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**Association between phytoestrogens, glucose homeostasis and risk of diabetes in women: A systematic review and meta-analysis**

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Phytoestrogens might have advantageous effects on diabetes in women. We performed a systematic review and meta-analysis to determine the effect of phytoestrogens on glucose homeostasis and risk of type 2 diabetes (T2D) among women. Randomized clinical trials (RCT) and prospective observational studies that assessed associations of phytoestrogens (supplementation, dietary intake or biomarkers) with fasting glucose or insulin, homeostatic model assessment of insulin resistance (HOMA-IR), or with risk of T2D were included. We identified 18 RCTs (n=1,687 individuals) investigating the effect of phytoestrogen supplementation on glucose homeostasis, and 9 prospective population-based studies (n=212,796 individuals) examining the association between phytoestrogen intake and risk of T2D. As compared to placebo, phytoestrogen supplementation resulted in improvements in fasting glucose and HOMA-IR, the pooled mean differences of changes were -0.12 mmol/L (95% CI -0.20 to -0.03) and -0.24 microU/mol/L (95%CI: -0.45 to -0.03) respectively. While there was no significant decrease in insulin levels with overall phytoestrogen supplementation, pooled mean difference of changes was -0.98 pmol/L (95%CI: -4.64 to 2.67). However, the results of RCTs would vary by type of phytoestrogens, soy derived isoflavones and genistein improved glucose homeostasis, isoflavone mix and daidzein had no or were associated with adverse glycemic profile. Higher dietary phytoestrogen intake was associated with a 10% lower risk of developing T2D in observational studies (pooled relative risk; 0.90 [95% CI, 0.85 to 0.96] for highest versus the lowest quantiles). Results were similar when the analyses were restricted only to medium and high-quality studies. Overall phytoestrogens may have a positive influence on glycaemia and could be used for diabetes prevention in women. However, for some individual types of phytoestrogens, such as mixed isoflavones, caution is needed in demonstrating their use in women, as their use could lead to adverse glycemic profile in women.

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