Let food be thy medicine: How GMO tomatoes could help Parkinson's patients

An apple a day might keep the doctor away, but soon the garden's preventative prescription for 60 thousand Americans might be a tomato.

The neurodegenerative disease called Parkinson Disease (PD) is a common affliction shared by Michael J. Fox, Muhammad Ali, Neil Diamond and Linda Ronstadt, among 1 million sufferers in the US and 10 million worldwide.

"I'm no good with secrets," the rock star Ozzie Osbourne, another sufferer, confessed. "I cannot walk around with it anymore 'cause it's like I'm running out of excuses."

It's a terrible affliction, with no known cures. But now researchers at the John Innes Centre, a UK-based institute focused on cutting-edge agricultural research using genetic modification, think they may have a treatment for this disease. Extraordinarily, it begins with a genetically engineered tomato.

The scientists' research focused on turning tomatoes into a sort of factory to produce Levodopa (L-DOPA), a major Parkinson's therapeutic. L-DOPA has been the gold standard drug for the management of PD symptoms since 1967, but it is typically obtained from synthetic sources. There are serious concerns about a shortage of the drug as incidences of PD rise. Turning tomato plants into factories to make this natural compound carries several benefits over synthetic versions or having L-DOPA synthesized naturally by other plants.

Why the GMO Parkinson's treatment could be a breakthrough

Parkinson's Disease is a disorder in which the nerves in the brain are damaged. That leads to symptoms such as tremors, difficulty with walking and balance, and poor coordination. As the disease and the neural damage it causes progress, the symptoms become worse. Difficulty talking and a sense of helplessness often lead to mental and behavioral issues such as sleep problems, memory deterioration, and depression. Dementia is reported in a significant number of PD sufferers. The precise cause and cure for PD remain elusive, even though the disease has been researched since the early 1800s.

[You can learn more about effective and affordable treatments for Parkinson's Disease at the Parkinson's Foundation website or you can call their Parkinson's helpline for more information.]

One common hypothesis is that the decreased levels of the neurotransmitter dopamine may be the basis of the symptoms of PD. Dopamine is necessary for neurological function in motor movement, cognitive function, and many other processes. Decreased levels would explain the loss of coordination and several other PD symptoms. Unfortunately, administering dopamine to directly correct the deficiency is not possible because it cannot physically cross the brain's protective membrane. However, a similar molecule, the amino acid L-DOPA, transits this barrier unimpeded.

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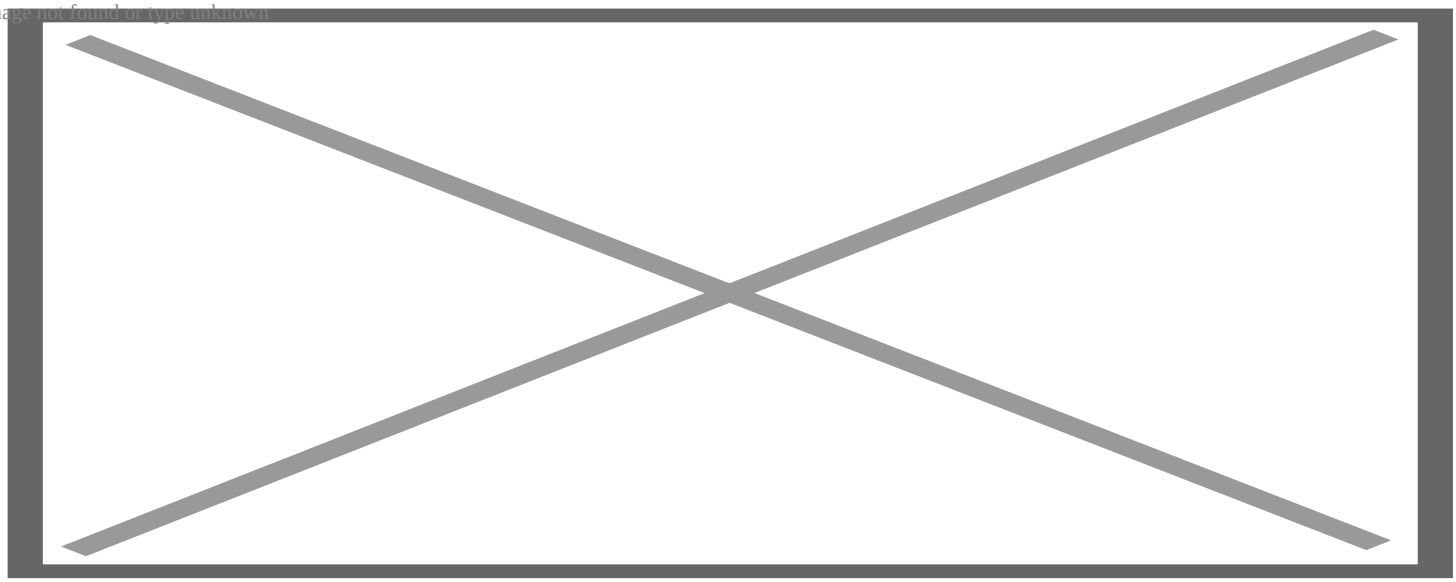

L-DOPA (also known as L-3,4-dihydroxyphenylalanine) is an amino acid that can pass from the bloodstream into the brain, where it is then converted to dopamine. The increased dopamine allows patients to regain normal function, restore dignity, and it slows the progression of neurological decline. The majority of L-DOPA used in PD treatment is produced synthetically and branded as Sinomet or Madopar. But synthetic treatments cause side effects such as nausea and lightheadedness. Prolonged treatment can lead to tolerance against the drug, causing symptoms to return and the disease progresses at a faster rate. The dosage may be increased, but then there is an increased risk of involuntary movements and increased intolerance.

L-DOPA can be produced naturally by some plants

The plant-produced compound does not cause these side effects and costs less than the synthetic versions. Initial trials were performed with L-DOPA extracted from velvet beans (*Mucuna pruriens*) and showed promise, even to the point where recipes for "Parkinson Cuisine" were developed. Some even went as far as naming it the "dopamine bean" and using slick, and misleading, marketing campaigns like "dopamine for a happier brain and healthier mood".

But use of velvet beans presented a different set of challenges. The velvet bean plant is covered in tiny hairs that contain mucunian and serotonin, chemicals that cause irritation, blisters, and allergic reactions in field workers responsible for harvesting and handling the crop. The accessory compounds in velvet beans have also caused hallucinations in patients with PD, further compromising their value.

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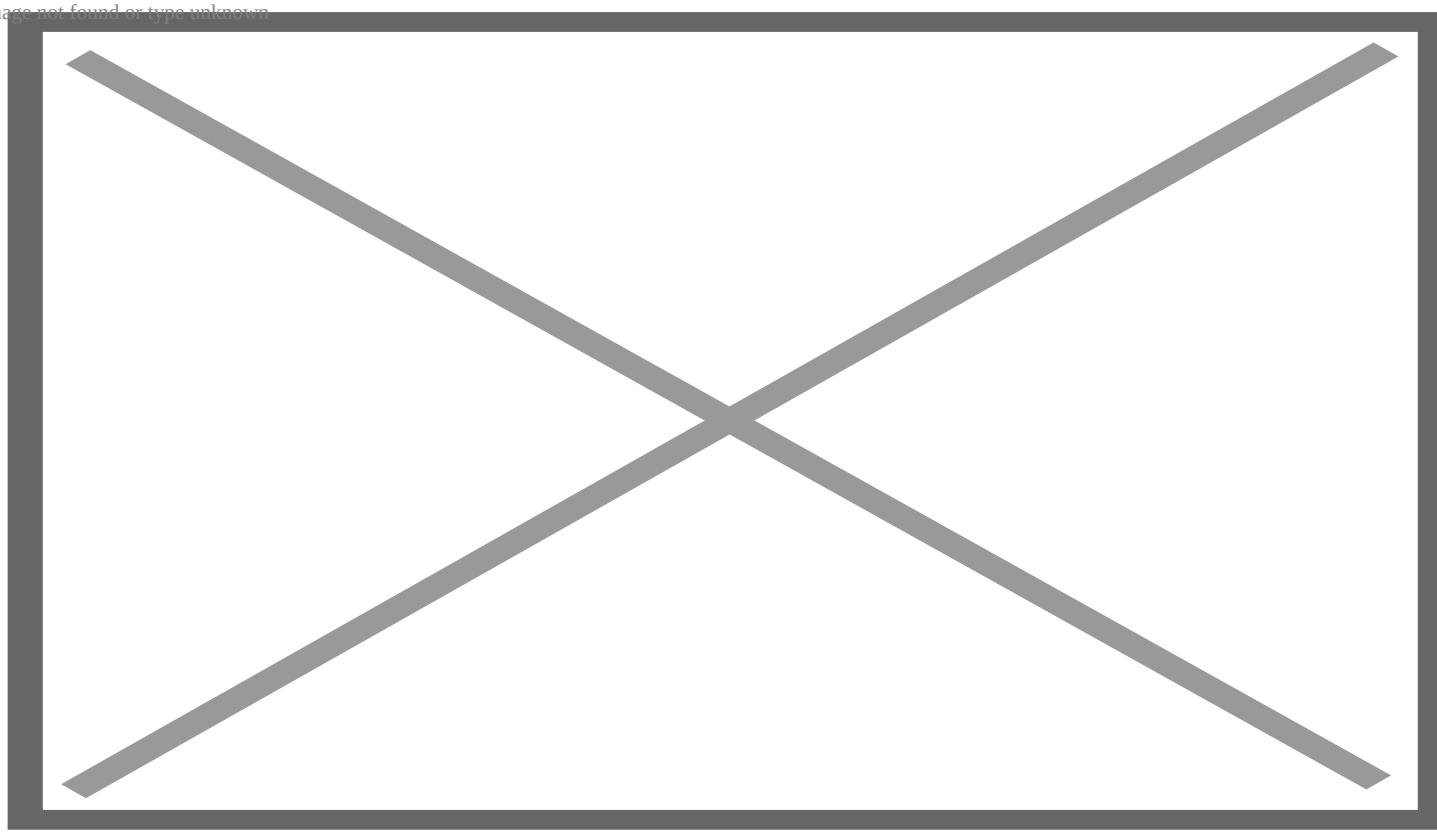

Figure 1: Velvet beans (Mucuna pruriens) contain L-DOPA but also accessory compounds which cause irritation and hallucinogenic reactions

What if L-DOPA could be produced in a plant without the compounds that induce the deleterious side effects? A gene was identified in beets (*Beta vulgaris*) that catalyzes the production of L-DOPA. This gene was isolated and placed into tomato plants, where it is exclusively expressed in the fruits. The resulting genetically modified tomatoes are rich in L-DOPA, creating a new source of the non-synthetic compound.

What are the benefits?

Using tomatoes as L-DOPA factories eliminates the risk of severe irritation or hallucinations from additional chemical products. And there are production advantages. Tomatoes grow easily in a variety of horticultural settings, from gardens to elaborate greenhouses. This opens the opportunity for these plants to be grown in several different settings and hopefully different areas. This decentralization would allow for widespread production to occur instead of being limited to one specific region. Extraction of L-DOPA from tomatoes can be performed easily, with fewer infrastructure needs and other production barriers required for production of synthetic L-DOPA.

The breakthrough may have significant implications in the developing world, where there is limited access to synthetic drugs, while tomatoes can be grown in abundance. The chemistry of the ripe tomato also helps to stabilize the L-DOPA produced, retaining its therapeutic properties days after harvest, meaning the medicine is more likely to be available. Breakthroughs like these are important and are becoming more prevalent as research in genetically engineered plants uncovers novel ways to access inexpensive biopharmaceutical production without sacrificing quality or safety.

The adage “Let food be thy medicine” takes on new meaning in the age of synthetic biology. While clinical applications are forthcoming, the work demonstrates that engineering natural plant compounds into other commonly consumed fruits is a viable way to produce crucial compounds for human health.

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