

# **Aspirin's Forgotten Anticancer Function**

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#### STORY AT-A-GLANCE

- > Aspirin, traditionally used for pain relief, shows promising anticancer properties. Recent research highlights its potential in cancer prevention and treatment, with a more potent analog, 2,6-dihydroxybenzoic acid, showing even greater promise
- > Combining aspirin with vitamin C demonstrates superior results in shrinking tumors and extending survival times compared to either compound alone or conventional chemotherapy drugs, while being gentler on healthy cells
- > Long-term, low-dose aspirin use (75 mg+ daily for several years) can significantly reduce colorectal cancer incidence and mortality, with benefits most pronounced for proximal colon cancers and after 20+ years of use
- > Aspirin's cancer-fighting potential extends beyond colorectal cancer, showing promise in reducing risks for esophageal, stomach, lung, prostate and breast cancers, with overall cancer incidence potentially reduced by 20% to 30% after three to five years of use
- > For maximum benefit, choose immediate-release aspirin without additives. Optimal dosage ranges from 82 mg to 325 mg daily, taken with meals. Genetic testing may help personalize aspirin use for cancer prevention in the future

Aspirin is a staple in medicine cabinets worldwide, known primarily for its pain-relieving and anti-inflammatory properties. However, recent research is shedding light on a potentially game-changing role for this common medication: cancer prevention and treatment.<sup>1</sup>

While aspirin's anticancer properties have been hinted at in various studies over the years,<sup>2</sup> this function has largely been overlooked in favor of newer, more expensive drugs. Now, groundbreaking experiments are not only reaffirming aspirin's potential in fighting cancer but also uncovering a more potent analog that could revolutionize our approach to cancer treatment.

This forgotten function of aspirin, and its even more powerful cousin, may offer new hope in the battle against one of humanity's most persistent health challenges. Let's explore the exciting developments that are causing researchers to take a fresh look at this familiar drug.

### Aspirin and Cancer: Introducing 2,6-Dihydroxybenzoic Acid

In my interview with Georgi Dinkov, above, he discusses his experiments with mice using a combination of B vitamins — B1, B3 and B7 — and aspirin to combat a highly lethal form of human mantle cell lymphoma. He found that while the vitamins alone stopped tumor growth, adding aspirin at a human-equivalent dose of about 1.5 grams per day led to complete tumor regression in all three test subjects.

Building on the success with aspirin, Dinkov introduced a more potent analog of aspirin known as 2,6-dihydroxybenzoic acid. Not only is it much stronger, it's also much more lipophilic, meaning it has a greater affinity for lipids (fats) than water. Lipophilic compounds tend to be more easily absorbed through cell membranes.

Dinkov explains the theoretical basis for using this compound, which is based on lowering intracellular pH to induce cancer cell death:<sup>3</sup>

"One of Ray [Peat]'s main theories was that ... cancer cells ... [are] metabolically dysfunctional, we all know that, and typically a cell like that commits apoptosis. But in order to commit apoptosis, that mechanism is controlled almost entirely by the intracellular pH. And in order for apoptosis to occur, it needs to be in the acidic range.

But the cancer cells are alkaline due to exporting lactate and hydrogen ions. So, if anything can drop the intracellular pH, those cancer cells, because they're deranged, should actually disappear by themselves.

And one of Peat's suggestions at the time was, 'Why don't you use the drug acetazolamide?' which as a carbonic anhydrase inhibitor, increases carbon dioxide. Carbon dioxide is acidic, and then that should allow cancer cells to commit apoptosis.

There are some studies in vitro and in vivo showing that acetazolamide may work, but it didn't really cure the tumors. It was a slower growth, partial regression, but it showed that the idea was on the right track.

So, I said, 'Let's find something that's much more acidic than carbon dioxide.'
And that is this 2,6-dihydroxybenzoic acid, which is just one extra hydroxyl
group on top of aspirin. Salicylic acid, really, which is 2-hydroxybenzoic acid.
And then this thing is about 10 times more potent than aspirin."

Follow-up studies have yielded promising results, with tumors regressing after one week. Dinkov notes that 2,6-dihydroxybenzoic acid is, "Freely available. No patent, nothing on it. Quite a few studies back in the day, but really a very generic molecule ... Dirt cheap, too. Cheaper than aspirin."

Just as aspirin was developed from a natural source (willow bark), other natural compounds, including those derived from the leaves of the medicinal plant Lithraea molleoides,<sup>5</sup> also show cytotoxic effects, adding to the growing body of evidence that plant-derived compounds can have significant anticancer potential. Compounds isolated from Mangifera zeylanica, a species of mango tree native to Sri Lanka, also have cytotoxic and apoptotic effects.<sup>6</sup>

# **Aspirin-Vitamin C Combination Treats Solid Tumors Better Than Chemo**

While research suggests 2,6-dihydroxybenzoic acid could be a promising tool against cancer, aspirin also shows immense promise. Your body may benefit even more when aspirin is combined with vitamin C, which also has antitumor effects. Recent studies have shown that this combination can be more effective against cancer cells while remaining gentler on healthy cells compared to conventional chemotherapy drugs like doxorubicin.<sup>7</sup>

In laboratory tests, the aspirin-vitamin C combination showed a strong cytotoxic effect on liver cancer cells but was much less harmful to normal lung cells.8 This selectivity is crucial for reducing the side effects associated with cancer treatments. The synergy between these two common substances appears to enhance their individual anticancer properties, offering a safer alternative to harsh chemotherapies.

The potential of aspirin and vitamin C extends beyond the lab, with encouraging results in animal studies. When tested on rats with chemically induced liver cancer, the combination therapy showed remarkable results. After 90 days of treatment, the livers of treated rats had significant improvement in both appearance and function.

Importantly, most of the liver tissue appeared normal under microscopic examination. This combination therapy outperformed doxorubicin in restoring liver health and reducing tumor markers.

## **Aspirin Works Synergistically with Vitamin C**

In another study, the combination of aspirin, also known as acetylsalicylic acid (ASA), and vitamin C, or ascorbate (AS), showed superior results in shrinking tumors compared to either compound alone. When mice with solid tumors were treated with the combination, their tumor volume decreased by 46%, versus 40% with ASA alone and 36% with AS alone.

This synergistic effect likely stems from combining aspirin's anti-inflammatory properties with vitamin C's potent antioxidant capabilities. The two compounds appear

to work together to create a more hostile environment for cancer cells, impeding their growth and proliferation.

By attacking tumors through multiple mechanisms simultaneously, the aspirin-vitamin C combination may overcome some of the adaptations cancer cells typically develop to evade single-compound treatments.

Beyond just shrinking tumors, the aspirin-vitamin C combination significantly extended survival times and appeared to improve overall health in the tumor-bearing mice. Mice treated with the combination survived an average of 93.5 days, compared to just 54 days for untreated tumor-bearing mice — a 73% increase in lifespan.<sup>11</sup>

The combination also outperformed either compound alone in normalizing various biomarkers of liver, kidney and heart function that had been disrupted by the cancer. Notably, the combination was able to increase hemoglobin levels, potentially alleviating the anemia often associated with cancer.

These improvements in organ function and blood parameters suggest the aspirinvitamin C treatment may have wide-ranging benefits for overall health and quality of life, beyond just its antitumor effects.

A key mechanism behind the aspirin-vitamin C combination's effects appears to be its powerful modulation of oxidative stress and inflammation in the body. The study found that tumor-bearing mice had significantly elevated levels of oxidative stress markers like malondialdehyde (MDA) and nitric oxide (NO), along with depleted antioxidant defenses.

Treatment with aspirin and vitamin C dramatically reversed these imbalances, decreasing MDA and NO while boosting total antioxidant capacity, glutathione and catalase activity. By creating a less inflammatory, less oxidative environment in the body, the combination may make it harder for cancer cells to thrive and spread.

This rebalancing of the redox state could have far-reaching effects throughout the body, potentially explaining the improvements seen in multiple organ systems. The study's

findings underscore the importance of addressing chronic inflammation and oxidative stress as part of a comprehensive approach to cancer treatment and prevention.

## **Aspirin's Promising Role in Colorectal Cancer Prevention**

Aspirin may also significantly reduce the risk of colorectal cancer (CRC), one of the leading causes of cancer-related deaths worldwide. Studies have shown that taking at least 75 milligrams (mg) of aspirin daily for several years can decrease both the incidence and mortality of CRC.<sup>12</sup>

Interestingly, the beneficial effect appears to be most pronounced for proximal colon cancers, which are typically harder to prevent through standard screening methods like colonoscopy or sigmoidoscopy. Long-term aspirin use, particularly for over 20 years, has been associated with a remarkable 35% reduction in CRC incidence.<sup>13</sup>

These findings suggest that incorporating low-dose aspirin into your long-term health strategy could offer significant protection against this common form of cancer.

Beyond its preventive effects, aspirin may also improve outcomes for those already diagnosed with colorectal cancer. Research indicates that regular aspirin use after a CRC diagnosis is linked to reduced risks of both overall and CRC-specific mortality. This benefit appears to be particularly pronounced in tumors that overexpress cyclooxygenase-2 (COX-2).<sup>14</sup> Moreover, aspirin's protective effects aren't limited to colorectal cancer alone.

Studies have shown that long-term aspirin use can reduce the 20-year risk of death from any cancer by 20%, with an even more substantial 35% reduction in gastrointestinal cancer deaths. 15 These findings suggest that if you're at increased risk for cancer or have already been diagnosed, aspirin use could be a valuable part of your treatment and prevention strategy.

Studies suggest aspirin may help suppress tumor growth, reduce metastasis and even enhance the effectiveness of other cancer treatments.<sup>16</sup> This multi-pronged approach makes aspirin a particularly promising agent in the fight against colorectal cancer. For

individuals at higher risk of CRC, such as those with a history of colorectal neoplasia or genetic predisposition, aspirin may offer even more promise.

A systematic review of studies involving people with previous colorectal neoplasia found a non-statistically significant reduction in advanced neoplasia with low-dose aspirin use.<sup>17</sup> Additionally, for carriers of Lynch syndrome genes, high-dose aspirin for two years was associated with a decreased risk of colorectal cancer.<sup>18</sup>

Individuals with Lynch syndrome have a significantly higher lifetime risk of developing colorectal cancer. The National Institute for Health and Care Excellence recommends patients diagnosed with Lynch Syndrome begin daily aspirin therapy to reduce the risk of colorectal cancer.<sup>19</sup>

### **Aspirin's Broad Cancer-Fighting Potential**

Analyses of long-term cardiovascular trials have also revealed aspirin's unexpected power in fighting cancer across multiple sites.<sup>20</sup> Studies show significant reductions in deaths from esophageal and stomach cancers among long-term aspirin users, and data indicate it may also lower your risk of lung, prostate and breast cancers.

Perhaps most exciting is the potential for a 20% to 30% reduction in overall cancer incidence after just three to five years of daily low-dose aspirin use.<sup>21</sup> Further, studies consistently show that low doses — as little as 75 mg to 100 mg daily — are just as effective as higher doses in reducing cancer risk.<sup>22</sup>

The effectiveness of low-dose regimens also points to a unique mechanism of action. Rather than directly affecting tissues throughout your body, aspirin may work by inhibiting platelets, which play a crucial role in both early cancer development and later metastasis.<sup>23</sup> While some benefits of aspirin use may appear within a few years, other reductions in cancer risk emerge with long-term use.

Studies tracking participants for 20 years or more have found that aspirin's protective effects against gastrointestinal cancers become more pronounced over time. For colorectal cancer, significant reductions in incidence and mortality were observed 10 to

20 years after the start of aspirin use.<sup>24</sup> This long-lasting effect suggests that aspirin may be altering fundamental processes in cancer development, offering enduring protection against this disease.

Aspirin's potential as a repurposed drug for cancer therapy is another exciting area of research.<sup>25</sup> Aspirin works by inhibiting COX enzymes, particularly COX-1 and COX-2. This mechanism not only helps prevent heart attacks but may also combat cancer in multiple ways. By inhibiting COX-1, aspirin reduces platelet aggregation around tumor cells, making these malignant cells more visible to your immune system.<sup>26</sup> This could help prevent cancer from spreading throughout your body.

Additionally, aspirin's effect on COX-2 may directly impact tumor growth. COX-2 produces prostaglandin E2, which stimulates tumor cell growth. By reducing prostaglandin E2 production, aspirin could slow or prevent tumor development.<sup>27</sup>

The future of aspirin in cancer prevention may lie in personalized medicine. Emerging research has identified several genetic markers that could help predict who will benefit most from aspirin therapy. For example, certain variations in genes like UGT1A6 and ALOX12 have been associated with enhanced aspirin efficacy in reducing colorectal cancer risk.<sup>28</sup>

Additionally, your expression levels of enzymes like 15-PGDH may influence how well you respond to aspirin's cancer-fighting properties.<sup>29</sup> These genetic insights open up exciting possibilities for tailoring aspirin use to your individual genetic profile. In the coming years, genetic testing could become a routine part of determining whether aspirin is right for you and at what dose.

#### Willow Bark: Nature's Time-Tested Pain Reliever

For those with aspirin sensitivity, salicylic acid or willow bark supplements may be alternatives worth considering. When you consume aspirin, your body converts the acetylsalicylic acid into salicylic acid, which is responsible for aspirin's anti-

inflammatory, analgesic and antithrombotic properties. Willow bark naturally contains this compound.

This ancient medicinal plant carries with it centuries of therapeutic wisdom, offering a compelling alternative to modern pharmaceuticals. Willow bark's efficacy stems from its long-standing relationship with human physiology. Unlike laboratory-created drugs, the active compounds in willow bark have been interacting with our biochemistry for thousands of years.

This extended coexistence has fostered a natural compatibility that many synthetic medications struggle to achieve.

Our ancestors' consistent, albeit minimal, consumption of these compounds over generations has allowed our bodies to develop an efficient means of processing and utilizing them. This evolutionary adaptation underscores the potential advantages of natural remedies over their synthetic counterparts. Further, research suggests that some of willow bark's therapeutic properties are due to synergistic effects,<sup>30</sup> offering benefits beyond those of salicylic acid alone.

The pharmaceutical industry's development of aspirin in the 19th century marked a significant shift from nature-based to laboratory-derived medicine.<sup>31</sup> While this transition led to the creation of a patentable product, it didn't necessarily improve upon the original source material. In fact, the enduring popularity of willow bark serves as a testament to the power of plant-based remedies.

For those considering willow bark as an alternative to aspirin, particularly individuals with aspirin sensitivity, understanding proper dosage is important. While willow bark and aspirin share similar active compounds, their metabolism and bioavailability differ, necessitating distinct dosing strategies.

So, while 240 mg to 600 mg of willow bark extract (15% salicin) is often estimated to provide a salicin dose that is roughly equivalent to 325 mg of aspirin, the total amount of willow bark extract needed is typically larger:

- To approximate the effects of 81 mg of aspirin, a dose of 400 mg to 800 mg of willow bark extract (standardized to 15% salicin) is typically required.
- For effects similar to 111 mg of aspirin, a dose of 500 mg to 1 gram of willow bark extract (standardized to 15% salicin) is generally needed.

#### **Tips for Aspirin Dosage and Duration**

When selecting aspirin, choose immediate-release formulations rather than coated extended-release versions to avoid unnecessary additives. Immediate-release aspirin is available on Amazon. Examine the inactive ingredients list carefully; ideally, corn starch should be the only additive listed.

After extensive research, I identified a product meeting these specifications. The appropriate dosage ranges from 82 mg to 325 mg daily, taken with your largest meal, depending on your individual needs.

Based on my research into aspirin's preventive benefits, I personally take 111 mg daily using Health Natura's USP grade 60 gram aspirin powder, which costs less than \$20. This 99% pure USP aspirin powder appeals to me due to its prometabolic, antilipolytic, anti-inflammatory, anticortisol and anti-estrogen effects. Its safety profile is well-established.

When it comes to cancer prevention, the dosage and duration of aspirin use appear to be crucial factors. Low doses of aspirin (75 to 300 mg/day) have been shown to be as effective as higher doses in reducing CRC-related mortality,<sup>32</sup> suggesting that you don't need to take large amounts to reap the potential benefits. However, consistency and long-term use seem to be key.

Studies indicate that the benefits of aspirin increase with duration of use, with the most significant reductions in cancer risk observed after five to 7.5 years of regular use.<sup>33</sup> As research progresses, aspirin may prove to be a powerful new tool in your cancer prevention and treatment arsenal — one that's been in your medicine cabinet all along.

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