Effects of Willow Bark (*Salix alba*) and Its Salicylates on Blood Coagulant

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Abstract

The herb white willow (*Salix alba*), also known as willow bark, is used to treat pain and fever. It is also used for myalgias, osteoarthritis, dysmenorrheal, gouty arthritis, rheumatoid arthritis, gout, common cold, influenza, and weight loss. White willow contains a substance (salicine) that is converted by the body into a salicylate similar to the blood-thinner aspirin. Over the last twenty years, another use for aspirin has emerged connected with the discovery of its anti-thrombotic action.

Keywords: Willow bark, Blood coagulant, Salicine

1. Introduction

The concentration of salicin is actually much lower in willow bark than in other salix species. Willow bark has several different components, including flavonoids, tannins, and salicin. Salicin is considered the main active ingredient as it is metabolized to salicylic acid. The other components of willow bark are thought to have lipoxynagenase-inhibiting and antioxidant effects as well as prevent prostaglandin and cytokine release. The active substance of the common white willow, a glycoside of salicylic acid known as salicin, was isolated in 1829 by Leroux, who also demonstrated its antiplatelet properties (Chrubasik and Shvartzman 1999). The effects of willow bark attributed to the salicin compounds include analgesic, anti-inflammatory, antipyretic, and antiplatelet activity (Fiebich and Apel 2003).

Salicylic acid is one of numerous phenolic compounds, defined as compounds containing an aromatic ring with a hydroxyl group or its derivative, found in plants. There has been considerable speculation that phenolics in general function as plant growth regulators (Aberg 1981).

Willow species contain only a low quantity of the pro-drug salicine which is metabolized during absorption into various salicylate derivatives. Herbs with salicylate constituents help to reduce platelet aggregation and prevent blood clotting. Salicylate inhibits the platelets' production of a compound called thromboxane $A_2$ which controls the ability of the platelet to adhere to other platelets. Salicylate is the basis of aspirin. Herbs containing salicylate include meadowsweet, poplar and willow or willowbark (Vlachojannis et al. 2011).

2. The Mechanisms of Action

A variety of stimuli, including thrombin, adenosine diphosphate (ADP), and collagen, are known to cause platelet activation, spreading, and aggregation. Adenosine diphosphate is stored within the dense granules of platelets and is released upon cell activation, but it causes only modest reversible aggregation. Nonetheless, ADP plays an important role in initiating signals that lead to platelet shape changes and to the synthesis of thromboxane $A_2$, which is a potent activator of platelets. When a platelet is activated and its dense granules release their contents, ADP binds to its receptors on the same and neighboring platelets, as does thromboxane $A_2$ to its receptor. Adenosine diphosphate amplifies the platelet’s response to other agonists.

This adhesion cascade leads to the formation of large platelet aggregates that are both procoagulant and pro-inflammatory. The resulting thrombus can easily occlude the lumen of an already narrowed atherosclerotic coronary artery, thereby causing a myocardial infarction (Quick 1966, Ruggeri 2002).

Aspirin impairs both ADP release and secondary ADP-dependent platelet aggregation. Weiss reported that aspirin’s effect on platelets was rapid and irreversible, inhibiting platelet aggregation for the duration of a platelet’s life. Together with the findings from several other groups, Dr. Weiss’s discovery was a key step in understanding the mechanism by which low doses of aspirin could prevent coronary and cerebral thrombosis (Weiss and Aledort 1967).

The peculiar effectiveness of aspirin in thrombosis is based on its irreversible inhibition of the COX enzyme in platelets which make thromboxane $A_2$ ($\text{TXA}_2$), the potent
pro-aggregatory and vasoconstrictive prostaglandin. Of all the aspirin-like drugs, only aspirin permanently inactivates the enzyme (by attaching an acetyl group close to the active site), and thus makes the Arachidonic acid metabolism, controlled by cyclooxygenases. Arachidonic acid is liberated from the cells by phospholipase A₂ and converted by cyclooxygenases via unstable endoperoxides to prostaglandins.

In endothelial cells prostacyclin is preferentially produced, while blood platelets generate thromboxane A₂, platelet incapable of synthesizing TXA₂ for the rest of its life (about 10 days). Regular low doses of aspirin have a cumulative effect and inactivate platelet COX without affecting much the synthesis in blood vessels of prostacyclin—which exert potent vas-dilatory and anti-platelet effects (Szczeklik et al. 1979).

It is important to realize that salicin from willow can be split off by the body to create salicylic acid, providing anti-inflammatory and pain-relieving actions with the same COX-2 inhibition properties as aspirin; although salicin will not function as an anticoagulant (blood thinner) like aspirin (Bradley 1992, Newall et al. 1996).

This effect on the urine may lead to decreased blood levels and therapeutic effects of several drugs, including aspirin and other salicylates (choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate). It may be advisable to avoid these citrate compounds during therapy with aspirin or salicylates except under medical supervision.

White willow contains a substance that is converted by the body into a salicylate similar to aspirin. It is therefore possible that taking NSAIDs and white willow could lead to increased risk of side effects, just as would occur if you combined NSAIDs with aspirin.

To some extent salicylate-containing herbs work by treating the cause of the pain and by interfering with pain transmission. These herbs are generally not as effective for psychogenic pain or pain not related to inflammation or tissue destruction. Salicylates may also have activity in the central nervous system to reduce pain sensation.

3. Conclusion

Willow bark contain high concentrations of salicylates have been reported to exhibit antiplatelet activity. Preparations from Salix species, the natural NSAID, contain a total of more than 1% salicylates. Salicylate concentrations in the range causing analgesia are achieved with daily consumption of extract standardized at least on 240 mg Salicilin (ESCOP Monograph). Salicylate side-effects may occur during treatment. However, blood coagulation is less affected than with acetylsalicylate (Chrubasik and Shvartzman 1999).

Toxicity is far less with willow bark than with aspirin due to the low levels of salicylates in the plant products. There is a potential for interaction with salicylate-containing medications and other non-steroidal anti-inflammatory medications (NSAIDs). There is not expected to be a negative interaction with anticoagulant medications. Tannins may interfere with absorption of other medications. Nowadays, synthetic acetylsalicylic acid is used not only as an analgesic and antipyretic, but to prevent myocardial infarctions, strokes and colorectal cancer. Some herbalists recommend willow bark extract as a natural substitute for aspirin to achieve these same benefits. In Germany, willow bark is often taken along with aspirin to enhance the therapeutic effects while minimizing side effects (Peirce 1999).

Willow bark is an important bitter tonic with marked astringent properties, making it useful in chronic hypersecretory states, such as mucus discharges, passive hemorrhage, leukorrhea, humid asthma, diarrhea and dysentery. In the treatment of inflammatory joint disease Willow is unlikely to provide the same relief as aspirin, and if applied as a simple for its salicin content, will typically require such large doses that the tannins become potentially toxic (Bergner 2001). Usual dosage of salicin recommended for back pain is 120–240 mg, with the higher dose found to be more effective. Up to a week of therapy may be needed before benefit is seen. Willow bark has been used for up to 3 months without adverse effects (Food and Drug Administration 2003). Aspirin is composed of synthetic acetylsalicylic acid. Natural salicylic acid is reported to produce fewer side effects than synthetic acetylsalicylic acid (Hathcock 1997).

The solubility increases markedly in alkaline pH and is more than 100-fold higher for the sodium salts as compared to the free acids. Salicylates, in contrast to aspirin, have unique physicochemical properties. These are caused by the close steric neighborhood of the acetate hydroxyl group to the carboxyl group. This allows the formation of a chelate ring structure and facilitates the release of protons. The major functional consequence is the action of salicylate as protonophore, for example, in mitochondrial membranes, to uncouple oxidative phosphorylation because of the abolition of the membrane impermeability to protons. Neither aspirin nor other salicylates exhibit comparable physicochemical properties (Blumenthal et al. 1998, Schröer 2009). Unlike ASA (synthetic acetylsalicylic acid, naturally occurring salicine (salicylic acid) does not irreversibly inhibit platelet aggregation, reducing the potential for a bleeding disorder.
Willow is certainly a giving herb. Numerous species have a long history of use as a safe and effective pain-relieving medicine. As is the case when using all of nature’s healers, it is recommended that you consult with a trained herbalist or other complementary medicine practitioner before use.

4. References


