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Review Article

Inulin-Type Fructan Supplementation and Glycaemic Control in Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Trial

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Abstract

Background: Inulin-type fructans (ITFs) are fermentable dietary fibres proposed to improve glycaemic control in type 2 diabetes mellitus (T2DM) through gut microbiota-mediated mechanisms.

Objective: To synthesise RCT and meta-analytic evidence on ITF supplementation and glycaemic outcomes in T2DM.

Methods: Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies of inulin and oligofructose in T2DM.

Findings: Meta-analyses of 9-34 RCTs show ITF supplementation (5-40 g/day, 6-24 weeks) reduces fasting glucose by 0.42-0.60 mmol/L and HbA1c by 0.58-0.69%, with less consistent insulin-resistance effects; benefit is attributed to bifidogenic and short-chain fatty acid mechanisms, though flatulence is common.

Conclusions: ITF supplementation, at doses of approximately 10 g/day sustained for six weeks or longer, produces modest but reproducible glycaemic benefit in T2DM, warranting confirmation in larger, longer-duration trials.

Keywords: Inulin-type fructans; Type 2 diabetes mellitus; Glycaemic control; Gut microbiota; Short-chain fatty acids

Abstract

Background: Inulin-type fructans (ITFs) are fermentable dietary fibres proposed to improve glycaemic control in type 2 diabetes mellitus (T2DM) through gut microbiota-mediated mechanisms. **Objective:** To synthesise RCT and meta-analytic evidence on ITF supplementation and glycaemic outcomes in T2DM. **Methods:** Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies of inulin and oligofructose in T2DM. **Findings:** Meta-analyses of 9-34 RCTs show ITF supplementation (5-40 g/day, 6-24 weeks) reduces fasting glucose by 0.42-0.60 mmol/L and HbA1c by 0.58-0.69%, with less consistent insulin-resistance effects; benefit is attributed to bifidogenic and short-chain fatty acid mechanisms, though flatulence is common. **Conclusions:** ITF supplementation, at doses of approximately 10 g/day sustained for six weeks or longer, produces modest but reproducible glycaemic benefit in T2DM, warranting confirmation in larger, longer-duration trials.

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Introduction

Type 2 diabetes mellitus (T2DM) affects an estimated 537 million adults worldwide, with prevalence projected to rise further over coming decades [1]. Dietary fibre is a cornerstone of nutritional management, and among fermentable fibres, inulin-type fructans (ITFs) — inulin and its shorter-chain derivative oligofructose, extracted principally from chicory root — have attracted particular interest because they are selectively fermented by colonic bifidobacteria and lactobacilli, generating short-chain fatty acids (SCFAs) implicated in glucose and appetite regulation [2,3]. ITFs meet the internationally accepted definition of a prebiotic: a substrate selectively utilised by host microorganisms conferring a health benefit [4].

Interest in ITFs for glycaemic management has expanded into a substantial randomised trial literature in prediabetes and T2DM populations [5]. Proposed mechanisms include SCFA-mediated stimulation of glucagon-like peptide-1 (GLP-1) and peptide YY secretion via free fatty acid receptors on enteroendocrine L-cells, delayed gastric emptying, and favourable remodelling of a dysbiotic gut microbiota characteristic of T2DM [6,7,8]. However, the clinical trial evidence has been mixed, with some meta-analyses reporting clinically meaningful reductions in fasting glucose and glycated haemoglobin (HbA1c) and others finding effects that are small, inconsistent, or dependent on outlier studies [9,10]. Unlike pharmacological glucose-lowering agents, ITFs act upstream on substrate availability and microbial ecology rather than directly on insulin secretion or peripheral insulin action, positioning them as a plausible adjunct rather than a replacement for standard glucose-lowering therapy. Because T2DM itself alters gut barrier function, circulating endotoxin, and low-grade inflammation, an intervention capable of favourably remodelling the colonic microbiota carries theoretical appeal beyond glycaemia alone, extending to lipid and inflammatory risk markers relevant to cardiovascular complications. This review synthesises the randomised trial, meta-analytic, and mechanistic literature on ITF supplementation and glycaemic control specifically in patients with T2DM, as a narrative synthesis rather than a report of a single new trial.

Inulin-Type Fructans: Structure, Sources, and Mechanisms of Action

ITFs are linear fructose polymers linked by β(2→1) bonds with a terminal glucose unit, classified by degree of polymerisation as oligofructose (2-10 units) or longer-chain inulin (up to ~60 units); native chicory inulin is a mixture of both [2]. Neither form is hydrolysed by human small-intestinal enzymes, so ITFs reach the colon

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largely intact, where selective fermentation by *Bifidobacterium* and related taxa yields acetate, propionate, and butyrate [3,2]. In a landmark trial, a high-fibre diet enriched in ITF-type substrates promoted SCFA-producing gut bacteria and improved glycaemic control in Chinese patients with T2DM, linking compositional microbiota change directly to metabolic benefit [8]. Metagenomic profiling has independently shown that T2DM is characterised by depletion of butyrate-producing taxa, providing a mechanistic rationale for fibre-based restoration [7]. SCFAs, particularly propionate, activate free fatty acid receptors on intestinal L-cells, stimulating GLP-1 release and improving insulin secretion and gastric emptying-mediated glucose handling [6,11]. Consistent with this pathway, combined butyrate-and-inulin supplementation increased circulating GLP-1 alongside improvements in fasting glucose, HbA1c, and lipid profile in a placebo-controlled T2DM trial [12].

Evidence from Randomised Controlled Trials

Individual RCTs in T2DM populations have generally, though not universally, favoured ITF supplementation. In a triple-blind trial, 10 g/day high-performance inulin for eight weeks reduced fasting plasma glucose by 8.5% and HbA1c by 10.4% relative to placebo in women with T2DM, alongside improved antioxidant status [13]. A companion analysis of the same cohort reported concurrent reductions in fasting insulin, HOMA-IR, and inflammatory markers including hs-CRP, TNF-α, and endotoxin [14]. A combined inulin-oligofructose supplement improved several cardiovascular risk markers in a similarly designed trial [15], while enriched chicory inulin favourably affected liver enzymes without adverse effects on calcium homeostasis over eight weeks [16]. Conversely, not all trials have shown benefit: a placebo-controlled crossover study using 16 g/day of a 50:50 oligofructose-inulin blend for six weeks found a bifidogenic effect and increased faecal SCFAs [17] but no significant improvement in appetite hormones, and 64% of participants reported worsened flatulence versus 4% on placebo [18]. Similarly, an earlier controlled feeding study found that short-chain fructooligosaccharides did not alter basal hepatic glucose production or insulin resistance in T2DM despite adequate dosing [19], and a pilot RCT of 10 g/day inulin for six weeks in adults at elevated diabetes risk found reduced HOMA-IR but no change in intravenous glucose tolerance test-derived insulin sensitivity [20] (Table 1).

Table 1: Selected randomised controlled trials of inulin-type fructan supplementation in type 2 diabetes mellitus reviewed here [13,14,15,16,12,17,18,19,20].

Study	Population	Dose and duration	Key glycaemic finding
Gargari 2013	Women with T2DM (n=49)	10 g/day inulin, 8 weeks	Fasting glucose -8.5%, HbA1c -10.4% vs placebo
Dehghan 2014	Same cohort (companion analysis)	10 g/day inulin, 8 weeks	Fasting insulin -34.3%, HOMA-IR -39.5%
Aliasgharzadeh 2015	Women with T2DM	10 g/day inulin+ oligofructose, 8 weeks	Improved cardiovascular risk markers
Farhangi 2016	T2DM patients	Enriched chicory inulin, 8 weeks	Improved liver enzymes; calcium unaffected
Roshanravan 2017	T2DM patients	Butyrate + inulin, 8 weeks	GLP-1 increased; glycaemic status improved
Birkeland 2020/2021	T2DM patients (n=25-29)	16 g/day ITF, 6-week crossover	Bifidogenic/SCFA rise; no appetite-hormone change; more flatulence
Luo 2000	T2DM patients	Short-chain FOS, 4 weeks	No change in hepatic glucose production or insulin resistance
Mitchell 2021	Adults at elevated T2DM risk	10 g/day inulin, 6 weeks	HOMA-IR reduced; IVGTT insulin sensitivity unchanged

Meta-Analytic and Dose-Response Evidence

Pooled analyses provide the most informative summary of this heterogeneous literature (Table 2; Figures 1 and 2). A

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GRADE-assessed dose-response meta-analysis of 33 RCTs (1,346 participants) found high-certainty reductions in fasting glucose (weighted mean difference [WMD] -0.60 mmol/L, 95% CI -0.71 to -0.48) and HbA1c (WMD -0.58%, 95% CI -0.83 to -0.32), with lower-certainty reductions in fasting insulin and HOMA-IR; benefit was concentrated at daily doses near 10 g sustained for six weeks or longer [5]. An independent meta-analysis restricted to insulin-resistance outcomes in 11 studies (634 T2DM patients) reported significant post-intervention HbA1c (mean difference -0.58%, 95% CI -0.78 to -0.39) and HOMA-IR reductions after accounting for baseline body-mass index [21]. A further systematic review of nine RCTs (661 participants) reported standardised mean reductions in fasting glucose (SMD -0.55), HbA1c (SMD -0.69), and HOMA-IR, with effects strengthening in interventions lasting eight weeks or more [22]. However, a broader meta-analysis of 20 RCTs (607 participants, mixed populations) found a non-significant fasting glucose effect in the T2DM subgroup despite a significant fasting-insulin reduction [9], and a subsequent critique highlighted that its lipid findings were substantially driven by a single outlier trial, urging caution in over-interpreting ITF metabolic benefits [10]. A meta-analysis of inulin-type fructan intake across body-weight, glucose, and lipid endpoints similarly found favourable but modest pooled effects on glycaemia [23], while a 2024 meta-regression focused on weight outcomes found that glycaemic benefit and adiposity reduction tend to co-occur, suggesting shared mechanisms [24].

Table 2: Summary of meta-analyses of inulin-type fructan supplementation and glycaemic outcomes in type 2 diabetes mellitus [5,21,22,9,23].

Meta-analysis	RCTs (participants)	Fasting glucose	HbA1c	HOMA-IR / insulin
Wu 2019	33 RCTs (1,346)	-0.60 mmol/L	-0.58%	HOMA-IR -0.69 (low certainty)
Rao 2019	11 studies (634)	Not reported	-0.58%	HOMA-IR -0.99 (post-intervention)
Zhang 2020	9 RCTs (661)	SMD -0.55	SMD -0.69	SMD -0.81
Liu 2017	20 RCTs (607, mixed)	-0.42 mmol/L (ns in T2DM)	Not reported	Fasting insulin -4.01 pmol/L
Li 2021	Pooled RCTs, mixed populations	Modest reduction	Modest reduction	Not reported

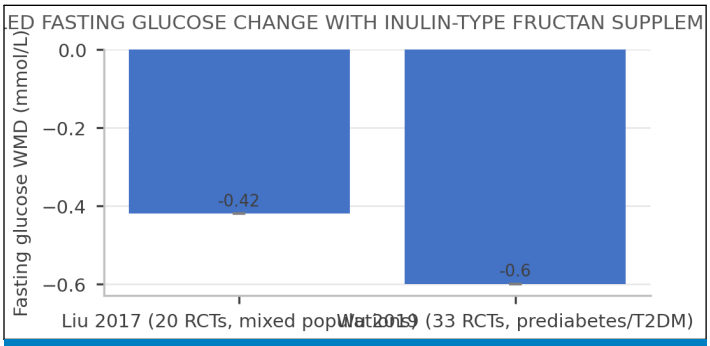

Figure 1: Pooled fasting glucose reduction with inulin-type fructan supplementation in a meta-analysis of 20 randomised controlled trials in mixed populations (non-significant in the type 2 diabetes subgroup) [9] versus a GRADE-assessed dose-response meta-analysis of 33 randomised controlled trials (1,346 participants) in prediabetes and type 2 diabetes [5].

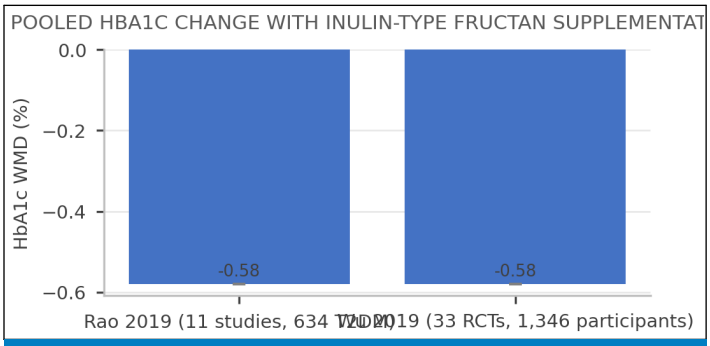

Figure 2: Concordant pooled HbA1c reductions with inulin-type fructan supplementation from two independent meta-analyses: 11 studies (634 patients with type 2 diabetes) [21] and 33 randomised controlled trials (1,346 participants) [5].

Dose, Formulation, and Patient Selection

The trial evidence suggests that not all ITF formulations or doses are equivalent. Dose-response modelling indicates that benefit is most reliably observed at approximately 10 g/day and requires at least six weeks of continuous

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exposure, with shorter or lower-dose regimens more likely to yield null results [5]. Chain length also appears relevant: longer-chain native inulin and high-performance inulin preparations, fermented more slowly and distally along the colon, have shown more consistent glycaemic benefit in T2DM trials than short-chain oligofructose or fructooligosaccharide preparations fermented rapidly in the proximal colon [13,19]. Combination formulations pairing ITFs with a preformed SCFA such as butyrate have produced some of the largest reported GLP-1 and glycaemic responses, raising the possibility that fibre-alone regimens under-deliver relative to their fermentation potential in some individuals [12]. Baseline adiposity and background glucose-lowering medication also modify response: meta-regression suggests that participants with higher baseline body-mass index or less well-controlled diabetes may derive greater relative benefit, while insulin-sensitivity outcomes in individuals with lower cardiometabolic risk have been less consistently favourable [21,20]. These considerations argue for stratified reporting of dose, chain length, and baseline metabolic status in future trials, rather than treating "inulin-type fructans" as a single homogeneous exposure.

Safety, Tolerability, and Limitations

ITFs are generally well tolerated at the doses used in these trials, but gastrointestinal symptoms — principally flatulence, bloating, and mild abdominal discomfort — are common and dose-dependent, occurring in the majority of participants at 16 g/day in controlled feeding studies [18]. No trial reviewed reported serious adverse events attributable to ITF supplementation. Interpretive limitations are nonetheless substantial: trials are predominantly small (n=20-70), short in duration (6-12 weeks), and drawn disproportionately from a small number of research groups, raising concerns about generalisability and, in at least one instance, about outlier-driven pooled estimates [10]. Reporting of HbA1c, fasting insulin, and HOMA-IR is inconsistent across trials, definitions of T2DM and background glucose-lowering therapy are heterogeneous, and blinding of a fibre supplement against an inert placebo is complicated by its distinctive gastrointestinal effects. Mechanistic work in chicory-derived ITF models, including a rodent study showing suppression of hepatic JNK and MAPK inflammatory signalling with amelioration of hyperglycaemia [25], reviewed comprehensively elsewhere [26], supports biological plausibility for hepatic and inflammatory pathways but cannot substitute for adequately powered clinical trials in T2DM.

Conclusion

Across a substantial and growing randomised trial and meta-analytic literature, inulin-type fructan supplementation at approximately 10 g/day for six weeks or longer produces modest, reasonably consistent reductions in fasting glucose and HbA1c in patients with type 2 diabetes, plausibly mediated through bifidogenic shifts in gut microbiota, short-chain fatty acid production, and enhanced GLP-1 signalling. Effects on insulin resistance are less uniform, gastrointestinal tolerability limits some patients, and at least one influential positive meta-analysis has been challenged as outlier-driven. Larger, longer, and more rigorously standardised trials are needed before ITFs can be recommended as an adjunct glycaemic therapy rather than a general dietary fibre source. Future trials should standardise dose (approximately 10 g/day), chain length, and treatment duration (at least 12 weeks), report HbA1c alongside fasting glucose and HOMA-IR, and pre-specify subgroups by baseline body-mass index and background glucose-lowering therapy, so that the true clinical magnitude and durability of ITF-associated glycaemic benefit in type 2 diabetes can be established with greater confidence.

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