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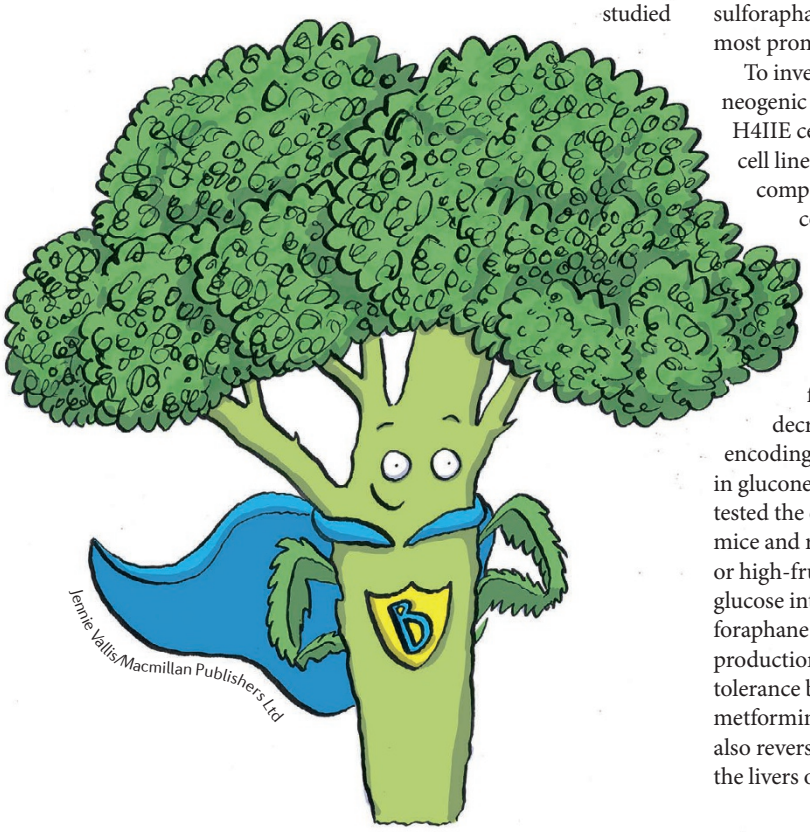
DIABETES

Could broccoli have a role in combating type 2 diabetes mellitus?

> …sulforaphane suppressed hepatic glucose production and improved glucose tolerance…

In a new study published in *Science Translational Medicine*, broccoli sprout extract (BSE) containing the active ingredient sulforaphane is shown to reduce hepatic gluconeogenesis and improve glycaemic control in patients with obesity and poorly controlled type 2 diabetes mellitus (T2DM). If the findings are confirmed in larger clinical trials, BSE could become an important addition to existing treatments for T2DM.

Frustrated by the fact that many promising drugs fail when tested in patients, Anders Rosengren and colleagues adopted a new strategy to find compounds with antidiabetic properties. "Researchers have traditionally studied single genes or proteins and attempted to target them as specifically as possible; however, T2DM does not involve a single gene but rather a large network of genes," explains Rosengren. As exaggerated hepatic glucose production is a central disease mechanism in individuals with obesity and T2DM, the investigators used a combination of gene expression profiling and mathematical modelling to identify a 50-gene disease signature for T2DM in liver tissue. The team then screened 3,852 drug signatures (groups of genes whose expression is affected when cells are treated with a particular drug) to identify compounds that could reverse the T2DM signature; sulforaphane was identified as the most promising candidate.



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To investigate a possible gluconeogenic effect of sulforaphane, H4IIE cells (a rat hepatoma cell line) were treated with the compound. Compared with controls, sulforaphane (3 μM) suppressed glucose production by 41%, which was dependent on translocation of nuclear factor erythroid 2-related factor 2 to the nucleus and decreased expression of genes encoding key enzymes involved in gluconeogenesis. Next, the team tested the effect of sulforaphane in mice and rats that were fed high-fat or high-fructose diets to induce glucose intolerance. Remarkably, sulforaphane suppressed hepatic glucose production and improved glucose tolerance by a similar magnitude as metformin. Moreover, sulforaphane also reversed the disease signature in the livers of these diabetic animals.

Finally, Rosengren and his team conducted a clinical trial to test whether sulforaphane was effective in people with T2DM. "We utilized the fact that sulforaphane is present at high concentrations in cruciferous vegetables such as broccoli and provided BSE or placebo to 97 patients with T2DM (60 with well-controlled disease; 37 with poorly controlled disease, 17 of whom also had obesity). Daily intake of BSE for 12 weeks reduced fasting blood levels of glucose and improved levels of HbA_{1c} in patients with poorly controlled T2DM and obesity (BMI >30 kg/m^2). Reassuringly, no major adverse effects of BSE were reported, only transient gastrointestinal effects (8 in the BSE group; 7 in the placebo group).

Importantly, as all except three patients in the trial were on concomitant metformin treatment (the first-line therapy for T2DM), the observed effects of sulforaphane were on top of those of metformin. "We are now contemplating a further clinical trial of BSE in patients with prediabetes mellitus to study the effects of sulforaphane in isolation and also to investigate its potential in improving glycaemic control in individuals on the verge of developing T2DM," comments Rosengren. "In addition, we are working towards making BSE available to people as a functional food preparation to improve glycaemic control."

David Holmes

ORIGINAL ARTICLE Axelsson, A. S. *et al.* Sulforaphane reduces hepatic glucose production and improves glucose control in patients with type 2 diabetes. *Sci. Transl Med.* **9**, eaah4477 (2017)
FURTHER READING Martel, J. *et al.* Anti-obesogenic and antidiabetic effects of plants and mushrooms. *Nat. Rev. Endocrinol.* **13**, 149–160 (2017)