A chemical found in ayahuasca has the potential to regenerate pancreas cells that have been lost to diabetes.

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“In children and adults with type 1 diabetes, they’ve lost 99 percent of their beta cells, so they cannot make enough insulin. That’s the cause of their diabetes,” said Andrew Stewart, director of the Diabetes, Obesity and Metabolism Institute at the Icahn
School of Medicine at Mount Sinai, New York City and senior author of the study, in an interview with Healthline. “People with type 2 diabetes also have about a 50 or 60 percent reduction in their number of beta cells in their pancreas, and so they too cannot make enough insulin.”

**Learn More About Diabetes »**

**Growing Beta Cells**

Although many drugs exist to control the symptoms of diabetes, there currently is no reliable way to replace beta cells and cure the disease. Stewart joined with lead author Peng Wang and others on a multidisciplinary team to tackle the problem.

“In the world of beta cell regeneration, you can do it in two ways. You can either use stem cells, create stem cells and then transplant them. Or you could take a drug that makes your own beta cells grow,” Stewart explained.
Although the stem cell transplant research is promising, it involves an invasive procedure and will have difficulty meeting the massive demand, he said.

Diabetes affects more than 20 million Americans, according to the Centers for Disease Control and Prevention (CDC).

“The need vastly outstrips the stem cell islet supply,” said Stewart. “It would be simply much simpler to take a pill to make your beta cells grow.”

Using a high-volume screening method, Stewart’s team checked more than 100,000 different chemicals to see which had the potential to make beta cells grow. They identified 86 possible solutions and tested each manually. Of these, a single drug triggered beta cell growth: harmine.

Harmine occurs naturally in a number of plants around the world. It’s one of the ingredients in the psychoactive mixture ayahuasca, which is used by some indigenous people for religious purposes.
The Path to New Treatments

To confirm that harmine would cause beta cell growth, the team took islets from the pancreases of deceased human organ donors.

Then, they transplanted the islets into diabetic mice. They used far fewer than were necessary to cure the mice’s diabetes. Dosing the mice with harmine triggered the beta cells to multiply enough that they could restore the mice’s blood sugar levels to normal.

Stewart cautions that harmine itself isn’t the answer. Instead, harmine might inspire similar drugs that hone in on beta cells and leave the rest of the body, especially the brain, alone.

*We have no way to target drugs specifically to human beta cells. That’s what we need to do next.*

Andrew Stewart, Icahn School of Medicine
“We have no way to target drugs specifically to human beta cells,” Stewart said. “That’s what we need to do next. We need to figure out a way to get harmine directed to beta cells specifically and to no other tissue.”

It also won’t cure diabetes on its own. Even if the beta cells regrow, there’s still the problem that damaged them in the first place.

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**Related News: Scientists Make Insulin-Producing Cells from Stem Cells to Cure Type 1 Diabetes »**

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It also won’t cure diabetes on its own. Even if the beta cells regrow, there’s still the problem that damaged them in the first place.

For example, in people with type 1 diabetes, the body’s own immune system has attacked and destroyed the beta cells. Without complementary drugs to keep the immune system in check, newly grown beta cells might also be destroyed.

Still, the team’s discovery is another important step toward developing a medication that may someday reverse diabetes.

Stewart adds that this research would not have been possible without the support of the National Institutes of Health and the Juvenile Diabetes Research Foundation.
Harmine drug that restores beta cells seen as key diabetes treatment

A chemical called harmine, which occurs naturally in a number of plants around the world, has been shown to regenerate pancreatic cells lost in diabetes.

Type 1 diabetes is characterised by the immune system attacking insulin-producing pancreatic beta cells, while beta cell deficiency has been observed as a contributor to type 2 diabetes.

What is harmine?

Harmine is derived from Harmal, a flowering plant, but the drug is known for its psychoactive effects on the brain. It is an ingredient in the psychoactive mixture ayahuasca and is reportedly used in spiritual ceremonies.

Researchers at the Icahn School of Medicine at Mount Sinai, United States screened over 100,000 potential drugs to assess whether they had the potential to make beta cells grow.

To do this, they designed a sensor to glow following activation of a DNA snippet responsible for turning on the c-MYC gene, a regulator gene. 86 solutions caused the brightest glow, but harmine was the only drug that triggered beta cell growth.

When pancreatic islet cells were transplanted into diabetic mice, harmine treatment tripled the number of beta cells and restored the blood sugar levels of the mice to normal.

Key step forward

Dr Andrew Stewart, Director of the Diabetes, Obesity and Metabolism Institute at the Icahn School of Medicine in the US, concluded: "We believe these results represent a key step toward more effective treatment of diabetes.

"Our results provide a large body of evidence demonstrating that the harmine drug class can make human beta cells proliferate at levels that may be relevant for diabetes treatment. We still have a lot of work to do in improving the specificity and potency of the harmine and related compounds," Stewart added.

The study was funded by grants from JDRF and the National Institutes of Health, with the results published online in Nature Medicine.
Harmala alkaloid

_Harmala alkaloid_ 

*Peganum harmala*, commonly known as Syrian Rue

Several **alkaloids** that function as **monoamine oxidase inhibitors** (MAOIs) are found in the **seeds** of *Peganum harmala* (also known as *Harmal* or *Syrian Rue*), as well as **tobacco** leaves including **harmine**, **harmaline**, and **harmol**, which are members of a group of substances with a similar chemical structure collectively known as **harmala alkaloids**. These alkaloids are of interest for their use in Amazonian shamanism, where they are derived from other plants. The harmala alkaloid **harmine**, once known as **telepathine** and **banisterine**, is a naturally occurring **beta-carboline** alkaloid that is structurally related to **harmaline**, and also found in the vine *Banisteriopsis caapi*. **Tetrahydroharmine** is also found in *B. caapi* and *P. harmala*. Dr. Alexander Shulgin has suggested that harmine may be a breakdown product of harmaline. **Harmine** and **harmaline** are **reversible MAOIs** of the **MAO-A** isoenzyme of the enzyme, and can stimulate the central nervous system by inhibiting the metabolism of monoamine compounds such as **serotonin** and **norepinephrine**.

The harmala alkaloids occur in *Peganum harmala* in concentrations of roughly 3%, though tests have documented anywhere from 2-7% or even higher, as natural sources tend to vary widely in chemical makeup. Harmala alkaloids are also found in the **sacramental beverage** Ayahuasca, in concentrations that range between 0.31-8.43% for harmine, 0.03-0.83% for harmaline and 0.05-2.94% for tetrahydroharmine. Although other psychoactive plants are occasionally added to Ayahuasca to achieve visionary states of consciousness, the recipes vary greatly and no single combination is common. *Peganum harmala*, normally consumed as a tea or used as an incense, is mentioned in classical Persian literature both as a sacred sacrament and as a medicine. The harmala alkaloids are not especially psychedelic, even at higher dosages, when hypnagogic visions, alongside vomiting and diarrhea, become the main effect.

Harmala alkaloids are also found in many other plants, such as **passion flower**. The leaves of *P. incarnata* have been reported variously to give 0.005%, 0.12 mg%, and nil, of harman alkaloids.

**Telepathine**

**Telepathine** was originally thought to be the active chemical constituent of *Banisteriopsis caapi*, a key plant ingredient in the preparation of ayahuasca; a sacramental beverage from the Amazon. This isolated chemical was so named because of the reported effects of Ayahuasca among the indigenous users, including: collective contact with and/or visions of jaguars, snakes, and jeweled birds, and ancestral spirits; the ability to see future events; and as the name suggests, **telepathic** communication among tribal members. It was assumed to be a newly
discovered chemical at the time, however, it was soon realized that Telepathine was already more widely known as "harmine" from its previous discovery in *Peganum harmala* (Syrian Rue).

**Uses**

Harmaline and harmine fluoresce under ultraviolet light. These three extractions indicate that the middle one has a higher concentration of the two compounds.

As mentioned above, some harmala alkaloids can be used as an monoamine oxidase inhibitor (MAOI) to facilitate the ingestion of DMT and other tryptamines; while not generally used as a hallucinogen alone, there are reports of such use.[8] In high doses, it acts as purgative. Harmala alkaloids from *Banisteriopsis caapi* have been used to treat Parkinson's disease[citation needed], As abenzodiazepine site inverse agonist, harmala alkaloids are used as a model for Essential Tremor (ET) when injected to animals. Rats being treated with harmaline exhibit severe tremors after 5–7 minutes. Individuals diagnosed with Essential Tremor have been found to have elevated blood levels of harmala alkaloids.[6]

Unlike many synthetic pharmaceutical MAOIs such as phenelzine, harmine is reversible and selective meaning it does not have nearly as high a risk for the "cheese syndrome" caused by consuming tyramine-containing foods, which is a risk associated with monoamine oxidase A inhibitors, but not monoamine oxidase B inhibitors.[7] Both MAO-A and MAO-B break down tyramine, but large doses of harmala alkaloids begin to affect MAO-B as well.

**Anticancer**

Isolated harmine was found to exhibit a cytotoxic effect on HL60 and K562 leukemic cell lines. This action might explain the previously observed cytotoxic effect of *P. harmala* on these cancer cells.[9]

**Neuroprotective**

Norharmane exerts neuroprotective properties by suppressing kynurenine neurotoxic metabolites such as quinolinic acid, 3OH-kynurenine and nitric oxide synthase.[9]

**Legal Status**

**Australia**

Harmala alkaloids are considered Schedule 9 prohibited substances under the Poisons Standard (October 2015).[10] A Schedule 9 substance is a substance which may be abused or misused, the manufacture, possession, sale or use of which should be prohibited by law except when required for medical or scientific research, or for analytical, teaching or training purposes with approval of Commonwealth and/or State or Territory Health Authorities.[10]

Exceptions are made when in herbs, or preparations, for therapeutic use such as : (a) containing 0.1 per cent or less of harmala alkaloids; or (b) in divided preparations containing 2 mg or less of harmala alkaloids per recommended daily dose.[10]
Chemical forms

- **Harmine**: C$_{13}$H$_{12}$N$_2$O
  7-Methoxy-1-methyl-9H-pyrido[3,4-b]indole

- **Harmaline**: C$_{13}$H$_{14}$N$_2$O
  4,9-Dihydro-7-methoxy-1-methyl-3H-pyrido[3,4-b]indole

- **Harmalol**: C$_{12}$H$_{12}$N$_2$O
  1-Methyl-4,9-dihydro-3H-pyrido[3,4-b]indol-7-ol

- **Tetrahydroharmine**: C$_{13}$H$_{14}$N$_2$O
  1,2,3,4-tetrahydro-harmine

- **Harmalan**: C$_{12}$H$_{10}$N$_2$
  1-Methyl-3,4-dihydro-beta-carboline. Harmalan occurs in foodstuffs.\[12\]
• **Harmine acid**: methylester: 
  Methyl-7-methoxy-\textit{beta}-carboline-1-carboxylate

• **Harmilinic acid**: 
  7-Methoxy-3,4-dihydro-\textit{beta}--carboline1-carboxylic acid

• **Harmanamide**: 
  1-Carbamoyl-7-methoxy-\textit{beta}-carboline

• **Acetylnorharmine**: 
  1-Acetyl-7-methoxy-\textit{beta}-carboline

**See also**

- Harmane
- Beta-carboline (norharmane)
- Monoamine oxidase inhibitor
- Reversible inhibitor of monoamine oxidase A (RIMA)

**References**


11. Edward J. Massaro, Handbook of Neurotoxicology