Development of the first way to make large amounts of promising anti-cancer substance

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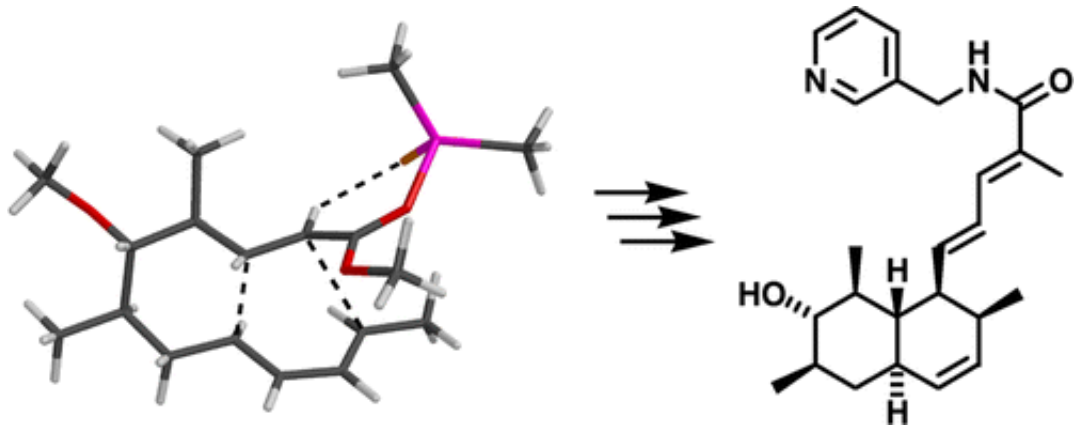

Scientists are reporting development of the first practical way to make large amounts of a promising new anti-cancer substance that kills cancer cells differently than existing medicines. Their article on synthesis of the substance, and tests demonstrating its effectiveness in the laboratory, appears in ACS' *Journal of Medicinal Chemistry*.

Isamu Shiina and colleagues explain that the substance, AMF-26, showed promise against certain forms of cancer in laboratory studies, fostering excitement about its potential for development as a new anti-cancer drug. That excitement centered on AMF-26's action in targeting a structure in cells, the Golgi apparatus, that had never been exploited in the past. The Golgi apparatus sorts and modifies hormones, enzymes and

other key proteins for transport elsewhere.

However, AMF-26 had been available in only small amounts by semisynthesis starting from AMF-14, which was extracted from the common soil mold of the genus Trichoderma.

Their report describes the first successful practical synthesis of AMF-26 and laboratory tests showing that the synthetic AMF-26 is just as effective as its natural counterpart. "The large-scale production of AMF-26 and its derivatives for the development of novel anticancer drugs are now in progress in this laboratory," the report states.

More information: "Total Synthesis of AMF-26, an Antitumor Agent for Inhibition of the Golgi System, Targeting ADP-Ribosylation Factor 1" J. Med. Chem., 2013, 56 (1), pp 150–159. DOI: 10.1021/jm301695c

Abstract
An effective method for the total synthesis of 1 (AMF-26), a potentially promising new anticancer drug that disrupts the Golgi system by inhibiting the ADP-ribosylation factor 1 (Arf1) activation, has been developed for the first time. The construction of the chiral linear precursor (a key to the synthesis) was achieved by the asymmetric aldol reaction followed by the computer-assisted predictive stereoselective intramolecular Diels–Alder reaction. The global antitumor activity of the totally synthetic 1 against a variety of human cancer cells was assessed using a panel of 39 human cancer cell lines (JFCR39), and it was shown that the synthetic 1 strongly inhibited the growth of several cancer cell lines at concentrations of less than 0.04 μM. Biological assays of novel derivatives, 26 and 31, which have different side-chains at the C-4 positions in the Δ1,2-octalin backbone, disclosed the importance of the suitable structure of the side-chain containing conjugated multidouble bonds.

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