

# The role of the kidney and emerging novel therapies in diabetes

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Diabetes is increasing at an alarming rate here in Singapore. Just last year, diabetes-related problems were amongst the most common reasons for Singaporeans visiting polyclinics. People with poorly controlled diabetes are at increased risk of developing potentially serious and life threatening complications such as kidney failure, stroke, heart disease and blindness.

Fortunately, with the right medical and lifestyle management, these complications can be prevented. Though exercise and diet are one of the cornerstones of diabetes management, more than 80% of people with diabetes eventually need some form of medical therapy to keep their sugars under control.

At the present time, there are numerous medications available for the treatment of people with type 2 diabetes. These range from an assortment of different oral medications and injectable treatments. These treatments work in various ways

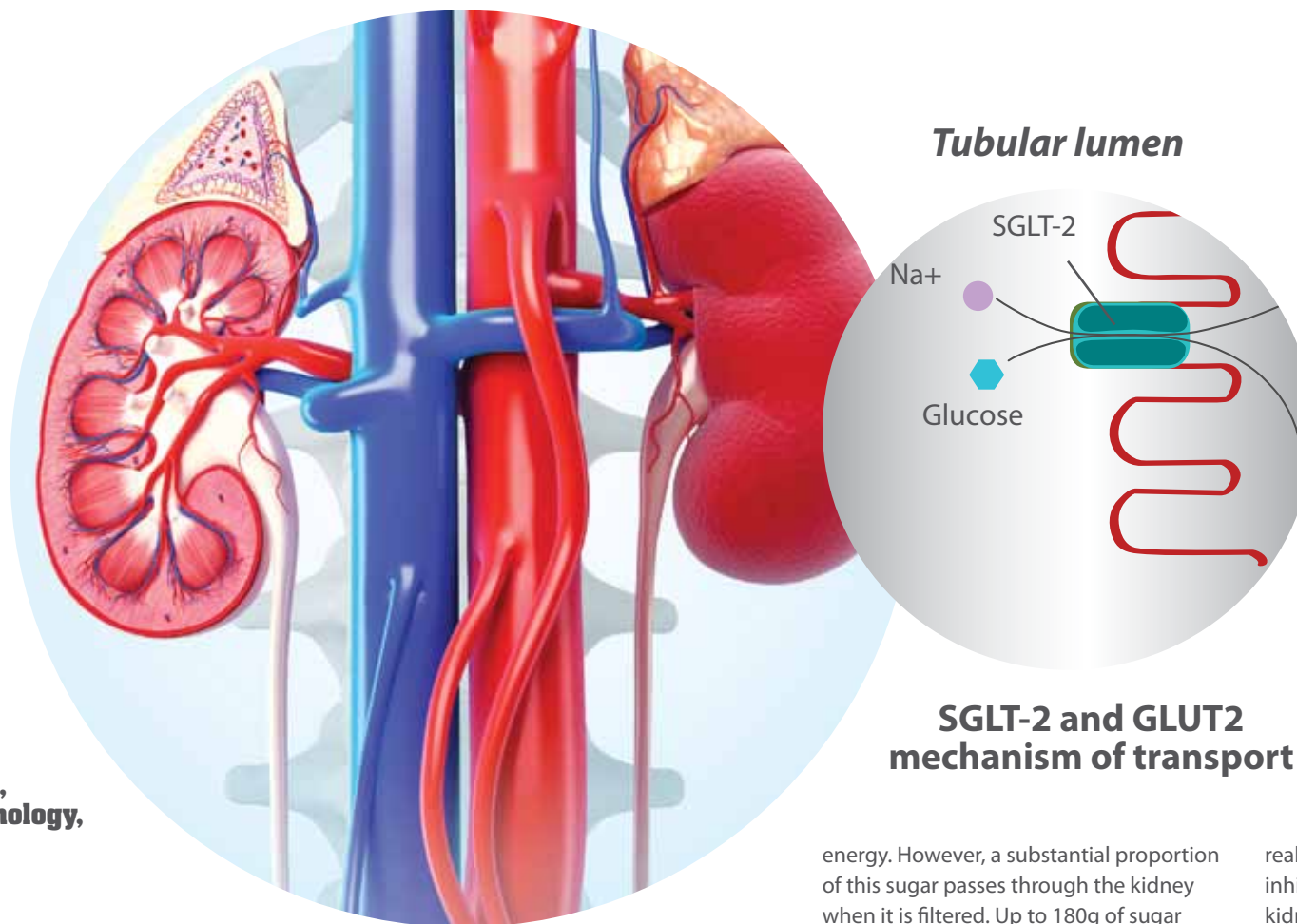
to address the high blood sugars such as increasing insulin release in to the blood stream, enabling the muscles and other parts of the body to take up sugar more effectively and reducing the amount of sugar absorbed from the intestines. Despite the various medical therapies that are available, many people still suffer from diabetes complications as a result of high sugar levels and it is clear that more agents that can help to reduce blood sugar levels are needed.

Hopefully from early next year, there will be a novel class of drug for type 2 diabetes patients available in Singapore – the sodium glucose cotransporter-2 inhibitors (SGLT-2). Its major difference from other medications currently used in diabetes is that it works in a different way from other medications to reduce blood sugar, i.e., by blocking a glucose transporter, called sodium-glucose cotransporter 2 (SGLT-2), in the kidney and causing the body to remove more glucose from the urine.

## How is the kidney involved with blood glucose levels?

It is well known that the kidneys play a crucial role in regulating the water and electrolytes (such as sodium and potassium) in the system and also in removing the toxins from our body. However, an often overlooked fact is that the kidneys play a very important role in sugar balance as well.

The kidney is involved in sugar balance via several mechanisms. One of the most important mechanisms lie in the reabsorption of sugar from the urine back into the blood stream. When we eat food, sugar from the food is absorbed into our blood stream and then distributed across the body to important organs such as the brain which then converts this sugar into



energy. However, a substantial proportion of this sugar passes through the kidney when it is filtered. Up to 180g of sugar (that's four and half cans of cola) is filtered through the kidneys every day. In a normal person, almost all the sugar is reabsorbed back into the body. This process of sugar reabsorption is enabled via a special 'gate mechanism' called the sodium glucose cotransporter.

## What are SGLT-2 inhibitors and how do they work?

The active ingredient in SGLT-2 inhibitors has been made to be very similar to a compound called phloroizin which can be found in the root bark of the apple tree. Scientists have known about phloroizin since the early 1800s. However, the potential sugar reducing effects have only been used for medicinal purposes, and only very recently.

Simply put, these novel agents work by inhibiting the sodium glucose transporter 2 (SGLT-2) which is responsible for the

reabsorption of sugar in the kidney. By inhibiting SGLT-2, sugar which enters the kidney from the body passes through the urine without being reabsorbed back into the blood stream. That way, an individual on SGLT-2 treatment 'loses' sugar from the kidney and that results in a lower blood sugar level in his or her body.

This way, not only does the individual's own sugar level drop (as it is passed out via urine) but it also has the added advantage of weight loss as the accompanying calories in the sugar are similarly passed out in the urine.

Scientific studies have shown patients on SGLT-2 inhibitors to have better sugar control with the added benefit of weight loss and a drop in their blood pressure. In addition to this, as it does not increase insulin activity in the body, SGLT-2 inhibitors have not been found to cause hypoglycaemia or low blood sugars. Furthermore, SGLT-2 inhibitors can be used safely in combination with many other diabetic agents without cross reaction.

However, some participants in the clinical trials reported some problems with genital infections likely as a result of the high sugar content in the urine.

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SGLT-2 inhibitors have the potential to aid clinicians in the battle against diabetes mellitus. It has been proven to be effective in lowering HbA1c levels and is a welcome addition to the current array of therapies available.

Despite the potential benefits of this form of therapy, this treatment may not be suitable for all people who have diabetes, so please consult your doctor to discuss on whether this is a suitable drug for you.

In summary, SGLT-2 inhibitors are a new, medication for sugar control which can be used on its own or in combination with current drugs, and it has shown much promise. It has already been approved in Europe where it is currently being prescribed.

This drug may be available in Singapore as early as the first quarter of 2014. If you need more information, speak with your doctor. Just like any new drug in diabetes, its long term effects are still under surveillance, though it appears to be an effective option in managing blood glucose.