

How Dangerous Could be the Receiving of a Ricin-Contaminated Letter?

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Most recently, we read in the news about sending of ricin-exposed letter to some governmental important people. Ricin is a toxalbumin derived from castor bean (*Ricinus communis*; Euphorbiaceae), whose oil is employed in medicine. Ricin is a potent and highly dangerous protein, where its exposure can cause severe toxicity in different organs and then death. Because there are many possible ways to expose (including skin, mucosal, gastrointestinal and pulmonary routs) and also regarding to its importance, which is abused as a kind of biological killing weapons, and its potential to affect many people via extremely low dosages, the main headlines attributed to its toxicity signs and symptoms, various probable routs of exposure especially via skin and mucosal contacts have been reviewed here. Nevertheless ricin is an easily produced toxin with known application in biological weapons; it is hard to consider it as a quick bio-killing poison to terror someone via exposed letter.

Most recently, we read in the Yahoo news about sending of ricin-exposed letter to some governmental important people (1).

The first point came to our mind was to see whether ricin can be absorbed by touching the letter and how much it can be dangerous. Although there are a number of reviews and reports on diverse aspects of this poison, toxicokinetic of ricin has not been cleared completely. For this reason, remarked points of view around this concern have been reviewed and considered in this article.

Ricin, a well-known toxalbumin isolated from *Ricinus communis* (Euphorbiaceae), is found as an extremely toxic natural protein (Figure 1). A main source of ricin, *R. communis*, is a woody bush, growing up to 1-4 m height, and cultivated as an ornamental plant especially in north of Iran due to its attractive inflorescences in purple during vegetation period. Moreover, its leaves are generally alter-

nate and divided with toothed lobes, and also the remarkable capsules are ordinary green-purple ovoid (up to 1.5 cm) with smooth spines (2). Review of traditional documents reveals that *R. communis* has been used for various purposes such as antidote, cathartic, cyanogenic, emetic, emollient, expectorant, insecticide, poison, purgative, tonic, while castor oil is introduced as an ingredient in folk remedies for abscess, arthritis, asthma and many other illnesses. Additionally, castor oil is well-known for its cathartic activity to induce labor in natural deliveries, where ricinoleic acid, the main active fatty acid in the oil has been employed in contraceptive jellies (3-7).

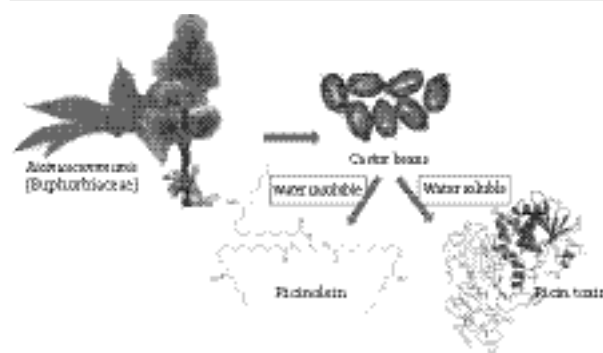


Figure 1. Castor beans from *Ricinus communis* has been used to produce both ricin toxin and castor oil.

Ricin, a toxic protein in the seeds acts as a blood coagulant. Interestingly, too small amount of this peptide is able to kill a man when exposes via injection or inhalation ($LD_{50} = 22 \mu\text{g.Kg}^{-1}$), while oral exposure to ricin is less toxic ($LD_{50} = 20\text{-}30 \text{ mg.Kg}^{-1}$) (6). Actually, ricin is a globular (with around 60-65 kDA) heterodimer peptide in its tertiary structure and found as glycosylated. Two

Implication for health policy/practice/research/medical education:
For plant studies and medical sciences

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diverse chains of ricin including A and B chains showed very similar molecular weights about 32 and 34 (kDa), respectively (4, 8). Ricin is stable in solid powder or liquid form even at high temperatures while it dissolves in aqueous and weak acids. Although castor bean is the main source for accumulation of ricin, it can be stored in whole parts of the plants.

Toxicity may occur when castor beans are swallowed or chewed by accident especially in children, thus gastrointestinal (GI) intake is a common exposure pathway (9). Other exposure routes of ricin are highly unlikely such as inhalation, skin or mucosal penetration and intravenous injection, which may be used in terroristic attacks. Symptoms of ricin inhalation may be observed as early as 4 hours after exposure including cough related to hard breathing, which is developed quickly by fluid accumulation inside the lungs followed by respiratory collapse and probably death during 36-72 hours after exposure. Although ricin is less toxic via ingestion, the common symptom is diarrhea which can lead to dehydration, circulatory collapse and death in severe situations. The known mechanism of toxicity is interfering with protein synthesis followed by cell death (9, 10).

Regarding data obtained from literature, ricin usually falls in the category of biological weapons of mass destruction and is not transmitted person-to-person but the main concern rises as "Does touching the ricin letter result in serious toxicity and death as a biological killing toxin?" It seems that ricin is unlikely absorbed through normal skin but may result in eye contact or ingestion from hand finally. Furthermore, there is possibility of lacrimation, conjunctivitis, redness, bleeding from membrane in the rear (retinal hemorrhage), impaired vision even blindness, when eye exposure happens. Systemic toxicity might occur after eye exposure. However, injured skin and mucosa are of important routes of exposure, where absorption of ricin through mucous membranes may create serious irritation and inflammation. In case of skin absorption, there is a potential for allergic reactions such as erythema and blistering. Another exposure route is inhalation of ricin powder. Inhalation can cause a number of signs including fever, cough, storage of liquids in the lungs or edema, respiratory distress, and finally death due to airways obstruction. It is difficult to think that ricin may reach to blood to cause systemic toxicity. However, this way is dangerous route by itself because of the high risk of severe dyspnea, difficult breathing as well as highly risk of death.

Taking together, ricin may penetrate through irritated or injured skin and also through normal skin if mixed with a solvent carrier but in solid powder form (Figure 2). Anyhow, it is possible to inhale the fine powders of ricin dispersed in the air by breathing, so that inhalation toxicity might occur when a person open an envelope consisted of ricin in solid powder form. Chronic toxicity may

be correlated to cytotoxic activity of this peptide on the liver, central nervous system (CNS), kidneys, and adrenal glands (11). There is a little information on carcinogenicity, developmental toxicity, or reproductive toxicity via repeated exposure to ricin.

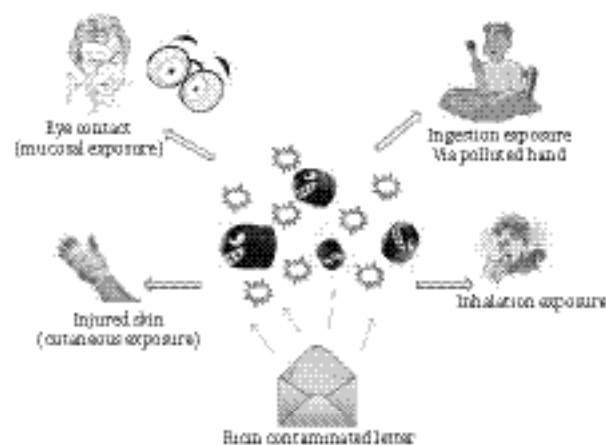


Figure 2. Different exposure routes for ricin toxicity via opening a contaminated letter

There is not antidote available for ricin. Although some vaccines have been introduced, their efficacy and safety is under debate. Immediate removing the victim from the source of exposure is the first and important aid and management for ricin toxicity. In case of eye exposure, washing the eyes with large amounts of water for at least 15 min is essential. Also decontamination procedure is acquired for skin exposure. Regarding the emergency of the matter, getting advice from a local poison information center (PIC) is highly recommended. They can triage the patients to skilled divisions within the hospitals for rapid management. The PIC system presently operating in Iran and the US both are comparably helpful (11).

Nevertheless ricin is an easily produced toxin with known application in biological weapons; it is hard to consider it as a quick bio-killing poison to terror someone via exposed letter. Regarding the potential of ricin to be replicated by *Escherichia coli* bacteria to which the ricin gene has been transferred, ricin became of interest as a chemical weapon agent. According to Organisation for Prohibition of Chemical Weapons (OPCW), in 1978, ricin was used in the "umbrella murder" in London where a ricin-treated bullet was used to shoot a Bulgarian defector who died within a day. Then ricin was included in schedule 1 of the Chemical Weapons Convention and it is now under control (13).

Authors' Contribution

Authors have participated equally in manuscript preparation.

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