

## REPORT

### The Multiple Benefits of Metformin

Metformin (brand name "Glucophage") has been used in the treatment of type II diabetes for the past 40 years.(1) This drug counteracts many of the underlying factors that result in the manifestation of this insidious disease. Metformin also produces helpful side benefits that can protect against the lethal complications of type II diabetes. Frequently prescribed anti-diabetic drugs fail to address the fundamental causes of type II diabetes and can induce serious side effects.

by JoAnn Knorr, MMS

Type II diabetes affects between 16 to 19 million Americans. About 75% of type II diabetics will die from a cardiovascular-related disease. Conventional doctors often prescribe drugs for the purpose of lowering blood sugar levels. These drugs do not adequately address the multiple underlying pathologies associated with the type II diabetic state.

Type II diabetes is characterized by cellular insulin resistance. The result is excess accumulation of glucose in the bloodstream as cells become resistant to the effects of insulin.

As the type II diabetic condition progresses, many people gain weight and develop more fat cells.(2) Treating type II diabetes with insulin-enhancing therapy increases the risk of cardiovascular complications, induces weight gain, and fails to correct the underlying cause of the disease. Many type II diabetics produce too much insulin in a futile attempt to drive glucose into insulin-resistant cells. When doctors prescribe insulin-enhancing drugs to these type II diabetics, a temporarily reduction of serum glucose may occur, but the long-term effects of this excess insulin can be devastating.

An ideal anti-diabetic drug would enhance cellular insulin sensitivity, inhibit excess intestinal absorption of sugar, reduce excess liver production of glucose, promote weight loss and reduce cardiovascular risk factors. Metformin (Glucophage) is the one drug that does all of this and more.

Metformin works by increasing the number of muscle and adipocyte (fat cell) insulin receptors and the attraction for the receptor. It does not increase insulin secretion, it only increases insulin sensitivity. Therefore, metformin is not associated with causing hypoglycemia. This activity reduces insulin levels by increasing the sensitivity of peripheral tissues to the effects of insulin by rejuvenating the response, and restoring glucose and insulin to younger physiological levels that may cause weight loss and most certainly a decrease in the body's total fat content.(3-7)

In an study published by the American Diabetes Association, metformin was found to decrease the fasting plasma glucose concentration by -60 to -70mg/dl in patients with non-insulin dependent type II diabetes.(1) Metformin also reduced hemoglobin A1C levels, a blood measurement of glycosylation. One of the most devastating consequences of diabetes is protein degradation caused by the formation of advanced glycated end products. Reductions in serum hemoglobin A1C levels are a good indicator of consistent glucose control in the diabetic patient.

Dr. Ward Dean is a specialist in anti-aging and life extension medicine, author of over a 100 articles on the biology of aging, and founder and Medical Director of the Center for Bio-Gerontology in Florida. He recommends taking 500 mg of metformin two or three times per day to all his patients over 40 who do not have kidney or liver problems, or a history of congestive heart failure.(4,5)

According to Dean, aging causes insulin resistance. Metformin increases hypothalamo-pituitary sensitivity that declines with age. As we get older, there is a loss of sensitivity of the hypothalamus and the peripheral tissues to the effects of insulin, which causes elevated blood insulin levels (hyperinsulinemia).(4,5)



Type II diabetes is characterized by cellular insulin resistance. The result is excess accumulation of glucose in the bloodstream because cells become resistant to the effects of insulin and fail to take up glucose.

A number of harmful and age-accelerating effects are associated with elevated blood insulin levels. These effects include: increased infections, microvascular complications like retinopathy (eye problems), nephropathy (kidney problems), neuropathies (nerve problems), hypercholesterolemia, hypertension, premature atherosclerosis and obesity, which eventually evolve into cardiovascular problems.(1,3-5,8)

## The cardiovascular system

Patients with type II diabetes often present with a cluster of cardiovascular risk factors like visceral obesity, hypertension, high triglyceride and low high density lipoprotein (HDL) cholesterol levels, and hypofibrinolysis, all of which form insulin resistance and potentially contribute to increased cardiovascular risk.(8) In the United Kingdom Prospective Diabetes Study, metformin was the only medication that reduced diabetes related deaths, heart attacks and strokes.(1,8)

In the Fontbonne and Associates BIGPRO 1 trial, the individuals with visceral obesity treated with metformin showed greater weight loss, a greater decrease in fasting insulin levels and a smaller increase in low density lipoprotein (LDL) cholesterol concentrations than those who received placebo. A decrease in plasminogen activator inhibitor was most associated with the body weight loss in subjects.(8,9) In the trial, the effects of metformin were most notable on the level of endothelial (artery lining) damage that showed a decrease.

The microvascular complications of retinopathy, nephropathy and neuropathy improve due to metformin's ability to decrease damage to arterial lining.(2) These small blood vessels are somewhat unblocked to provide healthier blood supply to vital tissues surrounding the eyes, kidneys and nerves.(2)

The potentially preventive effects of metformin on type II diabetes and evolving cardiovascular complications include a decrease in total cholesterol and low density cholesterol (LDL), free fatty acids, tissue plasminogen activator antigen and insulin levels when patients present with symptoms of hypertension, dyslipidemia, visceral obesity or hyperglycemia.(8)

In non-diabetic patients with hypertension, 3 placebo controlled trials were done. These trials showed that metformin significantly reduced fasting insulin or C-peptide levels, as well as total cholesterol, low density lipids cholesterol or apolipoprotein B levels, fasting free fatty acids and tissue plasminogen activator antigen levels. Metformin had a significant effect on lowering blood pressure and fasting triglyceride levels in one of these trials.(8)

## Polycystic ovarian syndrome

Polycystic ovarian syndrome is characterized by irregular or absent menstrual periods, and elevated serum testosterone and androstenedione. These patients complain of abnormal bleeding, infertility, obesity, excess hair growth, hair loss and acne. Polycystic ovarian syndrome seems to have a genetic component in which those who are affected often have both male and female relatives with type II diabetes, obesity, elevated blood triglycerides or high blood pressure. They may also have female relatives with infertility, hirsutism or menstrual problems.



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For women in the reproductive age range, polycystic ovarian syndrome is a serious common cause of infertility because of the endocrine abnormalities that accompany elevated insulin levels. As women with polycystic ovarian syndrome maybe at greater risk for other medical conditions, testing is essential. They should be tested for blood lipids, diabetes and blood clotting factors that promote abnormal clotting. Metformin, at doses of 500 mg to 850 mg three times per day, has been shown to reverse these endocrine abnormalities. In women with polycystic ovarian syndrome, metformin reduced systolic blood pressure, hyperinsulinemia and insulin resistance, and facilitated menstrual regulation and pregnancy.(10,11)

## Cancer & cellular immunity

Metformin has been found to suppress the growth of some tumors and enhance the activity of anti-cancer drugs. By giving the immune system a boost, metformin can improve cellular immunity. It has also been found to reduce the incidence of chemically induced cancer in rats.(5,7)

The way metformin improves cellular immunity is linked to its blood sugar lowering effect by improving receptor sensitivity and number. Bacteria, fungi and some viruses tend to feed on sugar. By diminishing their fuel supply, we diminish them. That is why diabetics and other individuals with endocrine abnormalities tend to be more prone to infections.(2)

## Contraindications & side effects

Metformin is not recommended for people who have a history of kidney or liver disease, or a history of congestive heart failure. People with a history of alcohol abuse should also avoid taking the drug, as serious lactic acidosis can develop in these individuals.

Long term use of metformin may cause malabsorption of vitamin B12.(1,3-5,8) Because of the depletion of B12, supplementation is recommended.4-6 When a person begins to take metformin, they may experience some nausea and vomiting, stomach pain, bloating and diarrhea. The latter usually disappear once the person becomes accustomed to the drug.(1,5)

## Many helpful side benefits

Metformin's multiple effects benefit individuals with a propensity to develop diabetes, cardiovascular problems, endocrine problems, retinopathies, nephropathies, cancer or decreased immunity, infections and weigh gain.(1-5,8)

As with diabetes, metformin has been shown to cause a reduction in appetite, weight, and the body's total fat content. In associated heart disease conditions, there is plaque build-up that lines the arteries. This build-up of plaque can lead to atherosclerosis.(8) Metformin reduces or lowers the chances of developing atherosclerosis and reduces the rate of pro-aging cross linkages of collagen, which plays a role in the scar tissue build-up that occurs during wound healing.(4)

Metformin has been shown to reduce the amount of supplemental insulin needed by type II diabetics who become insulin-dependent. They are able to take a lower insulin dose in conjunction with metformin without the risk of becoming hypoglycemic. For 40 years metformin has been used to control blood glucose levels in patients with type II diabetes. Physicians are recommending it to patients who are predisposed to diabetes for the prevention of developing the disease.(8)

With the cluster of cardiovascular problems associated with hyperinsulinemia, metformin has proven effective in lowering total cholesterol, low density lipids, free fatty acids, tissue plasminogen activator antigen and insulin levels when patients present with symptoms of hypertension dyslipidemia, visceral obesity or hyperglycemia. Metformin prevents the acceleration of atherosclerosis and reduces the rate of pro-aging cross linking of collagen. The microvascular complications of hyperinsulinemia are improved by metformin due to the arterial clearance in small blood vessels of the eyes, kidneys and nerves.

There are other positive effects associated with metformin: decreased tumor growth and improved cellular immunity in individuals who are prone to chronic infections associated high blood sugar levels. In non diabetics, metformin reduced low density lipid, total cholesterol, free fatty acids, tissue plasminogen activator antigen, blood pressure and fasting triglyceride levels.(1-5,8)

Women suffering from polycystic ovary syndrome have been treated with metformin. Benefits include: lipid lowering effects, reduction in systolic blood pressure, hyperinsulinemia and insulin resistance syndrome. Metformin has also been shown to aid in normal menstrual regulation and pregnancy.(10,11)

In conclusion, the scientific research points to metformin's multiple uses, with few drawbacks. Accordingly, the drug's numerous side benefits associated with the treatment and prevention of diabetes, as well as other disorders, appear to outweigh its limited side effects.



Metformin prevents the acceleration of atherosclerosis and reduces the rate of pro-aging cross linking of collagen.

## Metformin Dosage Suggestions

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