Comp Clin Pathol (2006) 15:211–213
DOI 10.1007/s00580-006-0633-3

ORIGINAL ARTICLE

Effects of garlic (*Allium sativum*) and its chief compound, allicin, on acute lethality of cyanide in rats

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Received: 2 May 2006 / Accepted: 30 July 2006 / Published online: 28 September 2006

Abstract Cyanide, known as a potent suicidal, homicidal and chemical warfare agent, is widely found in plants and used in industry. Cytochrome oxidase, the main enzyme in cell respiration, is inhibited by cyanide resulting to acute or chronic toxicity. The effects of garlic (*Allium sativum*) and its chief compound, allicin, on the acute lethality of cyanide were studied in rats. Three groups of rats were fed a diet containing 10%, 20% and 30% garlic powder for 48 h and then were challenged with 10 mg/kg cyanide. The lethality of cyanide intoxication was markedly reduced in rats which received garlic by diet and the rate of protection was dose-dependent. The effect of 1,000 ppm of allicin on cyanide lethality was equal to 20% of garlic in diet. These results suggest that sulfur compounds of garlic may have a protective effect against cyanide intoxication.

Keywords Allicin · Cyanide · *Allium sativum*

Introduction

Cyanide, a potent toxic agent, is present in some insecticides, rodenticides, metal polishes, electroplating solutions, gold and silver extraction and fumigants, and is used in a variety of metallurgical processes. The waste discharge from these industries can contain large amounts of cyanide and can act as a source of poisoning (Aslani et al. 2004). Cyanide is also widely used for suicide and homicide and has been used for chemical warfare (Baskin and Reagor 1997).

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A large number of plants contain cyanogenic glycosides, and their ingestion has been reported to cause acute cyanide toxicity and mortality in livestock (Radostits et al. 2000). Cyanide poisoning in humans has also been reported from eating plant material such as chokecherries, bitter almond, cassava beans, apricot pits and lima beans (Baskin and Reagor 1997).

In addition to acute toxicity, the chronic pathologic effects of cyanide on various organs are known in animals and in humans (Okolie and Osagie 2000). Cyanide inhibits cellular oxidizing enzymes that contain ferric iron such as cytochrome oxidase. Inhibition of cytochrome oxidase causes intracellular respiratory cessation and tissue anoxia, mainly leading to the dysfunction of neural cells and symptoms of the central nervous system failure (Baskin and Reagor 1997; Nagahara et al. 2003).

Cyanide can be metabolized by different endogenous intracellular mechanisms, and different pathways exist for its detoxification. The predominant pathway is that of cyanide conversion to thiocyanide by the enzyme rhodanese, a sulfur-trasferase, in the presence of thiosulfate (Megarbane 2003).

Garlic (*Allium sativum*) is considered as a natural product that has an immense therapeutic potential in many pathologic conditions. The plant is rich in sulfur-containing amino acids. In this study, garlic and its chief active component, allicin , were tested for their potential to reduce lethality of cyanide in acutely intoxicated rats.

Materials and methods

Animals and feeding

Fifty NMRI rats, male and female of equal number, weighing 220–250 g, were purchased from the Mashhad

branch of Razi Institute. The animals were maintained under standard animal house conditions with food (product of Javaneh, Khorasan-Mashhad) and water ad lib for 7 days before the commencement of the experiment.

Chemicals

Potassium cyanide (KCN, Merck, Germany) and allicin (ALLIMAX, Nopex, UK) were used. Fresh garlic (*A. sativa*) bulbs were also purchased from the market, cleaned, sliced and dried at room temperature, then ground to powder.

Experimental design

The rats were divided into five (10 in each) groups: four experimental and one control. KCN as a 2.5% solution was injected subcutaneously into the control group as a single dose of 10 mg/kg body weight (LD50). Animals of groups 2, 3 and 4 were maintained on a ration containing 10, 20 and 30% garlic, respectively, for 48 h and then dosed with 10 mg/kg KCN as the animals of the control group. Rats of group 5 received 1,000 ppm allicin in drinking water for 48 h and were then challenged with KCN as the animals of control group.

Results

The effects of the different amounts of garlic on acute cyanide lethality in rats are shown in Table 1. Feeding rats with rations containing 10, 20 and/or 30% garlic developed a dose-dependent, low level of protection against cyanide lethality. The protection effect of 1,000 ppm allicin was equal to feeding 20% garlic.

Garlic and allicin also prolonged the survival time of intoxicated animals.

Discussion

The results clearly demonstrate that garlic in the diet of rats can reduce, dose-dependently, the toxicity of cyanide. On the other hand, allicin in concentration of 1,000 ppm in drinking water of rats led to a protection rate equal to 20% of garlic in the diet.

Table 1 Effect of different amounts of garlic in diet on cyanide mortality in rats

Rat no.	Garlic in diet (%)	Mortality (%)
10	0	50
10	10	40
10	20	20
10	30	10

Although various medical properties of garlic and its potential to lower the risk of some diseases are widely known, therapeutic or protective effects of garlic against cyanide toxicity have not been reported in the literature. Garlic contains many sulfur compounds, and the concentration of these compounds in garlic is higher than any other species of *Allium* (Newall et al. 1996). Dried, powdered garlic contains approximately 1% alliin (*S*-allyl cystein sulfoxide). One of the most biologically active compounds, allicin (diallyl thiosulfinate) does not exist in garlic until it is crushed or cut. Injury to the garlic bulb activates the enzyme allinase, which metabolizes alliin to allicin (Block 1996). The exact protective mechanism of garlic against cyanide toxicity is unknown, but, according to the metabolism pathways of cyanide, the protective effect of garlic against lethality may be related to the sulfur compounds of garlic.

Different pathways exist to neutralize cyanide. The predominant pathway is that of cyanide conversion to less toxic thiocyanide by the enzyme rhodanese, a sulfurtransferase, in the presence of thiosulfate (Megarbane 2003; Nagahara et al. 2003). Another effective pathway of cyanide detoxification is via mercaptopyruvate sulfurtransferase, which uses thiosulfate as a substrate to metabolize cyanide to thiocyanate. Thiosulfate reductase and cystathion γ lyase also participate in the detoxification of cyanide (Nagahara et al. 2003).

These enzymes have a broad substrate specificity, and various sulfur compounds may substitute for thiosulfate or cyanide (Nagahara and Nishino 1996). Even though these enzymatic routes are efficient, they do not have sufficient capacity for the detoxification of cyanide in acute poisoning because of lack of sulfur donors (Baskin et al. 1997). Experimental sulfur donors have been shown to protect mice against exposure to lethal dose of cyanide (Baskin et al. 1999).

Sodium nitrite and sodium thiosulfate, which are conventional antidotes to cyanide, could not be used prophylactically because each exhibits a number of side effects (Baskin et al. 1992). On the other hand, sodium thiosulfate utility is limited due to its short biological half-life and its small volume of distribution (Baskin et al. 2003). However, the safety, efficacy and correct indication of those drugs are frequently debated (Bhattacharya 2000), and search for new drugs is encouraged.

In addition to acute cyanide intoxication, chronic toxicity of cyanide has frequently been reported in recent years, and it is suggested that the most widespread problems arising from cyanide are from chronic dietary, industrial and environmental sources (Mathangi and Namasivayam 2000). Acute cyanide toxicity is lethal,

resulting in death due to respiratory failure while chronic exposure has been implicated in the etiology of tropical ataxic neuropathy and spastic paresis, various ocular pathologies such as amblyopia and retrobulbar neuropathy of pernicious anemia. Chronic cyanide intoxication has also been reported in sheep, cattle and horses, affecting the central nervous system and causing ataxia and urinary incontinence (Soto-Blanco et al. 2002). Sublethal doses of cyanide in laboratory animals alter many physiological parameters, including memory and brain neurotransmitters, when administered over a period of time (Mathangi and Namasivayam 2000).

It should be noted that in humans, malnutrition increases susceptibility to trace amounts of cyanide in these subjects. A low level of sulfur amino acids has also been reported in patients suffering from tropical ataxic neuropathy. The damage to the nervous tissues might be related to the inhibition of oxidative systems by cyanide whose potency can be increased in the absence of sufficient sulfur amino acids to detoxify it to thiocyanate (Tewe and Iyayi 1989).

Acknowledgement We wish to thank Dr. P. Josling from Nopex-UK for supplying allicin.

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