

Toxic avenger at the ribosome

In 1978, Georgi Markov, a Bulgarian journalist who had written articles critical of the then-Communist government of Bulgaria, was living in exile in London. As he stood one evening at a bus stop near Waterloo Station, a man—possibly a Bulgarian secret agent—brushed up against him and, seemingly by accident, poked him with an umbrella. Markov felt a sharp pain. Within a few hours, he started to feel weak. A high temperature, vomiting, and more severe symptoms soon followed. Two days later he was dead.

Police investigators found a tiny perforated pellet embedded in Markov's leg, and in that pellet was a small amount of ricin, a highly toxic molecule isolated from the seeds of the tropical castor bean plant, *Ricinus communis*. The seeds of *Ricinus* have been used for centuries as a source of castor oil, a natural product once frequently administered to children to «clean out» the digestive tract. Castor oil is used today in the plastics industry. The toxin ricin is a protein that is not present in the seed oil, and people found

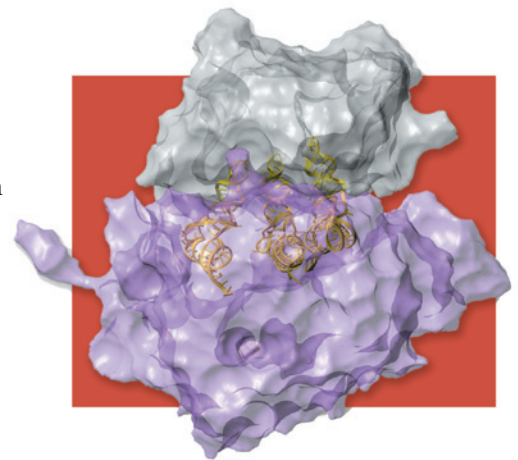
out the hard way that it is one of the most poisonous substances made by any organism. About 1 milligram (an amount the size of the head of a pin) can kill a human.

Markov's murder is not the only case of deliberate use of ricin. Small amounts of ricin were found in caves in Afghanistan occupied by the terrorist group Al-Qaeda, and the poison may have been used in the war between Iran and Iraq that raged throughout much of the 1980s. In the 1990s, four members of an anti-tax group were arrested for plotting to use home-grown ricin to kill a U.S. government official. And on February 3, 2004, the U.S. Senate offices were closed when ricin was found in a mailroom.

Much has been written about the possible ways ricin might be used in a terrorist attack. That is unlikely, however, because relatively large amounts of it would be needed to harm a significant number of people. Unlike bacteria such as those that cause anthrax, ricin molecules are proteins; they do not reproduce.

The Castor Bean Plant

This brightly colored tropical plant produces ricin, a lethal toxin that inhibits protein synthesis at the ribosome.



Ricin's Target Ricin inactivates the ribosome, which is the site of protein synthesis. Ribosomes are large aggregates of macromolecules, containing dozens of proteins and ribosomal RNA in two subunits (violet and gray) and three molecules of transfer RNA (gold).

Ricin enters cells by binding to membrane glycoproteins and glycolipids that contain the sugar galactose. Since many cell surface molecules contain this sugar, ricin can bind to most cells. After being endocytosed and released into the cell cytoplasm, ricin kills the cell by blocking protein synthesis. More specifically, it catalyzes the modification and cleavage of one of the large RNA molecules that make up the eukaryotic ribosome—the «workbench» of protein synthesis. A single ricin molecule in the cytoplasm can modify 1500 ribosomes, killing the cell in minutes.

Proteins are the major phenotypic expression of the genotype—the genetic information encoded in a cell's DNA. Ricin inhibits the cell's ability to express the genotype as phenotype through protein synthesis, and therefore ricin-poisoned cells cannot survive.

Answer the questions

- What happened in 1978 to Georgi Markov?
- What is ricin?

