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## Answers to Diabetes Part 3: Type 2 Diabetes

Dr. Bryan Ardis D.C.



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# Type 2 Diabetes

Type 2 diabetes happens when your body can't use insulin properly. Without treatment, Type 2 diabetes can cause various health problems, like heart disease, kidney disease and stroke.

You can manage this disease by making lifestyle changes, taking medications and seeing your healthcare provider for regular check-ins.

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>



# What is Type 2 diabetes?

Type 2 diabetes (T2D) is a chronic condition that happens when you have persistently high blood sugar levels (hyperglycemia).

Healthy blood sugar (glucose) levels are 70 to 99 milligrams per deciliter (mg/dL). If you have undiagnosed Type 2 diabetes, your levels are typically 126 mg/dL or higher.

T2D happens because your pancreas doesn't make enough insulin (a hormone), your body doesn't use insulin properly, or both. This is different from Type 1 diabetes, which happens when an autoimmune attack on your pancreas results in a total lack of insulin production.

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>

## How common is Type 2 diabetes?

Type 2 diabetes is very common. More than 37 million people in the U.S. have [diabetes](#) (about 1 in 10 people), and about 90% to 95% of them have T2D.

★ Researchers estimate that T2D affects about 6.3% of the world's population. T2D most commonly affects adults over 45, but people younger than 45 can have it as well, including children.

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>





## Type 2 Diabetes

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### KEY POINTS

- About 1 in 10 Americans has diabetes; most have type 2.
- More children, teens, and young adults are developing type 2 diabetes than in the past.
- Type 2 diabetes can be prevented or delayed with lifestyle changes.



### Overview

More than 38 million Americans have diabetes (about 1 in 10), and about 90% to 95% of them have type 2 diabetes. Type 2 diabetes most often develops in people 45 or older, but more and more [children, teens](#), and young adults are also developing it.

#### ON THIS PAGE

[Overview](#)[Symptoms](#)[Risk factors](#)

<https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html>

## Overview

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- ★ More than 38 million Americans have diabetes (about 1 in 10), and about 90% to 95% of them have type 2 diabetes. Type 2 diabetes most often develops in people 45 or older, but more and more [children](#), [teens](#), and young adults are also developing it.

## Symptoms

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Type 2 diabetes [symptoms](#) often develop over several years and can go on for a long time without being noticed. Sometimes there aren't any noticeable symptoms at all.

<https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html>



## TYPE 2

## Body can't use insulin properly



Can develop at  
any age



Most cases **can**  
be prevented

90-95%

In adults, type 2 diabetes  
accounts for approximately  
**90-95%** of all diagnosed  
cases of diabetes.

nearly  
**5,300**

Nearly **5,300** youth  
diagnosed each year in  
2017 and 2018

### Risk factors for type 2 diabetes:



Being  
overweight



Having a family  
history



Being physically  
inactive



Being 45 or  
older

**1.2 Million**

People **18 years or older**  
diagnosed with diabetes  
in 2021

<https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html>

## What are the symptoms of Type 2 diabetes?

Symptoms of Type 2 diabetes tend to develop slowly over time. They can include:

- Increased thirst ([polydipsia](#)).
- [Peeing more frequently](#).
- Feeling hungrier than usual.
- [Fatigue](#).
- Slow healing of cuts or sores.
- Tingling or [numbness in your hands](#) or feet.
- [Blurred vision](#).
- [Dry skin](#).
- [Unexplained weight loss](#).

★ Women may experience frequent [vaginal yeast infections](#) and/or [urinary tract infections \(UTIs\)](#).

### Symptoms of Type 2 diabetes



**Increased thirst.**



**Unexplained weight loss.**



**Increased hunger.**



**Fatigue.**



**Slow healing.**



**Numbness in hands or feet.**



**Blurred vision.**



**Frequent urination.**



**Dry skin.**

 Cleveland Clinic

Symptoms of Type 2 diabetes tend to develop slowly over time. It's important to see a healthcare provider if you have them.

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>



## What are the risk factors for Type 2 diabetes?

You're more likely to develop Type 2 diabetes if you:

- Have a family history of Type 2 diabetes (biological parent or sibling).
- Are older than 45.
- Have [overweight](#) or obesity (a [BMI](#) greater than 25). ★
- Are physically active less than three times a week. ★
- Are Black, Hispanic, Native American, Asian American or Pacific Islander.
- Had [gestational diabetes](#) while pregnant.
- Have [high blood pressure](#) and/or [high cholesterol](#). ★
- Have [prediabetes](#). ★
- Have [polycystic ovarian syndrome \(PCOS\)](#).

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>

## Type 2 diabetes medications

Your healthcare provider may recommend taking medication, in addition to lifestyle changes, to manage Type 2 diabetes. These include:

- **Oral diabetes medications:** These are medications that you take by mouth to help manage blood sugar levels in people who have T2D but still produce some insulin. There are several types. The most commonly prescribed one is metformin. Your provider may prescribe more than one oral diabetes medication at a time to achieve the best blood glucose management.
- **GLP-1 and dual GLP-1/GIP agonists:** These are injectable medications that mainly help manage blood sugar levels in people with T2D. Some GLP-1 agonists can also help treat obesity.
- **Insulin:** Synthetic insulin directly lowers blood sugar levels. There are several types of insulin, like long-acting and short-acting types. You may inject it with syringes or pens, use inhaled insulin, or use an insulin pump.

<https://my.clevelandclinic.org/health/diseases/21501-type-2-diabetes>





## What These Prescribed "Medications" Actually Do!!

# Metformin

**Generic name:** metformin [ *met-FOR-min* ]

**Brand names:** Fortamet, Glucophage, Glucophage XR, Glumetza, Riomet

**Drug class:** Non-sulfonylureas



Medically reviewed by Melisa Puckey, BPharm. Last updated on Aug 22, 2023.

[Uses](#) | [Warnings](#) | [Before taking](#) | [Dosage](#) | [Side effects](#) | [Interactions](#) | [FAQ](#)

## What is metformin?

- ★ Metformin is an FDA-approved antidiabetic agent that manages high blood sugar levels in type 2 diabetes patients. It reduces glucose absorption from the intestines, lowers liver glucose production, and improves insulin sensitivity. Metformin is recommended with dietary changes and exercise for better results.

<https://www.drugs.com/metformin.html>

# Metformin

**Generic name:** metformin [ *met-FOR-min* ]

**Brand names:** Fortamet, Glucophage, Glucophage XR

**Drug class:** Non-sulfonylureas



Medically reviewed by Melisa Puckett

[Uses](#) | [Warnings](#) | [Before taking](#)

## What is metformin?

Metformin is an FDA-approved antidiabetic medication for type 2 diabetes patients. It reduces glucose absorption in the intestines and improves insulin sensitivity. Metformin is recommended for the treatment of type 2 diabetes.

## Important warnings

This medicine can cause some serious health issues

**Oral route (tablet; tablet, extended release; solution; suspension, extended release)**

Death, hypothermia, [hypotension](#), and resistant bradyarrhythmias have been reported due to metformin-associated [lactic acidosis](#).

Onset may be subtle and include nonspecific symptoms such as malaise, myalgia, respiratory distress, somnolence, and abdominal distress; laboratory abnormalities include low pH, increased anion gap and elevated blood lactate.

The risk of lactic acidosis increases with renal or hepatic impairment, aged 65 years or older, having a radiological study with contrast, surgery, or other procedures, hypoxic states, and excessive alcohol intake.

If lactic acidosis is suspected, metformin hydrochloride should be discontinued, supportive measures started in a hospital setting.

Prompt [hemodialysis](#) is recommended.

<https://www.drugs.com/metformin.html>



Under certain conditions, too much metformin can cause lactic acidosis. The symptoms of lactic acidosis are severe and quick to appear, and usually occur when other health problems not related to the medicine are present and are very severe, such as a heart attack or kidney failure. Symptoms of lactic acidosis include abdominal or stomach discomfort, decreased appetite, diarrhea, fast or shallow breathing, a general feeling of discomfort, severe muscle pain or cramping, and unusual sleepiness, tiredness, or weakness.

This medicine may cause some premenopausal women who do not have regular monthly periods to ovulate. This can increase the chance of pregnancy. If you are a woman of childbearing potential, you should discuss birth control options with your doctor.

This medicine may cause hypoglycemia (low blood sugar). This is more common when this medicine is taken together with certain medicines. *Low blood sugar must be treated before it causes you to pass out (unconsciousness). People feel different symptoms of low blood sugar.* It is important that you learn which symptoms you usually have so you can treat it quickly. Talk to your doctor about the best way to treat low blood sugar.

Hyperglycemia (high blood sugar) may occur if you do not take enough or skip a dose of your medicine, overeat or do not follow your meal plan, have a fever or infection, or do not exercise as much as usual. *High blood sugar can be very serious and must be treated right away. It is important that you learn which symptoms you have in order to treat it quickly.* Talk to your doctor about the best way to treat high blood sugar.

<https://www.drugs.com/metformin.html>

# Metformin Side Effects

Medically reviewed by Drugs.com. Last updated on Jun 11, 2025.

[Serious side effects](#) | [Other side effects](#) | [Professional info](#) | [FAQ](#)

Applies to **metformin**: oral solution, oral suspension extended release, oral tablet, oral tablet extended release, oral tablet extended release 24 hr.

## Metabolic

- **Common** (1% to 10%): Hypoglycemia ★
- **Very rare** (less than 0.01%): Lactic acidosis <sup>[Ref]</sup>

## Gastrointestinal

- **Very common** (10% or more): Diarrhea (53.2%), nausea/vomiting (25.5%), flatulence (12.1%)
- **Common** (1% to 10%): Indigestion, abdominal discomfort, abnormal stools, **dyspepsia**, loss of appetite <sup>[Ref]</sup>

<https://www.drugs.com/metformin.html>

## Dermatologic

- **Common (1% to 10%):** Rash, nail disorder, increased sweating
- **Very rare (less than 0.01%):** Erythema, pruritus, urticaria<sup>[Ref]</sup>

## Hematologic

- **Very rare (less than 0.01%):** Subnormal vitamin B12 levels<sup>[Ref]</sup>

## Other

- **Common (1% to 10%):** Asthenia, chills, flu syndrome, accidental injury<sup>[Ref]</sup>

## Cardiovascular

- **Common (1% to 10%):** Chest discomfort, flushing, palpitation<sup>[Ref]</sup>

## Endocrine

- **Frequency not reported:** Reduction in thyrotropin (TSH) levels<sup>[Ref]</sup>

<https://www.drugs.com/metformin.html>



## Immunologic

- Very common (10% or more): Infection (20.5%)<sup>[Ref]</sup>

## Musculoskeletal

- Common (1% to 10%): Myalgia<sup>[Ref]</sup>

## Nervous system

- Common (1% to 10%): Lightheadedness, taste disturbances<sup>[Ref]</sup>

## Psychiatric

- Common (1% to 10%): Headache<sup>[Ref]</sup>

## Respiratory

- Common (1% to 10%): Rhinitis<sup>[Ref]</sup>

<https://www.drugs.com/metformin.html>

## Serious side effects of metformin

Metformin can potentially cause some serious side effects.

### Lactic acidosis

Although it is rare, metformin's most serious side effect is [lactic acidosis](#). Metformin has a boxed warning — also called a black box warning — about this risk. A boxed warning is the most severe warning the FDA issues.

Lactic acidosis is a rare but serious problem resulting from a buildup of metformin in your body, which causes a pH imbalance. It's a medical emergency that must be treated immediately in the hospital.

<https://www.healthline.com/health/diabetes/metformin-side-effects#serious-side-effects>

## Serious side effects of metformin

Symptoms can include:

- extreme tiredness
- weakness
- decreased appetite
- nausea
- vomiting
- trouble breathing
- dizziness
- lightheadedness
- a fast or slow heart rate
- a cold feeling
- muscle pain
- flushing or sudden reddening and warmth in your skin
- stomach pain combined with any of these other symptoms

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Contact a doctor right away if you have any symptoms of lactic acidosis. If you have trouble breathing, call 911 or your local emergency number or go to the nearest emergency room.

Metformin-associated lactic acidosis has an estimated death rate of up to 50%.

Taking some other medications, including corticosteroids and blood pressure medications, with metformin may increase your risk of lactic acidosis. See the risk factors section for more information about factors that raise your risk of this complication.

<https://www.healthline.com/health/diabetes/metformin-side-effects#serious-side-effects>



## Serious side effects of metformin

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<https://www.healthline.com/health/diabetes/metformin-side-effects#serious-side-effects>

# Acarbose

**Generic name:** acarbose [ *ah-KAR-bose* ]

**Brand name:** Precose

**Dosage form:** oral tablet (100 mg; 25 mg; 50 mg)

**Drug class:** Alpha-glucosidase inhibitors



Medically reviewed by Drugs.com on Apr 9, 2024. Written by Cerner Multum.



[Uses](#) | [Side effects](#) | [Warnings](#) | [Before taking](#) | [Dosage](#) | [Interactions](#)

## What is acarbose?

★ Acarbose slows the digestion of carbohydrates in the body, which helps control blood sugar levels.

Acarbose is used together with diet and exercise to treat [type 2 diabetes](#). Acarbose is sometimes used in combination with insulin or other diabetes medications you take by mouth.

<https://www.drugs.com/mtm/acarbose.html>

Acarbose does not cause [hypoglycemia](#) (low blood sugar). However, low blood sugar can occur if you take acarbose with another type of diabetes medicine, delay or miss a meal or snack, exercise more than usual, drink alcohol, or cannot eat because of nausea or vomiting. Symptoms of low blood sugar must be treated before they lead to unconsciousness (passing out). Different people may feel different symptoms of low blood sugar. It is important that you learn which symptoms of low blood sugar you usually have so that you can treat it quickly.

Symptoms of low blood sugar include [anxiety](#); behavior change similar to being drunk; blurred vision; cold sweats; confusion; cool, pale skin; difficulty in thinking; drowsiness; excessive hunger; [fast heartbeat](#); [headache](#) (continuing); nausea; nervousness; nightmares; restless sleep; shakiness; slurred speech; or unusual tiredness or weakness.

[Hyperglycemia](#) (high blood sugar) may occur if you do not take enough or skip a dose of your antidiabetic medicine, overeat or do not follow your meal plan, have a fever or infection, or do not exercise as much as usual.

Symptoms of high blood sugar include blurred vision; drowsiness; [dry mouth](#); flushed, dry skin; fruit-like breath odor; increased urination; ketones in urine; loss of appetite; stomachache, nausea, or vomiting; tiredness; troubled breathing (rapid and deep); unconsciousness; or unusual thirst.

<https://www.drugs.com/mtm/acarbose.html>



# Acarbose Side Effects

Medically reviewed by Drugs.com. Last updated on Feb 26, 2025.

[Common side effects](#) | [Serious side effects](#) | [Professional info](#)

Applies to [acarbose](#): oral tablet.

## Gastrointestinal

- **Very common** (10% or more): Abdominal pain (19%), diarrhea (31%), flatulence (74%)
- **Uncommon** (0.1% to 1%): Nausea,, vomiting, [dyspepsia](#)
- **Postmarketing reports:** Ileus/subileus, pneumatosis cystoides intestinalis<sup>[Ref]</sup>

## Hepatic

- **Very common** (10% or more): Serum transaminase elevations (14%) ★
- **Postmarketing reports:**★ Fulminant hepatitis with fatal outcome, [jaundice](#) and/or hepatitis and associated liver damage<sup>[Ref]</sup>

<https://www.drugs.com/mtm/acarbose.html>

## Hematologic

- Frequency not reported: Small reductions in hematocrit
- Postmarketing reports: Thrombocytopenia<sup>[Ref]</sup>

## Dermatologic

- Frequency not reported: Acute generalized exanthematous pustulosis<sup>[Ref]</sup>

## Hypersensitivity

- Postmarketing reports: Hypersensitivity skin reactions (e.g. rash, erythema, exanthema, urticaria)<sup>[Ref]</sup>

## Cardiovascular

- Postmarketing reports: Edema<sup>[Ref]</sup>

## Metabolic

- Frequency not reported: Hypoglycemia, low serum calcium, low plasma vitamin B6 levels<sup>[Ref]</sup>

<https://www.drugs.com/mtm/acarbose.html>

# Ozempic

**Pronunciation:** *oh-ZEM-pick*

**Generic name:** semaglutide injection

**Dosage form:** Single-patient-use injection pen (multiple-strengths)

**Drug class:** GLP-1 receptor agonists



Medically reviewed by Melisa Puckey, BPharm. Last updated on June 16, 2025.

[Uses](#) | [Side effects](#) | [Warnings](#) | [Cost](#) | [Dosage](#) | [Interactions](#) | [FAQ](#)

## What is Ozempic?

**Ozempic (semaglutide) is a prescription medication used for adults with type 2 diabetes to lower their blood sugar levels (A1C).** It is also used to reduce the risk of kidney function decline in diabetics with [chronic kidney disease](#) (CKD) and lower the risk of [heart attack](#) or [stroke](#) in certain patients with type 2 diabetes and heart disease.

**Ozempic works by increasing insulin release, slowing stomach emptying, and reducing sugar production by the liver,** which results in improved blood sugar levels, prolonged fullness, and controlled appetite, which may lead to weight loss.

<https://www.drugs.com/ozempic.html>

## Common side effects

Common Ozempic side effects include nausea, vomiting, diarrhea, stomach pain, constipation, upset stomach, heartburn, burping, gas, bloating, loss of appetite, runny nose or sore throat, stomach flu symptoms or headache, dizziness, tiredness, and low blood sugar (in people with type 2 diabetes).

Stomach or gastrointestinal side effects are common but tend to be mild and clear up in a few weeks in most people and will not interfere with long-term treatment. Stomach side effects can be more common with higher doses.

The most common gastrointestinal side effect is nausea, which occurs in 15.8% to 20.3% of people taking Ozempic at doses of 0.5 mg or 1 mg, according to clinical trials.

- Others include vomiting (5% to 9.2%), diarrhea (8.5% to 8.8%), stomach-area pain (7.3% to 5.7%), and constipation (5% to 3.1%).

## ★ Serious side effects ★

Ozempic can cause serious side effects such as inflammation of the pancreas, vision changes, low blood sugar levels, kidney problems, and serious allergic reactions, and it can also increase the risk of food or liquid getting into your lungs during surgery or a medical procedure (see Ozempic side effects to watch for).

<https://www.drugs.com/ozempic.html>



This medicine can cause other serious side effects. Call your healthcare provider at once if you have:

- vision changes;
- unusual mood changes, thoughts about hurting yourself; ★
- pounding heartbeats or fluttering in your chest;
- a light-headed feeling, like you might pass out;
- signs of a thyroid tumor - swelling or a lump in your neck, trouble swallowing, a hoarse voice, feeling short of breath; ★
- symptoms of pancreatitis - severe pain in your upper stomach spreading to your back, nausea with or without vomiting, fast heart rate; ★
- gallbladder problems - upper stomach pain, fever, clay-colored stools, jaundice (yellowing of the skin or eyes);
- low blood sugar--headache, hunger, weakness, sweating, confusion, irritability, dizziness, fast heart rate, or feeling jittery; ★
- kidney problems - swelling, urinating less, blood in urine, feeling tired or short of breath
- stomach flu symptoms - stomach cramps, vomiting, loss of appetite, diarrhea (may be watery or bloody) ★
- symptoms of ileus (stomach paralysis) - bloating, stomach cramps or pain, nausea or vomiting, constipation or diarrhea, loss of appetite. ★

<https://www.drugs.com/ozempic.html>

## Ozempic Faces \$2 Billion in Lawsuits Over Severe Side Effects Including Stomach Paralysis and Vision Loss

2 months ago 4 min read



Feedback

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### Key Insights

- Over 1,800 lawsuits have been filed against Novo Nordisk's Ozempic in US federal courts, with legal analysts estimating total liability could exceed \$2 billion.
- Patients report severe complications including gastroparesis (stomach paralysis), intestinal blockages, gallbladder disease, and sudden vision loss linked to NAION.
- The litigation has been consolidated into multidistrict litigation in Pennsylvania, with bellwether trials expected to begin in early 2026.

Novo Nordisk's blockbuster **diabetes** and weight-loss drug **Ozempic** is facing one of the largest pharmaceutical legal battles in recent years, with over 1,800 lawsuits consolidated in US federal courts and potential damages estimated to exceed \$2 billion. The litigation represents a growing challenge for the Danish pharmaceutical giant as patients report severe, life-altering side effects they claim were inadequately disclosed.

<https://trial.medpath.com/news/e5ef868ff717e201/ozempic-faces-2-billion-in-lawsuits-over-severe-side-effects-including-stomach-paralysis-and-vision-loss>

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# Prescription Drugs That CAUSE HIGH Blood Sugar!

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DIABETES

## High Blood Sugar? It Could Be a Side Effect of These Medications

Written by [Jewels Doskicz, RN, BA](#) | Reviewed by [Farzon A. Nahvi, MD](#)  
Updated on November 22, 2024



RichLegg

**Key takeaways:**

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>



# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 1. Corticosteroids, like prednisone

Steroids, like [prednisone](#), are used to treat inflammation in lots of conditions, from rheumatoid arthritis and asthma to chronic obstructive pulmonary disease (COPD) and inflammatory bowel disease.

Steroids — either as pills or injection — can raise blood sugar levels while you're taking them (this is much less likely with inhaled steroids). This can be a problem in people who already have diabetes and in people who don't have diabetes.

Increased blood sugar is more likely if you take higher doses of steroids over the long term. It's also more common in people with risk factors for diabetes. This includes:

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 2. Beta blockers, like atenolol, metoprolol, and propranolol

[Atenolol](#), [metoprolol](#), and [propranolol](#) are beta blockers that treat heart problems like irregular heart rates and high blood pressure. But they can increase blood glucose in people with diabetes and cause new Type 2 diabetes in people who didn't have it before. This seems to happen because the beta blockers reduce how much insulin the pancreas makes.

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

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## 3. Hydrochlorothiazide and metolazone

Some other blood pressure medications, such as thiazide diuretics and thiazide-like diuretics, can have a similar effect. Like beta blockers, [hydrochlorothiazide](#) (HCTZ) and [metolazone](#) can [increase blood sugar](#) levels. They can also cause new Type 2 diabetes in as little as [9 to 18 weeks](#).

This seems to be more common the longer someone takes the medication. This also happens more often in people who have a higher risk of Type 2 diabetes. It's not clear exactly how it happens. But it's likely to be related to insulin production and how well the body responds to that insulin.

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 4. Statins, like simvastatin, atorvastatin, and rosuvastatin

There may be a link between regular use of statins — medications that treat high cholesterol — and a [small increase in glucose levels](#) in certain people. Other [studies](#) have suggested a slight increase in [A1C levels](#) (your average blood sugar levels over about 3 months). Statins seem to cause cells in the body to become resistant to insulin, the hormone that helps move glucose out of the blood and into cells.

But there are mixed results, so more research is needed to better understand how statins affect glucose management.

The risk is higher in people who take larger doses of statins, like 40 mg to 80 mg [atorvastatin](#) (Lipitor) or 20 mg to 40 mg [rosuvastatin](#) (Crestor) and [simvastatin](#). The risk is also higher for:

- Older adults
- People with risk factors for diabetes
- People who already have [prediabetes](#)

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>



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- Older adults
- People with risk factors for diabetes
- People who already have [prediabetes](#)

For most people, especially those who [already have diabetes](#), the benefit of taking statins far [outweighs](#) the small increased risk of Type 2 diabetes.

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 5. Quinolone antibiotics, like gatifloxacin

One class of antibiotics — quinolones — has [been linked](#) to both high and low blood sugar levels in people with Type 2 diabetes. This is most common with the quinolone antibiotic [gatifloxacin](#).

It's probably best to avoid quinolone antibiotics if you're older than 65 and have other risk factors for Type 2 diabetes. Other quinolones, like [ciprofloxacin](#) and [moxifloxacin](#), don't seem to have this effect.

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

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## 6. Leuprolide and goserelin

Many men with [prostate cancer](#) get [androgen deprivation therapy](#) with medications like:

- [Lupron](#) (leuprolide)
- [Zoladex](#) (goserelin)
- [Trelstar](#) (triptorelin)
- [Firmagon](#) (degarelix)

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 7. Antipsychotics, like olanzapine and clozapine

Newer antipsychotics, like [clozapine](#) and [olanzapine](#), cause an [increase in blood sugar levels](#) in people with diabetes and [increase the risk](#) of getting new Type 2 diabetes. This is most likely because they cause weight gain. But this link hasn't been seen with all antipsychotics.

[Risperidone](#) (Risperdal) and [quetiapine](#) (Seroquel) cause an increase in body weight. But [studies are mixed](#) on whether these medications are linked to an increase in diabetes.

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# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 8. Protease inhibitors to treat HIV

Protease inhibitors are one of six major classes of antiretroviral therapies for people living with HIV. But they have a long history of being linked to:

- Weight gain
- Metabolic syndrome
- [Raised blood sugar levels](#)
- New diabetes

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- Weight gain
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- [Raised blood sugar levels](#)
- New diabetes

In people with other risk factors for diabetes, it's probably a good idea to avoid medications like [atazanavir](#), [darunavir](#), and [ritonavir](#).

<https://www.goodrx.com/conditions/diabetes/drugs-that-raise-blood-sugar>

# Prescription Drugs That CAUSE HIGH Blood Sugar!

## 9. Some immunosuppressants, like cyclosporine, sirolimus, and tacrolimus

Calcineurin inhibitor medications are commonly used medications after organ transplants. Examples of these are cyclosporine, sirolimus, and tacrolimus. They've been linked to an increased risk of diabetes, especially in older adults and those who also take steroids. As many as [1 in 4 people](#) develop new diabetes in the 3 years after a kidney transplant.

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# Prescription Drugs That CAUSE HIGH Blood Sugar!

## Birth Control Pills

Birth control pills and other contraceptives have proven effective in preventing unwanted pregnancy. For women with diabetes, patches, implants, pills, injections, and rings have been checked to be safe options. However, it's no news that some present specific side effects when used.

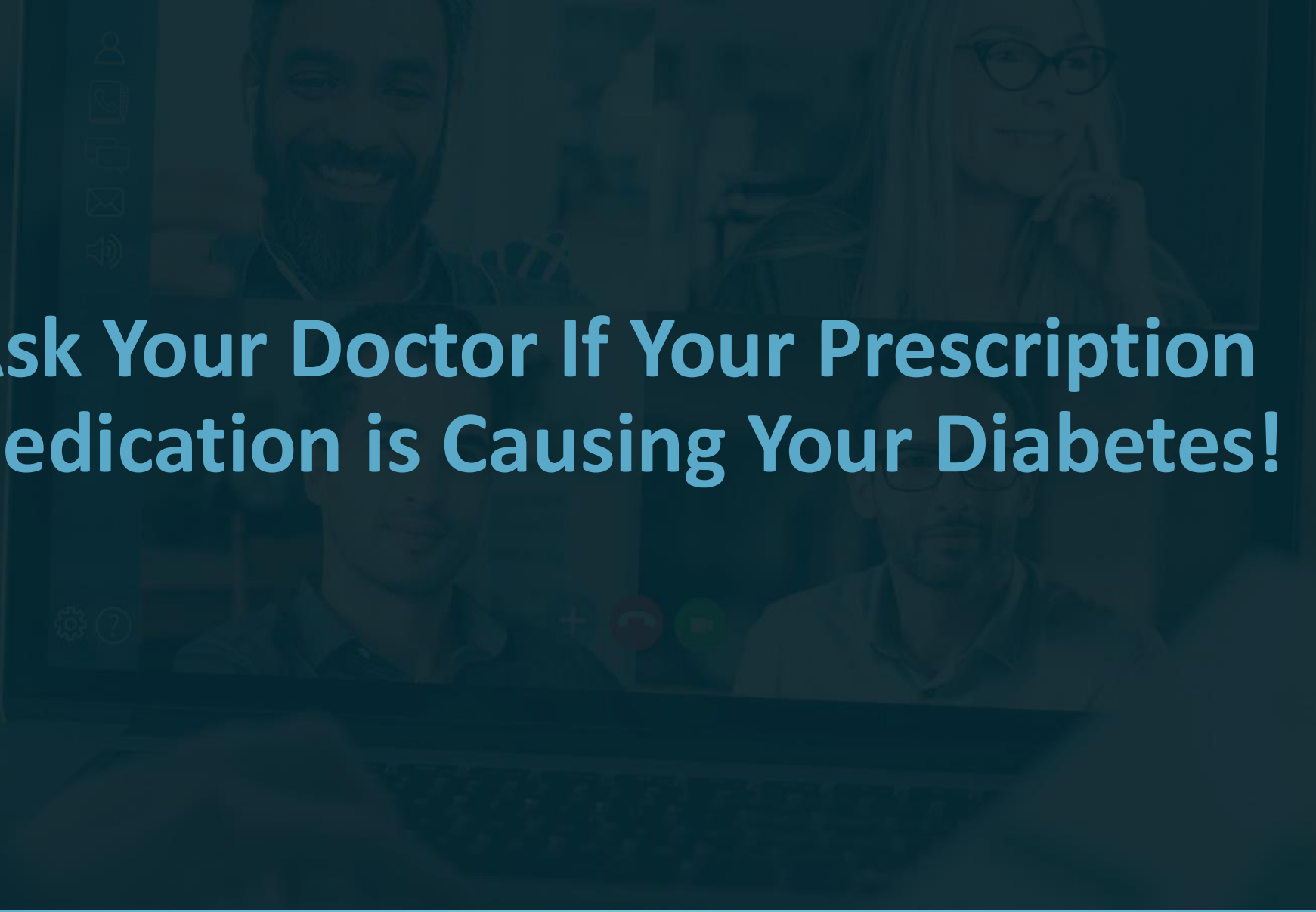
Several researchers have looked into the relationship between diabetes and birth control methods. For example, some claimed that estrogen in birth control pills could cause insulin resistance in some patients, eventually leading to blood sugar spikes. In contrast, others didn't find variation in blood glucose levels in women with diabetes taking birth control pills.

However, we can't overrule the findings of this research. Hence, physicians often recommend birth control pills with the minimum estrogen level for women with diabetes. At the same time, some physicians avoid prescribing birth control pills to women living with diabetes.

Furthermore, other researchers have linked birth control pills to some diabetic complications, especially when taken for over two years.

<https://mydiabetes.health/blog/drugs-that-raise-blood-sugar-levels/>








**Ask Your Doctor If Your Prescription  
Medication is Causing Your Diabetes!**



## Natural Ways to Handle Prediabetes!!



# Synergistic therapeutic effect of Guggul gum resin on antidiabetic activity of saxagliptin

Shalini Jain <sup>a</sup>, Mukesh Kumar Sharma <sup>b</sup>, Asad Syed <sup>c</sup>, Ali H. Bahkali <sup>c</sup>, Surendra Nimesh <sup>d</sup>, Nidhi Gupta <sup>e</sup>  , Sreemoyee Chatterjee <sup>e</sup> 

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(GE)= Guggul extract  
(SAXA)= Saxagliptin

Oxidative stress is the primary cause of the onset and progression of long-term diabetic complications. Also, it is a critical factor in the pathogenesis of diabetic complications, as excessive reactive oxygen species (ROS) contribute to cellular dysfunction. Persistent hyperglycemia may induce oxidative stress and cause liver, kidney, and pancreas ( $\beta$ -cell destruction) tissue damage [34,35]. In the present study, the increase in specific biomarker levels in the case of diabetic control suggests organ damage [36,37]. The restored levels of biochemical parameters, when GE was administered alone and in combination with SAXA, could be due to the numerous compounds present in GE. Guggul has been reported to contain 38 % oleo-gum resin [30]. Although this resin constitutes many compounds (such as steroids, flavones, lignans, tannins, cembrenoids and terpenes), it is now accepted that its pharmacological action can be owed to guggulsterone [30,38]. The two isomers E & Z guggulsterone have pronounced anti-inflammatory properties. These phytosterols can neutralize the generated reactive oxygen species (ROS), inhibit lipid peroxidation, and even induce metal chelation [39]. Both phytoconstituents are even antagonists for the farnesoid X receptor (FXR, a bile receptor), which is an important regulator of bile/cholesterol homeostasis [40]. Hence, the hypolipidemic activity and ability to reverse tissue damage (through minimizing oxidative stress) can be attributed majorly to these two phytosterols.

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## Saxagliptin Tablets

# Saxagliptin

**Generic name:** saxagliptin [ SAX-a-GLIP-tin ]

**Brand name:** Onglyza

**Dosage form:** oral tablet (2.5 mg; 5 mg)

**Drug class:** Dipeptidyl peptidase 4 inhibitors



Medically reviewed by Drugs.com on May 1, 2018

[Uses](#) | [Side effects](#) | [Warnings](#) | [E](#)

## What is saxagliptin?

Saxagliptin is used together with diet and exercise to treat [diabetes mellitus](#). Saxagliptin is not for treating

This medicine may cause serious allergic reactions, including [anaphylaxis](#), [angioedema](#), and serious skin reactions. These conditions may be life-threatening and require immediate medical attention. Check with your doctor right away if you have a rash, itching, a large, hive-like swelling on the face, eyelids, lips, tongue, throat, hands, legs, feet, or sex organs, skin flaking or peeling, trouble with breathing, or chest tightness while you are using this medicine.

This medicine may cause [hypoglycemia \(low blood sugar\)](#). This is more common when this medicine is taken together with certain medicines. *Low blood sugar must be treated before it causes you to pass out (unconsciousness). People feel different symptoms of low blood sugar.* It is important that you learn which symptoms you usually have so you can treat it quickly. Talk to your doctor about the best way to treat low blood sugar.

[Hyperglycemia \(high blood sugar\)](#) may occur if you do not take enough or skip a dose of your medicine, overeat or do not follow your meal plan, have a fever or infection, or do not exercise as much as usual. High blood sugar can be very serious and must be treated right away. It is important that you learn which symptoms you have in order to treat it quickly. Talk to your doctor about the best way to treat high blood sugar.

<https://www.drugs.com/mtm/saxagliptin.html>

(SOD)=  
superoxide  
dismutase

(GSH)= reduced  
glutathione  
levels

present study, the observed restoration of GSH levels and SOD activity in the liver and kidney following treatment with SAXA and GE suggests a significant enhancement of the antioxidant defense system in diabetic conditions. Previous studies have highlighted the protective effects of various herbal extracts on oxidative stress. For instance, GE has demonstrated substantial antioxidant properties in several assays, including DPPH, TAC, and FRAP [44]. The combination of SAXA and GE may synergistically enhance the bioavailability and efficacy of their active compounds, leading to improved antioxidant activity. Such interactions may involve multiple pathways, including modulation of the Nrf2 pathway, which regulates antioxidant responses [45]. Research has shown that increased oxidative stress is a critical factor in the progression of diabetes and its complications [46]. The observed results align with findings by other researchers, who reported similar protective effects of natural antioxidants in diabetic models [47]. These results underscore the potential of SAXA and GE as effective agents in mitigating oxidative stress, thereby contributing to better management of diabetes and its associated complications.

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The diabetes induction using STZ leads to progressive hyperglycemia with normal non-fasting insulin levels and damage to the preserved  $\beta$ -cell mass. The blood glucose level in T2DM rises due to insulin resistance and hence excess glucose is not converted into glycogen [48]. Hence the diabetic control showed low levels of total glycogen content. Guggulsterone, an active constituent of GE, possesses antioxidant properties that can inhibit the lipid peroxidation reaction and thus restore  $\beta$ -cell damage [6]. In the case groups treated with GE, the antioxidants present in the extract might have reversed the tissue damage of the pancreas which may lead to enhanced production of insulin. Hence, GE-treated groups have higher glycogen content than drugs. In the case of a combination dose, as both GE and SAXA are insulin enhancers, this treatment showed the highest glycogen content among all three treatment groups.

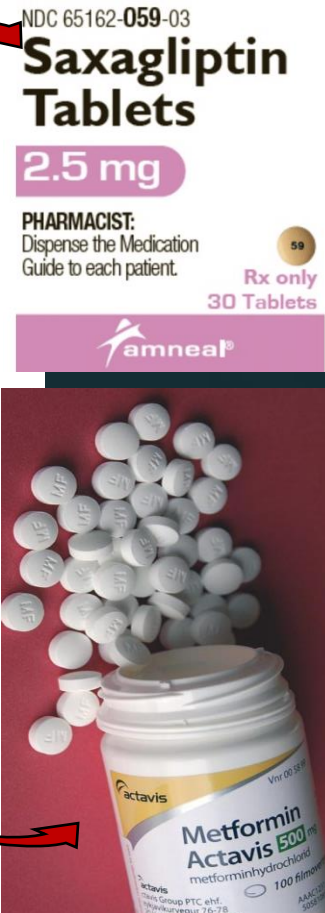
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high blood glucose level leads to the formation of ample reactive oxygen species (ROS) leading to the deterioration of renal tissue [50]. A similar type of damage in kidney and liver tissues is reflected in the induced-diabetic (diabetic control) group in the study. The induction of diabetes using STZ also led to  $\beta$ -cell necrosis [51] (shown by empty spaces) (Fig. 4b'). Although saxagliptin has been reported to attenuate liver inflammation and improve liver steatosis conditions, there is a case report stating saxagliptin-induced hepatotoxicity where steatohepatitis and intra-hepatic cholestasis were reported after consumption of Kombiglyze (Saxagliptin + Metformin) [52]. The drug is also reported to reduce renal tubulointerstitial inflammation but not glomerulosclerosis in *in vivo* mice models [53]. Hence, the SAXA-treated liver and kidney samples showed signs of damage and thus altered levels of biochemical parameters. The gliptins represent the only class of drugs that have the potency to improve  $\beta$ -cell health [3]. This drug is not only efficacious but also safe as it does not cause significant hypoglycemia. So, the  $\beta$ -cell architecture was restored in SAXA-treated pancreatic tissue but not the normal architecture was not reattained (Fig. 4c'). However, GE supplementation mitigated these histological changes,

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GE was observed to reduce the elevated levels of CYP3A11 expression in induced diabetes whereas SAXA was not able to significantly reduce the same when given alone. The STZ-induced diabetes results in an elevation in hepatic bile acids (due to liver damage) which further leads to indirect activation of constitutive androstane receptor (CAR). CAR activation, in turn, mediates the induction of CYP3A11 (murine homolog of CYP3A4) [59]. Also, it has been reported that the functional activity and expression (both mRNA and protein) of CYP3A4 increases during experimental diabetes (induced using STZ) due to the activity of various fatty acids. A similar type of elevation in the CYP3A11 level was observed in the case of STZ treatment in the current study [60]. The GE, when given in combination with SAXA, not only helped in controlling the BGL compared to the drug alone, but it also reduced the hepatic mRNA expression of CYP3A11. The results of histopathology can be corroborated here which indicates that the treatment of GE restored liver damage which further lowers the levels of hepatic bile acids and thus CAR-mediated induction of CYP3A11. The alone treatment of SAXA, on the other hand, could

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mediated induction of CYP3A11. The alone treatment of SAXA, on the other hand, could not significantly reduce these mRNA expression levels signifying that although it controls the levels of serum biomarkers and BGL, cannot aid in the significant reversion of liver tissue damage caused by STZ (as shown in Fig. 2b) compared to the condition where GE was given alone and in combination with SAXA [61]. As SAXA was not able to reverse diabetes-induced liver tissue damage, the CYP3A11 level is seen as high in this case when compared with other treatments. Saxagliptin is the only member of the class gliptin which is a substrate of CYP3A4. In humans, CYP3A4 metabolizes saxagliptin into an active metabolite, 5-hydroxy saxagliptin (5-OH SAXA), which is only half as potent as the parent drug [62,63]. The decrease in expression of CYP3A11 mRNA expression in mice after SAXA and GE administration alone or in combination here probably signifies that the parent drug will remain in the body longer, resulting in a prolonged pharmacological effect i.e. DPP-4 inhibition and thus restoration of BGL and other diabetes-induced alterations. However, to confirm the further induction or inhibition of this enzyme in the presence of GE, pharmacokinetic studies could be conducted in the future.

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## 5. Conclusions

From the present study, it can be concluded that GE can synergistically aid in improving the allopathic treatment of diabetes and its related secondary complications in the induced T2DM mice model. The combined GE + SAXA treatment showed a significant reduction in blood glucose levels and appropriate serum biomarkers along with an improved total lipid profile. The combination treatment also demonstrated synergistic effects by improving glucose tolerance and insulin sensitivity. The combination of SAXA and GE also demonstrated significant antioxidant effects, effectively restoring GSH levels and SOD activity, suggesting its potential as a therapeutic strategy for mitigating oxidative stress in diabetes. Moreover, several anti-inflammatory components (like

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# Effects of *guggulsterone* isolated from *Commiphora mukul* in high fat diet induced diabetic rats

Bhavna Sharma<sup>a</sup>, Rajani Salunke<sup>a</sup>, Swati Srivastava<sup>a</sup>, Chandrajeetbalo Majumder<sup>b</sup>, Partha Roy

<sup>a</sup>  

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Partially purified fraction of gum resin, commonly known as guggul lipid, has been well documented for its lipid lowering effects (Urizar and Moore, 2003). Results from our study have further proved the efficacy of the purified *guggulsterone* in lowering TG, LDL, TC and improvement in the level of HDL. Histopathological examination of the liver sections from diabetic group showed significant steatosis (also called fatty liver change) i.e. abnormal retention of lipids within the liver cells which can be correlated to abnormal synthesis and elimination of TG. However, treatment with *guggulsterone* showed improvement in TG accumulation as demonstrated by absence of steatosis in treated group. This can be correlated with various studies where guggul lipids and synthetic derivatives of *guggulsterone* have been intensively studied for their hypolipidemic effects. In these studies, synthetic *guggulsterone E* and *Z* isomers were proposed as antagonist for farnesoid X receptor (FXR) a nuclear receptor that inhibits bile acid production from cholesterol via inhibiting cholesterol 7 $\alpha$ -hydroxylase (CYP7A1) gene transcription (Sinal and Gonzalez, 2002, Deng et al., 2007). So far majority of studies

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gene transcription (Sinal and Gonzalez, 2002, Deng et al., 2007). So far majority of studies focused on the medicinal properties of *guggulsterone* and/or its synthetic isomers, with major emphasis on lipid metabolism. However, to the best of our knowledge for the first time we propose here the direct effect of isolated *guggulsterone* on carbohydrate metabolism. Expression profile of various genes related to glucoregulation i.e. glucokinase, phosphoenolpyruvate carboxykinase, and glucose-6-phosphatase from diabetic and treated group clearly showed the direct effect of *guggulsterone* on glucoregulation. High G6Pase and low hexokinase activity is a characteristic feature of insulin resistance which results in hyperglycemia. Treatment with *guggulsterone* resulted in the inversion of this condition in the treated group which can be further correlated with a parallel change in the expression profiles of these enzymes when compared to the diabetic group.

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Remarkable changes were observed in the adipose tissue of *guggulsterone* treated group along with a significant improvement in the expression profile of different target genes providing a preliminary idea about the mechanism of action of *guggulsterone*. Increased expression of glut-4 and at the same time reduced expression of TNF- $\alpha$  explains improvement in insulin resistance. PPAR, a sub-family of the 48-member steroid and nuclear receptor superfamily, are ligand dependent transcription factors that controls energy homeostasis by regulating carbohydrate and lipid metabolism (Shen et al., 2006).

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They exist in three different subtypes: PPAR $\alpha$ , PPAR $\beta/\delta$  and PPAR $\gamma$  out of which PPAR $\alpha$  is expressed in liver, kidney, heart, muscles and are involved in lipoprotein metabolism while PPAR $\gamma$  are predominantly expressed in adipose tissue and are involved in controlling insulin resistance, adipocyte differentiation and lipid storage. Due to their insulin receptor sensitizing activity, the agonists for these receptors (thiazolidinediones) are used in treatment of type II diabetes mellitus. In our study, activity of PPAR $\gamma$  showed significant improvement during different levels of analysis. Improvement in PPAR $\gamma$  activity was clearly evident from the expression profile and western blot analysis of the target genes. Transactivation assay further proved the role of guggulsterone in transactivating exclusively the PPAR $\gamma$  gene in a dose dependent manner, although the effect was marginal (20%) as compared to rosiglitazone. This compound however failed to transactivate the PPAR $\alpha$ . This conclusively proved that the phytochemical specifically acts as PPAR $\gamma$  activator. However, a recent finding showed that the *guggulsterone* did not

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Taken together, it is clearly evident from above results and observations that guggulsterone has immense potential for the treatment of diabetes not only as a hypolipidemic agent but also by its ability to act directly on different critical nodes of carbohydrate and lipid metabolic pathways. One of the most interesting features of this molecule is that it inhibited the differentiation of 3T3-L1 preadipocytes unlike any potent PPAR $\gamma$  agonist. This unique feature of *guggulsterone* as PPAR $\gamma$  ligand suggested that the mechanisms underlying the increased insulin sensitivity and adipogenicity may be separate. One possible explanation for the inhibition of adipocyte differentiation by *guggulsterone* could be the absence of coordination of PPAR and C/EBP family of protein in these cells, which are the prerequisite for the differentiation of adipocyte (Yang et al., 2008). Reduced blood cholesterol and TG levels can also provide a possible explanation for the increased insulin sensitivity and improved peripheral glucose clearance during OGTT. Further a significant inhibition of 3T3-L1 adipocyte supports the anti-obesity potential of *guggulsterone*. In brief, the obtained results give us an idea that this phytochemical could be probably utilized for the development of novel drugs having multiple potentialities for cure and management of type II diabetes. However, further

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## PPAR Agonists: Definition and Overview

BY ROBERT S. DINSMOOR | JUNE 15, 2006

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### What is a PPAR agonist?

PPAR agonists are a family of drugs that activate certain proteins in the body called peroxisome proliferator-activated receptors (PPARs). The PPAR agonists can help to improve blood glucose levels and levels of blood lipids (fats and [cholesterol](#)) and may also reduce risks of [atherosclerosis](#) because PPARs regulate the expression of genes that affect blood lipid metabolism, the generation of adipocytes (fat cells), and blood glucose control.



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Since the commonly used insulin sensitizer  
thiazolidinediones,  
have been reported to be associated with increased risk of massive hepatic necrosis, heart  
failure, and bladder cancer in patients treated with these drugs [\[6\]](#)–[\[8\]](#)

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#### JOURNAL ARTICLE

## Nighttime Administration of Nicotine Improves Hepatic Glucose Metabolism via the Hypothalamic Orexin System in Mice <sup>FREE</sup>

Hiroshi Tsuneki ✉, Takashi Nagata, Mikio Fujita, Kanta Kon, Naizhen Wu,  
Mayumi Takatsuki, Kaoru Yamaguchi, Tsutomu Wada, Hisao Nishijo, Masashi Yanagisawa  
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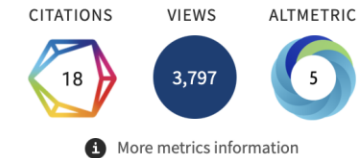
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### Abstract

Nicotine is known to affect the metabolism of glucose; however, the underlying mechanism remains unclear. Therefore, we here investigated whether nicotine promoted the central regulation of glucose metabolism, which is closely linked to the circadian system. The oral intake of nicotine in drinking water, which mainly occurred during the nighttime active period, enhanced daily hypothalamic *prepro-orexin* gene expression and reduced hyperglycemia in type 2 diabetic *db/db* mice without affecting body weight, body fat content, and serum levels of insulin.



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The hypothalamus regulates glucose homeostasis by synchronizing metabolic functions with sleep/wake and fasting/feeding cycles under the control of the circadian clock system (30). Hypothalamic orexin has been shown to coordinate these functional links (31). In the present study, we explored the role of the nicotinic cholinergic system in the central regulation of glucose metabolism using nicotine. Although the observed effects of nicotine on blood glucose levels were moderate, we found that the daily nicotinic stimulation improved hepatic glucose metabolism via the hypothalamic orexin system with unique chronopharmacological profiles especially under the severe insulin resistant condition.

<https://academic.oup.com/endo/article/157/1/195/2251841>



Nicotine is one of the constituents of tobacco. The oral intake of drinking water containing nicotine at 60  $\mu\text{g/mL}$ , similar to the doses used in our study (20–50  $\mu\text{g/mL}$ ), was previously reported to increase plasma nicotine concentrations up to 0.2  $\mu\text{M}$  in mice, which is similar to the plasma levels observed in smokers (32). Nicotine (<100  $\mu\text{g/mL}$  in drinking water) has been shown to have no effect on body weight, food intake, locomotor activity, or addictive behaviors (32–34). Under such conditions, we observed that nicotine preferentially caused glucose-lowering effects in mice. These findings suggest that low-dose nicotine has the capacity to improve glucose metabolism at least in rodents.

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The disruption of circadian rhythms triggers the development of glucose intolerance and insulin resistance, whereas the restoration of circadian rhythms by genetic rescue, time-of-day-restricted feeding, and pharmacological agents targeting biological clock components improves glucose metabolism in type 2 diabetic animals (37). A major result of the present study was that the glucose-lowering effects of nicotine depended on the treatment-time-of-day. Namely, the ad libitum intake of nicotine-containing water, which was largely restricted to the nighttime active period, reduced blood glucose levels in the daytime resting state (at ZT 2) in diet-induced obese mice. Moreover, the nighttime injection of nicotine (at ZT 14) reduced hyperglycemia in the daytime resting state (at ZT 2) in db/db mice. Previous studies have consistently demonstrated that chronic daily injections of nicotine (administered more frequently or for a longer period of time than in our study) or the ad libitum oral intake of a nicotine-containing solution increased insulin sensitivity in rodents (9, 10, 38),

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Another major result of the present study was that the chronic oral nicotine treatment suppressed hepatic gluconeogenesis via the hypothalamic orexin system in mice, whereas an injection of nicotine acutely elevated blood glucose levels in an orexin-independent, but sympathetic nerve pathway-dependent manner. Moreover, the chronic effects of nicotine disappeared in parasympathectomized mice. These results suggested that the daily oral consumption of nicotine according to the light/dark cycle promoted the daily action of endogenous orexin, leading to the suppression of hepatic gluconeogenesis via the parasympathetic nervous system. In fact, the chronopharmacological profiles of nicotine-induced glucose reduction were similar to those of orexin A in *db/db* mice, as shown in our previous study (15). In addition,

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# Orexin ←

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Orexin, also known as hypocretin, is defined as an endogenous peptide that exists in two forms, orexin-A and orexin-B, and is involved in regulating feeding behavior, metabolism, the sleep-wake cycle, and the endocrine system. It specifically binds to orexin receptors OX1R and OX2R, with orexin-A having high affinity for both receptors and orexin-B selectively binding to OX2R.

<https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/orexin>



nicotine selectively increased the expression of orexin in the hypothalamus of type 2 diabetic *db/db* mice in the late phase of the active period. Thus, it appears that both nighttime administration of orexin and nighttime activation of the orexin system by nicotine facilitate the daily glucose oscillation via bidirectional regulation of hepatic glucose production, leading to the delayed glucose-lowering effect in the daytime resting state in mice. Because the expression of orexin is down-regulated by hyperglycemia (39) and because the diurnal rhythm in orexin gene expression is dampened in diet-induced obese mice (40), a timely nicotinic stimulation may represent a valuable approach to restore impaired orexin function in the diabetic state.

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Hepatic glucose production is regulated by the central and autonomic nervous systems, in addition to hormonal systems (1). Neural signals from the brain through the autonomic nervous system have been shown to elicit IL-6-STAT3 signaling in the liver, thereby suppressing hepatic gluconeogenesis (43) or preventing hepatic inflammation relevant to insulin resistance (44). Although the precise mechanisms responsible remain unclear, the parasympathetic nerve pathway is considered to be involved in the production of IL-6 by Kupffer cells in the liver (45). Nicotine has been shown to promote IL-6 production (46) and STAT3 phosphorylation in the liver of normal rodents (9, 47). We consistently observed that the chronic nicotine treatment increased the expression of IL6 and phosphorylation of STAT3 in the liver of db/db mice. The effects of nicotine were accompanied by decreases in the expression of G6Pase, but not *Pepck*, resulting in a partial suppression of hepatic gluconeogenesis. This may explain

<https://academic.oup.com/endo/article/157/1/195/2251841>



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## **Chronic Exposure to Nicotine Enhances Insulin Sensitivity through $\alpha 7$ Nicotinic Acetylcholine Receptor-STAT3 Pathway**

[Tian-Ying Xu](#)<sup>1,#</sup>, [Ling-Ling Guo](#)<sup>1,#</sup>, [Pei Wang](#)<sup>1</sup>, [Jie Song](#)<sup>1</sup>, [Ying-Ying Le](#)<sup>2</sup>, [Benoit Viollet](#)<sup>3,4</sup>, [Chao-Yu Miao](#)<sup>1,\*</sup>

Editor: Srikumar P Chellappan<sup>5</sup>

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<https://pmc.ncbi.nlm.nih.gov/articles/PMC3520975/>

Insulin resistance occurs in 20%–25% of the human population [1]. It is a chief component of type 2 diabetes mellitus and an important risk factor for cardiovascular disease as well as certain forms of cancer [2]–[5]. Since the commonly used insulin sensitizer thiazolidinediones, selective agonists for nuclear peroxisomal proliferator-activated receptor- $\gamma$ , have been reported to be associated with increased risk of massive hepatic necrosis, heart failure, and bladder cancer in patients treated with these drugs [6]–[8], it is of great value to identify new therapeutic targets for development of novel therapy against insulin resistance.

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<https://pmc.ncbi.nlm.nih.gov/articles/PMC3520975/>

## What are thiazolidinediones?

TZDs, also known as “glitazones,” are used in [the treatment of Type 2 diabetes](https://www.singlecare.com/drug-classes/thiazolidinediones). TZDs help with blood sugar control and insulin resistance.

<https://www.singlecare.com/drug-classes/thiazolidinediones>

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### List of thiazolidinediones

Drug name	Learn more	See SingleCare price
Actos	<a href="#">Actos details</a>	<a href="#">Actos price</a>
Actoplus Met	<a href="#">Actoplus-Met details</a>	<a href="#">Actoplus-Met price</a>
Duetact	<a href="#">Duetact details</a>	<a href="#">Duetact price</a>
Oseni	<a href="#">Oseni details</a>	<a href="#">Oseni price</a>

<https://www.singlecare.com/drug-classes/thiazolidinediones>

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thiazolidinediones,  
have been reported to be associated with increased risk of massive hepatic necrosis, heart  
failure, and bladder cancer in patients treated with these drugs [\[6\]](#)–[\[8\]](#)

Oseni	<a href="#">Oseni details</a>	<a href="#">Oseni price</a>
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<https://www.singlecare.com/drug-classes/thiazolidinediones>



In our previous study, we were surprised to find that chronic nicotine treatment can significantly reduce HOMA of insulin resistance (HOMA-IR) in normal rats, suggesting that nicotine may enhance insulin sensitivity [16]. In the present study, to further study this phenomenon, we treated normal rats with nicotine for 6 weeks and examined insulin sensitivity by detecting blood glucose and insulin levels, and performing insulin tolerance test and glucose tolerance test. Nicotinic acetylcholine receptor (nAChR) antagonist,  $\alpha 7$ -nAChR agonist, signal transducer and activator of transcription 3 (STAT3) inhibitor,  $\alpha 7$ -nAChR knockout ( $\alpha 7$ -nAChR<sup>-/-</sup>) and AMP-activated kinase- $\alpha 2$  knockout (AMPK $\alpha 2$ <sup>-/-</sup>) mice were used to indentify the nAChR subtypes mediating the effect of nicotine on insulin sensitivity and explore the underlying mechanisms. We demonstrated that chronic treatment of nicotine enhanced insulin sensitivity in normal rodents through  $\alpha 7$ -nAChR-STAT3 pathway which is independent of the anti-inflammatory effect of nicotine. Activation of  $\alpha 7$ -nAChR also improved insulin sensitivity in AMPK $\alpha 2$ <sup>-/-</sup> mice, a model of insulin resistance.

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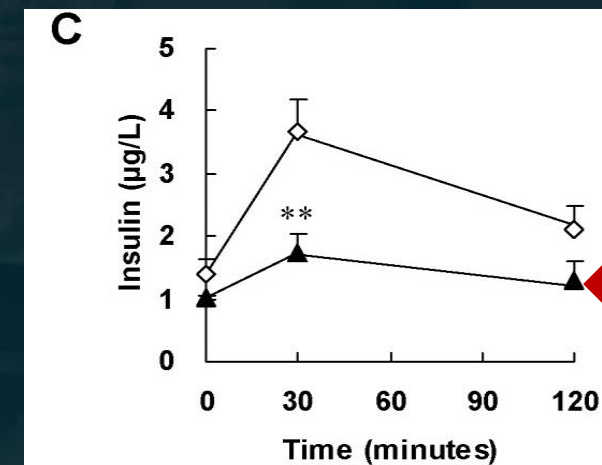
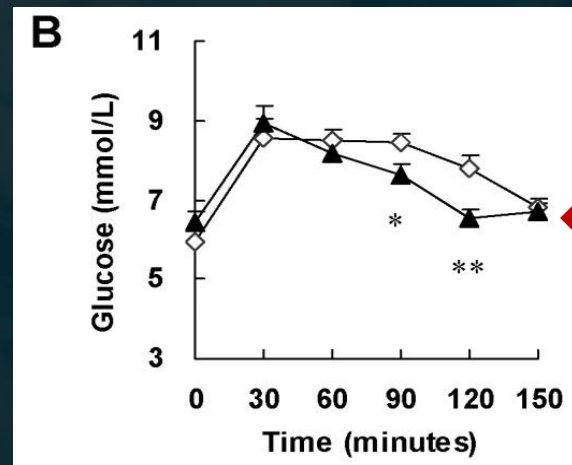
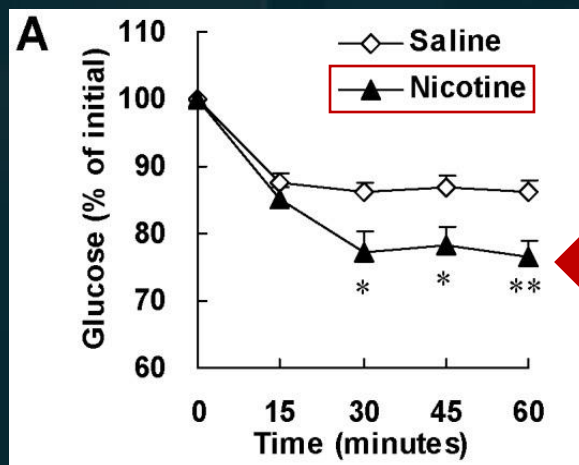
After 6 weeks of treatment, the weight gain in nicotine-treated rats was only 57% of that in saline-treated rats (Fig. 1A). Blood triglyceride levels showed a 40% reduction after nicotine treatment (Fig. 1B). Nicotine treatment significantly reduced 65% basal insulin level (Fig. 1D) but had no effect on glucose level (Fig. 1C), indicating a higher insulin sensitivity in nicotine treated rats. Nicotine treated-rats reduced HOMA-IR to 35% and elevated QUICKI indexes to 112% of that in saline-treated rats (Fig. 1, E and F), supporting that chronic nicotine treatment enhances insulin sensitivity.

<https://pmc.ncbi.nlm.nih.gov/articles/PMC3520975/>

(ITT)=  
Insulin  
tolerance  
test

(GTT)=  
Glucose  
tolerance  
test

We further performed ITT and GTT to evaluate insulin sensitivity. ITT showed significant decrease of blood glucose levels at 30, 45 and 60 minutes after insulin injection in nicotine-treated rats compared with those in saline-treated rats ([Fig. 2A](#)), suggesting that nicotine treatment enhances insulin sensitivity. Meanwhile, GTT showed a more rapid glucose clearance ([Fig. 2B](#)) but lower insulin levels ([Fig. 2C](#)) in nicotine-treated rats compared with saline-treated animals. Thus, results from both ITT and GTT confirmed that chronic nicotine treatment enhanced insulin sensitivity in normal rats.



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After nicotine treatment for 6 weeks,  $\alpha 7$ -nAChR<sup>-/-</sup> mice reduced  $2.3 \pm 0.44$  g, 9.2% of initial bodyweight (Fig. 4B). The blood glucose levels in nicotine-treated mice were within normal range and had a tendency to increase compared with those in saline-treated mice (Fig. 4C).  $\alpha 7$ -nAChR knockout reversed the reduction of blood insulin level and HOMA-IR index as well as the increase of QUICKI index induced by nicotine (Fig. 4, D-F). These results further support that nicotine enhances insulin sensitivity through activation of  $\alpha 7$ -nAChR.

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## Diabetology & Metabolic Syndrome

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### Effect of supplementation with vitamins D3 and K2 on undercarboxylated osteocalcin and insulin serum levels in patients with type 2 diabetes mellitus: a randomized, double-blind, clinical trial

[J. I. Aguayo-Ruiz](#), [T. A. García-Cobián](#), [S. Pascoe-González](#), [S. Sánchez-Enríquez](#), [I. M. Llamas-Covarrubias](#), [T. García-Iglesias](#), [A. López-Quintero](#), [M. A. Llamas-Covarrubias](#), [J. Trujillo-Quiroz](#) & [E. A. Rivera-Leon](#) 

*Diabetology & Metabolic Syndrome* **12**, Article number: 73 (2020) | [Cite this article](#)

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<https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-020-00580-w>

Patients with type 2 diabetes mellitus (T2DM) are characterized by chronic hyperglycemia as a consequence of decreased insulin sensitivity, which contributes to bone demineralization and could also be related to changes in serum levels of osteocalcin and insulin, particularly when coupled with a deficiency in the daily consumption of vitamins D3 and K2. The objective of this study was to evaluate the effect of vitamin D3 and vitamin K2 supplements alone or in combination on osteocalcin levels and metabolic parameters in patients with T2DM.

<https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-020-00580-w>

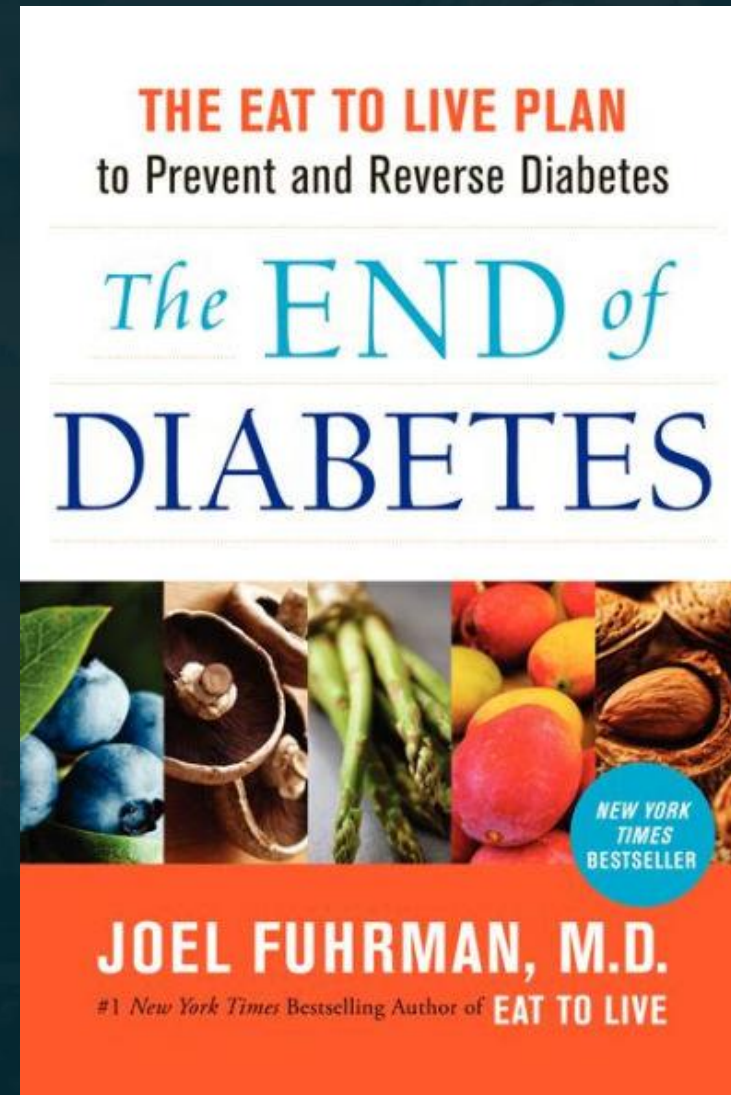
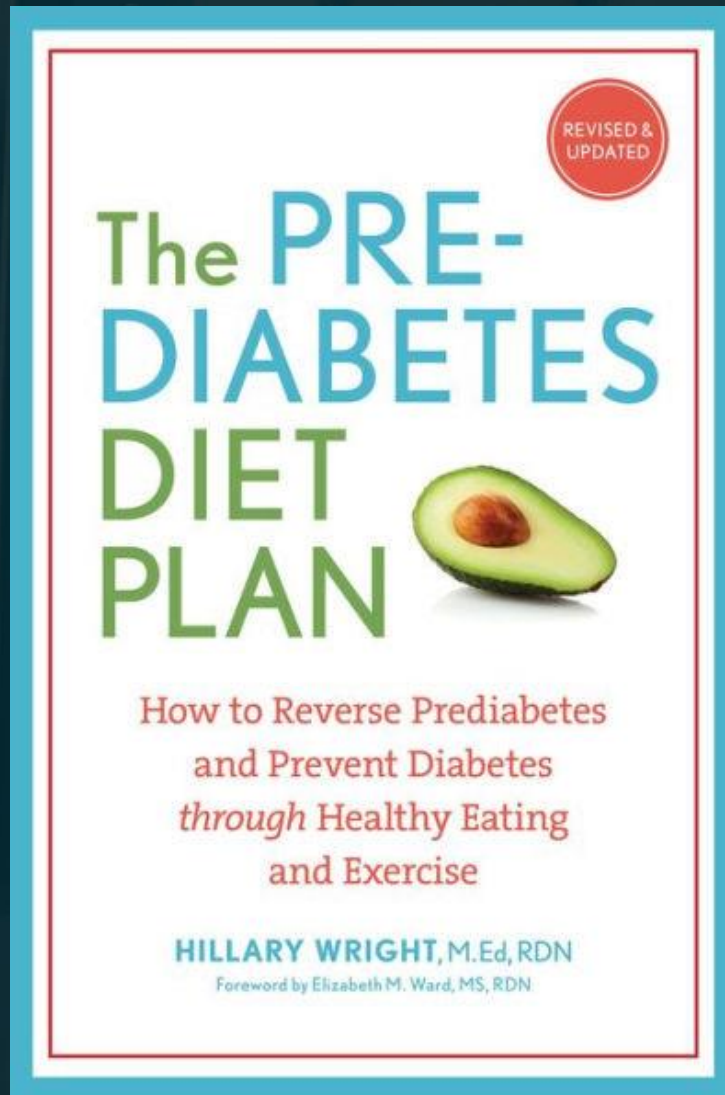
## Conclusion

Individual or combined supplementation with vitamins D3 and K2 significantly decreases the glucose levels and % of functional pancreatic beta cells, while D3 and D3 + K2 treatments also induced a reduction in the uOC/cOC index. Only in the group with vitamin D3 supplementation, it was observed a reduction in undercarboxylated osteocalcin while vitamin K2 increased the carboxylated osteocalcin levels.

*Trial registration* NCT04041492

<https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-020-00580-w>

<https://www.barnesandnoble.com/w/the-prediabetes-diet-plan-hillary-wright-med-rdn/1115292565>



<https://www.barnesandnoble.com/w/the-end-of-diabetes-joel-fuhrman/1111651264?ean=9780062219985>





## 100 Years of Sugar Consumption - When did it become too much?



**Kamila Laura Sitwell**

Guiding midlife reinvention through relocation, career change, slow travel and freedom living. Founder of Portugal's leading women's network. Global correspondent sharing real-life pivots from around the world.

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**Natural Society** conducted research into the average consumption of sugar from 1700 to the present day, and found that:

- In 1700, the average person consumed approximately 4.9 grams of sugar each day (1.81 kg per year).
- In 1800, the average person consumed approximately 22.4 grams of sugar each day (10.2 kg per year).
- In 1900, the average person consumed approximately 112 grams of sugar each day (40.8 kg per year).
- In 2009, 50 per cent of Americans consumed approximately 227 grams of sugar each day - equating to 81.6 kg per year.

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- In 1900, the average person consumed approximately 112 grams of sugar each day (40.8 kg per year). **89.76 Lbs**
- In 2009, 50 per cent of Americans consumed approximately 227 grams of sugar each day - equating to 81.6 kg per year. **179.52 Lbs**

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## Here's how much sugar is safe per day, according to expert doctors

According to the 2020-2025 Dietary Guidelines for Americans, everyone aged two years and older should keep their added sugar consumption below 10% of their daily calorie intake. For someone following a 2,000-calorie diet, this means no more than 50 grams of added sugar, or approximately 12.5 teaspoons, per day.

The American Heart Association says the daily sugar limit is even more conservative.

- Men should aim to consume no more than 36 grams (or nine teaspoons, 150 calories) of added sugar daily.
- Women should aim to consume no more than 25 grams (or six teaspoons, 100 calories) of added sugar daily.

To put this into perspective, a single 12-ounce soda can contain up to 32 grams (eight teaspoons) of added sugar. "If a woman is consuming one of those sodas a day, she's already gone over on her sugar," Tilton says.

<https://www.thehealthy.com/nutrition/how-much-sugar-should-you-eat-in-a-day-dietitians/>





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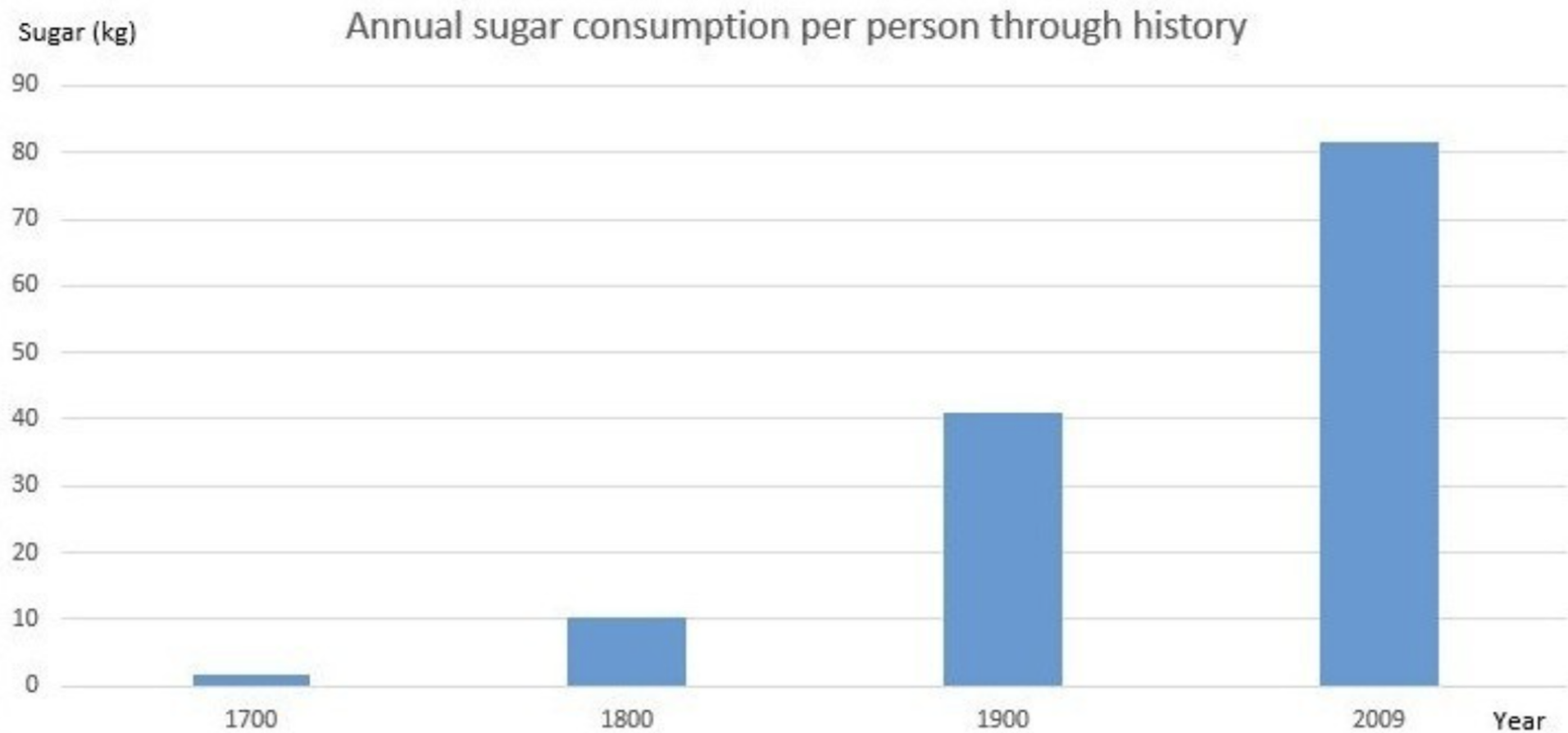


Figure: Sugar consumption on average by approximate year

<https://www.linkedin.com/pulse/100-years-sugar-consumption-when-did-become-too-much-sitwell>

## 144 Ways Sugar Ruins Your Health by Nancy Appleton, ND

1. Sugar can suppress the immune system
2. Sugar upsets the mineral relationships in the body
3. Sugar can cause hyperactivity, anxiety, difficulty concentrating, and crankiness in children
4. Sugar can produce a significant rise in triglycerides
5. Sugar contributes to reduced defense against bacterial infection
6. Sugar causes a loss of tissue elasticity and function, the more sugar you eat the more elasticity and function you lose.
7. Sugar reduces high density lipoproteins
8. Sugar leads to chromium deficiency
9. Sugar leads to cancer of the breast, ovaries, prostate, and rectum
10. Sugar can increase fasting levels of glucose
11. Sugar causes copper deficiency
12. Sugar interferes with absorption of calcium and magnesium
13. Sugar can weaken eyesight
14. Sugar raises the level of neurotransmitters: dopamine, serotonin, and norepinephrine
15. Sugar can cause hypoglycemia
16. Sugar can produce an acidic digestive tract
17. Sugar can cause a rapid rise of adrenaline levels in children
18. Sugar mal absorption is frequent in patients with functional bowel disease
19. Sugar can cause premature aging
20. Sugar can lead to alcoholism
21. Sugar can cause tooth decay
22. Sugar contributes to obesity
23. High intake of sugar increases the risk of Crohn's disease & ulcerative colitis
24. Sugar can cause changes found in person with gastric or duodenal ulcers
25. Sugar can cause arthritis
26. Sugar can cause asthma
27. Sugar greatly assists the uncontrolled growth of Candida Albicans (yeast infections)
28. Sugar can cause gallstones
29. Sugar can cause heart disease
30. Sugar can cause appendicitis
31. Sugar can cause multiple sclerosis
32. Sugar can cause hemorrhoids
33. Sugar can elevate glucose and insulin responses in oral contraceptive users
34. Sugar can lead to periodontal disease
35. Sugar can contribute to osteoporosis
36. Sugar contributes to saliva acidity
37. Sugar can cause a decrease in insulin sensitivity
38. Sugar can lower the amount of Vitamin E in blood
39. Sugar can decrease growth hormone
40. Sugar can increase cholesterol
41. Sugar can increase the systolic blood pressure
42. Sugar can cause drowsiness and decreased activity in children
43. High sugar intake increases advanced glycation end products (AGEs) (Sugar that is bound non-enzymatically to protein)
44. Sugar can interfere with the absorption of protein
45. Sugar causes food allergies
46. Sugar can contribute to diabetes
47. Sugar can cause toxemia during pregnancy
48. Sugar can contribute to eczema in children
49. Sugar can cause cardiovascular disease
50. Sugar can impair the structure of DNA
51. Sugar can change the structure of protein
52. Sugar can make our skin age by changing the structure of collagen
53. Sugar can cause cataracts
54. Sugar can cause emphysema
55. Sugar can cause atherosclerosis
56. Sugar can promote an elevation of low density lipoproteins (LDL)
57. High sugar intake can impair the physiological homeostasis of many systems in the body
58. Sugar lowers the enzymes ability to function
59. Sugar intake is higher in people with Parkinson's disease
60. Sugar can cause a permanent altering the way the proteins act in the body
61. Sugar can increase the size of the liver by making the liver cells divide
62. Sugar can increase the amount of liver fat
63. Sugar can increase kidney size & produce pathological changes in the kidney
64. Sugar can damage the pancreas
65. Sugar can increase the body's fluid retention
66. Sugar is enemy number 1 of the bowel movement
67. Sugar can cause myopia (nearsightedness)
68. Sugar can compromise the lining of the capillaries
69. Sugar can make the tendons more brittle
70. Sugar can cause headaches, including migraine
71. Sugar plays a role in pancreatic cancer in women
72. Sugar can adversely affect school children's grades & cause learning disorders
73. Sugar can cause an increase in delta, alpha, and theta brain waves
74. Sugar can cause depression
75. Sugar and cause dyspepsia (indigestion)
76. Sugar can increase your risk of getting gout
77. Sugar can increase the levels of glucose in an oral glucose tolerance test over the ingestion of complex carbohydrates
78. Sugar can increase the insulin responses in humans consuming high-sugar diets compared to low sugar diets

## 144 Ways Sugar Ruins Your Health by Nancy Appleton, ND

79. High refined sugar diet reduces learning capacity
80. Sugar can cause less effective functioning of two blood proteins, albumin, and lipoproteins, which may reduce the body's ability to handle fat and cholesterol
81. Sugar can contribute to Alzheimer's disease
82. Sugar can cause platelet adhesiveness
83. Sugar can cause hormonal imbalance; some hormones become under active and others become overactive
84. Sugar can lead to the formation of kidney stones
85. Sugar can lead to the hypothalamus to become highly sensitive to a large variety of stimuli
86. Sugar can lead to dizziness
87. Diets high in sugar can cause free radicals and oxidative stress
88. High sucrose diets of subjects with peripheral vascular disease significantly increases platelet adhesion
89. High sugar diet can lead to biliary tract cancer
90. Sugar feeds cancer
91. High sugar consumption of pregnant adolescents is associated with a twofold increased risk for delivering a small-for-gestational-age (SGA) infant
92. High sugar consumption can lead to substantial decrease in gestation duration among adolescents
93. Sugar slows food's travel time through the gastrointestinal tract
94. Sugar increases the concentration of bile acids in stools and bacterial enzymes in the colon
95. Sugar increases estradiol (the most potent form of naturally occurring estrogen) in men
96. Sugar combines and destroys phosphatase, an enzyme, which makes the process of digestion more difficult
97. Sugar can be a risk factor of gallbladder cancer
98. Sugar is an addictive substance
99. Sugar can be intoxicating, similar to alcohol
100. Sugar can exacerbate PMS
101. Sugar given to premature babies can affect the amount of carbon dioxide they produce
102. Decrease in sugar intake can increase emotional stability
103. The body changes sugar into 2 to 5 times more fat in the bloodstream than it does starch
104. The rapid absorption of sugar promotes excessive food intake in obese subjects
105. Sugar can worsen the symptoms of children with attention deficit hyperactivity disorder (ADHD)
106. Sugar adversely affects urinary electrolyte composition
107. Sugar can slow down the ability of the adrenal glands to function
108. Sugar has the potential of inducing abnormal metabolic processes in a normal healthy individual and to promote chronic degenerative diseases
109. I.Vs (intravenous feedings) of sugar water can cut off oxygen to the brain
110. High sucrose intake could be an important risk factor in lung cancer
111. Sugar increases the risk of polio
112. High sugar intake can cause epileptic seizures
113. Sugar causes high blood pressure in obese people
114. In Intensive Care Units: Limiting sugar saves lives
115. Sugar may induce cell death
116. Sugar may impair the physiological homeostasis of many systems in living organisms
117. In juvenile rehabilitation camps, when children were put on a low sugar diet, there was a 44% drop in antisocial behavior
118. Sugar can cause gastric cancer
119. Sugar dehydrates newborns
120. Sugar can cause gum disease
121. Sugar increases the estradiol in young men
122. Sugar can cause low birth weight babies
123. Greater consumption of refined sugar is associated with a worse outcome of schizophrenia
124. Sugar can raise homocysteine levels in the blood stream.
125. Sweet food items increase the risk of breast cancer.
126. Sugar is a risk factor in cancer of the small intestine.
127. Sugar may cause laryngeal cancer.
128. Sugar induces salt and water retention.
129. Sugar may contribute to mild memory loss.
130. As sugar increases in the diet of 10 years olds, there is a linear decrease in the intake of many essential nutrients.
131. Sugar can increase the total amount of food consumed.
132. Exposing a newborn to sugar results in a heightened preference for sucrose relative to water at 6 months and 2 years of age.
133. Sugar causes constipation.
134. Sugar causes varicose veins.
135. Sugar can cause brain decay in pre-diabetic and diabetic women.
136. Sugar can increase the risk of stomach cancer.
137. Sugar can cause metabolic syndrome.
138. Sugar ingestion by pregnant women increases neural tube defects in embryos.
139. The higher the sugar consumption the more chances of getting irritable bowel syndrome.
140. Sugar could affect central reward systems.
141. Sugar can cause cancer of the rectum.
142. Sugar can cause endometrial cancer.
143. Sugar can cause renal (kidney) cell carcinoma.
144. Sugar can cause liver tumors.



SUGAR ADDICTION UPSETS  
YOUR WHOLE BODY CHEMISTRY.  
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# LICK THE SUGAR HABIT

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foreword by **NINA TEICHOLZ**

**DR. JASON FUNG**  
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# THE DIABETES CODE

PREVENT AND  
REVERSE  
TYPE 2 DIABETES  
NATURALLY

<https://www.barnesandnoble.com/w/the-diabetes-code-dr-jason-fung/1127226881?ean=9781771642651>



## Supplement Facts

Serving Size: 1 Capsules    Servings Per Container: 30

Amount Per Serving		% Daily Value
Calories	5	
Total Carbohydrates	1g	<1%*
Guggulsterone (as Guggul Resin Extract)	70mg	†

\*Percent Daily Value (DV) are based on a 2000 calorie diet.

†Daily Value (DV) not established.

**OTHER INGREDIENTS:** Cellulose (Capsule), Rice Flour

## Nature Wins Guggul Resin (30 Count)

Nature Wins    SKU: GUGGUL001-listing

\$22.99

☆☆☆☆☆ (No reviews yet) + [Write a Review](#)

SIZE: \*

1 Bottle

3 Bottles

6 Bottles

<https://thedrardisshow.com/nature-wins-guggul-resin-30-count/>





## Supplement Facts

Serving Size: 0.5ml (17 drops)  
Servings Per Container: 30

Amount Per Serving	% Daily Value	
Vitamin D (as Vitamin D3) 5000IU	125mcg	625%
Vitamin K (as Vitamin K2)	50mcg	42%

**Ingredients:** Vitamin K2 (menaquinone-7 (all-trans))  
Vitamin D3-Cholecalciferol, 100% organic MCT oil.

## D3+K2 Organic

Nature Wins SKU: D3K2001

\$27.99

☆☆☆☆☆ (No reviews yet) + [Write a Review](#)

ONE-TIME PURCHASE OR SUBSCRIPTION: \*

One Time Purchase

Ships every 30 days

Ships every 90 days

Ships every 180 days

<https://thedrardisshow.com/>



## Supplement Facts

Serving Size: 1 Capsule    Servings Per Container: 30

Amount Per Serving	% Daily Value
Copper (from Cu1 [cuprous nicotinic acid]) 0.9mg	100%

### Other Ingredients:

Organic Gum Acacia, Vegetable Capsule (Cellulose)

## Bio-Active Copper (30 Count)

SKU: COPPER001

\$49.99

★★★★★ (15 reviews) + [Write a Review](#)

ONE-TIME PURCHASE OR SUBSCRIPTION?: \*

One Time Purchase

Ships every 30 days

Ships every 90 days

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[https://thedrardisshow.com/bio-active-copper-30-count/?searchid=3552517&search\\_query=copper](https://thedrardisshow.com/bio-active-copper-30-count/?searchid=3552517&search_query=copper)



<https://www.amazon.com/TOLEVITA-Transparent-Cravings-Healthier-Lifestyle/dp/B0DYND7N87/>

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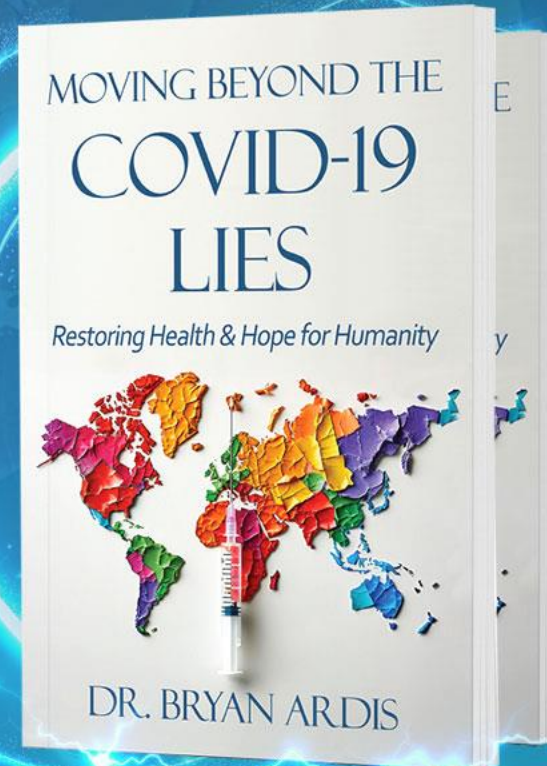


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