

MANAGEMENT OF ACUTE ALUMINUM PHOSPHIDE TOXICITY IN RAT MODEL WITH A NOVEL INTERVENTION, A TRIAL OF BORIC ACID

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ABSTRACT

Aluminum phosphide (AIP) or rice tablet is a cheap pesticide. When it comes in contact with acid (gastric acid) or moisture, it releases phosphine (PH₃) gas. The heart, lungs, liver are the main targets in acute Aluminum phosphide (AIP) poisoning. Most deaths occur due to cardiovascular toxicity. Recently, boric acid has been proposed theoretically as an antidote for AIP poisoning. With the formula B (OH)₃, boric acid can accept electrons as it is a Lewis acid with an empty p orbital. **The aim** of the present study was to investigate the possible protective role of boric acid in management of aluminum phosphide poisoning and its possible use as an effective antidote to reduce ALP poisoning mortality. **Forty albino rats, all of which were adults and males** were equally divided into four groups, group 1: control (given distilled water), group 2: given boric acid only (100mg/kg nontoxic dose), group 3: given aluminum phosphide (12.5 mg/kg), group 4: given aluminum phosphide followed by boric acid. Rats in group 1 and 2 was killed by cervical dislocation, while rats in group 3 and 4 were left to die, then all were dissected out. Fixation in situ was performed by perfusion technique then the chest and the abdomen were carefully incised to reveal the heart and the liver. The liver and the heart were washed with saline then quickly dissected, excised then blotted for histological preparation. Blood samples were collected from each rat (immediately after death) for measuring liver enzymes (SGOT, SGPT, ALK (alkaline phosphatase) and cardiac troponin. Rats treated with ALP followed by boric acid showed significant increase in their survival time, marked improvement in histopathological changes and also showed significant improvement in biochemical parameters including liver and cardiac markers (SGOT, SGPT, and cardiac troponin) compared with rats intoxicated with AIP. **Conclusion:** This study may increase the hope of using boric acid as a new effective antidote for ALP poisoning and opens the door of opportunity for larger experimental and then clinical trials to reevaluate the role of boric acid in acute ALP poisoning.

Key words: Aluminum phosphide, Boric acid, Toxicity, Cardiac troponin, Antidote.

INTRODUCTION

Aluminum phosphide (AIP) is a solid cheap fumigant pesticide (rice tablet) which protects stored grains from insects and rodents with a fatal dose between 0.15 and 0.5 grams (0.0053 and 0.0176 oz) (Wahab et al., 2008). When it comes into contact with moisture or acid, it releases phosphine

(PH₃); a colorless, inflammable, water insoluble, and highly toxic gas (Moghadammia 2012; Bumbrah et al., 2012). While odorless in its pure form, PH₃ can smell of garlic or decaying fish due to the presence of impurities such as substituted phosphines and diphosphines (Wahab et al., 2009).

Phosphine gas (PH₃) is a Lewis base and a strong nucleophile. It is a reducing agent with a lone-pair electron which reduces cytochrome c oxidase and interferes with the electron transfer from complex III to complex IV of the mitochondrial respiratory chain, ultimately resulting in the inhibition of oxidative phosphorylation, adenosine triphosphate depletion and cell death (Soltani et al., 2013).

Aluminum phosphide is usually taken in suicidal attempt. It was reported that AIP has a mortality rate more than 50% of intoxicated cases (Moghadamnia 2012). After ingestion of aluminum phosphide, phosphine gas is released in the stomach and after absorption; symptoms and signs of poisoning occur rapidly (Wahab et al., 2008) which include nausea, vomiting, garlic breath smell, retrosternal and epigastric pain, anxiety, agitation, and dyspnea (Mostafazadeh 2012 & Popp et al 2002).

The heart, lungs and liver are the main target organs in acute AIP poisoning, although multi-organ system failure may also occur. Most deaths occur within the first 12-24 hours, usually because of cardiovascular toxicity (Perry 2007).

Patients are usually managed conservatively, and their outcome is very bad as there is no efficient antidote has been discovered for AIP poisoning till now (Moghadamnia 2012).

Recently, boric acid has been proposed theoretically as an antidote for AIP poisoning. With the formula B(OH)₃, boric acid is a Lewis acid which can accept electrons as it has an empty p orbital (Soltani et al., 2013). Boric acid is a colorless, odorless, transparent material used in industrial sector for preparation of disinfectants and drugs. However, it is primarily beneficial for

humans in nutritional amounts, and is thus found in animal and human tissues at low concentrations (Environmental Protection Agency 2004). It is considered as a weak acid and it is non-toxic in rats with a median lethal oral dose of 5.14 g kg⁻¹ (Perelygin and Chistyakov 2006).

In the study done by Soltani et al., (2016), at Sultan Qaboos University on chemical reaction between boric acid and phosphine, they concluded that boric acid significantly reduced the rate of phosphine gas evolution (P <0.01) and that boric acid may be an efficient and non-toxic antidote for PH₃ poisoning.

AIM OF THE STUDY

This study aimed to investigate the possible antidotal role of boric acid in management of Aluminum phosphide toxicity and its protective role on AIP-induced biochemical and histopathological changes in liver and heart of adult male albino rats.

MATERIALS & METHODS

This experiment was carried out in the animal laboratory in Faculty of Medicine, Menoufia University.

Animals: Forty adult male albino rats weighed 150-240 grams were used in this experiment. Animals were purchased from a small animal breeding center in Shebin El-kom, Menoufia, Egypt. All ethical protocols for animal treatment were followed. This experimental protocol was accepted by the Ethical Committee of Menoufia faculty of medicine.

Materials: Aluminum phosphide used in experiment was in the form of 3 gm tablets (57% concentration, Excel crop care Ltd, India), and contains two compounds: aluminium phosphide and

aluminium carbonate in a ratio of 57:43.

Aluminum phosphide Purchased from local pesticide shop in Shebin El-Kom.

Boric acid was obtained from toxicology laboratory in toxicology department (boric acid powder dissolved in hot distilled water and given in a dose of 100 mg/kg dose), Menoufia Faculty of medicine. Substances of experiment were given by gavage (oral tube).

Experimental design:

Rats were housed in polypropylene cages. Food and water were provided ad libitum (on desired). Rats were given two days' time to get acclimatized with the laboratory conditions prior to experiment. All rats were fasted for 24 hours just before starting the experiment (in order to empty gastro intestinal tract and abolishing interactions of food components with the tested substance) (vermeulen et al., 1997).

Rats were divided into four groups, each containing ten rats (n=10).

Group 1: Control (given distilled water)

Group 2: Boric acid only (+ve control) in a dose, (100 mg/kg nontoxic dose), (Ince et al., 2010).

Group 3: Given aluminum phosphide (12.5 mg/kg) (Baeri et al., 2013).

Group 4: Given aluminum phosphide (12.5 mg/kg) followed by boric acid (100mg/kg).

Rats in group 1 and 2 was killed by cervical dislocation, while rats in group 3 and 4 were left to die, then all were dissected out.

Histological specimen preparation:

Fixation in situ was performed by perfusion technique then the chest and

the abdomen were carefully incised to reveal the heart and the liver. The heart and the liver were washed with saline then quickly dissected, excised then blotted.

I- Histological study: Tissue samples were fixed in 10% formol saline for 2-5 days then washed in tap water, dehydrated in ascending grades of alcohol (50%, 70%, 90% over night and 100% for 3 hours), cleared in xylene and embedded in paraffin wax. Paraffin sections of 5-6 micrometer thickness were cut and stained with hematoxylin & eosin (H &E).

II-Immunohistochemical study: Caspase-3: sections were stained with the primary rabbit polyclonal anti caspase-3 antibody (Thermo Scientific, Lab Vision, USA) (Sanii et al., 2012).

Immunostaining by caspas3 show if there is apoptosis or not, as we want to know if ALP produce effect at the level of the nucleus or not.

Biochemical analysis:

Blood samples were collected from each rat (immediately after death) for measuring liver enzymes (SGOT, SGPT, ALK (alkaline phosphatase) and cardiac troponin. Blood was centrifuged at 3000 rpm to obtain the plasma, then SGOT, SGPT activity were determined (Ritman and Frankel 1957). Activity of alkaline phosphatase was determined (Babson and Read 1959), and the levels of cardiac troponin were also measured by enzyme linked immunoassay (ELISA) technique using a standard kit (Glory Science Co., Ltd, USA).

Statistical analysis:

The collected data were organized, tabulated and analyzed using SPSS version 16 software (Spss Inc, Chicago, ILL Company). The t-test was used to compare between mean \pm SD of two groups. Also, normally quantitative

data expressed in mean \pm SD and was compared using F test (ANOVA), and the Sig. between groups was done using Post Hoc Test (Tukey). The abnormally distributed quantitative data was expressed in median (Min. - Max.), and compared using Kruskal Wallis test, where Sig. between groups was done using Post Hoc Test (Dunn's multiple comparisons test). The accepted level of significance was stated ≤ 0.05 .

RESULTS

A-Histopathological & immunoreactivity changes:

• Liver sections

Sections of the control group (group 1) showed hepatocytes arranged in plates radiating from central vein and separated by blood sinusoids. The hepatocytes characterized by vesicular central nuclei and acidophilic cytoplasm (**Fig.1 A**). Immunostaining for Caspase 3 showed -ve reaction (**Fig.1 C**).

Sections of the boric acid treated group (group 2) showed picture of liver similar to control group which appeared completely normal (**Fig. 2 A&C**).

Sections of the liver of rats intoxicated with Aluminium phosphide (group 3) showed destructive changes in the form of hydropic degeneration of hepatocytes, presence of many hepatocytes with pyknotic nuclei (**Fig.3 A1**). Many vacuoles were also seen among hepatic tissue. Dilated distorted and congested blood sinusoids were noticed (**Fig.3 A2**). Central vein showed dilation and congestion. Mononuclear cells infiltrated the area around central vein and blood sinusoids (**Fig.3 A3**). Immunostaining for Caspase 3 showed + ve reaction (**Fig.3C**).

Liver sections in rats intoxicated with aluminum phosphide then treated with boric acid (group 4) showed marked improvement of the degenerative changes as the hepatocytes showed acidophilic cytoplasm with central vesicular nuclei (**Fig.4 A1**). There was marked decrease in the presence of vacuoles. The blood sinusoids showed normal appearance. The disappearance of monocells infiltrates was also noticed (**Fig.4 A2**). Immunostaining by Caspase 3 showed -ve reaction (**Fig. 4 C**).

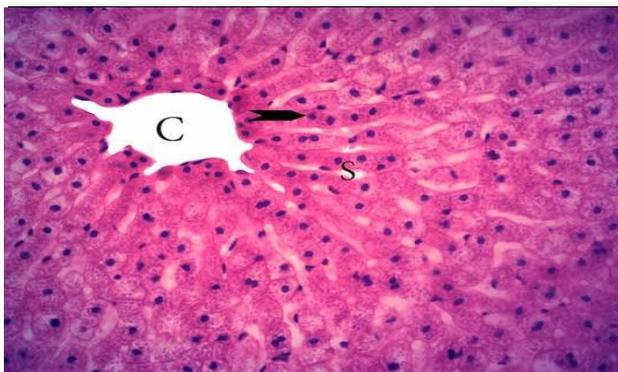


Figure (1A): A photomicrograph in a section of control rat liver showing hepatocytes (►) arranged in plates that radiate from the central vein (C), and separated by blood sinusoids (S). H. and E. x 400

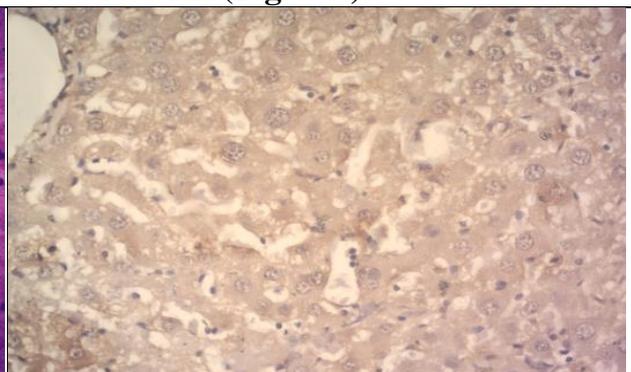


Figure (1C): photomicrograph in a section of control rat liver showing -ve Caspase 3 reaction. x 400.

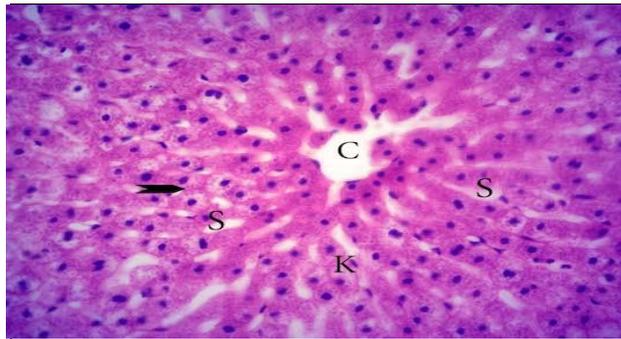


Figure (2A): A photomicrograph in a section of rat liver treated with Boric acid showing normal hepatocytes (▶) radiating from central vein (C) and separated by blood sinusoids (S) as control group. H. and E. x 400.

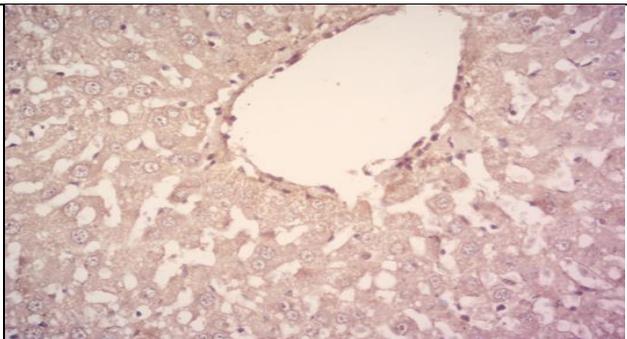


Figure (2C): A photomicrograph in a section of rat liver treated with Boric acid showing -ve Caspas 3 reaction x 400.

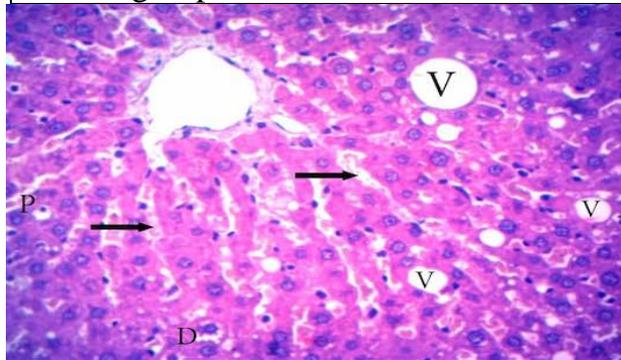


Figure (3A2): A photomicrograph in a section of rat liver treated with aluminum phosphide showing distorted, dilated, congested blood sinusoids (→), and many cytoplasmic vacuoles (V) were noticed. Some hepatocytes showing hydropic degeneration (D) and pyknotic nuclei (P). H. & E. x 400.

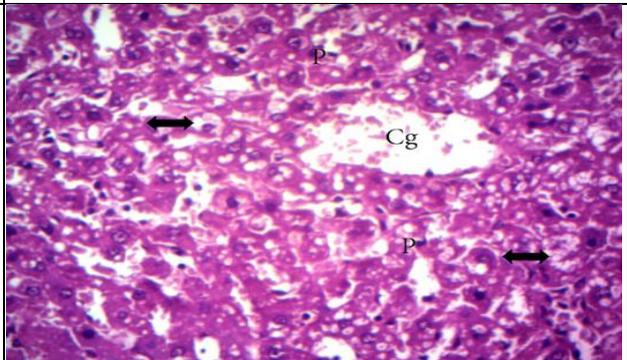


Figure (3A2): A photomicrograph in a section of rat liver treated with aluminum phosphide showing cytoplasmic vacular degeneration (↔), pyknotic nuclei (P) in the affected hepatocytes and dilated congested central vein (Cg). H. & E. x 400.

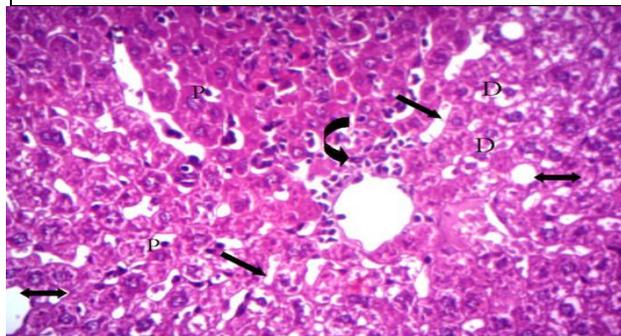


Figure (3A): A photomicrograph in a section of rat liver treated with aluminum phosphide showing monocellular infiltration (⊖). Cytoplasmic vacuoles (↔) were seen. Hydropic degeneration of hepatocytes (D) and pyknotic nuclei (P) were also noticed H. & E. x 400

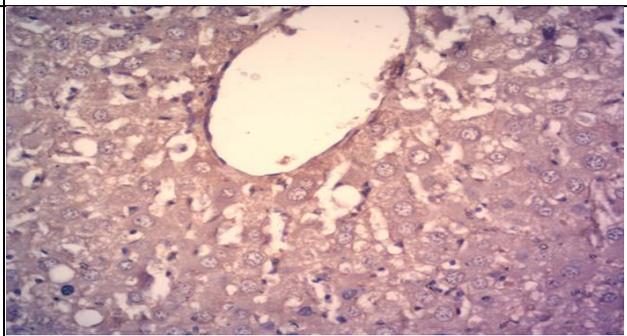


Figure (3C): A photomicrograph in a section of rat liver treated with aluminum phosphide showing strong +ve Caspas reaction. X 400.

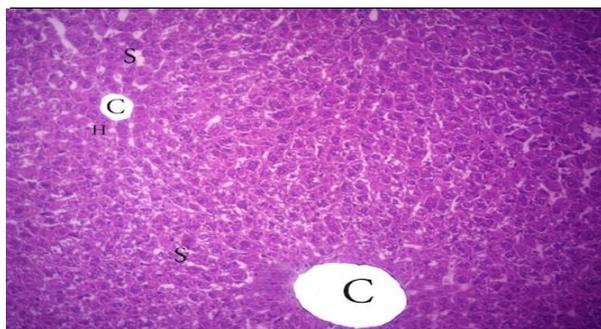


Figure (4A1): A photomicrograph in a section of rat liver treated with aluminum phosphide and Boric acid showing normally arranged hepatocytes. Only few blood sinusoids are dilated (→)
x400

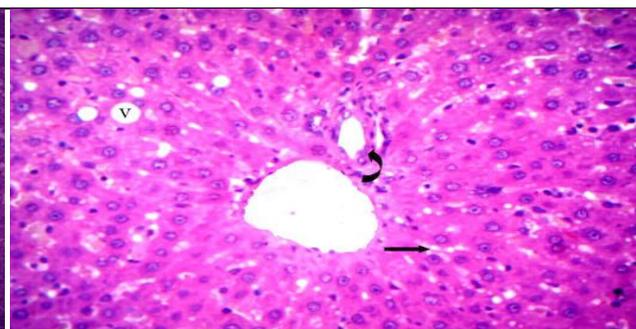


Figure (4A2) A photomicrograph in a section of rat liver treated with aluminum phosphide and Boric acid showing return of liver tissue to its normal appearance. Improvement of sinusoidal dilation (→), absence of monocellular infiltration but few vacuoles are still present (V)
H. & E. x 400

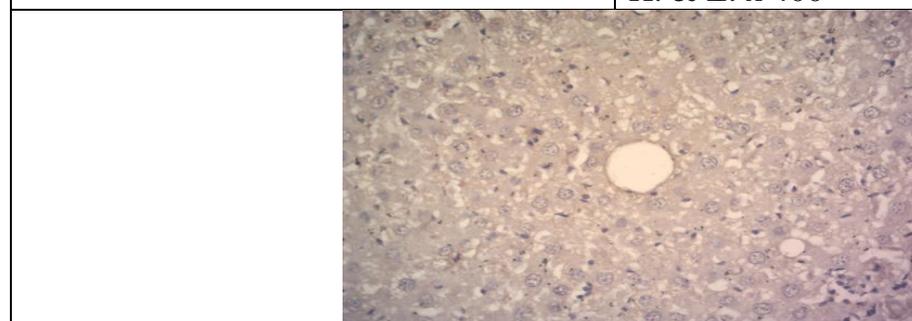


Figure (4C): A photomicrograph in a section of rat liver treated with aluminum phosphide and Boric acid showing -ve Caspas reaction. X 400

• Heart sections

In control group (group 1), Cardiac myocytes appeared cylindrical with acidophilic striated sarcoplasm and centrally located oval nuclei. Fibroblasts with its deeply stained flattened nuclei were noticed at the C.T (connective tissue) endomysium (**Fig. 5A**). Immunostaining for Caspase 3 showed -ve reaction (**Fig. 5 C**).

In group 2 (Boric acid treated), examination by light microscope showed cardiac myocytes with acidophilic striated sarcoplasm and centrally located elongated vesicular nuclei, nearly as picture in control group (**Fig. 6 A & C**).

Microscopic changes noticed in group 3 (Aluminum phosphide) were in the form of fragmentation of muscle

fibers of the heart, many cytoplasmic vacuoles and hyaline materials were noticed. Also, pyknotic nuclei were present in the affected fibers (**Fig.7 A1& A2**). Widening of interstitium between cardiac myocytes was noticed, which contained hemorrhage and infiltration with mononuclear cells. There was congestion of blood vessels (**Fig.7 A3**). Caspase 3 immunostaining revealed strong +ve reaction (**Fig.7 C**).

In group 4 (Aluminum phosphide and Boric acid treated), examination by light microscopic showed appearance of cardiac myocytes more or less similar to control group (**Fig.8 A1 & A2**). Also Caspase 3 Immunostaining showed -ve reaction (**Fig.8 C**).

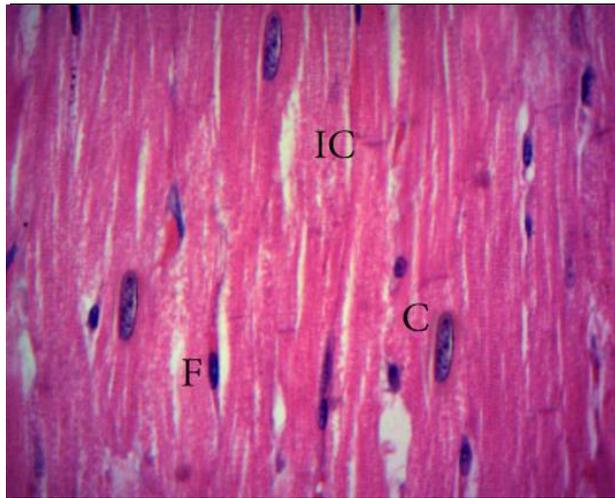


Figure (5A): A photomicrograph in a section of control rat heart showing long cylindrical cardiac muscle fiber (C) with acidophilic striated sarcoplasm and centrally located oval nuclei. The cardiac muscle fibers are connected by intercalated discs (IC). Flattened deeply stained nuclei of fibroblast are noticed (F). H.& E. x 1000

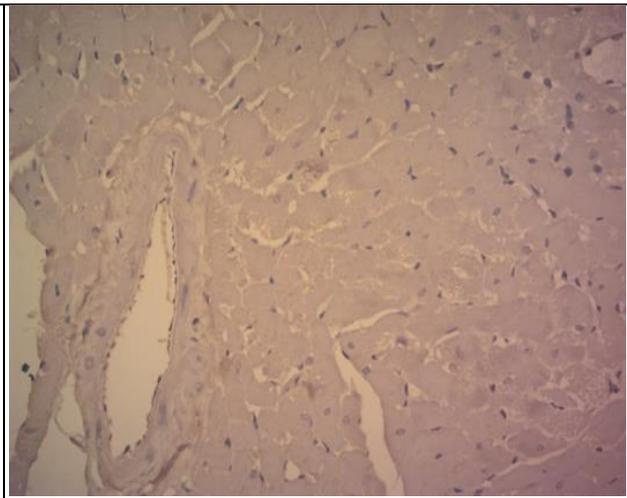


Figure (5C): A photomicrograph in a section of control rat heart showing -ve Caspas 3 reaction. x 400

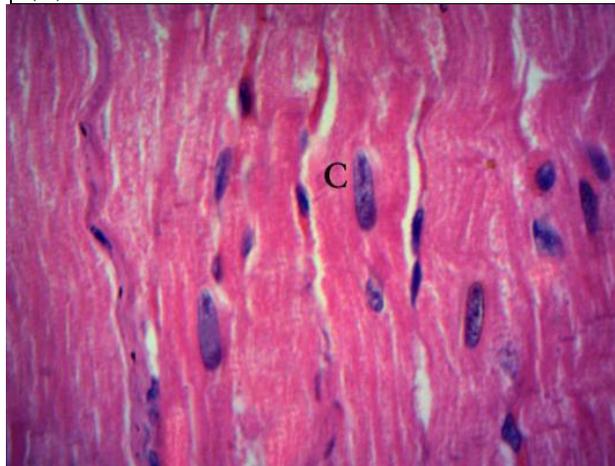


Figure (6A): A photomicrograph in a section of rat heart treated with Boric acid showing cardiac muscle fibers with acidophilic sarcoplasm (C) and central vesicular nuclei similar to control group. H. &E. x 1000

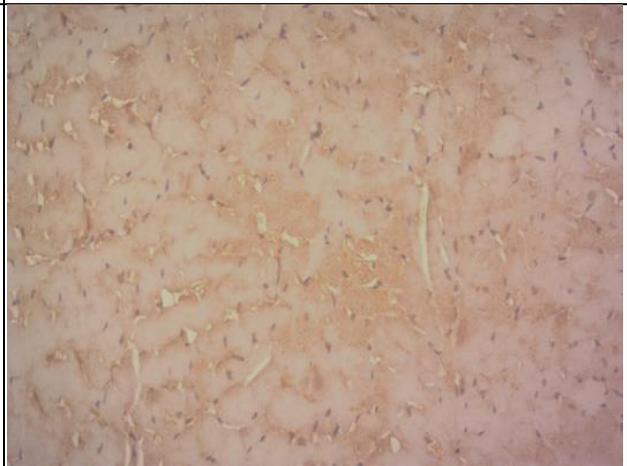


Figure (6C): A photomicrograph in a section of rat heart treated with Boric acid showing -ve Caspas 3 reaction. X400

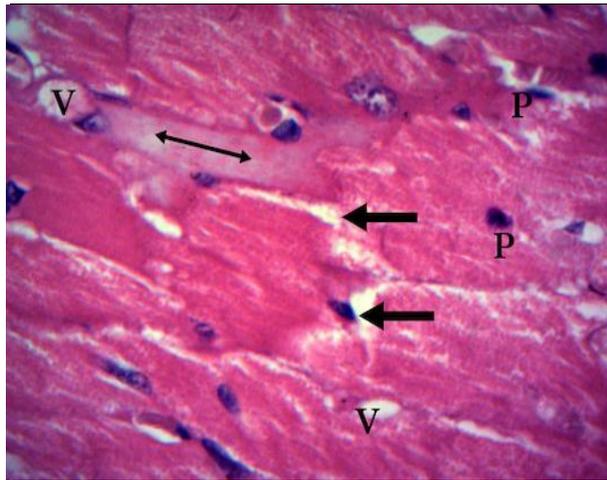


Figure (7A1): A photomicrograph in a section of rat heart treated with aluminum phosphide showing fragmentation of cardiac muscle fibers (\leftrightarrow), cytoplasmic vacuolation (V) and hyaline material accumulation (\leftrightarrow). Notice the pyknotic nuclei (P) in some cardiac myocytes. H.& E. x 1000

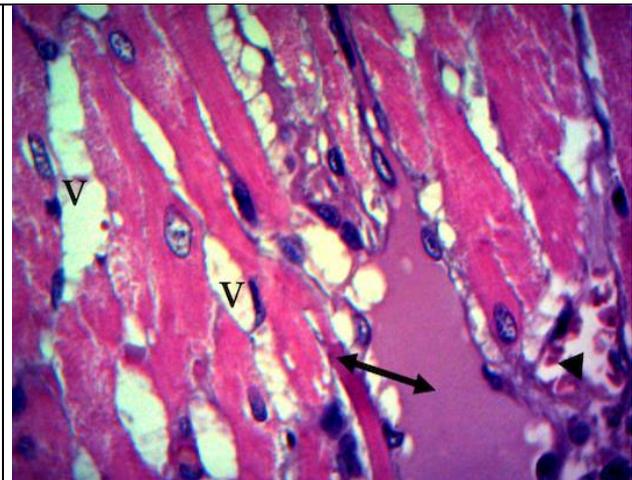


Figure (7A2): A photomicrograph in a section of rat heart treated with aluminum phosphide showing marked hyalinization (\leftrightarrow) and cytoplasmic vacuolation (V). Widening of the interstitial space separating the cardiac myocytes (\blacktriangleright), containing hemorrhage and mononuclear cells infiltrate. H. & E. x 1000



Figure (7A3): A photomicrograph in a section of rat heart treated with aluminum phosphide showing marked interstitial edema (\blacktriangleright), congested blood vessels are also seen (Cg). H. & E. x 1000

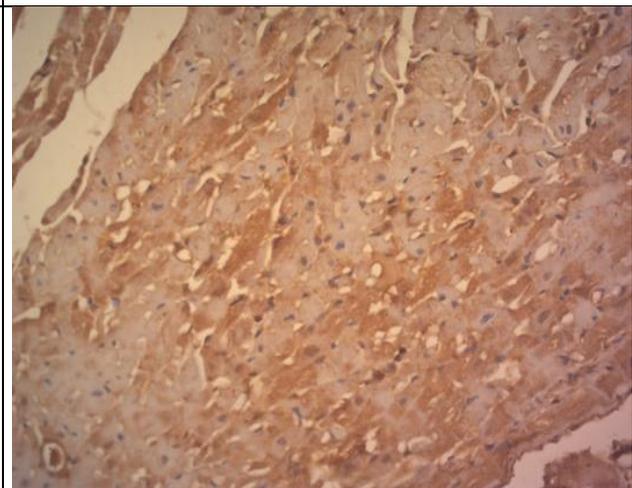


Figure (7C) A photomicrograph in a section of rat heart treated with aluminum phosphide showing +ve Caspas 3 reaction. X 400

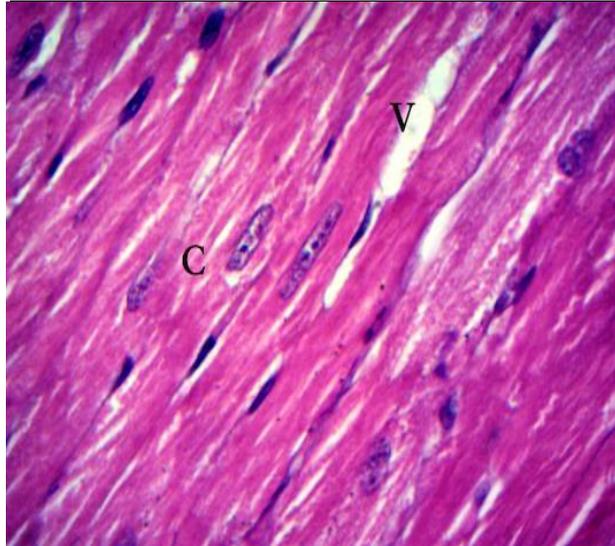


Figure (8A1): A photomicrograph in a section of rat heart treated with aluminum phosphide and Boric acid showing normal structure of cardiac myocytes (c) with its centrally located oval vesicular nuclei. Few vacuoles are still present (V).H. & E. X 1000

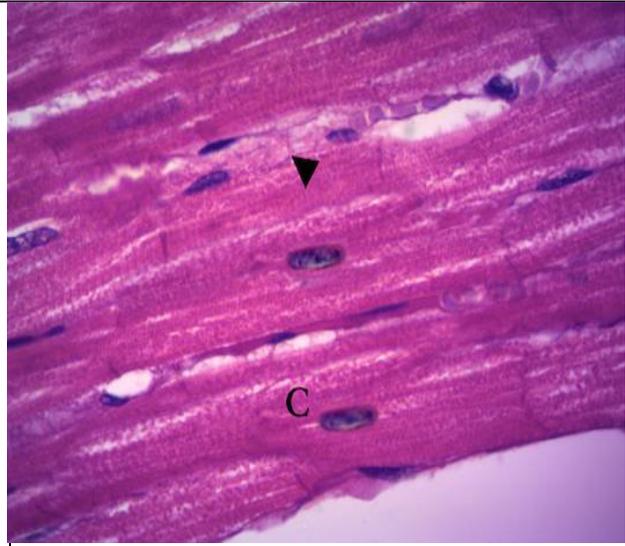


Figure (8A2): A photomicrograph in a section of rat heart treated with aluminum phosphide and Boric acid showing minimal interstitial edema. The cardiac muscle fibers regain its normal shape and structure. H. & E. x 1000

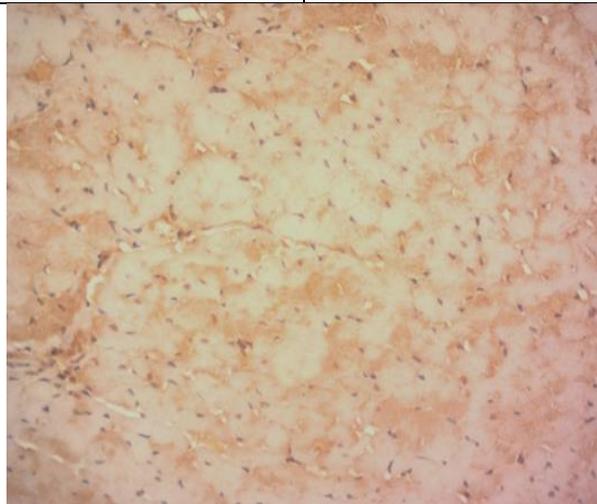


Figure (8C): A photomicrograph in a section of rat heart treated with aluminum phosphide and Boric acid showing –ve Caspas 3 reaction. x 400.

B- Biochemical results: Liver enzymes, and cardiac troponin:**Table (1):** Comparison between the different studied groups according to liver enzymes (SGOT, SGPT, ALK) and cardiac troponin.

	Control (n= 10)	Boric (n= 10)	ALP (n= 10)	ALP+boric (n= 10)	P
SGOT U/L	47 ± 2.5	45.5 ± 2.3	68.7 ^{ab} ± 1.5	51.9 ^{abc} ± 2.4	<0.001*
SGPT U/L	36.6 ± 2.5	36.2 ± 2.8	75.6 ^{ab} ± 7.8	61.3 ^{abc} ± 5.6	<0.001*
ALK U/L	319 (313–420)	325 (300–420)	490 ^{ab} (444–570)	450 ^{ab} (430–500)	<0.001*
Troponin Ug/L	0.03 (0.02–0.04)	0.03 (0.02–0.05)	0.26 ^{ab} (0.09–0.40)	0.06 ^{abc} (0.03–0.20)	<0.001*

Normally quantitative data was expressed in mean ± SD and was compared using F test (ANOVA), Sig. bet. grps was done using Post Hoc Test (Tukey) abnormally distributed quantitative data was expressed in median (Min. - Max.) and was compared using Kruskal Wallis test, Sig. bet. grps

Data of the current work showed that group of Alp poisoned rats showed a highly significant increase in liver enzyme activity and cardiac troponin compared to their levels in rats of either control or boric acid groups (P value <0.001). In group 4 (Boric acid and

was done using Post Hoc Test (Dunn's multiple comparisons test)

a: significant with control

b: significant with boric

c: significant with ALP

*: Statistically significant at $p \leq 0.05$

ALP) there was a significant decline in liver enzymes activity (SGOT, SGPT) compared with ALP group. Concerning cardiac troponin, its level was significantly decreased compared with its level in group 4 (Boric acid and ALP group) (Table 1).

Table (2): Survival time in mean ± SD of rats intoxicated with ALP compared with that treated with boric acid with ALP.

	ALP group	ALP + Boric acid	t - value	P value
Survival time in minutes	98.6 (±7.06)	511.3 (±11.84)	94.67	< 0.0001

Using t- test

Statistically significant at $p \leq 0.05$

Mean survival time was 98.6 min (±7.06) after a single dose of aluminum phosphide of 12.5mg/kg. Increased to 511.3min (±11.84) in AIP group treated with boric acid (group4) with much increase in survival time and this increase was highly significant (P value

<0.0001) (Table 2).

DISCUSSION

Acute intoxication with phosphides is a serious health problem either accidental or suicidal in Menoufia governorate, Egypt as in 2016, at

Menoufia poison control center (MPCC), phosphides were the cause of about 80 % of mortality of poisoned cases.

Until 2012, the main line of management for ALP intoxicated patients was just supportive due to absence of proper antidote (**Mostafazadeh, and Farzaneh 2012**).

Boric acid is considered as a safe product and its toxicity is unusual (**Kaymaz 2015**), so we tried in our study to test the possible use of this substance as an antidote for ALP poisoning in rat models, based on the theoretical study of **Soltani et al., (2016)**.

In the current study, the mean survival time was 98.6 (± 7.06) after a single dose of aluminum phosphide of 12.5mg/kg. That increased to 511.3 (± 11.84) in AIP group treated with boric acid.

There was much increase in survival time with administration of boric acid after aluminum phosphide which entail that this substance (boric acid) may be the missed antidote for ALP poisoning specially if we compare it with other proposed antidotes like N - acetyl cysteine (138 ± 13 min with NAC dose=50mg/kg) or vitamin C (250 ± 17 min with vitamin C dose=500mg/kg) (Moghadamnia, 2000)

Histopathology & immunoreactivity of the liver.

There were histopathological changes in the rat liver tissues in the form of disorganization of hepatocytes, hydropic degeneration, sinusoidal dilation and some hepatocytes showed pyknotic nuclei in ALP group in comparison with control and boric acid only groups. These changes were markedly decreased when rats were treated with boric acid after ALP. As boric acid act to maintain the oxidant

/antioxidant balance and it inhibits lipid peroxidation (**Turkez et al., 2011**). These pathological changes due to phosphine gas effects liberated after ALP ingestion and cause inhibition of respiration mitochondria in rat liver (**Okolie et al., 2004**).

In India, **Saraf et al. (2015)**, reported that zinc phosphide is the most common cause of drug/toxin-induced human irreversible acute liver failure.

The histopathological results of our research are in agreement with the experimental study done by **Sinha et al. (2003)**, who recorded histopathological changes in the rats liver after ALP intoxication in the form of congestion in central veins, haemorrhage degeneration, hyperplasia in Kupffer cell, sinusoidal dilation, mononuclear cells infiltration, centrilobular necrosis and fatty changes.

Mehrpour et al. (2010), recorded liver tissues changes with aluminum phosphide, in the form of mononuclear infiltration, congestion of veins and degeneration of hepatocytes.

Musshoff et al. (2008), found congestion, centrilobular necrosis, edema of liver tissue after ALP poisoning. While **Saleki et al. (2007)** found fine cytoplasmic vacuolization of hepatocytes and sinusoidal congestion were observed after only one-day phosphine gas poisoning.

Moghaddammia et al., (2000), showed hepatic congestion and liver necrosis with ALP poisoning at different doses.

Pyknotic nuclei in some hepatocytes of ALP group were noticed in the current study. This finding was confirmed with the apparent increase in Caspase 3 immunoreactivity in liver sections. This could be explained by DNA damage and inhibition of DNA

synthesis.

Hydropic degeneration and pyknotic changes of hepatocytes were also reported by **Olurin et al. (2016)**.

Heart histopathology:

Heart examination of ALP rat group revealed fragmentation of muscle fibers, cytoplasmic vacuolation and hyalinization, widening of interstitium between cardiac myocytes, hemorrhage, mononuclear cellular infiltration and congestion of blood vessels compared with that of boric acid (only) and control groups. These changes were markedly decreased in ALP and boric acid group.

These effects on heart tissue were due to Phosphine gas liberated after ALP ingestion which induces myocardial contractility impairment and leads to circulatory failure and pulmonary edema (**Sogut et al, 2011**).

Many pyknotic nuclei were seen in the affected cardiac muscle fibers. This was confirmed by an apparent increase of Caspase 3 immunoreactivity in ALP treated rats. Some investigators stated that a strong relation is found between heart tissue injury and cellular hypoxia - induced mitochondrial dysfunction following ALP poisoning (**Karamaz et. at., 2013**).

Boric acid help protection of nucleic acids from damage by free radicals results in ALP exposure. This explains our result of -ve Caspase 3 immunoreactivity in rats of ALP treated with boric acid. (**Turkez et al., 2011**).

In accordance to our results, **Arora et al. (1995)** also observed histopathological changes in various organs (e.g. heart) in the form of congestion, leucocytic infiltration and edema in ALP.

Shah et al. (2009), recorded myocardial toxic effects of ALP in the form of myocyte vacuolation and

myocytolysis and degeneration which suggestive of myocardial injury, and they also found areas of increased waviness of myocardial fibers that indicate an episode of myocardial infarction.

Rahbar et al. (2010) revealed congestion, leucocytes infiltration and necrosis in myocardial tissue in their study on aluminum phosphide.

Biochemical changes.

As regards data of the current work, the activities of liver enzymes SGOT and SGPT, alkaline phosphatase (ALP) and cardiac troponin in plasma of ALP intoxicated rats showed a significant increase compared with its activity in rats groups of control and boric acid only; these elevations were decreased in group 4 (ALP and boric acid) which showed a significant decrease as regards liver enzymes (SGOT and SGPT) and cardiac troponin.

These biochemical results were in agreement with **Hamdan and Bonin (1999)**, as they also recorded increased serum alkaline-phosphatase (ALP) activity in rats after exposure to phosphine gas. Significant increasing in activity of ALT with ALP toxicity also recorded by **Morgan et al., (1995)**.

In the current study there was also a significant decrease in cardiac troponin in "ALP and boric acid" group compared with ALP group, which means that boric acid carry a beneficial effect in case of ALP poisoning.

El Hangouche et al., (2017), found elevated cardiac troponin level in human patients intoxicated with ALP.

Myocardial injury with elevated cardiac biomarkers (CPK, CK-MB, and Troponin-T) was also noticed in the work of **Soltaninejad et al. (2012)**.

CONCLUSION

Rats given boric acid after ALP showed increase in their survival time, marked improvement in the histopathological and biochemical parameters including liver and cardiac markers compared with rats given only ALP.

So this study opens the door of opportunity for larger experimental and then clinical trials to reevaluate whether the early use of boric acid in ALP poisoning will improve outcome in this highly fatal poisoning or not. Also, it may increase the hope of using boric acid as a new effective antidote in ALP poisoned cases.

RECOMMENDATIONS:

- Further researches needed to study the possible beneficial effect of boric acid in treatment of ALP toxicity in human.

- Increase awareness about the danger of phosphide poisoning between publics especially farmers - Selling of zinc and aluminum phosphide from pesticide shops should be restricted and replaced by other less or nontoxic forms.

- Restriction of availability of these highly toxic poisonous materials which are used mainly for suicide.

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الملخص العربي للبحث

عنوان البحث

**علاج التسمم الحاد لفوسفيد الألومنيوم في نموذج الجرذان بتدخل جديد :
تجربه حمض البوريك**علا عبد الهادي منصور^a، فاطمة شعبان قنديل^a، داليا عبد الرازق نويه^bقسم الطب الشرعي والسموم الإكلينيكية^a - قسم الهستولوجي^b - كلية الطب - جامعة المنوفية**مقدمة البحث:**

فوسفيد الألومنيوم هو من المبيدات الحشرية الرخيصة (قرص الأرز). فعندما يحدث تلامس بينه وبين الرطوبة أو أي حمض يطلق غاز الفوسفين (PH₃). القلب والكبد والرئتين هي الأجهزة المستهدفة الرئيسية في التسمم الحاد بفوسفيد الألومنيوم. معظم الوفيات في الآونة الأخيرة، تحدث بسبب سمية القلب والأوعية الدموية. وقد اقترح حمض البوريك نظريا كترياق للتسمم بفوسفيد الألومنيوم. مع الصيغة B(OH)₃، حمض البوريك هو حمض لويس مع المداري p التي يمكن أن تقبل الإلكترونات.

الهدف من البحث:

تهدف هذه الدراسة إلى التحقيق في الدور المحتمل لحمض البوريك كترياق في علاج تسمم فوسفيد الألومنيوم ودورها الوقائي على التغيرات البيوكيميائية والتغيرات النسيجية المرضية في الكبد والقلب في الفئران البيضاء واستخدامها المحتمل كترياق فعال للحد من وفيات التسمم بفوسفيد الألومنيوم.

مواد وطرق البحث:

أجرى هذا البحث على أربعين من ذكور الجرذان البيضاء و قد قسموا إلى أربع مجموعات كالتالي: المجموعة الأولى المجموعة الضابطة السلبية) والتي اعطيت ماء مقطرا بالفم، المجموعة الثانية (الضابطة الإيجابية) التي تم إعطاؤه حمض البوريك فقط، المجموعة الثالثة وتم إعطاؤها فوسفيد الألومنيوم، المجموعة الرابعة وتم إعطاؤها فوسفيد الألومنيوم وحمض البوريك بنفس الجرعات السابق وصفها. جميع الجرعات تم إعطاؤها بالفم مره واحده ثم تم التضحية بالجرذان عن طريق خلع فقرة العنق ثم تم التشريح واستئصال الكبد والقلب والاحتفاظ بها في فورمالين لفحصها هيستولوجيا. كما تم اخذ عينات من الدم لتحليل انزيمات الكبد وتروبونين القلب.

نتائج البحث:

وكانت النتيجة ان خلايا المجموعة الضابطة السلبية والضابطة الإيجابية كانت طبيعية ولا يوجد بها أي تغيرات هيستوباثولوجية أو بيوكيميائية في حين أن هناك تغيرات كبيرة وجدت في خلايا الكبد والقلب للجرذان التي تم إعطاؤها فوسفيد الألومنيوم. كما إن هناك زيادة في معدل إنزيمات الكبد و التروبونين. كثير من هذه التغيرات قلت بصورة ملحوظة في خلايا الجرذان التي تم إعطاؤها حمض البوريك بعد فوسفيد الألومنيوم.

الاستنتاج:

هذه الدراسة تفتح الباب أمام إجراء دراسات تجريبية أكبر ثم تجارب سريرية لإعادة تقييم دور حمض البوريك في علاج التسمم بفوسفيد الألومنيوم. وزيادة الأمل في استخدام حمض البوريك باعتباره ترياق فعال جديد.