The modulation of glucose metabolism by leaf tea constituents – a systematic review of recent clinical and pre-clinical findings

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Background

Leaf teas are widely consumed for their potential in managing or preventing metabolic disease. Studies in humans and laboratory animals have indicated that tea consumption may reduce body weight and alleviate metabolic disturbances associated with increased type 2 diabetes mellitus (T2DM) risk. However, the published evidence is scattered and the mechanisms underlying these beneficial effects are in many instances not well documented.

Aim

This systematic review aimed to 1) catalog the evidence for the regulation of glucose metabolism by tea constituents in humans and laboratory animals, and 2) identify tissue-level and cellular mechanisms involved in the modulation of glucose metabolism by tea constituents.

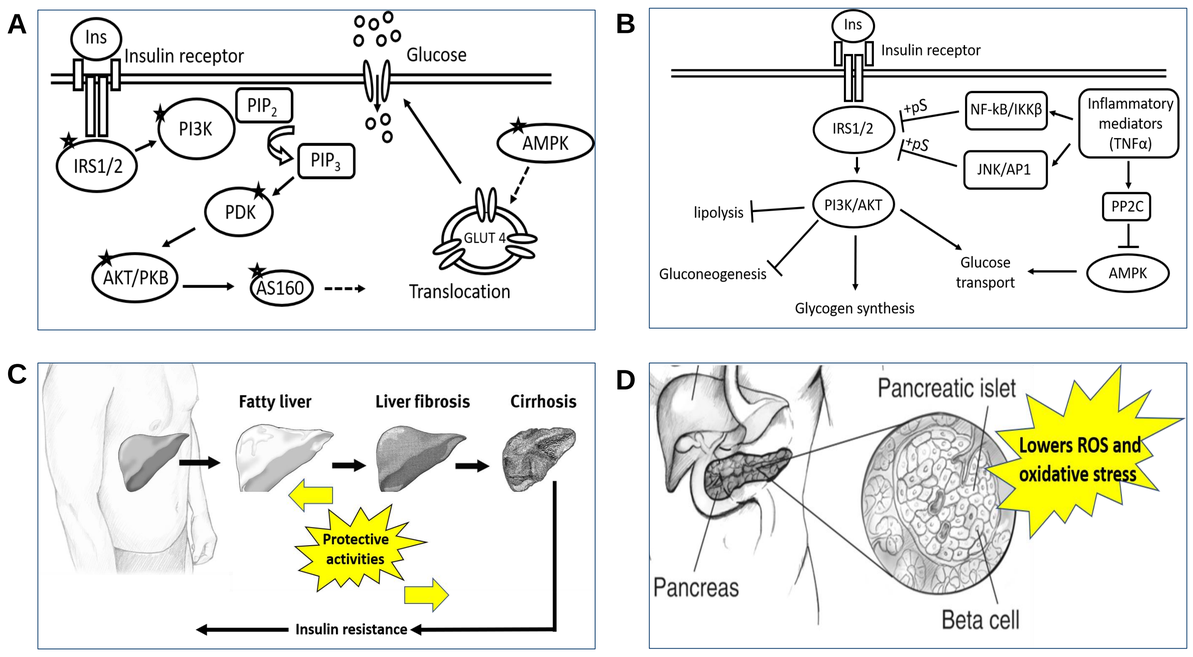

Figure 2. Regulation of glucose metabolism by leaf tea administration as identified in animal and tissue culture models. A) Effects of tea on insulin-dependent (IRS/PI3K/AKT) and insulin–independent (AMPK) signalling pathways. B) Normalization of insulin signalling through anti-inflammatory actions. C) Protective effects on liver function and non-alcoholic liver disease. D) Protection of pancreatic function.

Methods

A systematic search for articles of interest in PubMed, ScienceDirect and Web of Science was conducted. The search strategy included articles from January 2013 to May 2019. Keywords and MeSH terms included: 'tea', 'insulin', 'antidiabetic', 'glycaemia' and 'diabetes'. Inclusion criteria were: 1) a study examining the effects of a specific type of tea (hot or cold, leaf-brewed beverage of a plant nature) and/or 2) its bioactive constituent on an aspect of glucose metabolism. Studies focusing on fruit, flower or root teas were excluded.

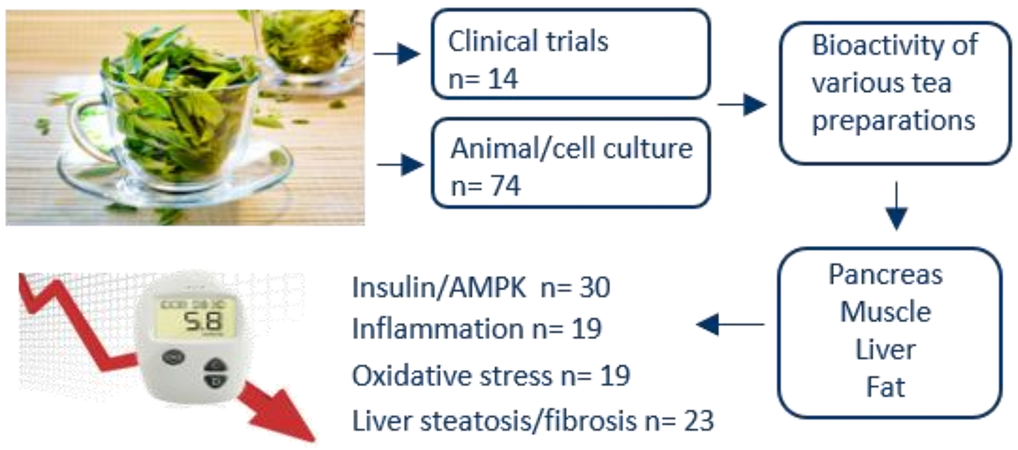

Figure 1. Clinical and pre-clinical intervention studies examining the administration of teas and their bioactive constituents were retrieved and analyzed for possible glucose-and insulin-related metabolic effects in pancreas, muscle, liver and adipose tissue.

Results

1) **The majority of studies retrieved focused on *C. sinensis*-derived teas**, with comparatively few studies on teas derived from other plant species.
2) Overall, these studies provided evidence that **various types of tea may have beneficial and protective effects** on glucose metabolism outcomes in humans and animals, although not all studies agree.
3) Of the **14 randomized controlled trials** (RCTs) identified, 13 utilized green and black tea extracts of *C. sinensis*, with 6 trials showing improved glycemic control and 7 trials showing no effect on glucose homeostasis, even when body composition measures were improved.
4) In contrast to the clinical trials, **studies in animal models have demonstrated mostly positive results** for the regulation of glucose metabolism, impacting on glucose- and insulin-related metabolism, function and intracellular signalling in the pancreas, muscle, liver and adipose tissue.

Results (continued)

5) **50 animal studies (31 on *C. sinensis* teas and 19 on other tea species) observed improved glycemic control** after consumption of tea constituents, against the background of a variety of metabolic insults, including diet-induced obesity and genetic obesity, chemically-induced diabetes and gene knock-outs.

6) In contrast, **3 studies in animal models reported neutral or adverse effects** on glucose metabolism after tea consumption (2 of these studies on green *C. sinensis* tea). These exceptions, although in the minority, correspond with the findings in human trials that the impact of tea consumption on glucose metabolism is not always positive.

7) **Recurring mechanisms** (figure 2) for the promotion of insulin sensitivity by different tea constituents in animals include:

- upregulation and activation of **IRS/PI3K/AKT signalling** pathway components in liver and muscle, with associated increase in glucose transporters;
- insulin-independent glucose disposal through the **AMPK/GLUT4** glucose uptake pathway in liver, muscle and adipose tissue;
- **suppressing inflammatory cytokine production** by adipose tissue;
- **preserving liver morphology/function** by downregulating hepatic lipogenesis;
- **protection of pancreatic β-cell viability/function** by reducing oxidative stress.

Discussion and future perspectives

- Although several epidemiological studies have indicated that tea consumption may reduce the risk of developing T2DM, **supporting evidence from human intervention studies is weak.**
- Only a small number of clinical intervention studies have been performed, with **mixed results**, in contrast to mostly positive findings from animal and *in vitro* cell culture studies.
- **Human trials varied widely** in base-line pathologies, tea dose, duration and glucose measures, complicating comparisons between trials.
- Available mechanistic information was mostly obtained from non-human studies.
- **Larger and better designed human intervention studies, including RCTs examining a wider variety of tea extracts beyond *C. sinensis*, are therefore needed** before any substantiated recommendations can be made on the use of tea bioactive compounds to improve glucose and insulin metabolism in humans.

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