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Aspirin appears to curb colorectal cancer recurrence and tumor growth, study finds

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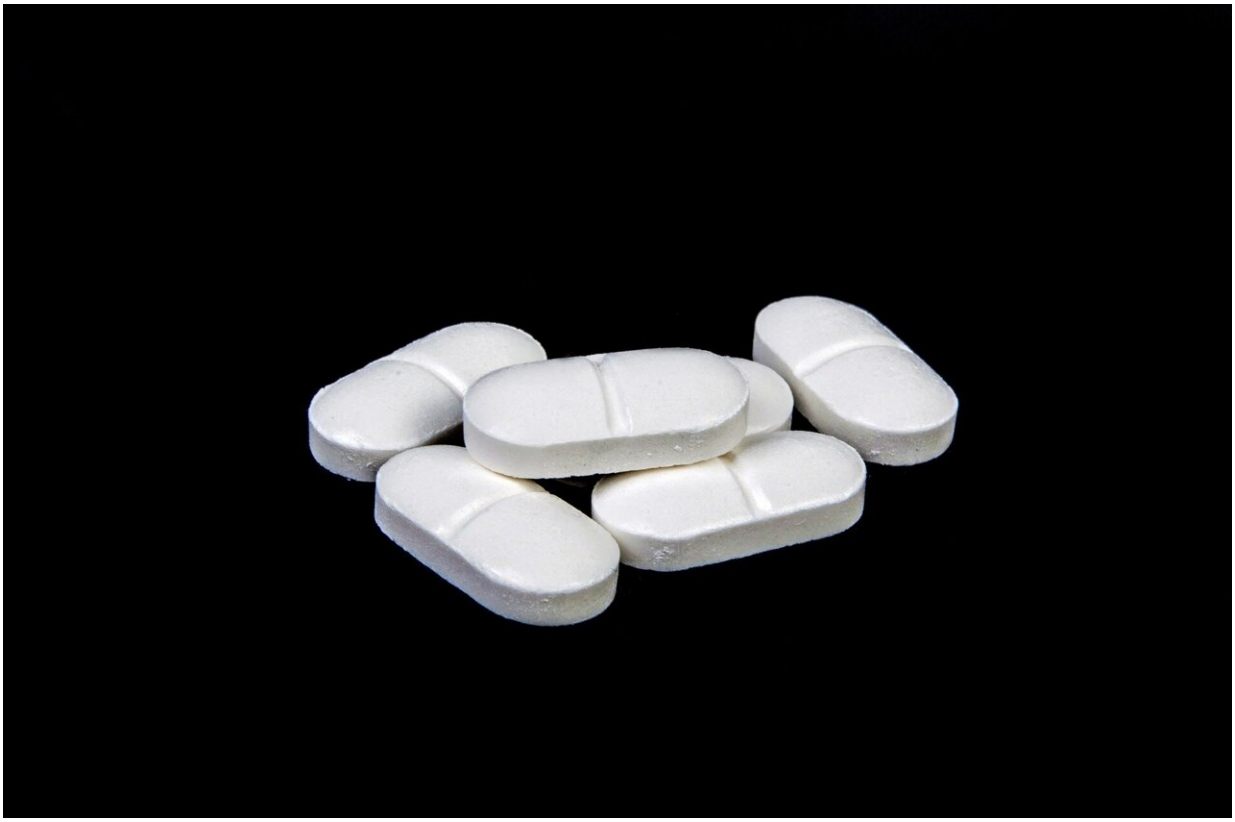

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The benefits of a daily aspirin may extend beyond heart health to colorectal cancer treatment, say City of Hope researchers who have found aspirin appears to reduce tumor growth and inhibit recurrence of

the disease.

The trick now, researchers say, is to determine the right dosage of aspirin that can be used as a daily prophylactic without triggering dangerous side effects such as stomach and brain bleeds.

"Some might say aspirin is a 'miracle drug' because of its potential to prevent diseases that result from chronic inflammation, such as cancer, Alzheimer's, Parkinson's and arthritis," said Ajay Goel, Ph.D., senior author of a new study and chair of the Department of Molecular Diagnostics, Therapeutics and Translational Oncology at City of Hope.

"The reason aspirin isn't currently being used to prevent these diseases is because taking too much of any anti-inflammatory eats at the stomach's mucus lining and causes gastrointestinal and other problems. We are getting closer to discovering the right amount of daily aspirin needed to treat and prevent colorectal cancer without causing scary side effects."

The study, published in the journal *Carcinogenesis* on Jan. 6, used mouse models and mathematical modeling to parallel the amount of daily aspirin people in the U.S. and Europe are taking in clinical trials. The City of Hope-led research found that as the aspirin doses increased, the rate of cell death increased while the division rates of cells decreased, meaning tumor cells were more likely to die and not proliferate.

"We are now working with some of the people conducting those human clinical trials to analyze data and use mathematical modeling. This process adds a layer of confidence to the findings and guides future human trial designs," Goel said, adding that colorectal cancer is among the top five cancers diagnosed every year.

Research details

Goel and his colleagues tested three varying daily doses of aspirin in four colorectal cancer cell lines, including tumors with microsatellite instability and mutations in the PIK3CA gene, which has been tied to increased risk of endometrial, colon and aggressive breast cancers.

Then the researchers divided 432 mice into four groups: control, low-dose aspirin (15mg/kg), medium-dose aspirin (50mg/kg) and high-dose aspirin (100mg/kg) - the mouse equivalent of 100mg, 300mg and 600mg for humans. The tumors from three mice in each treatment group were analyzed on days three, five, seven, nine and 11.

Researchers inspected "cellular apoptosis" (programmed cell death) and found that the percentage of cells programmed to die increased in all cell lines. Exactly how much, however, depended on the amount of aspirin that was consumed, suggesting that aspirin triggers a domino effect of cell death in all colorectal cell lines regardless of genetic background.

Notably, the scientists observed that low-dose aspirin was especially effective in suppressing tumor growth in animal models that had more PIK3CA genes. The finding was significant because the mutated version of these genes has been associated with increased risk of certain cancers.

To further validate the findings, the scientists applied mathematical modeling to the experimental data. They measured the rates of cell division and cell death and used mathematical modeling to determine the probability that tumor cell colonies could survive and develop into actual tumors.

"Speaking metaphorically, they were building a hurricane model to predict the path a cyclone would take," said Russell Rockne, Ph.D., a mathematical oncology scientist at City of Hope who was not involved in the study. "Mathematics and computational biology increasingly play a larger role in basic and translational research in cancer. Mathematical

oncologists like myself take data, separate it into discreet parts and use math to explain why something like aspirin could have an inhibitory effect against colorectal cancer."

Provided by City of Hope

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