

Researchers discover ingredient in cough medicine may help with Type 2 diabetes

March 17 2015, by Bob Yirka



Cough suppressant improves blood sugar levels in diabetes mellitus

(Medical Xpress)—A large team of researchers with members from across the globe has found that an ingredient in popular cough medicines may help people with Type 2 diabetes. They have published a description of their research and their findings in the journal *Nature Medicine*.

Type 2 diabetes is the kind of diabetes that people normally get as adults, it is characterized by the pancreas producing less insulin, a hormone that helps the body regulate and use glucose. The cause of diabetes is not known and there is no cure. Patients must typically modify their diet and



take medications or insulin to maintain their health. In this new effort, the researchers report that they were conducting a study of dextromethorphan, the active ingredient in many cough suppressants—prior research had shown that when ingested, as the body works on it, a byproduct called dextrorphan is formed—a compound that suppresses the activity of certain brain receptor cells which reduces the urge to cough. Prior research had shown that it also had an impact on receptor cells in the pancreas, but it was not known what that impact was. The team reports that they were expecting the compound to worsen insulin production, but found instead that it apparently caused the receptor cells to nudge the pancreas as a whole into producing more insulin.

Intrigued, the researchers tested the impact of the compound on mice, and then on human pancreatic tissue. Then, because it is already approved and used in humans for cough suppression, the researchers were able to set up a clinical trial right away to see what impact it might have on <u>diabetes</u> patients. They enlisted the assistance of 20 male patients, and ran a single dose trial to see what happened. They report that the volunteers "showed enhanced serum insulin concentrations and glucose tolerance."

The researchers point out that their findings are still preliminary, and thus caution diabetics against self medicating with cough medicine to see if it will help manage their disease. They are hoping that their findings will cause others to set up much larger and more in-depth clinical trials to determine if dextromethorphan might be a useful way to treat diabetics.

More information: "Characterization of pancreatic NMDA receptors as possible drug targets for diabetes treatment." *Nature Medicine*, Feb 2015. DOI: 10.1038/nm.3822



Abstract

In the nervous system, NMDA receptors (NMDARs) participate in neurotransmission and modulate the viability of neurons. In contrast, little is known about the role of NMDARs in pancreatic islets and the insulin-secreting beta cells whose functional impairment contributes to diabetes mellitus. Here we found that inhibition of NMDARs in mouse and human islets enhanced their glucose-stimulated insulin secretion (GSIS) and survival of islet cells. Further, NMDAR inhibition prolonged the amount of time that glucose-stimulated beta cells spent in a depolarized state with high cytosolic Ca2+ concentrations. We also noticed that, in vivo, the NMDAR antagonist dextromethorphan (DXM) enhanced glucose tolerance in mice, and that in vitro dextrorphan, the main metabolite of DXM, amplified the stimulatory effect of exendin-4 on GSIS. In a mouse model of type 2 diabetes mellitus (T2DM), longterm treatment with DXM improved islet insulin content, islet cell mass and blood glucose control. Further, in a small clinical trial we found that individuals with T2DM treated with DXM showed enhanced serum insulin concentrations and glucose tolerance. Our data highlight the possibility that antagonists of NMDARs may provide a useful adjunct treatment for diabetes.

Press release

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