock, developed adult respiratory distress syndrome and multi -organ failure (MOF) [1,2].

In the 1990s showed a dramatic increase in the number of intentional poisoning cases and deaths caused by suicidal ingestion, particularly in India [1]. However, AIP has been reported as the most common cause of suicidal poisoning in rural and sub-urban regions in of the developing countries like Iran [5-9].

In Iran, AIP known as "Rice tablet" is used as a formulated in a 3g tablets in dark gray or greenish-gray colors packaged

in metallic box and is available under various brands such as Celphos®, Phosfume®, Quickphos® and mainly under brand name Phostoxin®. Each tablet contain AIP, urea, and ammonium carbamate which usually able to produce about 1g PH<sub>3</sub> in the presence of water or moisture [3].

Following studies showing both a high morbidity and mortality due to acute AIP poisoning in Iran [10,11], the National Pesticide Control Board authorities banned the importation, distribution, and use of AIP tablets and excluded it from the Iran's list of allowed pesticides in 2007 [5,12]. Unfortunately, from this date, the use of smuggled forms of rice tablets available in black markets was distributed and sold by profiteers. Between 2000-2019, the Iranian Legal Medicine Organization (LMO) has been reported the 600-900 fatal AIP poisoning cases, annually [13].

In this article, we have reviewed the recent published studies on acute AIP poisoning and related deaths to know the current status of the manner and characteristics of acute AIP poisoning in Iran. These studies were collected using searches by PubMed and Google Scholar databases using the keywords 'Aluminum phosphide', 'poisoning' and 'Iran' from 2014 to 2024 (20th September). The initial search identified 52 publications. Based on the screening, 28 duplications and ineligible were removed. We performed full-text review of the remaining 24 eligible articles, excluding an additional 11 papers based on irrelevant and/or insufficient data. Finally, 13 articles included in this review.

## Findings

Shokerzade M, et al. [14] was reported the prevalence of AIP fatal poisoning in Mazandaran province (North of Iran) according to the data obtained from the autopsy files in the forensic medicine center from 2009 to 2011. From total 2446 autopsy cases during this period, 42 fatal cases (17.8%) due to AIP poisoning. Male to female ratio was reported 1.6. The common age range of decedents was 21-30 years old. The mortality was frequently observed in married individuals [14].

In another study was performed by Shokerzadeh M, et al. [15] on the AIP poisoning cases in Golestan Province (North of Iran) during 2008-2016, all autopsy files at Golestan forensic medicine center were evaluated. In this period, from total of 420 deaths due to poisoning, 105 (25%) fatal cases due to AIP poisoning. Sixty- seven (68.7%) of the cases were male and the common age range was 20-29 years old. Majority of cases were married (n=49, 46.7%). Also, 87 (82.9%) of cases were living in urban areas. However, 104 (99%) of fatal deaths caused by suicidal AIP poisoning [15].

Kordrostami R, et al. [16] performed a study on self-poisoning related suicidal deaths on autopsy cases in forensic

medicine center in Tehran (Capital of Iran) from 2011 to 2015. They showed from 674 cases of suicidal poisoning deaths were investigated in the study period, of which 68.55% were male. The most often used suicide method was self-poisoning in young population. ALP was the most toxic agent used in suicidal poisoning (619 cases) followed by opioids, methamphetamine, organophosphates, cyanide and strychnine [16].

Navabi SM, et al. [6] evaluated all patients with acute ALP poisoning referred to a referral hospital in Kermanshah Province (northwestern of Iran) during 2014- 2015. In this study, total 77 poisoned cases (48 patients were male and 29 patients were female) were enrolled. The average age of the survivors and non-survivors was 28.7 and 31.3 years, respectively. All cases (100%) of ALP poisoning were committed suicide. The main predictive variables of mortality in acute ALP poisoning were low blood pressure, decrease of blood pH, and time elapsed from ingestion to beginning of treatment [6].

Valipour R, et al. [17] performed a study on forensic autopsies on suicidal deaths between 2010-2016 at the legal medicine center of Zanjan Province (Northwest of Iran). During this period, from total of 181 cases of suicide deaths, 74% were male and ALP was the most frequent poison detected in the fatal suicidal cases (33 cases, 18.2%) followed by opioids [17].

Dorooshi G, et al. [3] were investigated the outcome of ALP intoxicated patients admitted to the clinical toxicology ward of an university hospital in Isfahan city (center of Iran) from 2017 to 2019 via a chart-review study. The most common clinical presentations at admission were low of consciousness (41.9%) and vomiting (32.2%). There was no significant change in blood glucose, pH, base excess (BE), and venous blood bicarbonate concentration during hospitalization ( $P > 0.05$ ). Treatment outcomes had a significant relationship with blood pH, 2- hour and 6- hour after admission and the BE 6- hour after admission ( $P < 0.05$ ). There was also a significant relationship between the outcome and the length of stay, initial ejection fraction (EF), and EF in predischarge echocardiography ( $P < 0.05$ ). Out of 31 patients, 24 (77.4%) died within 72 hours, 5 cases (16.1%) recovered without any complication, and 2 patients (6.5%) recovered with complications [3].

Bagherian F, et al. [18] performed a systematic review and meta-analysis on the mortality rate of ALP poisoning cases in Iran. The mortality rate in ALP poisoning in male and female patients was 62.3% (95% CI: 53.5%-70.8%) and 37.7% (95% CI: 29.2%-46.5%), respectively ( $p < 0.01$ ). According to this study, they concluded that the mortality

rate of ALP poisoning in Iranian population is about 27.3% (95% CI: 18.9%- 36.5%) after the trim-and-fill correction on corrected pooled mortality rate. However, males having a higher fatality rate than females. Also, intoxication at a younger age is associated with better outcome [18].

Astaraki P, et al. [19] studied a descriptive-analytical study on patients in an academic referral hospital in Khorramabad city (Lorestan Province, west of Iran) due to ALP acute poisoning and methadone from 2015 to 2020. From total of 19,238 patients with poisoning referred to this center, 412 patients (2.41%) were due to acute ALP poisoning. Among these patients, 56 cases (13.59%) died. In ALP poisoned cases, male patients with 53.57% was the majority group. The common age group in these patients was 15-35 years old. The duration of hospitalization and the time of referral to the emergency department to the death of the patient was significantly correlated with mortality in both the groups. The common manner of poisoning was reported as suicide [19].

In another study, Dorooshi G, et al. [20] performed a cross-sectional descriptive analytical study to investigate the frequency of fatal poisoning during 5-year (from 2014 to 2019) in a referral teaching hospital in Isfahan (Center of Iran). From total 264 fatal poisoned cases during this period, paraquat ( $n = 48$ , 18.1%) and ALP ( $n = 45$ , 17%), were the common cause of fatal poisoning. All of poisoning cases were suicidal [20].

Jamshidi F, et al. [21] evaluated the data of the clinical laboratory parameters in ALP poisoned cases who referred to Razi hospital (Ahvaz city, Southwest of Iran) within the period of 2010-2015. A total of 23 cases, the mean age of the patients was  $27.2 \pm 7.3$  years and majority of them were male (60.9%). In majority of the ALP poisoned cases, the levels of serum sodium and potassium were normal. However, 8.7% of the patients had hyponatremia and 21.7% of the patients had hypokalemia. Metabolic acidosis and serum bicarbonate was reduced in the majority of cases (91%) [21].

Gholami N, et al. [22] reported case fatality rate among poisoned children (age, 0-12 years) who admitted to a referral university hospital in Tehran (Capital of Iran) via a retrospective review of patient data recorded in the Hospital Information System over the 10-year period from March 2010 to March 2020. Of 8158 children admitted for poisoning, 28 cases (0.3%) died, among whom 19 (67.9%) were boys and 9 (32.1%) girls. The median age was 42 months (range: 2 to 144 months). The most common cause of mortality in acute poisoning was methadone ( $n = 13$ , 46.4%), followed by opium ( $n = 5$ , 17.9%), ALP, carbon monoxide, and toxic mushrooms ( $n=2$  deaths each, 7.1%). Tramadol, colchicine,

and petroleum involved for one death each (3.6%) [22].

Kojidi HM, et al. [23] performed a descriptive cross-sectional study on all AIP intoxicated patients admitted to an university hospital in Rasht city (North of Iran) from April 2016 to the October 2017. The most gastrointestinal symptoms were nausea and vomiting (86.7%). neurological problems were reported in 12.4% of patients. The majority of cases having paresis (68.3%). Suicidal poisoning was documented in 96.2% of cases via oral ingestion. Hypotension, cardiac, and respiratory complications were observed in 25.2%, 30.8%, and 25% of the patients, respectively [23].

Dadpour B, et al. [24] reported an outbreak of AIP poisoning in Mashhad (Northeast of Iran) due to accidental phosphine inhalation. On 6 June 2015, the accidental AIP poisoning was occurred in Saudi Arabian tourists. Thirty six Saudi tourists (mean age 15 years; range: 1-45) staying in a hotel in Mashhad were admitted to the university hospital for symptoms of acute AIP poisoning. One of them died on admission to the hospital. They inhaled PH<sub>3</sub> gas liberated from AIP powder which was placed in their rooms for pest control. Four patients died before or soon (4-6 h) after admission. The main clinical presentations of deceased cases on admission was shock and severe metabolic acidosis, which was refractory to treatment. In addition to shock, the fourth deceased patient had a massive pulmonary hemorrhage due to DIC. This is the first scientific report of accidental mass poisoning due to phosphine liberated from AIP tablets in Iran [24].

## Conclusion

Despite the prohibition of AIP tablets in Iran since 2007, the present study shows that the number of poisonings caused by this poison is frequent in Iran. AIP is considered as one of the most important causes of fatal poisonings in Iran. Also, AIP is considered as one of the most important poisons used in suicidal poisoning. In Iran, the mortality rate in acute AIP poisoning is estimated at 27%. This type of poisoning has been reported mostly in married men aged between 20 -30 years old and in the route of oral consumption. AIP poisoning is reported mostly from Tehran and the northern, western and central provinces of Iran. Although the incidence of accidental AIP poisoning in the country is low, but the accidental inhalation of phosphine as a mass poisoning pattern have been reported in Iran. Considering the prevalence of AIP poisoning in the country, it is suggested to take legal measures to limit the distribution and sale of smuggled AIP tablets in the black markets. Also, to increase general education to the community and specialized training to medical professionals with the aim of reducing the prevalence of poisoning with this poison are recommended.

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