

What is Metformin

Metformin is popularly known as Glucophage, and is usually the first medication people who have type 2 diabetes and are overweight are told to get. Although Metformin is mostly used in the treatment of type 2 diabetes, it is not the only illness it treats. For instance, women who have cysts or boil-like formations on their ovaries are often advised to take metformin.

The first time metformin was discovered was in the year 1922 however it was in the 1950s that a French doctor called Jean Sterne began to check out its effect on humans. Probably due to the success of Dr. Jean's experiment, Metformin, was accepted to be used as a medication in the US in 1955 and in France, his home country in the year 1957. Metformin is not advisable for people who have health problems with their liver and that's because it works with the liver. Inducing an already ailing organ to carry out a function when it ought to be left to recover isn't a wise thing to do.

Interestingly, in 2019, Metformin was the fourth most needed medication in the United States. About 17 million people who suffered from diabetes had metformin prescribed to them about 85 million times. Metformin is listed among the World Health Organization's list of essential medicines; these are medicines that are considered to be safe and effective to treat the most important health problems in a health system.

However, in this article, we will be talking about the use of metformin for weight loss. We will consider the truth, the myths and you will find answers to every question you may have concerning the use of metformin for weight loss.

How does Metformin work?

Currently, scientists are trying to ascertain the particular process metformin goes through in the body. There are some propositions such as limiting the activities of the mitochondrial respiratory chain, the initiation of the AMP- activated protein kinase, the slowing down of the process where by glucagon influences the increase of cAMP where cAMP is cyclic



adenosine monophosphate, the reduction of glycerol-induced hepatic gluconeogenesis; gluconeogenesis is a process which happens in the body where glucose is sourced from food materials that are not carbohydrates.

Some scientists also believe that the effect of metformin use is completely as a result of its action on gut bacteria.

Nevertheless, there are proven effects of metformin use which you would likely experience when you start taking it as a medication. For instance, it usually causes people to eat less amount of food and as a consequence cut down on foods that have high calorie. Metformin also disrupts the actions of the liver such that more glucose is not processed. Normally, glucose is more readily processed from carbohydrate rich foods such as bread, rice and cereals but the liver can also make glucose from non-carbohydrate foods substrates. It does that in a process called gluconeogenesis which metformin does inhibit. This is one reason why metformin is prescribed for patients with type 2 diabetes. It cuts down on glucose production from the liver.

For metformin's inhibitory effect on the liver to take place, AMPK or AMP-activated protein kinase has to be activated. As an enzyme, AMPK plays a role in the signaling of insulin and how your body metabolizes glucose and fats. There are two genes that are related to gluconeogenesis in the liver which are phosphoenolpyruvate carboxykinase and glucose 6-phosphatase. AMPK triggers the production of a substance which inhibits the expressions of these genes. In the long run, less glucose is produced by the liver.

Aside from reducing the production of glucose in the liver, metformin also increases insulin sensitivity. This is important for you if you want to cut down on your weight. The cells of your body require glucose to produce the energy your body uses to carry out involuntary functions like the movement of food in your guts, the pumping action of your heart, the coordination of your nervous system and the blinking of your eyes among others. It also provides energy for voluntary actions such as walking, running, lifting



objects and every other activity you can control. However, when your cells are not sensitive to insulin or when they reject insulin, they fail to get enough glucose across the cell membrane which acts as a protective wall around the content of the cell. This is because insulin is needed to get glucose into your cells.

When glucose doesn't get into your cells, they remain in the blood from where they are either stored as glycogen in the liver or get converted to fat and then distributed to other parts of your body.

This is why metformin is sometimes prescribed to increase insulin sensitivity so that your cells will use more glucose and your body would not have to convert glucose to fat.

How does Metformin help with weight loss?

The Food and Drug Administration has not given the go-ahead for metformin to be prescribed as a medication for weight loss. Despite that, it is still being used as a weight loss pill. The use of metformin as a weight loss aid has recorded quite varying results. As an off-label augment, not much research has been done to ascertain the pathway of metformin use for weight loss. However, to ensure that you have an explanation for why you are shedding off weight when you use metformin, health practitioners have monitored users under controlled systems to come up with useful explanations.

You should note that weight loss due to metformin use is a side effect and not the target function of the medication. The most traceable impact of metformin in weight loss is its influence on gut bacteria. A study was conducted where healthy people and people who had Type 2 Diabetes were treated with metformin. The result showed that there was significant reduction in the amount of *Roseburia*, *Subdoligranulum*, and butyrate-producing *Clostridiales* spp. *Escherichia* spp. recorded an increase in amount while there was reduced abundance of *Intestinibacter* spp. Also, *Akkermansia muciniphila* which is known to degrade mucin recorded an increase in abundance. The changes in relative abundance of these gut



bacteria are said to cause a loss of appetite which inadvertently causes reduction in weight.

Another theory goes that the changes in gut bacteria can cause stomach upset which may induce loss of appetite or it may cause diarrhea which reduces body fluid content and consequently some pounds. Also, there is a hormone in the body called *leptin*. Leptin is responsible for maintaining our body weight over a long period of time by regulating our crave for food. The amount of leptin that flows through our blood is determined by how much fat we have stored in our body. In a case where the activity of leptin is resisted, we will experience consistent hunger for food even after eating to our fill. Leptin is often influenced when you use metformin. Metformin increases the level of leptin in the blood which signals to the brain that the body needs less food. This causes a loss of appetite and as a consequence, loss in weight.

Another way metformin is believed to affect weight loss is its interaction with the hypothalamic region of the brain. Research was conducted to ascertain what regions of the brain are involved in metformin's effect on appetite and weight loss. It was discovered that the ventromedial hypothalamic nucleus of the treated rat's brain showed activity which influenced a state of anorexia. This showed that metformin use can make you avoid food intake due to its impact on the hypothalamic region of the brain.

What results have been obtained from research on metformin's impact on weight loss

For safety reasons, most research on medication use is carried out using mice because of the similarity between their metabolic processes and that of humans. A research was conducted using mice to test the effect of metformin on weight loss. According to research, the introduction of metformin registered alterations in the abundance of a number of gut bacteria which was followed by reduction in weight. Another study paid



more attention to the central nervous system of the rodents and discovered that the rodents displayed anorexia which led to weight loss.

The response of humans to metformin use with regards to weight loss has also been studied. In 2013, research was carried out on the effectiveness of metformin on weight loss in non-diabetic individuals with obesity. 154 people who had body mass indexes above 27 kg/m^2 . The research lasted for 6 months with an additional 45 people who would be untreated were used as control. A dosage of 2,500 mg was administered every day for these 6 months after a test was conducted to check if these people had insulin resistance. The result showed that metformin caused a weight loss with a mean of $5.8 \pm 7.0 \text{ kg}$ while the untreated people gained weight instead with a mean of $0.8 \pm 3.5 \text{ kg}$ between that period. Those whose bodies were resistant to insulin lost more weight than those whose bodies weren't. The distribution of weight loss wasn't dependent on age, gender or body mass index. This shows that metformin is effective as a medication for weight reduction in healthy people.

What do people have to say about it?

Kathryn from California said that her mother lost a considerable amount of weight due to metformin use. Her mother was nauseous and couldn't eat enough food. Although after a month of continuous use, her mother's blood sugar level went below normal till she developed hypoglycemia. She believes that her mother's drastic reduction in weight of about ~50 lbs in a month worsened her mother's health problems. One Ada Townsend, believes that while metformin is prescribed for people who are finding it hard to lose weight, it is not a weight loss solution that works like magic. While she agrees that metformin helps with weight loss, she however says that it is not a quick fix solution as it may happen gradually. The extent of weight loss varies from one person to another and it usually happens between one to two years. Lisa from Alabama says that metformin alone doesn't take away much pounds. One may have to use a weight



loss diet also.

What do doctors think about metformin and weight loss?

Metformin's major function is to reduce blood sugar levels in people suffering from Type 2 Diabetes. However, as a side effect, it may also cause weight loss.

According to Dr. Sood, one should not expect a dramatic weight change if you still eat too much or do not engage in physical activities. You must comply with healthy eating habits such as cutting down on refined sugars and starchy foods especially if you are prone to have high insulin levels. You need to bear in mind that weight loss may be temporary and you may regain your normal weight if you stop using metformin and you return to your normal eating habits. This is why doctors advise that you lead a healthy lifestyle such as healthy diets, regular exercises, etc.

Doctors generally advise that before you use metformin as a medication for weight loss, seek counsel from your doctor.

Are there risks to using metformin for weight loss alone?

There are side effects associated with metformin use and their severity depends on how long you use it or if you have some health challenges.

Stomach pain is one frequently reported side effect of metformin use. This could be as a result of the way metformin alters the number and activities of bacteria in the gut; reducing the abundance of some and increasing that of others. According to a report, about 25% of people who used metformin complained about stomach or digestion related problems.

Also connected with stomach pain is diarrhea, vomiting, nausea and gas. Some metformin users noticed that they developed a swollen stomach after metformin use while a section of others complained about



constipation. Scientists believe that these problems are due to a shift in balance in gut bacteria caused by metformin. However, if it is used, starting with very low doses or as slow-release preparations, you may likely tolerate the side effects better. Although, about 5% of users don't feel better even after using low doses.

Study reveals that when you use metformin for prolonged periods, you are likely to develop increased levels of homocysteine. Homocysteine is an amino acid in the body whose increased levels are a possible sign of heart disease. Side effects of increased homocysteine levels include blood clots, dementia, heart attack, osteoporosis or stroke.

Long term use can also cause vitamin B₁₂ deficiency which may cause nerve problems such as peripheral neuropathy, weakness or vision loss. Researchers suggest that healthcare givers should employ screening and prevention methods when this happens.

Hypoglycemia or low blood sugar is often associated with metformin use during periods of fasting or strenuous physical activity. Also, when used as a combination pill with other medications especially in treating diabetes, it could cause low blood sugar.

Lactic acidosis is a rare occurrence but it has been reported as a side effect of metformin use. Research shows that only about 9 people in every 100,000 in a year ever get to experience lactic acidosis from metformin use. Although kidney problems can expose someone to lactic acidosis, it is still safe for use if the kidney problem is at a mild phase. At stages 4 and 5 of kidney disease, one is prone to lactic acidosis if the person uses metformin. Aside from kidney disease, excessive use, constant dehydration, excessive alcohol use, liver disease or being older than 65 years are risk factors to developing lactic acidosis from metformin use.

Lactic acidosis means that the lactic acid content of your body has gone beyond normal levels. Lactic acid is normally found in our body from which glucose can be sourced when glucose is not readily gotten from food.



Since metformin stops the production of glucose, lactic acid continues to build up till it reaches levels that are dangerous to health. Common symptoms associated with lactic acidosis include weakness, difficulty in breathing, stomach upset, and pains in the muscle.

These side effects usually wear off after two weeks of use when your body's tolerance to the drugs has improved. Nevertheless, to be safe, you should consult your doctor if you can use metformin especially if you have underlying health issues or if you could use lower doses.

Where can you buy metformin?

You can get metformin as tablets in 500 mg, 850 mg and 1000 mg but the 500 mg is mostly prescribed. You can find metformin in its generic or branded form. It could also be combined with other drugs. You will most likely find metformin medications with branded names such as Glucophage, Riomet, Fortamet, Glumetza and Glucophage XR. Metformin can be combined with canagliflozin in Invokamet and also with dapagliflozin in Xigduo.

In the U.S, you can get metformin after providing a prescription from a health provider. You can buy metformin from pharmacies and some registered online health stores.

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