Effectiveness of canagliflozin in treating type 2 diabetes

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Research led by the University of Dundee has found that one of a new breed of drugs, which have been approved for treatment of type 2 diabetes, may be particularly effective without the need to be used in combination with the existing drug, metformin.

Three drugs—canagliflozin, dapagliflozin and empagliflozin—that inhibit SGLT2 (sodium-glucose co-transporter-2) have been approved for treatment of type 2 diabetes in the USA and Europe within the last two years.

SGLT2 is the protein that reabsorbs glucose filtered out of blood by the kidneys back into the bloodstream. If you inhibit that process, more glucose appears in the urine and less in the blood, which is beneficial for a diabetic.

Research led by Professor Grahame Hardie, of the University of Dundee, working in collaboration with colleagues at the University of Glasgow and McMaster University in Canada, has suggested that one of the drugs, canagliflozin, may be particularly effective in treatment of type 2 diabetes.

"We have found that canagliflozin not only inhibits SGLT2 but also activates the AMP-activated protein kinase (AMPK), a signalling pathway that we discovered in Dundee back in the 1980s," said Professor Hardie. "Dapagliflozin and empagliflozin do not do this nearly so effectively.

"The significance of this is that activation of AMPK is also one of the main mechanisms of action of metformin, which is already the front-line drug for treatment of type 2 diabetes and is prescribed to more than 100 million people worldwide.

"Pharmaceutical companies are currently carrying out clinical trials to test the efficacy of combinations of SGLT2 inhibitors and metformin. Our results suggest that, in the case of canagliflozin, it may not be necessary to add metformin, because canagliflozin is already activating AMPK."

SGLT2 inhibitors are derived from phloretin, a natural product found in apples and first isolated in 1863. However, phloretin itself has side effects that the new synthetic derivatives avoid.

The University of Dundee is one of the world's leading centres for study into AMPK and its role in diabetes treatment.

The results of this new research are published in the journal *Diabetes*, and the research was supported by the Wellcome Trust and the British Heart Foundation.

More information: Simon A. Hawley et al. The Na/glucose co-transporter inhibitor canagliflozin activates AMP-activated protein kinase by inhibiting mitochondrial function and increasing cellular AMP levels, *Diabetes* (2016). DOI: 10.2337/db16-0058

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