Organometallic compounds as new drugs? Cobalt-containing aspirin complex with potential anti-tumor properties

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Despite considerable progress in modern chemotherapy, there remains a large demand for innovative anti-tumor agents. A new approach involves modeling the pharmacological properties of established drugs with organometallic fragments. As a team of scientists from Berlin and Bochum (Germany), Innsbruck (Austria), and Leiden (The Netherlands) report in the journal *Angewandte Chemie*, cobalt-aspirin complexes have potential as cytostatics.

Most drugs used today are purely organic compounds. Stimulated by the enormous success of the inorganic complex cisplatin in tumor treatment, interest in metal complexes has grown. Within cells, metal complexes can participate in reactions that are not possible with conventional organic substances.

Aspirin (acetylsalicylic acid) belongs to the family of nonsteroidal antirheumatics (NSAR), which have anti-inflammatory and pain-relieving effects. The pharmacological effects of NSARs stem from the inhibition of enzymes in the cyclooxygenase family (COX). These enzymes not only play a central role in inflammatory processes, they also seem to be involved in tumor growth. NSARs have thus come into focus as potential cytostatics. It may be possible to improve anti-tumor activity in the case of aspirin by binding it to an organometallic fragment.

Within the scope of the “Biological Function of Organometallic

Compounds" research group funded by the Deutsche Forschungsgemeinshaft (German Research Foundation, DFG), the team determined that "Co-Aspirin", a hexacarbonyldicoboalt-aspirin complex, inhibits COX activity differently to aspirin. Whereas the effect of aspirin stems from the acetylation of a serine residue in the active center of COX, Co-Asprin does not attack this side chain, instead acetylating several other sites. This may block access to the active center of the enzyme, resulting in a different activity spectrum for the drug.

Experiments with zebra fish embryos showed that in contrast to aspirin, Co-Aspirin inhibits both cell growth and the formation of small blood vessels (angiogenesis). Tumors are dependent on newly formed blood vessels for their nutrients and can be starved out by the inhibition of angiogenesis. In addition, Co-Aspirin modulates other tumor-relevant metabolic pathways. For example, it activates the enzyme caspase, which is involved in processes that lead to apoptosis (programmed cell death).

Paper: Ingo Ott, Modulation of the Biological Properties of Aspirin by Formation of Bioorganometallic Derivative, *Angewandte Chemie International Edition* 2009, 48, No. 6, 1160-1163, doi: 10.1002/anie.200803347

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