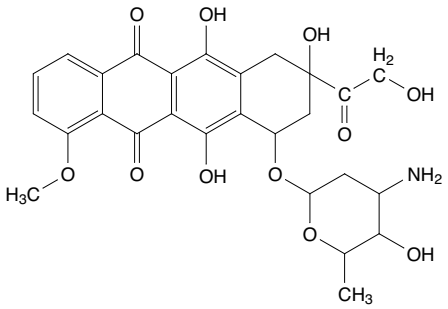
Adriamycin

CAS No. 23214-92-8

Reasonably anticipated to be a human carcinogen

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Adriamycin is a registered trademark of Pharmacia Company for doxorubicin hydrochloride (CAS No. 25136-40-9)



Carcinogenicity

Adriamycin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Adriamycin caused tumors in rats at several different tissue sites and by several different routes of exposure. A single intravenous injection of Adriamycin caused mammary-gland tumors in female rats in several studies. In rats of unspecified sex, single or repeated subcutaneous injections of Adriamycin caused cancer of the mammary gland and at the injection site (sarcoma) (IARC 1976, 1982).

Since Adriamycin was listed in the *Fourth Annual Report on Carcinogens,* additional studies in experimental animals have been identified. In rats of unspecified sex, instillation of Adriamycin into the urinary bladder resulted in a low incidence of benign urinary-bladder tumors (papilloma) and promoted the induction of urinary-bladder tumors by *N*-nitroso-*N*-(4-hydroxybutyl)-*N*-butylamine (IARC 1982, 1987). When Adriamycin was administered to rhesus and cynomolgus monkeys by intravenous injection, a single malignant tumor (fibrosarcoma) was observed at the injection site in one cynomolgus monkey (Thorgeirsson *et al.* 1994, Schoeffner and Thorgeirsson 2000).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to Adriamycin. However, some cancer patients who received Adriamycin in combination with alkylating agents and radiotherapy developed acute nonlymphocytic leukemia and bone tumors (osteosarcoma) (IARC 1982).

Properties

Adriamycin is an anthracycline antibiotic that is an almost odorless red crystalline solid. It is soluble in water and aqueous alcohols, moderately soluble in anhydrous methanol, and insoluble in nonpolar organic solvents (IARC 1976). It is stable at room temperature in closed containers under normal storage conditions (Akron 2009). Physical and chemical properties of Adriamycin are listed in the following table.

Property	Information
Molecular weight	543.5[a]
Melting point	229°C to 231°C[b]
Log K_{ow}	1.27 at pH 7.4[a]
Water solubility	20 g/L[a]
Vapor pressure	8.99×10^{-25} mm Hg[b]
Dissociation constant (pK_a)	8.33[a]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

Use

Adriamycin is a cytotoxic anthracycline antibiotic used in antimitotic chemotherapy. It is infused intravenously to treat neoplastic diseases such as acute leukemia, multiple myeloma, Hodgkin's disease, non-Hodgkin's lymphoma, soft-tissue and osteogenic sarcomas, Kaposi's sarcoma, neuroblastoma, Ewing's sarcoma, Wilms' tumor, and cancer (carcinoma) of the head and neck, breast, thyroid gland, genitourinary tract, and lung (IARC 1976, Chabner *et al.* 2001, HSDB 2009, MedlinePlus 2009). A liposomal doxorubicin product is available to treat AIDS-related Kaposi's sarcoma.

Production

In 2009, Adriamycin was produced by four manufacturers worldwide (two in Europe and one each in China and East Asia) (SRI 2009); doxorubicin hydrochloride was available from eight U.S. suppliers (ChemSources 2009), and five pharmaceutical companies produced 15 injectable pharmaceutical products approved by the U.S. Food and Drug Administration containing doxorubicin hydrochloride (FDA 2009). No data were found on U.S. imports or exports of Adriamycin.

Exposure

The primary source of human exposure is by intravenous injection of patients treated with Adriamycin. When Adriamycin is used as a single agent for treatment of adult patients, the most common dosage schedule is 60 to 75 mg/m^2 of body surface as a single intravenous infusion over 30 minutes at 21-day intervals until a total of 550 mg/m^2 is given (IARC 1976). The liposomal product is also administered intravenously at 21-day intervals at a dose of 20 mg/m^2 (Chabner *et al.* 2001). In 2009, 378 clinical trials with regimens including Adriamycin were in progress or recently completed (ClinicalTrials 2009). Healthcare professionals and support staff (including custodians) may be exposed to Adriamycin by dermal contact, inhalation, or accidental ingestion during drug preparation and administration or cleanup of medical waste, including excretions from treated patients (Zimmerman *et al.* 1981, NIOSH 2004). Adriamycin can be found unchanged in human excrement (RxMed 2009). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 17,132 health-services workers, including 11,918 women, potentially were exposed to Adriamycin (NIOSH 1990).

Regulations

Food and Drug Administration (FDA)

Adriamycin is a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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