Can you imagine how much damaging power a glucose molecule possesses? In patients with diabetes, long-term high blood glucose levels can lead to limb amputation, blindness, kidney dysfunction, or cardiovascular disease. Such an uncontrolled increase in blood glucose can be due to the autoimmune destruction of pancreatic β cells (type 1 diabetes) or insulin deficiency combined with insulin resistance (type 2 diabetes).

There have been many approaches to treat diabetes and its associated complications. The first-ever commercially available antidiabetic agent was insulin. Most antidiabetic drugs seek to lower blood glucose levels by increasing either insulin secretion by the pancreas or insulin sensitivity and, therefore, can lead to potentially fatal hypoglycaemia.

Sodium glucose co-transporter-2 (SGLT2) inhibitors, the most recently developed class of antidiabetic drugs, act independently of the insulin pathway. SGLT2 inhibitors include empagliflozin, canagliflozin, dapagliflozin, and ertugliflozin. Canagliflozin was the first to be approved in 2013 and, as of 2019, four drugs of this class have been approved by the FDA. These molecules act in the kidneys where they block SGLT2 proteins, which are the prime mediators of renal glucose reabsorption in the proximal tubules (Figure 1). Consequently, by removing excess glucose from the blood, SGLT2 inhibitors maintain normal blood glucose levels.

Although these clinical studies are promising, SGLT2 inhibitors may cause urogenital tract infections by increasing urinary glucose levels. SGLT2 inhibitors may also increase the risk of stroke and diabetic ketoacidosis (i.e., high blood ketone levels), although the mechanisms are not fully understood. SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

Although these clinical studies are promising, SGLT2 inhibitors may cause urogenital tract infections by increasing urinary glucose levels. SGLT2 inhibitors may also increase the risk of stroke and diabetic ketoacidosis (i.e., high blood ketone levels), although the mechanisms are not fully understood. SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

The most stunning result from clinical studies is that SGLT2 inhibitors confer cardiovascular benefits to patients with diabetes. In contrast to other antidiabetic drugs, the use of SGLT2 inhibitors reduce cardiovascular-related mortality risk in patients with type 2 diabetes.5 Because SGLT2 inhibitors do not affect insulin secretion or action, unlike other antidiabetic drugs (e.g., sulfonylureas), they have low risk of inducing hypoglycaemia. In clinical trials, SGLT2 inhibitors reduced fasting blood glucose and HbA1c levels that are the markers most commonly used for diagnosing diabetes.6 Interestingly, SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

Although these clinical studies are promising, SGLT2 inhibitors may cause urogenital tract infections by increasing urinary glucose levels. SGLT2 inhibitors may also increase the risk of stroke and diabetic ketoacidosis (i.e., high blood ketone levels), although the mechanisms are not fully understood. SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

Although these clinical studies are promising, SGLT2 inhibitors may cause urogenital tract infections by increasing urinary glucose levels. SGLT2 inhibitors may also increase the risk of stroke and diabetic ketoacidosis (i.e., high blood ketone levels), although the mechanisms are not fully understood. SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

The most stunning result from clinical studies is that SGLT2 inhibitors confer cardiovascular benefits to patients with diabetes. In contrast to other antidiabetic drugs, the use of SGLT2 inhibitors reduce cardiovascular-related mortality risk in patients with type 2 diabetes.5 Because SGLT2 inhibitors do not affect insulin secretion or action, unlike other antidiabetic drugs (e.g., sulfonylureas), they have low risk of inducing hypoglycaemia. In clinical trials, SGLT2 inhibitors reduced fasting blood glucose and HbA1c levels that are the markers most commonly used for diagnosing diabetes.6 Interestingly, SGLT2 inhibitors can cause weight loss and blood pressure reduction, probably by increasing glucose and sodium secretion.

References

Robin Sachdeva
KGK Science in London, Canada
srobin.iitg@gmail.com

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose

Figure 1. Mechanism of action of sodium glucose co-transporter-2 (SGLT2) inhibitors in a nephron.
Under physiological conditions, most of the glucose in the blood is filtered through the Bowman’s capsule and reabsorbed by SGLT2 proteins present in the proximal convoluted tubule. SGLT2 inhibitors normalise blood glucose levels by blocking glucose reabsorption and inducing the elimination of glucose through urine.

Glucose
Bowman’s Capsule
Proximal convoluted tubule
Collecting duct
Glucose
SGLT2 inhibitors
SGLT2

Glucose reabsorption

Glucose