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EFFECTS OF CHROMIUM(III) SUPPLEMENTATION ON INSULIN RESISTANCE AND DIABETES – A REVIEW

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ABSTRACT

Chromium(III) is a trace element traditionally associated with carbohydrate metabolism and insulin signaling. This review examines the effects of chromium supplementation on insulin sensitivity and glycemic control, particularly in individuals with type 2 diabetes mellitus (T2DM) and insulin resistance. Chromium picolinate (CrPic), typically administered at 100–1000 µg/day, is the most extensively investigated formulation. Numerous randomized controlled trials have reported significant reductions in fasting glucose, insulin concentrations, and glycated hemoglobin (HbA1c) in patients with T2DM following chromium supplementation. Improvements in glucose tolerance (OGTT) and insulin sensitivity assessed by hyperinsulinemic–euglycemic clamp studies have also been documented, although the number of studies employing these diagnostic techniques remains limited. Results across the literature, however, remain inconsistent, with several trials reporting no significant changes in glycemic markers or insulin sensitivity indices such as HOMA-IR and QUICKI. Chromium efficacy appears to depend on individual patient characteristics, baseline chromium status, and the presence of metabolic disorders, suggesting that those with chromium deficiency or pronounced metabolic impairment may derive greater benefit. Future research should enroll larger patient cohorts and incorporate comprehensive methods for assessing insulin sensitivity. To ensure comparability with earlier clinical trials, upcoming studies should also replicate key methodological assumptions – particularly those related to chromium dosage and participant health status. Although findings are promising in selected subpopulations, additional large-scale, rigorously controlled trials are required to establish optimal dosing strategies and long-term safety. In this review, we evaluated the effects of supplemental chromium(III) on major biochemical indices relevant to metabolic assessment, including fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), fasting insulinemia, HOMA-IR, QUICKI, oral and intravenous glucose tolerance tests (OGTT, IVGTT/FSIVGTT), and the hyperinsulinemic–euglycemic clamp. Detailed findings are presented in the following sections.

Keywords: chromium(III), supplementation, insulin resistance, diabetes

INTRODUCTION

Trivalent chromium (Cr III) continues to attract scientific attention because of its proposed involvement in glucose metabolism and insulin signaling. This trace element has been suggested to enhance insulin receptor phosphorylation and facilitate glucose transport in peripheral tissues (Asbaghi et al., 2020; Hua et al., 2012; Zhao et al., 2022). However, its therapeutic relevance for type 2 diabetes

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mellitus (T2DM) and insulin resistance (IR) remains uncertain.

Evidence from meta-analyses and systematic reviews assessing the efficacy of chromium(III) supplementation on glycemic outcomes and insulin sensitivity is inconsistent. In a meta-analysis by Asbaghi et al. (2020) comprising 25 randomized controlled trials (n = 1257), statistically significant reductions in fasting glucose, insulin, and HOMA-IR were reported, although substantial heterogeneity and variable methodological quality were noted. Similarly, Zhao et al. (2022), in a meta-analysis of 14 trials involving 875 patients with T2DM, observed a small but statistically significant reduction in glycated hemoglobin (HbA1c), whereas changes in fasting glucose did not reach statistical significance. The authors suggested that treatment responses may depend on factors such as chromium formulation, dosage, intervention duration, and patients' metabolic profiles.

Earlier work by Costello et al. (2016) reached comparable conclusions, emphasizing that although some studies report improvements in glycemic control, the overall strength of evidence supporting chromium as an effective therapeutic agent for T2DM remains limited.

There is also evidence that patient characteristics may influence responsiveness to supplementation. Individuals with higher baseline glucose or HbA1c levels may – though not consistently – exhibit more pronounced responses to chromium supplementation (Wang et al., 2010). While these findings are encouraging for certain subgroups, heterogeneity in study design, chromium formulations, and relatively short intervention periods limits the ability to draw broad clinical recommendations.

The aim of this review is to synthesize current evidence on the effects of Cr(III) supplementation on key metabolic indicators in individuals with insulin resistance and T2DM, including fasting glucose, insulin levels, HbA1c, HOMA-IR, QUICKI, OGTT, and insulin sensitivity tests. The review focuses on human clinical trials published in PubMed and Scopus after 2000, with attention to dosage, formulation, and specific chromium(III) compounds used in the management of insulin resistance and diabetes.

Fasting blood glucose

Fasting plasma glucose (FPG) remains one of the most widely used indicators for assessing insulin sensitivity and diagnosing type 2 diabetes mellitus (T2DM), owing to its simplicity, accessibility, and non-invasiveness (Munekawa et al., 2022).

Chromium picolinate (CrPic) is the most extensively studied chromium formulation in investigations of its potential effects on FPG. Early trials conducted between 2000 and 2006 in healthy individuals and in populations with overweight or obesity generally did not demonstrate significant benefits of CrPic supplementation (Amato et al., 2000; Kleefstra et al., 2006; Volek et al., 2006; Volpe et al., 2001). Amato et al. (2000) and Volpe et al. (2001) reported no improvements in FPG among healthy participants, and Kleefstra et al. (2006) found no meaningful effect after six months of supplementation (500–1000 µg/day) in patients with T2DM. Similarly, Volek et al. (2006) observed no changes in overweight but otherwise healthy adults. However, not all findings from this period were negative: Martin et al. (2006) reported a significant reduction in fasting glucose after six months of 1000 µg/day CrPic in individuals with T2DM.

Most subsequent research conducted from 2005 to 2018 likewise produced neutral results, with numerous trials reporting no glucose-lowering effect of CrPic supplementation (Ali et al., 2011; Amiri Siavashani et al., 2018; Anton et al., 2008; Ashoush et al., 2016; Brownley et al., 2013; Feiner et al., 2008; Gunton et al., 2005; Whitfield et al., 2016). Notably, one of the largest randomized controlled trials – Cefalu et al. (2010), involving 93 patients with T2DM receiving 1000 µg/day CrPic for 24 weeks – also reported no significant differences in fasting glucose compared with placebo.

Mixed results have been observed in women with polycystic ovary syndrome (PCOS). Ashoush et al. (2016) reported no improvement in fasting glucose after six months of high-dose supplementation (1000 µg/day) in 85 women, while Amiri Siavashani et al. (2018) likewise found no significant changes after eight weeks of supplementation at 200 µg/day.

In contrast, several trials have reported beneficial effects. Albarracin et al. (2008) conducted one of the largest randomized controlled trials to date, enrolling 348 overweight or obese individuals with T2DM, and

Table 1. Studies on chromium picolinate and fasting glucose

Study – author, year	Number of participants	Medical conditions	Chromium dose µg/day	Duration	Changes in fasting glucose
Martin et al., 2006	25	T2DM	1000 µg	24 weeks	↓
Albarracin et al., 2008	348	T2DM	600 µg (+2 mg biotin)	12 weeks	↓
Jamilian et al., 2018	40	PCOS	200 µg	8 weeks	↓
Jamilian et al., 2020	40	PCOS	200 µg	12 weeks	↓
Derosa et al., 2020	130	IGT, impaired fasting glucose	100 µg	12 weeks	↓
Farrokhian et al., 2020	64	Coronary artery disease; T2DM	200 µg	12 weeks	↓
Amato et al., 2000	19	None	1000 µg	8 weeks	–
Volpe et al., 2001	37	None	400 µg	12 weeks	–
Gunton et al., 2005	40	IGT	800 µg	12 weeks	–
Kleefstra et al., 2006	46	T2DM	500 or 1000 µg	24 weeks	–
Volek et al., 2006	16	None	600 µg	4 weeks	–
Anton et al., 2008	19	Increased carbohydrate craving	1000 µg	8 weeks	–
Feiner et al., 2008					–
Ali et al., 2011	59	IGT, impaired fasting glucose, or MetS	500 or 1000 µg	24 weeks	–
Brownley et al., 2013	19	BED, depression	1000 µg (group I), 600 µg (group II)	24 weeks	–
Whitfield et al., 2016	12	T2DM	200 µg	40 days	–
Ashoush et al., 2016	85	PCOS	1000 µg	24 weeks	–
Amiri Siavashani et al., 2018	34	PCOS	200 µg	8 weeks	–
Talab et al., 2020	41	T2DM	400 µg	8 weeks	–
Moradi et al., 2020	43	NAFLD	400 µg	12 weeks	–

↓ significant decrease; – no significant effects; T2DM – type 2 diabetes mellitus; PCOS – polycystic ovary syndrome; CrPic – chromium picolinate; IGT – impaired glucose tolerance; MetS – metabolic syndrome; BED – binge eating disorder; NAFLD – non-alcoholic fatty liver disease.

found that 600 µg/day CrPic plus 2 mg/day biotin for 12 weeks significantly reduced fasting glucose. Jamilian et al. (2018) similarly observed a significant FPG reduction after eight weeks of 200 µg/day CrPic in 40 women with PCOS. In a subsequent study, a 12-week combination of CrPic (200 µg/day) and L-carnitine also led to a significant reduction in FPG (Jamilian et al., 2020).

Moreover, Derosa et al. (2020) reported significant reductions in fasting glucose after 12 weeks of supplementation with 100 µg/day CrPic in 130 individuals with impaired glucose tolerance. Likewise, Farrokhian et al. (2020) found that 12 weeks of supplementation with 200 µg/day CrPic significantly lowered fasting glucose in 64 overweight or obese patients with T2DM.

Table 2. Effects of chromium yeast on fasting glucose levels

Study – author, year	Number of participants	Medical conditions	Chromium dose µg/day	Duration	Changes in fasting glucose
Bahijiri et al., 2000	78	T2DM	23 µg	8 weeks	↓
Racek et al., 2006	36	T2DM	400 µg	12 weeks	↓
Sharma et al., 2011	40	T2DM (newly diagnosed)	42 µg	12 weeks	↓
Racek et al., 2013	11	T2DM (insulin treatment)	100 µg (weeks 1–2); 200 µg (weeks 3–8)	8 weeks	↓
Nussbaumerova et al., 2018	65	MetS; IGT	300 µg	24 weeks	–

↓ significant decrease; – no significant effects; T2DM – type 2 diabetes mellitus; MetS – metabolic syndrome; IGT – impaired glucose tolerance.

In summary, although several recent studies have demonstrated beneficial effects of chromium picolinate on fasting glucose – particularly among metabolically burdened populations such as individuals with T2DM, impaired glucose tolerance, PCOS, or coronary artery disease – a considerably larger body of evidence, including many trials in healthy subjects and studies conducted throughout 2000–2018, has not confirmed a reproducible glucose-lowering effect (Ali et al., 2011; Amato et al., 2000; Ashoush et al., 2016; Kleefstra et al., 2006; Talab et al., 2020; Volpe et al., 2001; Whitfield et al., 2016). Overall, current evidence does not support a consistent or clinically meaningful effect of CrPic on fasting plasma glucose across diverse populations.

Several studies have reported beneficial effects of chromium yeast supplementation on glycemic control (Bahijiri et al., 2000; Racek et al., 2006; Racek et al., 2013; Sharma et al., 2011). In an early trial involving 78 individuals with type 2 diabetes (T2DM), Bahijiri et al. (2000) showed that 23 µg of chromium from brewer's yeast lowered fasting glucose more effectively than 200 µg of chromium chloride ($CrCl_3$). Yeast-bound chromium also produced a more sustained glycemic response and exhibited greater retention in the body (Bahijiri et al., 2000).

These findings are supported by additional clinical evidence. Racek et al. (2006) reported improvements in fasting glucose and other metabolic parameters with chromium-enriched yeast supplementation, and Sharma et al. (2011) observed comparable benefits in their trial. Further support comes from Racek et al. (2013), who again documented significant reductions in fasting glucose following chromium yeast intake.

More recent evidence, however, has been less consistent. Nussbaumerova et al. (2018) found that a higher dose of yeast-derived chromium (300 µg/day) administered for 24 weeks in 65 patients with metabolic syndrome and impaired glucose tolerance did not produce significant improvements in OGTT outcomes or overall glycemic control.

BLOOD HEMOGLOBIN A1C (HBA1C)

Glycated hemoglobin (HbA1c) reflects average blood glucose levels over the preceding 2–3 months and serves as a key diagnostic and prognostic marker of long-term glycemic control, particularly in individuals with diabetes. Its inclusion in studies of chromium supplementation therefore provides useful insights into the sustained metabolic effects of chromium intervention (Sherwani et al., 2016).

One of the earliest clinical trials examining chromium's effects on HbA1c was conducted by Racek et al. (2006), who supplemented 36 women with type 2 diabetes with 400 µg/day of brewer's yeast–derived chromium for three months. No significant reductions in HbA1c levels were observed.

More favorable outcomes were reported in two subsequent randomized controlled trials using chromium picolinate. Martin et al. (2006) found a statistically significant decrease in HbA1c following six months of supplementation with 1000 µg/day. Similarly,

Table 3. Effect of chromium supplementation on glycated hemoglobin (HbA1c)

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in HbA1c
Martin et al., 2006	25	T2DM	Chromium picolinate	1000 µg	24 weeks	↓
Pei et al., 2006	60	T2DM	Chromium--enriched milk	200 µg	16 weeks	↓
Albarracin et al., 2008	348	T2DM	Chromium picolinate	600 µg (+2 mg biotin)	12 weeks	↓
Cefalu et al., 2010	93	T2DM	Chromium picolinate	1000 µg	24 weeks	↓
Sharma et al., 2011	40	T2DM (newly diagnosed)	Yeast	42 µg	12 weeks	↓
Racek et al., 2013	11	T2DM (on insulin treatment)	Yeast	100 µg (weeks 1–2); 200 µg (weeks 3–8)	8 weeks	↓
Kleefstra et al., 2006	46	T2DM	Chromium picolinate	500 µg (I group); 1000 µg (II group)	24 weeks	–
Racek et al., 2006	36	T2DM	Yeast	400 µg	12 weeks	–
Aghdassi et al., 2010	46	HIV; hyperglycemia; IO	Chromium nicotinate	400 µg	16 weeks	–
Brownley et al., 2013	24	BED	Chromium picolinate	1000 µg (I group); 600 µg (II group)	24 weeks	–
Guimarães et al., 2013	42	T2DM	Chromium nicotinate	50 µg (I group); 200 µg (II group)	12 weeks	–
Guimarães et al., 2016	42	T2DM	Chromium nicotinate	50 µg (I group); 200 µg (II group)	12 weeks	–

↓ significant decrease; – no significant effects; T2DM – type 2 diabetes mellitus; BED – binge eating disorder; HbA1c – glycated hemoglobin; IR – insulin resistance.

Albarracin et al. (2008) demonstrated significant reductions in HbA1c and fasting plasma glucose in a trial involving 348 adults with T2DM after 90 days of supplementation with 600 µg/day of chromium picolinate combined with 2 mg/day of biotin.

However, other studies from this period failed to replicate these findings. Kleefstra et al. (2006) reported no significant improvement in HbA1c in patients with T2DM after six months of supplementation with 500–1000 µg/day of chromium picolinate. Brownley et al. (2013) likewise observed no HbA1c reductions, though their study had a small sample size and excluded individuals with type 2 diabetes, limiting generalizability.

A beneficial effect was later demonstrated in a trial of chromium-enriched yeast conducted by Sharma et al. (2011). In this three-month study of 40 participants, supplementation with 42 µg/day of chromium led to a significant reduction in HbA1c despite the relatively low dose. Similarly, Racek et al. (2013) observed a decrease in HbA1c following an eight-week intervention in 11 subjects; however, the small sample size and short duration substantially limit the interpretability of these results.

More recently, a retrospective analysis of NHANES 2015–2016 data by Chen et al. (2022) identified a significant association between lower habitual chromium intake and elevated HbA1c, suggesting that adequate dietary chromium may support improved long-term glycemic control.

Higher-dose chromium yeast supplementation was evaluated in a 24-week randomized study by Nussbaumerova et al. (2018). In this study, 65 individuals with metabolic syndrome and impaired glucose tolerance received 300 µg/day of yeast-derived chromium, but no significant changes in HbA1c or glycemic responses were observed.

Taken together, current evidence indicates that chromium supplementation – particularly in the form of chromium picolinate or yeast-bound chromium – may have the potential to reduce HbA1c levels; however, findings remain inconsistent. While several randomized trials in T2DM populations have shown significant improvements, other studies, including those using higher doses or longer intervention periods, have failed to confirm these effects. Further research is needed to clarify chromium's clinical relevance in modulating long-term glycemic regulation.

No significant reductions in HbA1c have been reported in studies evaluating chromium nicotinate, a form of chromium bound to vitamin B3 (niacin) (Aghdassi et al., 2010; Guimarães et al., 2013, 2016). One of the earliest trials assessing chromium in food form was conducted by Pei et al. (2006), who provided 60 patients with type 2 diabetes with milk enriched with 200 µg of chromium; no significant changes in HbA1c were observed.

The effects of chromium nicotinate were further evaluated in a 16-week intervention by Aghdassi et al. (2010) in 46 HIV-positive patients with hyperglycemia, with no significant change in HbA1c. Similarly, two trials by Guimarães et al. (published in 2013 and 2016; conducted in 2009 and 2011) each enrolled 42 patients with type 2 diabetes and reported no improvements in HbA1c after 90 days of supplementation with either 50 µg or 200 µg/day of chromium nicotinate.

FASTING INSULINEMIA

Fasting insulin concentration is commonly used as an indirect biomarker of insulin sensitivity. Similar to fasting glucose, it helps identify insulin resistance and early disturbances in glucose homeostasis. Hyperinsulinemia – characterized by elevated circulating insulin – typically reflects early compensatory stages of insulin resistance, during which peripheral insulin sensitivity declines and pancreatic insulin secretion increases (Galicia-Garcia et al., 2020).

Across the literature, chromium picolinate (CrPic) is the most extensively studied form in trials assessing fasting insulin (Ali et al., 2011; Anton et al., 2008; Ashoush et al., 2016; Cefalu et al., 2010; Derosa et al., 2020; Farrokhian et al., 2020; Gunton et al., 2005; Jamilian and Asemi, 2015; Jamilian et al., 2018; Jamilian et al., 2020; Kleefstra et al., 2006; Martin et al., 2006; Moradi et al., 2020; Volek et al., 2006; Volpe et al., 2001). Other forms investigated include chromium yeast (Nussbaumerova et al., 2018; Racek et al., 2006), chromium nicotinate (Aghdassi et al., 2010), chromium chloride (Kim et al., 2011), and chromium dinicocysteinate (Aghdassi et al., 2010; Jain et al., 2012).

Most early trials reported null effects. For example, one of the earliest studies by Volpe et al. (2001) found no significant change in fasting insulin following chromium picolinate supplementation. Similar results were observed by Gunton et al. (2005) in individuals with impaired glucose tolerance. Subsequent studies were likewise negative: Racek et al. (2006) found no reduction after chromium yeast supplementation in patients with T2DM, and Kleefstra et al. (2006) reported no improvement after 24 weeks of 500–1000 µg/day CrPic in insulin-treated T2DM patients.

Some studies reported reductions. Martin et al. (2006) found significant decreases after six months of 1000 µg/day CrPic in individuals with T2DM. However, several subsequent trials again reported null effects. Anton et al. (2008) observed no significant changes, Ali et al. (2011) found no reductions in individuals at risk for diabetes, and Kim et al. (2011), evaluating chromium chloride in overweight children, likewise noted no improvement.

Other trials documented benefits in specific populations. Aghdassi et al. (2010) showed that 400 µg/day of chromium nicotinate for 16 weeks reduced fasting insulin in HIV-positive adults with hyperglycemia and elevated HOMA-IR, although the specialized population limits broader generalizability. Jamilian and Asemi (2015) reported improvements with 200 µg/day CrPic in women with polycystic ovary syndrome (PCOS), a finding later corroborated by Jamilian et al. (2018) in a separate PCOS cohort.

Table 4. Effect of chromium supplementation on fasting insulin levels

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in FPI (fasting plasma insulin)
Ashoush et al., 2016	85	PCOS	Chromium picolinate	1000 µg	6 months	↓
Jain et al., 2012	74	T2DM	Chromium dinicocyst-einate (CDNC) Chromium picolinate	400 µg 400 µg	3 months	↓
Pei et al., 2006	60	T2DM	Chromium-enriched milk	200 µg	16 weeks	↓
Aghdassi et al., 2010	46	HIV; Hyperglyce-mia; IR	Chromium nicotinate	400 µg	16 weeks	↓
Kim et al., 2011	25	Overweight	Chromium chloride	400 µg	6 weeks	↓
Jamilian and Asemi, 2015	61	PCOS	Chromium picolinate	200 µg	8 weeks	↓
Jamilian et al., 2018	40	PCOS	Chromium picolinate	200 µg	8 weeks	↓
Farrokhian et al., 2020	64	Coronary artery disease & T2DM	Chromium picolinate	200 µg	12 weeks	↓
Jamilian et al., 2020	40	PCOS	200 µg of chromium picolinate + 1000 mg of carnitine	200 µg	12 weeks	↓
Moradi et al., 2020	43	NAFLD	Chromium picolinate	400 µg	12 weeks	↓
Volpe et al., 2001	37	None	Chromium picolinate	400 µg	12 weeks	–
Gunton et al., 2005	40	IGT	Chromium picolinate	800 µg	12 weeks	–
Kleefstra et al., 2006	46	T2DM 2	Chromium picolinate	500 or 1000 µg	24 weeks	–
Racek et al., 2006	36	T2DM	Chromium yeast	400 µg	12 weeks	–
Anton et al., 2008	40	Increased carbohy-drate craving	Chromium picolinate	1000 µg	8 weeks	–
Cefalu et al., 2010	93	T2DM	Chromium picolinate	1000 µg	24 weeks	–
Ali et al., 2011	59	IGT; Hyperglycemia na czczo lub MetS	Chromium picolinate	500 or 1000 µg	24 weeks	–
Liu et al., 2015	52	Hyperglycemia	Chromium chloride + cinnamon and carnosine	20 µg	16 weeks	–
Nussbaumerova et al., 2018	65	MetS; IGT	Chromium yeast	300 µg	24 weeks	–

↓ significant decrease; – no significant effects; T2DM – type 2 diabetes mellitus; PCOS – polycystic ovary syndrome; FPI – fasting plasma insulin; IR – insulin resistance; MetS – metabolic syndrome; NAFLD – non-alcoholic fatty liver disease; IGT – impaired glucose tolerance.

Favorable results were also observed with chromium dinicocysteinate. Jain et al. (2012) found significant reductions after 12 weeks of 400 μg/day in 74 obese patients with T2DM. In contrast, among individuals with metabolic syndrome and impaired glucose tolerance, Nussbaumerova et al. (2018) reported no improvements following six months of chromium yeast supplementation.

Additional PCOS research showed consistent benefit: Ashoush et al. (2016) demonstrated significant reductions with 1000 μg/day CrPic in 85 overweight or obese women, and Jamilian et al. (2020) again reported decreases following CrPic-based supplementation. In T2DM, Farrokhian et al. (2020) reported reductions observed after 12 weeks of 200 μg/day CrPic. Conversely, Cefalu et al. (2010) found no significant changes after 24 weeks of 1000 μg/day CrPic in a larger T2DM cohort, aligning with earlier findings by Kleefstra et al. (2006). Ali et al. (2011) and Moradi et al. (2020) likewise reported null effects in individuals with impaired glucose metabolism.

Derosa et al. (2020) identified reductions in fasting insulin in individuals with impaired glucose tolerance (IGT) receiving 100 μg/day of CrPic, suggesting chromium's effects may be more pronounced in earlier dysglycemic states.

In summary, findings on chromium's effects on fasting insulin remain highly inconsistent. Benefits are most consistently observed in women with PCOS and in studies using chromium dinicocysteinate or moderate CrPic doses, whereas large randomized trials in T2DM and those employing higher CrPic doses frequently report null outcomes. Overall, chromium's influence appears to depend on population characteristics, chromium formulation, baseline insulin resistance, and underlying metabolic status.

HOMA-IR INDEX

The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a calculated index derived from fasting blood glucose and insulin concentrations. It is widely used to estimate insulin resistance; however, a key limitation is that it does not capture the body's dynamic response to glucose intake (Derosa et al., 2020; Farrokhian et al., 2020; Jamilian et al., 2018).

Early studies examining chromium supplementation and HOMA-IR largely reported neutral findings. In a six-month trial, Kleefstra et al. (2006) observed no improvements in HOMA-IR among individuals with type 2 diabetes following chromium picolinate supplementation. Similarly, Ali et al. (2011) detected no effect of chromium supplementation on insulin resistance in individuals at risk for diabetes. Aghdassi et al. (2010) also reported no improvement after 16 weeks of chromium nicotinate in HIV-positive individuals with hyperglycemia, although the specialized study population limits comparability with typical metabolic cohorts.

More encouraging results were reported in later years. Jain et al. (2012) demonstrated that 400 μg/day of chromium dinicocysteinate significantly improved HOMA-IR in 74 obese patients with type 2 diabetes during a 12-week intervention. Kim et al. (2011) also noted modest improvements using chromium chloride, though the effect magnitude was small.

Positive findings have additionally been reported for chromium picolinate. Jamilian and Asemi (2015) found significant improvements in women with polycystic ovary syndrome (PCOS), and Jamilian et al. (2018) later confirmed significant reductions in an independent PCOS cohort receiving 200 μg/day of CrPic.

Other studies have produced mixed outcomes. Sala et al. (2017) observed no improvements after six months of chromium picolinate, suggesting that prolonged supplementation does not necessarily enhance insulin sensitivity. Similarly, Nussbaumerova et al. (2018) reported no changes after six months of chromium yeast in individuals with metabolic syndrome.

More recent trials have again suggested potential benefits. In a 12-week randomized trial of 130 participants with impaired glucose tolerance, Derosa et al. (2020) found that 100 μg/day of chromium picolinate combined with white mulberry extract significantly reduced HOMA-IR. Talab et al. (2020) likewise reported improvements in insulin resistance following CrPic supplementation.

Further evidence comes from Imanparast et al. (2020), who evaluated four groups of patients with type 2 diabetes over four months. Two groups received 500 μg/day of chromium picolinate, either alone or in combination with vitamin D3. In both chromium-treated groups, glucose and insulin levels remained

Table 5. Effect of chromium supplementation on the HOMA-IR

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in HOMA-IR
1	2	3	4	5	6	7
Pei et al., 2006	60	T2DM	Chromium-enriched milk	200 µg	16 weeks	↓
Aghdassi et al., 2010	46	HIV; Hyperglycemia; IR	Chromium nicotinate	400 µg	16 weeks	↓
Kim et al., 2011	25	Overweight	Chromium chloride	400 µg	6 weeks	↓
Jain et al., 2012	74	T2DM	Chromium dinicocysteinate (CDNC); Chromium picolinate	400 µg 400 µg	12 weeks	↓
Jamilian and Asemi, 2015	61	PCOS	Chromium picolinate	200 µg	8 weeks	↓
Sala et al., 2017	19	BED	Chromium picolinate	600 µg (I group) 1000 µg (II group)	24 weeks	improvement in insulin sensitivity index
Jamilian et al., 2018	40	Infertility; PCOS	Chromium picolinate	200 µg	8 weeks	↓
Imanparast et al., 2020	92	T2DM	Chromium picolinate (+ vitamin D3)	500 µg	16 weeks	↓
Moradi et al., 2020	43	NAFLD	Chromium picolinate	400 µg	12 weeks	↓
Derosa et al., 2020	130	IGT; Fasting hyperglycemia	Chromium picolinate + white mulberry (1 mg 1-deoxynojirimycin)	100 µg	12 weeks	↓
Farrokhian et al., 2020	64	Coronary artery disease and T2DM	Chromium picolinate	200 µg	12 weeks	↓
Jamilian et al., 2020	40	PCOS	Chromium picolinate (+carnitine)	200 µg	12 weeks	↓
Talab et al., 2020	41	T2DM	Chromium picolinate	400 µg	8 weeks	↓
Gunton et al., 2005	40	IGT	Chromium picolinate	800 µg	12 weeks	–
Kleefstra et al., 2006	46	T2DM	Chromium picolinate	500 or 1000 µg	24 weeks	–

Table 5 – cont.

1	2	3	4	5	6	7
Anton et al., 2008	40	Increased carbohydrate craving	Chromium picolinate	1000 µg	8 weeks	–
Ali et al., 2011	59	IGT; Fasting hyperglycemia or MetS	Chromium picolinate	500 or 1000 µg	24 weeks	–
Guimarães et al., 2013	42	T2DM	Chromium nicotinate	50 µg (I group); 200 µg (II group)	12 weeks	–
Liu et al., 2015	52	IGT	Chromium chloride (+ cinnamon and carnosine)	20 µg	16 weeks	–
Guimarães et al., 2016	42	T2DM	Chromium nicotinate	50 and 200 µg	12 weeks	–
Nussbaumerova et al., 2018	65	MetS; IGT	Yeast	300 µg	24 weeks	–
Kim et al., 2018	24	MetS	Chromium chloride	600 µg	24 weeks	–

↓ significant decrease; – no significant effects; T2DM – type 2 diabetes mellitus; PCOS – polycystic ovary syndrome; IR – insulin resistance; BED – binge eating disorder; NAFLD – non-alcoholic fatty liver disease; IGT – impaired glucose tolerance; MetS – metabolic syndrome.

stable, thereby preventing the rise in HOMA-IR observed in the control groups. Farrokhian et al. (2020) similarly documented significant reductions after 12 weeks of 200 µg/day CrPic in overweight and obese individuals with T2DM. Moradi et al. (2020) reported comparable improvements.

Despite these encouraging findings, several long-duration trials have consistently found no significant effects of chromium supplementation on HOMA-IR (Ali et al., 2011; Kim et al., 2018; Kleefstra et al., 2006; Nussbaumerova et al., 2018; Sala et al., 2017). These studies, conducted in populations with metabolic syndrome, hyperglycemia, or established T2DM, collectively suggest that extended chromium supplementation may not yield sustained improvements in insulin resistance.

In summary, improvements in HOMA-IR have been observed most frequently in short- to medium-duration trials involving chromium picolinate, chromium dinicocysteinate, and, in some cases, chromium nicotinate or chromium chloride. By contrast, long-term studies – including those with large sample sizes – have often reported null findings. Overall, evidence indicates that chromium's effect on insulin resistance is inconsistent and may depend on chromium form, intervention length, and the metabolic characteristics of the study population.

QUICKI

The QUICKI index (Quantitative Insulin Sensitivity Check Index), like HOMA-IR, is calculated from fasting glucose and insulin concentrations. QUICKI is considered a more precise and sensitive measure of insulin sensitivity, and – unlike HOMA-IR – higher values indicate improved insulin responsiveness (Kleefstra et al., 2006; Liu et al., 2015).

The earliest study evaluating the effects of chromium supplementation on QUICKI was conducted by Kleefstra et al. (2006). In this six-month trial of 46 predominantly male patients with type 2 diabetes and obesity, daily supplementation with 500 or 1000 µg of chromium picolinate produced no significant changes in QUICKI compared with placebo. Liu et al. (2015) similarly reported no improvement in QUICKI after a four-month intervention in 52 individuals with fasting hyperglycemia. Their null findings may be partly attributable to the very low chromium dose (10 µg/day) and the use of chromium chloride – a form with lower bioavailability – administered alongside cinnamon and carnosine.

Table 6. Effect of chromium supplementation on the QUICKI index

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in QUICKI
Kim et al., 2011	25	Overweight	Chromium chloride	400 µg	6 weeks	↑
Jamilian and Asemi, 2015	61	PCOS	Chromium picolinate	200 µg	8 weeks	↑
Jamilian et al., 2018	40	PCOS	Chromium picolinate	200 µg	8 weeks	↑
Farrokhian et al., 2020	64	Coronary artery disease and T2DM	Chromium picolinate	200 µg	12 weeks	↑
Moradi et al., 2020	43	NAFLD	Chromium picolinate	400 µg	3 months	↑
Jamilian et al., 2020	40	PCOS	Chromium picolinate (+carnitine)	200 µg	12 weeks	↑
Kleefstra et al., 2006	46	T2DM	Chromium picolinate	500 and 1000 µg	6 months	–
Liu et al., 2015	52	Hyperglycemia	Chromium chloride (+ cinnamon and carnosine)	20 µg	4 months	–

↑ significant improvement; – no significant effects; T2DM – type 2 diabetes mellitus; PCOS – polycystic ovary syndrome; IR – insulin resistance; NAFLD – non-alcoholic fatty liver disease.

The first study to demonstrate a beneficial effect was published by Kim et al. (2011), who observed increases in QUICKI after six weeks of chromium chloride supplementation in overweight individuals. Shortly thereafter, Jamilian and Asemi (2015) reported significant QUICKI improvements in 61 women with polycystic ovary syndrome (PCOS) receiving 200 µg/day of chromium picolinate for eight weeks.

Evidence published between 2018 and 2020 has largely been consistent. Jamilian et al. (2018) observed significant increases in QUICKI following eight weeks of 200 µg/day CrPic in women with PCOS, and comparable findings were reported in a three-month trial by Jamilian et al. (2020). In a 12-week randomized trial, Farrokhian et al. (2020) demonstrated a significant improvement in QUICKI among 64 overweight or obese adults with type 2 diabetes and coronary artery disease following daily supplementation with 200 µg of chromium picolinate. Moradi et al. (2020) also reported increased QUICKI values after three months of chromium picolinate in patients with NAFLD.

Overall, findings on the effects of chromium supplementation on QUICKI are mixed but lean positive. Early long-duration trials found no benefit – potentially due to severe baseline metabolic impairment or inadequate dosing. In contrast, most short- and medium-duration studies conducted after 2011, particularly those administering 200 µg/day of chromium picolinate, reported significant improvements. These results suggest that chromium supplementation may enhance insulin sensitivity in selected metabolic populations, especially individuals with PCOS or type 2 diabetes.

ORAL AND INTRAVENOUS GLUCOSE TOLERANCE AND INSULIN SENSITIVITY TESTS

Several studies have evaluated chromium's effects on post-load glucose and insulin dynamics using the oral glucose tolerance test (OGTT) (Ali et al., 2011; Bahijiri et al., 2000; Chen et al., 2014; Derosa et al., 2020; Gunton et al., 2005; Lucidi et al., 2005; Martin et al., 2006; Nussbaumerova et al., 2018). OGTT provides a more comprehensive assessment of glycemic regulation than fasting glucose, fasting insulin, or indices derived from them, and is therefore widely used in the diagnosis of insulin resistance and type 2 diabetes mellitus (T2DM).

Across these eight studies, five reported statistically significant improvements in OGTT-derived glucose or insulin responses following chromium

Table 7. Studies on the effect of chromium supplementation using the oral glucose tolerance test (OGTT)

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in OGTT
Bahijiri et al., 2000	78	T2DM	Yeast; Chromium chloride	23 µg 200 µg	8 weeks	↓ (glucose after 2 h)
Lucidi et al., 2005	10	PCOS	Chromium picolinate	200 µg	16 weeks	↓ (glucose after 1 and 2 hours)
Martin et al., 2006	25	T2DM	Chromium picolinate (+ sulfonylurea derivative	1000 µg	24 weeks	↑ (insulin sensitivity)
Pei et al., 2006	60	T2DM	Chromium-enriched milk	200 µg	16 weeks	↑ (insulin sensitivity)
Feiner et al., 2008	6	HIV and IR	Chromium picolinate	1000 µg	8 weeks	↑ (insulin sensitivity)
Chen et al., 2014	66	T2DM	Chromium chloride	200 µg	16 weeks	↑ (second-phase insulin release)
Derosa et al., 2020	130	IGT; impaired fasting glucose	Chromium picolinate (+ white mulberry (1 mg 1-deoxynojirimycin)	100 µg	12 weeks	↓ (glucose)
Gunton et al., 2005	40	IGT	Chromium picolinate	800 µg	12 weeks	–
Ali et al., 2011	59	IGT; Fasting hyperglycemia or MetS	Chromium picolinate	500 and 1000 µg	24 weeks	–
Nussbaumerova et al., 2018	65	MetS; IGT	Yeast	300 µg	24 weeks	–

↓ significant decrease; ↑ significant improvement; – no significant effects; T2DM – type 2 diabetes mellitus; PCOS – polycystic ovary syndrome; IR – insulin resistance; OGTT – oral glucose tolerance test; IGT – impaired glucose tolerance; MetS – metabolic syndrome.

supplementation (Bahijiri et al., 2000; Chen et al., 2014; Derosa et al., 2020; Lucidi et al., 2005; Martin et al., 2006).

The earliest positive findings were reported by Bahijiri et al. (2000), who showed that chromium derived from brewer's yeast significantly improved post-load glucose responses compared with chromium chloride, indicating superior OGTT glucose dynamics with yeast-bound chromium.

Lucidi et al. (2005) examined chromium picolinate (CrPic) in ten women with polycystic ovary syndrome (PCOS) and observed significant reductions in glucose concentrations at one and two hours after glucose ingestion, despite the small sample size.

In a subsequent six-month trial, Martin et al. (2006) demonstrated that chromium supplementation significantly reduced glucose area under the curve (AUC) compared with both baseline and placebo, indicating improved OGTT glycemic handling.

Further support comes from Chen et al. (2014), who studied 66 patients with T2DM and reported that 200 µg/day of chromium chloride for 16 weeks significantly enhanced insulin sensitivity and insulin response two hours after glucose intake. These improvements were significant both within the chromium group and in comparison with placebo.

More recently, Derosa et al. (2020) also found significant improvements in OGTT outcomes following chromium supplementation in individuals with impaired glucose tolerance.

In contrast, three studies did not observe improvements in OGTT outcomes. Gunton et al. (2005) reported no benefit of 800 µg/day CrPic in 40 individuals with impaired glucose tolerance. Ali et al. (2011) found no significant effects after 24 weeks of supplementation with 500 and 1000 µg/day CrPic in 59 participants. Similarly, Nussbaumerova et al. (2018) reported no significant changes in OGTT glucose or insulin responses after six months of yeast-derived chromium supplementation in 66 individuals with metabolic syndrome and impaired glucose tolerance.

Overall, the evidence from OGTT studies is mixed. Positive effects were more common in early and mid-period trials and in studies using brewer's yeast chromium, chromium picolinate, or chromium chloride. These typically showed improved post-load glucose responses or enhanced insulin sensitivity. However, several long-duration studies – particularly in individuals with impaired glucose tolerance – did not replicate these effects. Collectively, the findings suggest that chromium may improve OGTT outcomes under specific metabolic conditions, but its efficacy appears to depend on chromium form, dosage, metabolic status, and sample size.

FREQUENTLY SAMPLED INTRAVENOUS GLUCOSE TOLERANCE TEST AND HYPERINSULINEMIC-EUGLYCEMIC CLAMP

One study has applied the Frequently Sampled Intravenous Glucose Tolerance Test (FSIVGTT), a method that provides detailed information on glucose regulation, pancreatic β-cell function, and insulin sensitivity. In FSIVGTT, glucose is administered intravenously, and multiple blood samples are collected over time, producing a dynamic profile of glucose and insulin responses. Although widely used in research on type 2 diabetes, insulin resistance, and metabolic syndrome, its methodological complexity limits its use in routine clinical practice (Tompkins et al., 2010).

The earliest chromium-related FSIVGTT study was performed by Pei et al. (2006). In this randomized controlled trial, 60 adults consumed milk enriched with 200 µg/day of chromium chloride for 16 weeks. Chromium supplementation produced a statistically significant improvement in insulin sensitivity compared with placebo (Pei et al., 2006).

In addition to FSIVGTT, three trials employed the hyperinsulinemic-euglycemic clamp, considered the gold standard for evaluating insulin resistance. This technique employs controlled insulin and glucose infusion, enabling precise quantification of basal and maximal insulin sensitivity. It also distinguishes hepatic from peripheral insulin resistance by measuring hepatic glucose output suppression and peripheral glucose uptake (Tam et al., 2012).

The earliest clamp-based chromium trial, conducted by Martin et al. (2006), in individuals with T2DM, found a significant improvement in insulin sensitivity following chromium picolinate supplementation. A subsequent study by Feiner et al. (2008) also reported enhanced insulin sensitivity, although chromium was co-administered with another insulin-sensitizing

Table 8. Studies evaluating the effect of chromium supplementation using the euglycemic-hyperinsulinemic clamp (EHC)

Study – author, year	Number of participants	Medical conditions	Chromium compound	Chromium dose µg/day	Duration	Changes in EHC (insulin sensitivity)
Martin et al., 2006	25	T2DM	Chromium picolinate (+ sulfonylurea derivative)	1000 µg	24 weeks	↑ (improved insulin sensitivity)
Feiner et al., 2008	6	HIV and insulin resistance	Chromium picolinate	1000 µg	8 weeks	↑ (improved insulin sensitivity)
Derosa et al., 2020	130	IGT; impaired fasting glucose	Chromium picolinate (+ white mulberry with 1 mg DNJ)	100 µg	12 weeks	↑ (improved insulin sensitivity)

↑ statistically significant improvement; T2DM – type 2 diabetes mellitus; IGT – impaired glucose tolerance; EHC – euglycemic-hyperinsulinemic clamp.

agent, making chromium's isolated effect uncertain. A later trial by Derosa et al. (2020) similarly documented improvements in clamp-measured insulin sensitivity, but chromium was again combined with an additional bioactive compound, limiting attribution of the effect solely to chromium.

Overall, studies using FSIVGTT and the hyperinsulinemic-euglycemic clamp consistently report improvements in insulin sensitivity following chromium supplementation. However, because two of the three clamp-based trials involved chromium co-supplementation, the specific contribution of chromium remains partly unclear. Evidence from high-precision metabolic testing indicates potential benefits, but definitive conclusions about chromium's isolated effects require further targeted research.

SUMMARY

The available evidence suggests that supplementation with highly bioavailable trivalent chromium compounds – such as chromium picolinate, chromium nicotinate, and chromium-enriched yeast – may exert beneficial effects on insulin sensitivity and glycemic regulation, particularly in individuals with type 2 diabetes or established insulin resistance. Several studies have demonstrated improvements using robust diagnostic methods, including HbA1c measurements and advanced glucose- and insulin-infusion techniques. Retrospective analyses further indicate that inadequate dietary chromium intake may be associated with a higher risk of developing diabetes.

Nevertheless, many trials have failed to replicate these benefits. A substantial proportion relied only on fasting glucose and fasting insulin, which provide an incomplete picture of metabolic function. In several interventions, chromium was administered alongside other insulin-modulating agents, limiting the ability to attribute outcomes specific to chromium. Small sample sizes were also common, and the chromium dose–response relationship remains unclear, as both low and high doses have produced inconsistent results.

Interpreting the literature is additionally complicated by the broad temporal span of included studies. Evolving diagnostic criteria, analytic techniques, and shifts in population health over the past two decades may affect the comparability of trials. Geographical and environmental factors – such as regional dietary patterns, variability in food chromium content, and differences in nutritional status – may further modify baseline chromium exposure and shape supplementation responses.

Given these limitations, future research should involve larger and more heterogeneous study populations, employ standardized and comprehensive measures of insulin sensitivity, and incorporate regional dietary variability as well as temporal differences in study design. Such methodological refinement is essential to determine the true clinical relevance of trivalent chromium supplementation in metabolic disorders.

DECLARATIONS

Data statement

All data supporting this study has been included in this manuscript.

Ethical Approval

Not applicable.

Competing Interests

The authors declare that they have no conflicts of interest.

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