BY DR. SEAN GOLDEN

PART 6

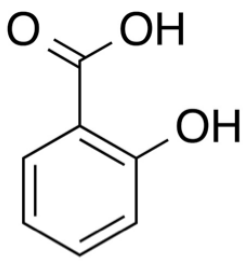
THE BIG "FOUR":

WHITE WILLOW BARK

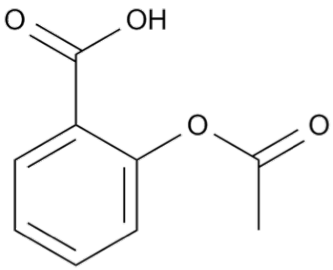
White Willow Bark is Literally Nature's Aspirin, but Better

White willow bark has been used for centuries now for pain and inflammation. White willow naturally contains salicin, which converts to salicylic acid in the colon. Over 100 years ago, we created synthetic aspirin by attaching an "acetyl" group onto the natural salicylic acid molecule found abundantly in nature. The acetyl group is essentially the acid that is in vinegar, which is why an old bottle of aspirin can develop a vinegar-like smell to it.

Thus, we turned *salicylic acid* into *acetyl-salicylic acid*:



Salicylic acid



Acetyl-salicylic acid (AKA aspirin)

(Don't worry if you're a little rusty with your chemistry, you won't need to memorize any of these structures!)

Attaching that acetyl group onto salicylic acid changes its properties. The biggest change is that **aspirin inhibits the COX enzymes** that can create inflammatory prostaglandins (similar to other anti-inflammatory medication like ibuprofen), while the natural **salicylic acid does not**.

This is what makes aspirin so damaging to the stomach lining.

One of the prostaglandins, PGE2, is needed for mucus production of the stomach and for proper blood flow to the lining of the stomach.[1] Since aspirin inhibits PGE2 production, it inhibits the ability for the stomach to secrete enough protective mucus and repair itself from small ulcers.

Natural salicylic acid, on the other hand, does not inhibit COX enzyme functioning. Actually, **salicylic acid has been shown to be protective** against stomach mucosal damage from other irritants and anti-inflammatory drugs.[2]

Most of the typical anti-inflammatory medications such as aspirin and ibuprofen inhibit inflammation by inhibiting the COX enzymes, which is also where many of their side effects come from. However, if salicylic acid doesn't inhibit the COX enzymes, then how does it lower inflammation?

Salicylic Acid Inhibits the "Master of All Inflammation"

As we learned in the last section on niacin, while some prostaglandins can promote inflammation, others can be very anti-inflammatory and even help to "resolve" existing inflammation.

When you block the COX enzymes with anti-inflammatory medications, you inhibit BOTH the pro- and anti-inflammatory prostaglandins. Thus, while they can sometimes help with the current inflammation you are having at the moment, they don't really do anything to solve the problem.

It turns out, one of that major ways that salicylic acid blocks inflammation is through down-regulating NF-kB, the "master regulator of inflammation".[3,4] NF-kB plays a central role in the response to inflammatory stimuli.

NF-kB has been found to be dysregulated in Crohn's and U.C., and this dysregulation increases both acute and chronic inflammation is these conditions.[5]

By targeting NF-kB, salicylic acid from white willow bark can powerfully block the heart of inflammation without the ulcer and bleed risk that comes with aspirin!

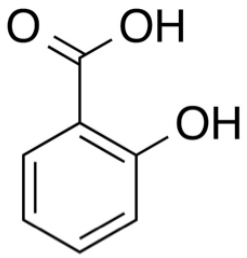
Pharmaceutical Companies Already Figured This Out!

Pharmaceutical companies saw the potential in aspirin to powerfully block inflammation in the colon from Crohn's or U.C., but they also saw the GI side effects of aspirin as a big downside.

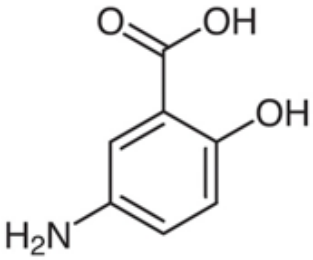
However, since salicylic acid didn't have the GI side effects of aspirin but still inhibited NF-kB, what if they could come up with a modified version of aspirin that didn't inhibit the COX enzymes but still inhibited NF-kB like salicylic acid. Even better, what if they could patent it?

This is exactly what they did: **enter the 5-amino-salicylates**

They ended up attaching an "amino" group on to salicylic acid instead of an "acetyl" group, like in aspirin. The structures are below:



Salicylic Acid



5-amino-salicylic acid

The Rise of the 5-amino-salicylates

After the companies realized this, prescribing 5-amino-salicylates became one of the first line treatments. They found that these, like salicylic acid and aspirin, also inhibited NF-kB.[7]

Brands such as Canasa, Delzicol, Asacol HD, Pentasa, Apriso, Lialda, and sfRowasa are all examples of 5-amino-salicylates (aka Mesalamine).

Since their inception, they have largely replaced sulfur-based salicylates (which have more side effects), and are used as a first-line of treatment.[6, 16]

While they have a high response rate (40-70%) and remission rate (15-20%), their main drawback is their cost.[6]

5-amino-salicylates are targeted to the colon... but so is white willow

Unlike aspirin, the body doesn't absorb the active molecule right away with white willow bark.

The molecule that starts off in white willow bark is actually salicin, which is mostly inactive. Once salicin makes its way down to the colon, the bacteria there convert salicin into salicylic acid.[8]

Thus, not only does the active molecule bypass the stomach, but this essentially ensures that salicylic acid will actually be in the colon to do its anti-inflammatory work, just like 5-amino-salicylates!

White Willow Bark is More Than Just Salicylic Acid

Besides the salicin / salicylic acid from white willow bark, it also contains an abundance of polyphenols, flavonoids, and proanthocyanidins.[9,10]

These compounds have been shown to also have powerful anti-inflammatory activity throughout the intestinal tract and are very likely responsible for some of the favorable response to white willow bark.[10,11] In fact, proanthocyanidins on their own achieve powerful effects in the rodent models of Ulcerative Colitis.[11]

Therefore, with white willow bark you are really getting the best of both worlds: A delivery of salicin / salicylic acid to the colon, as well as a multitude of other beneficial plant anti-inflammatory compounds!

White Willow Bark and Cancer

Both the compounds in white willow bark and the extract itself have been found to have broad-spectrum anti-cancer effects and inhibit the survival of colon cancer cells.[17,18,19]

While we can't say it will prevent colon cancer (there are many different risk factors to consider), this certainly isn't a bad "side effect" to have!

How to take White Willow Bark

White willow bark can easily be found in capsules in most health food stores and online. The kind standardized for 15% salicin is good, and the brand "NOW" makes a good product at an affordable price.

Usually the pills are 800 mg for 2 pills, or 400 mg for 1 pill. The standard dosage to start with is 3-4 pills a day, though you can test just one pill to make sure you don't have an allergy. Due to a good safety profile, you can discuss with your treating physician about doses higher than 4 pills.

The main side effect to look out for is ototoxicity, which can give you tinnitus or "ringing in the ears". This is very rare with white willow bark compared to aspirin, but theoretically any salicylate-based supplement or medication can cause this. If you start to notice any high pitched ringing in the ears, discontinue the supplement right away, and it should fade. After it fades, you can try a lower dose or skip this supplement altogether. **If you already have tinnitus, any salicylate-based drug / supplement, including white willow bark, can make it worse.** If you notice any worsening, stop the supplement immediately and it should revert. Again, tinnitus is a very rare side effect that the vast majority of the patients never get, and is temporary if you stop / reduce the dose, but I just want you to be aware of this possibility in case it comes up.

There is some evidence that taking glycine as a supplement can help prevent ototoxicity from salicylates, so if you are concerned for whatever reason, you can try taking 3-6 g of glycine a day with the white willow bark as well. Glycine happens to have its own beneficial anti-inflammatory effects too! (Magnesium and Gingko Biloba can also be somewhat effective for salicylate-induced tinnitus)[14,15]

To put this in context with aspirin, 4 pills of 15% salicin white willow bark contain 240 mg of salicin, less than 1 tablet of aspirin (325 mg acetyl-salicylic acid). Also, not all of that 240 mg of salicin will convert to salicylic acid; some of it ends up just going right through you.[8]

Make sure to discuss with your treating physician before making any changes or adding any new supplement to your regimen. This information is for educational purposes only and is not medical advise in any way!

Sincerely,

Dr. Sean Golden

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