

Safety Data Sheet

Abrin

Division of Safety
National Institutes
of Health



WARNING!

THIS COMPOUND IS ACUTELY TOXIC. IT IS ABSORBED THROUGH THE RESPIRATORY AND INTESTINAL TRACTS. IT MAY CAUSE SEVERE IRRITATION OF THE EYES, NOSE AND THROAT. AVOID FORMATION AND BREATHING OF AEROSOLS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND WATER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK OR WATER. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN AT ONCE.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

Introductory Remarks

1. Abrin is often referred to in the literature as a "lectin." The original definition of a lectin was a plant seed protein which causes agglutination of erythrocytes. While this property was originally believed to be associated with abrin, it is now known that the hemagglutinating function of the jequirity bean (the natural source of abrin) resides in a hemagglutinin with properties similar to, but distinct and separable from, the toxic abrin.

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Do not confuse abrin with "abrine" which is a constituent of the same natural source but is an entirely different molecule (N-methyl tryptophan).

The ultimate identity of "abrin" has not been completely established even though the protein has been available in crystalline form for some time. Recent studies in one laboratory have differentiated between two abrins ("Abrin A and C": Wei et al., 1974; Herrmann and Behnke, 1980, 1981) and in another between four ("Abrin a, b, c, d": Lin et al., 1981). All these have slightly different structural, physicochemical, and toxicological properties. Whether Abrin A and/or C are identical with any of Lin's isotoxins has not been established; it has been stated that Abrin C is more like the protein commonly called "abrin" (Herrmann and Behnke, 1981). Unless special mention is made of these six (or fewer?) isotoxins in the text below, "abrin" as usually isolated and crystallized and used in biological investigations may be any or a mixture of these.

Background

Abrin is a toxic glycoprotein found in the seeds of the jequirity plant (Abrus precatorius) where it occurs together with abrine (see Introductory Remarks), a hemagglutinin, abralin (a glycoside), and a lipolytic enzyme. Since the seeds are highly colored, they have been drilled, strung, and used as jewelry. The intact seeds present little toxicological hazard since they have a very hard shell and are usually excreted intact when swallowed. However, if drilled or chewed they are extremely toxic, one bean having been known to produce fatal poisoning after maceration (Dreisbach, 1983). Skin rashes are found in persons wearing strings of jequirity beans. Abrin is under investigation as a cytostatic drug in the treatment of some malignancies, alone or in conjunction with other cytostatics.

Earlier work on the chemical properties of abrin and its mechanism of action has been reviewed (Olsnes, 1976).

Chemical and Physical Data

1. Chemical Abstract No.: 1393-62-0
2. Synonyms: None for abrin. The jequirity seed is also known as: Crab's Eyes, Indian licorice seed, Jumble bead, Prayer bead.
3. Chemical structure and molecular weight: Abrin is a glycoprotein with an average molecular weight of 65,000; the isotoxins (see Introductory Remarks) vary in their molecular weights between 60,100 and 67,000. It consists of two chains (A and B) linked by a disulfide bond. Both chains (the B chain more so than the A chain) contain mannose and glucosamine moieties attached to

the polypeptide chain. The molecular weight of the B chain appears to be quite constant among the isotoxins at 35,000, variations in the overall molecular weight of abrin being due to the A chain. The amino and carboxy terminal amino acids have not as yet been identified. For toxicological information on abrin and its A and B chains see Section F.

Density: no data.

1%

Absorption spectroscopy: $E_{1\text{ cm}}$ at 280 nm for Abrin A and Abrin B is 11.8 and 12.9, respectively. Both have similar circular dichroic spectra with negative maxima at 286 and 293 nm. Their fluorescence near 335 nm is quenched by galactose (Herrmann and Behnke, 1980, 1981).

Isoelectric point: 6.1 for abrin, 4.6 for A chain, 7.2 for B chain (Olsnes, 1976).

Volatility: may be considered negligible.

Solubility: Since abrin has the properties of an albumin it is soluble in dilute salt solutions.

Description: white or yellowish-white powder or crystals.

Boiling point, melting point: not applicable.

Stability: Intact abrin is stable when heated to 60°C for 30 min but most of the toxicity disappears at 80°C for 30 min (Lin et al., 1969). Its solutions can be stored in frozen form even with repeated freezing and thawing. In the refrigerator these solutions are stable for several months on addition of 0.1 M galactose. Abrin is stable at acid pH (0.1 M acetic acid, 24 hr, room temperature) but is destroyed by alkali (0.1 M NaOH). The isolated chains are less stable. Intact abrin is resistant to attack by proteolytic enzymes (trypsin, chymotrypsin, pepsin, Pronase) while the isolated chains are sensitive to these enzymes (Olsnes et al., 1975).

Chemical reactivity: The polypeptide chains of abrin are susceptible to the usual protein reagents. Reductive methylation lowers toxicity only slightly, while periodate oxidation of methylated abrin, acetylation of tryosine residues, or succinylation strongly decrease toxicity (Note: the effect of these treatments on the inhibition of protein synthesis, the mechanism of toxic action of abrin, is far smaller than on animal toxicity. As will be explained in Section F, this indicates that the attack of these reagents is primarily on the B chain) (Sanvig et al., 1978). Treatment of abrin with 2-mercaptoethanol results in cleavage of the disulfide linkage between the A and B chains. This reaction is reversed by dialysis.

13. Flash point: not applicable.
14. Autoignition temperature: not applicable.
15. Explosive limits in air: not applicable.

Fire, Explosion and Reactivity Hazards

1. As a protein, abrin is inactivated under conditions of fire. The main hazards would be from the formation of dusts which could be toxic through breathing or skin exposure. Therefore, fire-fighting personnel should wear complete protective clothing and air-supplied respirators with full-face masks.
2. Flammability is likely to be low.
3. Conditions contributing to instability (and detoxification) are high temperatures and alkali.
4. No hazardous decomposition products are known.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving abrin.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environmental regulations.

1. Chemical inactivation: No validated method reported.
2. Decontamination: Turn off equipment that could be affected by abrin or the materials used for cleanup. Call the NIH Fire Department (dial 116) for assistance. Wipe off surfaces with 10% NaOH, then wash with copious quantities of water. Glassware should be rinsed (in a hood) with 10% NaOH, followed by soap and water. Animal cages should be washed with water.

3. **Disposal:** No waste streams containing abrin shall be disposed of in sinks or general refuse. Surplus abrin or chemical waste streams contaminated with abrin shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcass and bedding) containing abrin shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing abrin shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with abrin shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing abrin shall be handled in accordance with the NIH radioactive waste disposal system.
4. **Storage:** Store solid abrin and its solutions in dark-colored, tightly closed containers, preferably under refrigeration.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. **Sampling:** no data.
2. **Analysis:** There are no specific chemical methods available for the analysis of abrin since this protein molecule does not carry any signatory chemical groupings. A radioimmunoassay, useful for identification of poisoning with abrin and for monitoring patients under treatment, has been published. Blood concentrations down to 50-100 pg/ml blood can be determined by this method (Godal et al., 1981).

Biological Effects (Animal and Human)

1. **Absorption:** Abrin is absorbed and produces toxic effects by ingestion and parenteral administration. It is highly likely that inhalation of abrin dust also produces toxic symptoms; however, there is no published evidence to this effect. Abrin is also a potent irritant of eyes, nose, and skin but it is not known whether systemic effects are produced via any of these routes.
2. **Distribution:** Abrin labelled with ^{125}I (labelling occurs in both chains and does not affect toxicity) and administered intravenously or intraperitoneally is distributed, in order of

decreasing concentrations, to spleen, kidney, heart, liver, and thymus. At least up to 5 hours after injection the radioactivity is found mostly in the form of intact abrin. Considerable tissue radioactivity remains 40-50 hours after injection (Fodstad et al., 1976).

3. Metabolism and excretion: The mechanism of metabolism of abrin has not been investigated but presumably consists of proteolysis. No radioactivity due to parenteral administration of ^{125}I -labelled abrin is found in the feces; urinary radioactivity is low, and almost entirely in the form of trichloroacetic acid-soluble products (Fodstad et al., 1976).
4. Toxic effects: The intraperitoneal and intravenous LD50 in mice has been variously reported to be between 0.7 and 10 g/kg (Olsnes and Pihl, 1972; Fodstad et al., 1977; Fodstad and Pihl, 1978).* For the isotoxins abrin a through d (see Introductory Remarks) intraperitoneal LD50s of 10, 25, 16, and 31 g/kg (Lin et al., 1981), and for abrin A and C of 10 and 2.8 g/kg, respectively (Wei et al., 1974) have been reported. A review report (Olsnes and Pihl, 1978) states, without documentation, that "Lethal doses of abrin...are about 1 g toxin/kg body weight in the mouse, rat, and dog, whereas the rabbit is about 10 times more sensitive."

Rats that received an intraperitoneal dose of 25 g/kg (a dose that is fatal in 30-36 hours) show on death severe necrosis of the pancreatic cells but no morphological effects on liver, lung, heart, spleen, and intestine (Barbieri et al., 1979). (Note that this is markedly different from the effects of ricin which produces necrosis of the spleen and damage of the Kupffer cells) Neurological effects have also been demonstrated (Wiley et al., 1982). In man, the effects of chewing the toxic bean or of abrin are: severe gastroenteritis, nausea, and vomiting leading to dehydration, cyanosis, circulatory collapse, hematuria, and oliguria which may lead to uremia and death within 12 days. It is noteworthy that even with high doses the onset of toxic symptoms is rarely less than 2 hours after administration and may be delayed for several days (Arena, 1979; Dreisbach, 1983).

The mechanism of toxic action of abrin consists of a potent inhibition of protein synthesis by interfering with the incorporation of amino acids at the site of the 60S ribosomal subunit. This has been most clearly demonstrated in cell cultures and in cell-free systems (for reviews see Olsnes, 1976; Olsnes and Pihl, 1978). In exerting this effect in cell cultures, and to produce toxicity in animals, the intact abrin molecule is necessary; splitting of the molecule into the A and B chains by mercaptoethanol, or administration of either or both chains does not produce protein synthesis inhibition.

In cell-free systems, by contrast, the A chain is fully as active as intact abrin while the B chain does not contribute to activity. On the basis of these and other findings it is believed that the B chain ("haptomer") is responsible for binding the abrin molecule to the cell surface, allowing the A chain ("effectomer") to penetrate the cell interior and to exert its toxic effect. The binding to the cell surface appears to be via a galactose moiety on the cell, since each B chain contains one binding site for galactose or lactose, and the presence of lactose in a cell incubation medium prevents the toxic action of abrin.

5. **Carcinogenic effects:** No carcinogenic effects of abrin have been reported. On the contrary, abrin has a strong cytostatic effect against transplanted malignancies in mice (Lin et al., 1970; Fodstad et al., 1977). Its effect is enhanced on administration with cyclophosphamide (Gunderson and Fodstad, 1979). The mechanism is presumably the same as that described in the malignant cell. Abrin appears to show selectivity for malignant cells, and in addition has the advantage over other cytostatics in not depressing the level of white cells and having only a moderate effect on erythropoiesis and thrombopoiesis (Fodstad et al., 1977).
6. **Mutagenic and teratogenic effects:** None have been reported.

Emergency Treatment

1. **Skin and eye exposure:** For skin exposure, remove contaminated clothing and wash skin with soap and water. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.
2. **Ingestion:** Drink plenty of water or milk. Vomiting might reexpose the mouth and esophagus.
3. **Inhalation:** Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. **Refer to physician at once.**

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