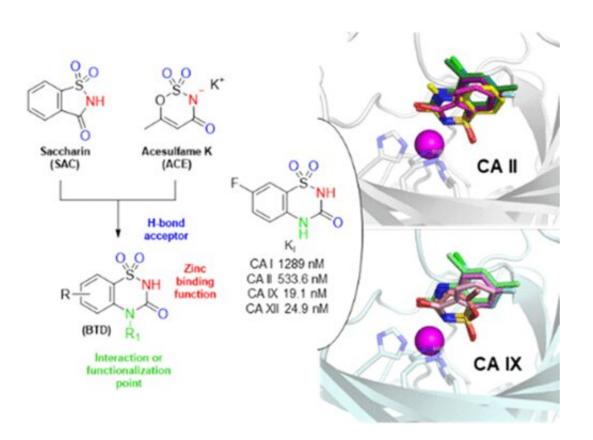


Saccharin derivatives give cancer cells a notso-sweet surprise

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Credit: American Chemical Society

Saccharin received a bad rap after studies in the 1970s linked consumption of large amounts of the artificial sweetener to bladder cancer in laboratory rats. Later, research revealed that these findings were not relevant to people. And in a complete turnabout, recent studies indicate that saccharin can actually kill human cancer cells. Now,



researchers reporting in ACS' *Journal of Medicinal Chemistry* have made artificial sweetener derivatives that show improved activity against two tumor-associated enzymes.

Saccharin, the oldest artificial sweetener, is 450 times sweeter than sugar. Recently, scientists showed that the substance binds to and inhibits an enzyme called carbonic anhydrase (CA) IX, which helps <u>cancer cells</u> survive in the acidic, oxygen-poor microenvironments of many tumors. In contrast, healthy cells make different—but very similar—versions of this enzyme called CA I and II. Saccharine and another <u>artificial</u> <u>sweetener</u> called acesulfame K can selectively bind to CA IX over CA I and II, making them possible anti-cancer drugs with minimal side effects. Alessio Nocentini, Claudiu Supuran and colleagues wondered whether they could make versions of the artificial sweeteners that show even more potent and selective inhibition of CA IX and another tumorassociated enzyme, CA XII.

The team designed and synthesized a series of 20 compounds that combined the structures of saccharin and acesulfame K and also added various chemical groups at specific locations. Some of these compounds showed greater potency and selectivity toward CA IX and XII than the original sweeteners. In addition, some killed lung, prostate or colon cancer cells grown in the lab but were not harmful to normal cells. These findings indicate that the widely used artificial sweeteners could be promising leads for the development of new anticancer drugs, the researchers say.

More information: Silvia Bua et al. "A Sweet Combination": Developing Saccharin and Acesulfame K Structures for Selectively Targeting the Tumor-Associated Carbonic Anhydrases IX and XII, *Journal of Medicinal Chemistry* (2019). DOI: 10.1021/acs.jmedchem.9b01669



Provided by American Chemical Society

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