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Arcamone F, Cassinelli G, Fantini G, Grein A, Orezzi P, Pol C & Spalla C.
Adriamycin, 14-hydroxydaunomycin, a new antitumor antibiotic from *S. peucetius* var. *caesius*. *Biotechnol. Bioeng.* 11:1101-10, 1969.
[Istituto Ricerche di Base della Soc. Farmaceutici Italia, Milan, Italy]

This paper describes the fermentative production, the isolation, and the chemical characterization of the new antitumor antibiotic adriamycin. The compound is the 14-hydroxy derivative of the antileukaemic anthracycline daunorubicin. Both compounds are produced by *Streptomyces peucetius* var. *caesius* and related strains. [The *SCI*® indicates that this paper has been cited in over 140 publications.]

An Antitumor Anthracycline from *Streptomyces*

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The anthracycline glycosides are pigments produced by microorganisms of the genus *Streptomyces*. The study of natural products, from both microbial and animal sources, has been carried out at Farmitalia Research Laboratories, Milan, since the early 1950s. The investigations in the field of steroid transformations by yeast, of peptides from amphibian skin, of antibiotics, and of ergot alkaloids can now be regarded as classical. Novel active principles of pharmacological relevance were derived from these different classes of natural substances. The discovery of antitumor anthracyclines represents the greatest achievement of our laboratories and has been a watershed in the medical treatment of cancer diseases.

The isolation of new antibiotics endowed with antitumor properties had been a major interest of mine and of Professor Aurelio Di Marco, head of the Section of Microbiology and Chemotherapy of the Istituto Ricerche Farmitalia. Fortunately, we enjoyed continued enlightened collaboration also after he joined the Istituto Nazionale Tumori, Milan, in 1964, where he was able to carry out the experimental chemotherapy investigations that were essential for the development of adriamycin (doxorubicin). The latter was obtained, as reported in our paper, from the mycelial extracts of a daunorubicin fermentation, where it was present in very small amounts.

At the beginning a formal adriamycin project did not exist, because of the low interest of the company's management in the drug market of the then-known cytostatics. It should be noted that the clinical development of the drug was fostered by the farsighted and generous effort of the US National Cancer Institute. The name *adriamycin*, derived from that of the Adriatic Sea near which the original daunorubicin strain had been collected, was readily popular.

Adriamycin was promptly identified as 14-hydroxydaunorubicin,[1] and its partial synthesis allowed the large-scale preparation of the antibiotic. This soon became, after its introduction in different countries and in the US in 1973, a base of many drug protocols used in medical oncology because of its high response rates and wide spectrum of activity against solid tumors.

Our paper is cited frequently because of the interest it has aroused in the chemistry and pharmacology of the antitumor anthracyclines. Many renowned organic chemists have worked on the total synthesis of the aglycones, daunosamine, and their derivatives.[2] More than 20 synthetic approaches to this aminosugar have been worked out, and a monograph dealing with 3-amino-2,3,6-trideoxyhexoses has appeared recently.[3] The search for new analogs resulted in the development of, among other compounds, the clinically useful epirubicin and idarubicin.[4]

My contributions to the field have been acknowledged by different awards, among them the Bristol-Myers International Award in 1981, the Gold Medal of the Italian Academy of Sciences in 1982, the RBS-Pharma Award in 1983, and, in 1985, the Bruce Cain Memorial Award from the American Association for Cancer Research.

1. Arcamone F, Franceschi G, Penco S & Selva A. Adriamycin (14-hydroxydaunomycin), a novel antitumor antibiotic. *Tetrahedron Lett.* (13):1007-10, 1969. (Cited 120 times.)
2. Pelyvas I F, Monneret C & Herczegh P. *Synthetic aspects of aminodeoxy sugars of antibiotics*. New York: Springer-Verlag, 1988. 244 p.
3. Kelly T R, ed. Recent aspects of anthracyclinone chemistry. (Whole issue.) *Tetrahedron* 40(22), 1984. 256 p.
4. Arcamone F. Antitumor anthracyclines: recent developments. *Med. Res. Rev.* 4:153-88, 1984. (Cited 30 times.)

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