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Screening the healing plants for effects on how our livers make and store sugar*

Purpose

This study screened the 17 Cree healing plants to see if they might affect how the liver makes, stores, and circulates sugar.

Where this study fits in

When we look at plants that might help with diabetes, we need to look for effects on all the different parts of our body that help make, store, or use up sugar. For each body part, we always begin by screening all 17 plants. That means we do lab tests using tissues from whichever body part we are interested in — say, muscle cells or gut cells. If a plant seems to have promise, we then go on to tests in live mice.

So far in the Anti-diabetic Plant Project, we have screened all 17 plants for

- Effects on fat, muscle, nerve, and pancreas cells
- Effects on how our guts move sugar into the blood
- Effects on AGEs—particles that damage our cells and can lead to heart disease

This study is another of the "screening" ones. This time, we screened the 17 plants to see if they affect the way our livers make, store, and circulate sugar.

About how the liver helps us balance our sugar levels

When we are healthy, there is a good balance in

- How much sugar our liver makes
- How much of that sugar gets taken out of the blood into our muscles and fat

- How much sugar gets stored in our liver or muscles as glycogen (a sort of medium-term storage)

Usually, insulin helps us to keep all these things in balance. But diabetes affects how our bodies make and handle insulin, and this throws off the balance. As a result, too much sugar stays in the blood, and this causes damage.

The way our livers make and store sugar is complex. It involves two pathways: the pathway that insulin uses, and another one. Each pathway has a lot of steps, and many different actors—enzymes that send signals to each other and trigger the various steps. We could not possibly look at all these steps and actors. Instead, we tested the Cree plants on a few key actors:

- An actor (enzyme) called G6Pase. We know that insulin works partly by quieting this actor. G6Pase is the last and decisive step through which the liver can make sugar available to the rest of the body. Because it affects how fast sugar can be made, we thought this enzyme was important for diabetes.
- An actor called GS that plays a large role in how much sugar gets put into medium-term storage. Again, insulin works in part through this actor, this time making it more active.
- An actor on the non-insulin pathway called AMPK. Like insulin, AMPK works to reduce how much sugar the liver makes, and to increase how much of it gets taken up or stored. The diabetes drug Metformin works by acting on AMPK.

Seven of the plants seem to help the liver make less sugar

In our lab tests, seven plants could quiet the G6Pase enzyme that normally allows sugar production. In particular, white spruce (Miinhikw) and balsam fir (Inaast) were almost as good as insulin at doing this. Yet the plants did not seem to be working through the usual actors to produce this effect. Perhaps they are working via some of the other actors that we didn’t measure.

Balsam fir and tamarack had strong effects on sugar storage

Next, we looked at how much sugar got put into medium-term storage through the action of the GS enzyme, and how big a role another upstream enzyme called GSK-3 was playing in that process. Several of the Cree plants were as good as insulin at helping put sugar into medium-term storage. Two plants stood out: balsam fir and tamarack (Waatinaakan). When you add insulin, the number of "actors" involved in storage doubles. But when you add balsam fir extract, you get an eleven-fold increase. With tamarack, we got a nine-fold increase. The plants seem to be acting partly through the GSK-3 enzyme that we thought was important. But they also seem to be using other actors that we didn't study.

Three plants to focus on

To sum up, in this study, three plants stood out for their effects on how liver cells make and store sugar:

White spruce

White spruce was the best at reducing the enzyme that controls how much sugar gets made by the liver and put into the blood. In our past studies, we found that white spruce did not help our muscles or fat cells to take in sugar. It did, however, seem to protect nerve cells against damage from too much sugar. Now we see that it's also good at reducing how much sugar the liver makes.

Tamarack

Tamarack had huge effects on sugar storage—much more effect than insulin in these particular tests. It did not affect how much sugar actually got made, but did seem to influence some of the key actors in the sugar-making process. We think that tamarack has important potential for fighting diabetes. In our past tests, we'd found that tamarack

- Stimulates cells in lab dishes to take in sugar or store it; and

- Reduces blood sugars in fat mice.

Now we see that tamarack may also act in the liver.

Balsam fir

Balsam fir had large effects on a lot of the key actors in how the liver makes and stores sugar. It was the only plant in these tests to have strong effects on both how sugar got made and how it got stored. And in our past tests, we found that it also helps muscle and fat cells to take in sugar. All of this makes balsam fir a top candidate for further study. We'd like to identify its active ingredients, and to test it in live animals.

Conclusions

We already knew that many of the Cree plants help with diabetes. This study leads us to believe that some of the plants work at least partly by acting on how our livers make and store sugar. These results provide further evidence that many of the Cree traditional medicines may be worth using either along with western medicine, or instead of it.

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[*] This is a plain-language summary of an article by Abir Nachar, Diane Vallerand, Lina Musallam, Louis Lavoie, Alaa Badawi, John Arnason, Pierre Haddad, called "The action of antidiabetic plants of the Canadian James Bay Cree traditional pharmacopeia on key enzymes of hepatic glucose homeostasis." It will be published in *Evidence-based Complementary and Alternative Medicine*. The summary was prepared by Ellen Bobet, and reviewed by Pierre Haddad and Abir Nachar.