Al-Rafidain J Med Sci. 2026;10(2):184-191.
DOI: https://doi.org/10.54133/ajms.v10i2.2841

AJMS

Online ISSN (3219-2789)

Research Article

Efficacy of Chromium Picolinate in Reducing Acanthosis Nigricans Severity in Adolescents with Insulin Resistance

Ghasak Kais Abd-Alhussain*
Department of Pharmacology, College of Pharmacy, Uruk University, Baghdad, Iraq
Received: 11 February 2026; Revised: 5 April 2026; Accepted: 13 April 2026

Abstract

Background: Acanthosis nigricans (AN) is a well-known skin condition characterized by the development of hyperpigmented skin patches associated with abnormal texture and is closely related to metabolic syndromes characterized by insulin resistance. Chromium picolinate supplementation, especially, is suggested to improve insulin function in peripheral tissue by stimulating the insulin receptors. Which might ultimately improve the severity of acanthosis nigricans. There is not enough evidence to support the significance of this correlation. ***Objective***: To determine the efficacy of chromium picolinate in reducing the clinical severity of acanthosis nigricans and improving insulin resistance in Iraqi adolescents and report any adverse effects. ***Methods***: 95 adolescent patients with insulin resistance and acanthosis nigricans were randomly allocated into two groups in a 1:1 ratio. Group I (n=48) received chromium supplementation for 24 weeks, while Group II (n=47) received identical placebo capsules for the same duration. Changes in the baseline insulin resistance status and Acanthosis Nigricans severity were then recorded during follow-up visits at 8, 16, and 24 weeks. ***Results***: Chromium supplementation significantly reduced Burke scores from baseline (mean 8.96±2.00) to 24 weeks (5.45±2.14) compared to placebo (9.04±1.92 to 8.00±1.88. HOMA-IR decreased markedly in the chromium group (4.10±0.92 to 2.75±0.89) versus placebo (3.96±0.84 to 3.62±0.85). Changes in HOMA-IR and Burke scores were strongly correlated (r=0.749, p<0.001). ***Conclusions***: Chromium supplementation effectively improves insulin resistance and acanthosis nigricans severity in at-risk adolescents, supporting its use as a safe adjunctive therapy for metabolic dysfunction.

Keywords: Acanthosis nigricans; Chromium picolinate; Insulin resistance; Metabolic syndrome.

فعالية بيكولينات الكروم في تقليل شدة التهاب الأكانثوس الأسود لدى المراهقين الذين يعانون من مقاومة الأنسولين

الخلاصة

الخلفية: الأكانثوس الأسود (AN) هو حالة جلدية معروفة تتميز بتطور رقع جلدية مفرطة التصبغ المرتبطة بملمس غير طبيعي، وهي مرتبطة ارتباطا وثيقا بمتلازمات الأيض التي تتميز بمقاومة الأنسولين. أن مكملات الكروم بيكولينات، بشكل خاص، تحسن وظيفة الأنسولين في الأنسجة الطرفية من خلال تحفيز مستقبلات الأنسولين. وقد يؤدي ذلك في النهاية إلى تحسين شدة مرض الأكانثوسيس الأسود. لا توجد أدلة كافية تدعم أهمية هذا الترابط. **الهدف**: تحديد فعالية الكروميوم بيكولينات في تقليل شدة الأكانثوز الأسود السريرية وتحسين مقاومة الأنسولين لدى المراهقين العراقيين والإبلاغ عن أي آثار جانبية. **الطرائق**: تم توزيع 95 مريضا مراهقا يعانون من مقاومة الإنسولين ومرض الأكانثوز الأسود بشكل عشوائي إلى مجموعتين بنسبة 1:1. تلقت المجموعة الأولى (n=48) مكملات الكروم لمدة 24 أسبوعا، بينما تلقت المجموعة الثانية (n=47) كبسولات وهمية متطابقة لنفس المدة. تم تسجيل تغييرات في حالة مقاومة الأنسولين الأساسية وشدة المرض خلال زيارات المتابعة في الأسبوع الثامن والعشرين والرابع والعشرين. **النتائج:** خفض تناول مكملات الكروم درجات بيرك بشكل ملحوظ من المعدل الأساسي (المتوسط 8.96±2.00) إلى 24 أسبوعا (5.45±2.14) مقارنة بالدواء الوهمي (9.04±1.92 إلى 8.00±1.88. انخفض HOMA-IR بشكل ملحوظ في مجموعة الكروم (4.10±0.92 إلى 2.75±0.89) مقابل الدواء الوهمي (3.96±0.84 إلى 3.62±0.85). كانت التغيرات في درجات HOMA-IR ودرجات بيرك مرتبطة بقوة (r=0.749، ص<0.001). **الاستنتاجات**: مكملات الكروم تحسن بشكل فعال مقاومة الأنسولين وشدة الأكانثوسيس الأسود لدى المراهقين المعرضين للخطر، مما يدعم استخدامه كعلاج مساعد آمن لخلل الأيض.

* ***Corresponding author***: Ghasak K. Abd-Alhussain. Department of Pharmacology, College of Pharmacy, Uruk University, Baghdad, Iraq ; Email: kassaq.kais@uruk.edu.iq
Article citation: Abd-Alhussain GK. Efficacy of Chromium Picolinate in Reducing Acanthosis Nigricans Severity in Adolescents with Insulin Resistance. *Al-Rafidain J Med Sci*. 2026;10(2):184-191. doi: https://doi.org/10.54133/ajms.v10i2.2841

INTRODUCTION

Acanthosis nigricans (AN) is a well-known skin condition characterized by the development of hyperpigmented skin patches that are brown and velvety in nature associated with abnormal skin texture [1]. These lesions are commonly distributed in the neck and the axillae and could be less commonly found on the elbows, knuckles, knees, or might even cover a large area of the skin or appear at the mucosal surfaces. Acanthosis nigricans affects both sexes and is usually symmetrical in distribution; unilateral variations of this condition may be represented as an epidermal nevus [2]. This condition is mainly asymptomatic except for a macerated and inflamed lesion in the skin folds that may become uncomfortable and malodorous [1,2]. This type of lesion is basically related to obesity and endocrine metabolic syndromes that are characterized by Insulin resistance, making it usually associated with the development of certain disorders, including type 2 diabetes mellitus

(T2DM) and polycystic ovarian syndrome (PCOS) [3]. Other causes of Acanthosis Nigricans include less frequently observed familial and genetic etiologies. Acanthosis nigricans can also rarely be a sign of malignancy [4,5]. The more common metabolic etiology is closely related to disorders characterized by insulin resistance, in which the development of hyperinsulinemia might lead to keratinocyte stimulation by direct effect on the insulin-like growth factor receptor-1 (IGFR1), leading to the development of the skin lesion defining this condition; otherwise, the exact mechanism of development of this condition is not fully understood and might be related to the stimulation of other contributing factors involving fibroblast growth factor receptor (FGFR) and epidermal growth factor receptor (EGFR) [1,6]. In a study of 236 children with acanthosis nigricans and 51 overweight children without the disorder, significant associations of acanthosis nigricans with insulin resistance and abnormal glucose homeostasis were detected [7]. Another United States-based study showed that the prevalence of Acanthosis Nigricans in young patients is significantly related to increased body mass index (BMI), which might ultimately lead to insulin resistance [8]. Although cases of asymptomatic insulin resistance and acanthosis nigricans do not prompt any sort of therapeutic intervention, literature studies associated with these conditions suggest that patients might benefit from certain adjunctive insulin-sensitizing agents, including metformin, as well as certain types of supplementation, including vitamin D and Chromium [9-11]. Chromium is a trace metal supplement that is widely hypothesized to aid in cases of insulin resistance and its associated metabolic disorders [9]. It is because chromium, especially in its picolinate form, improves insulin function on peripheral tissue by stimulating the insulin receptors. This theorized stimulation is based on an in vitro study fact that demonstrates chromium enhancement of insulin receptor-β activity, promotion of the movement of Glut-4 (a protein that enhances the glucose uptake to the surface of the cell), as well as reduction in the activity of PTP-1B (protein tyrosine phosphatase-1B), which slows insulin signaling [12,13]. Based on these theories, it is rational to hypothesize that chromium supplementation might improve insulin resistance, which might ultimately lead to a reduction in the clinical severity of associated conditions, including Acanthosis Nigricans. Unfortunately, this theory is rarely evaluated globally and regionally, and there is no strong evidence for the significance of this correlation. In this double-blinded randomized control trial (RCT), the goal is to determine the efficacy of chromium picolinate in reducing the clinical severity of acanthosis nigricans and improving insulin resistance in a sample of Iraqi adolescent patients and report any adverse effects. To bridge the current gap in clinically relevant research.

METHODS

Study design

The current study is a two-arm, double-blind, randomized controlled trial (RCT), conducted between January 1st, 2025, and January 1st, 2026, in the pediatric endocrine clinic and related facilities of a single specialized pediatric center. Written and informed consent was obtained from the patients and their guardians to participate in the study and undergo all the follow-up procedures. About 108 adolescent patients of both sexes clinically presented with acanthosis nigricans and confirmed insulin resistance—defined as homeostasis model assessment of insulin resistance (HOMA-IR) ≥ 2.5—were assessed for eligibility. A total of 95 patients were deemed eligible and allocated randomly into two groups in a 1:1 ratio. Group I (n=48) was labeled as the experimental group; patients in this group were assigned to receive chromium picolinate 200 mcg capsules once daily [14,15] for the upcoming 24-week study period. Group II (n=47) was labeled as the placebo comparator: patients in this group were assigned to receive an oral placebo capsule matching the shape, size, and color of chromium picolinate once daily for the upcoming 24-week study period. All patients were assessed clinically for the baseline severity of acanthosis nigricans using Burke's quantitative score, as well as the baseline insulin resistance indicator using a fasting blood sample to determine serum glucose and serum insulin and calculate HOMA-IR. Follow-up visits were then scheduled for each patient at 8 weeks, 16 weeks, and 24 weeks after the initiation of the allocated intervention to examine the changes in clinical severity of acanthosis nigricans and insulin resistance. Dietary intake, physical activity, and weight changes of the participants were not formally monitored during the study; however, general advice was given in a clinical context for the participants to maintain their ongoing usual lifestyle during the study period, which may have influenced the outcomes related to the efficacy of chromium picolinate in reducing the clinical severity of acanthosis nigricans and improving insulin resistance. The main outcome of the study was to determine the efficacy of chromium picolinate in reducing the clinical severity of acanthosis nigricans and improving insulin resistance in adolescents with both conditions as well as reporting any adverse effects. Five participants were lost to follow-up, leaving 90 participants for analysis (45+45). Figure 1 demonstrates the study design in a flow chart.

Blinding and randomization

The current study is double-blinded, in which neither the participant nor the outcome assessors performing the acanthosis nigricans clinical assessment, as well as the insulin resistance laboratory assessment are aware of the study group's allocation. The patients' sequence was

prelabeled in numbers, and the randomized allocation was done in a 1:1 ratio using the computer software (randomizer.org).

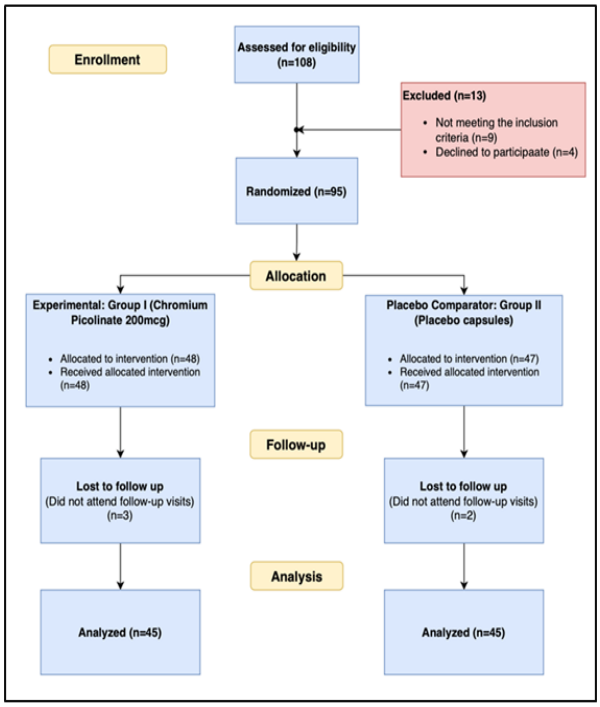

Figure 1: CONSORT Flowchart of the study.

Drug intervention

Patients in group I, which was labeled as the experimental group, received 200 mcg of chromium picolinate [14,15] (chromium picolinate 200 mcg, NOW®, Bloomingdale, Illinois, USA) dispensed by the investigational pharmacy per randomization to be taken once daily. Patients in group II, the placebo comparator, received inert capsules identical in appearance and packaging to the chromium picolinate 200 mcg NOW®, Bloomingdale, Illinois, USA, capsules (same size, shape, color, weight, and dosing schedule), manufactured without an active ingredient. The capsule shell is composed of gelatin or Hypromellose, matching the active capsules. The capsule is filled with inert excipients suitable for oral capsules, such as microcrystalline cellulose and magnesium stearate, to replicate the weight and flow properties of the active capsules. Optional coloring agents are included as needed to match the active product, ensuring that the appearance of the capsules is consistent with the active formulation for patient compliance and identification. Capsules were dispensed by the investigational pharmacy per randomization, to be taken once daily.

Inclusion criteria

Adolescent patients of both sexes, aged 12 to 18 years. Clinically diagnosed with acanthosis nigricans. Present Insulin resistance, defined as Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) ≥ 2.5. Willing to participate in the study, with written informed consent provided by both the patient and guardian.

Exclusion Criteria

Patients with type 1 or type 2 diabetes mellitus. Patients with a known hypersensitivity to chromium or any of the capsule excipients are excluded. Use of insulin-sensitizing medications (e.g., metformin, thiazolidinediones) within 3 months before screening. Use of systemic corticosteroids or other medications known to affect glucose metabolism within 3 months before screening. Presence of significant renal disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2) or liver disease (alanine aminotransferase or aspartate aminotransferase > 2.5 times the upper limit of normal). Pregnant or lactating females.

Sample size calculation

Because the primary endpoint of the study is a continuous variable (change in insulin resistance or skin score), the sample size formula for comparing two independent means was used:

$$n = \frac{2 \times (Z_{1-\alpha/2} + Z_{1-\beta})^2 \times \sigma^2}{\Delta^2}$$

Where n = required sample size in each group, $Z_{1-\alpha/2}$ = standard normal deviate corresponding to the two-sided significance level (α), $Z_{1-\beta}$ = standard normal deviate corresponding to desired power (1-β), σ = estimated standard deviation of the outcome measure, and Δ = minimum clinically important difference between groups. This formula is widely recommended for continuous outcomes in randomized controlled trials and is supported by general sample size methodology in RCTs [19]. The definition of statistical criteria is as follows: *Type I error (α):* 0.05 (two-sided), *power (1-β):* 0.80 (80%), and *effect size (Δ):* a conservative estimate based on prior studies investigating chromium picolinate effects on glucose metabolism or insulin resistance outcomes (changes in HOMA-IR or similar metabolic markers). For example, studies in metabolic disorders (e.g., T2DM or PCOS) using chromium picolinate have observed clinically relevant differences in insulin sensitivity or metabolic parameters between 0.3 and 0.8 SD units [20]. *Standard deviation (σ):* Estimated from similar interventions (chromium picolinate clinical trials assessing insulin sensitivity) to reflect anticipated variability in the adolescent insulin-resistant population. Using these parameters and assuming a moderate effect size (Cohen's d = 0.6), the predicted sample size was 44. Therefore, approximately 44 participants per arm are required to detect a moderate effect with 80% power [12].

Clinical assessment of acanthosis nigricans severity

The clinical severity of acanthosis nigricans was assessed by a single experienced physician at baseline and follow-up, utilizing Burke's quantitative scale for acanthosis nigricans [16,17]. This scale involves the summation of five parameters representing the severity of Acanthosis Nigricans, which are neck severity (0-4), neck texture (0-3), axilla severity (0-4), elbows (0 if absent, 1 if present), knuckles (0 if absent, 1 if present), and knees (0 if absent, 1 if present). The minimum score of this scale is 0, and the maximum is 14. Figure 2 demonstrates Burke's scale thoroughly.

Location	Score description
Neck severity	
0	Absent: not detectable on close inspection.
1	Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable.
2	Mild: limited to the base of the skull, does not extend to the lateral margin of the neck (usually <3 inches in breadth).
3	Moderate: extending to the lateral margins of the neck (posterior border of the sternocleidomastoid) (usually 3–6 inches), should not be visible when the participant is viewed from the front.
4	Severe: extending anteriorly (> 6 inches), visible when the participant is Viewed from the front.
Axilla	
0	Absent: not detectable on close inspection.
1	Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable.
2	Mild: localized to the central portion of the axilla, may have gone unnoticed by the participant .
3	Moderate: involving entire axillary fossa, but not visible when the arm is against the participant's side.
4	Severe: visible from front or back in the unclothed participant when the arm is against the participant's side.
Neck texture	
0	Smooth to touch: no differentiation from normal skin to palpation.
1	Rough to touch: clearly differentiated from normal skin.
2	Coarseness can be observed visually, portions of the skin clearly raised above other areas .
3	Extremely coarse: "hills and valleys" observable on visual examination.
Knuckles	Present
	Absent
Elbows	Present
	Absent
Knees	Present
	Absent

Figure 2: Burke's quantitative scale for acanthosis nigricans [14,15].

Assessment of insulin resistance

The assessment for insulin resistance was represented by calculating the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) [18]. Blood samples at baseline and in each follow-up visit were collected from the patients after fasting for at least 8 hours overnight. Fasting blood sugar assay was measured (utilizing blood glucose kits 3L82-21 on Abbott® ARCHITECT™ c4000 clinical chemistry analyzer), and fasting serum insulin assay was determined as well (utilizing serum insulin kits 08K4128 on Abbott® ARCHITECT™ i1000SR immunoassay device operating based on Chemiluminescent Microparticle Immunoassay principle). Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was then calculated using the following formula [18]:

$$HOMA - IR = \frac{(\text{Fasting insulin [µIU/mL]} \times \text{FBG [mg/dL]})}{405}$$

Ethical considerations and trial registration

The study was approved by the authorities and the institutional review board (IRB) in the College of Pharmacy, Uruk University in January 2025. This clinical trial is registered and published by clinicaltrials.gov (NCT07371169).

Statistical analysis

Data were entered into an Excel spreadsheet and then transferred to Jamovi version 2.6.45.0 for statistical analysis. Data normality was assessed using the Shapiro-Wilk test; consequently, continuous non-normal data were reported as median (interquartile range [IQR]) with range, while categorical variables were reported as frequencies (n) and percentages. The Mann-Whitney U test was used for continuous variables to compare between groups, and the Chi-square test for categorical variables' association. The paired-samples Wilcoxon signed-rank test was applied for within-group changes from baseline to 24 weeks. The Mann-Whitney U test is used for between-group comparisons at specific time points. Longitudinal changes in Burke acanthosis nigricans score and HOMA-IR were analyzed using repeated-measures analysis of variance (ANOVA) with Greenhouse-Geisser correction for violations of sphericity (confirmed via Mauchly's test). Post-hoc pairwise comparisons were performed with Bonferroni adjustment. Associations between changes in HOMA-IR and Burke scores were evaluated using Spearman's rank correlation coefficient. Statistical significance is set at $p< 0.05$.

RESULTS

Baseline clinical characteristics are summarized in Table 1. The median age was 15 years in both chromium and placebo groups ($p= 0.951$). Sex distribution was comparable between groups ($p= 0.832$). Baseline Burke acanthosis nigricans score and HOMA-IR values were also comparable between groups ($p= 0.823$ and 0.478, respectively). Fasting insulin levels did not differ significantly; however, fasting glucose was higher in the placebo group at baseline ($p= 0.016$). Longitudinal changes in the Burke score are presented in Table 2. In the chromium group, the mean Burke score decreased progressively from 8.96 ± 2.00 at baseline to 5.45 ± 2.14

at 24 weeks, whereas the placebo group changed from 9.04 ± 1.92 to 8.0 ± 1.88.

Table 1: Baseline participants' characteristics (n=45 in each group)

Variables	Group		Value	*p*-value
Age (year, median (IQR);[range]	I		15 (14-16); [12-18]	0.951*
	II		15 (14-17); [12-18]	
Sex n(%)	I	Male	26(57.78)	0.832**
		Female	19(42.22)	
	II	Male	25(55.56)	
		Female	20(44.44)	
Burke score for Acanthosis Nigricans at Baseline, median (IQR); [range]	I		9 (7-10); [6-12]	0.823*
	II		9 (8-11); [6-12]	
HOMA IR at Baseline, median (IQR); [range]	I		4.20 (1.81); [2.54-5.4]	0.478*
	II		3.97 (1.25); [2.62-5.43]	
Fasting glucose (mg/dl) at Baseline, median (IQR); [range]	I		96.30 (89.3-98.6); [85.1-108.6]	0.016*
	II		101.1 (93.2-104.0); [85.0-109.7]	
Fasting insulin (μIU/ml) at Baseline, median (IQR); [range]	I		17.4 (13.8-21.2); [10.5-24.7]	0.150*
	II		16.3 (13.40-19.0); [10.5-25.7]	

Group I: Chromium treated; Group II: Placebo treated. * Mann-Whitney U test, **Chi-square test.

Table 2: Burke's Score for Acanthosis Nigricans and HOMA-IR differences between groups

Timeline	Group	Mean±SD	Median	*p*-value*
Burke's Score for Acanthosis				
Baseline	I	8.96±2.0	9	<0.001
	II	9.04±1.92	9	
8-week	I	7.9±2.0	7.8	
	II	8.73±1.88	8.5	
16-week	I	6.86±2.04	6.7	
	II	8.42±1.87	8.0	
24-week	I	5.45±2.14	5.1	
	II	8.0±1.88	8.0	
HOMA-IR				
Baseline	I	4.1±0.924	4.2	<0.001
	II	3.96±0.84	3.97	
8-week	I	3.7±0.901	3.71	
	II	3.86±0.837	3.89	
16-week	I	3.29±0.889	3.28	
	II	3.76±0.837	3.83	
24-week	I	2.75±0.893	2.72	
	II	3.62±0.85	3.7	

Group I: Chromium treated; Group II: Placebo treated. * Paired Samples Wilcoxon rank test between baseline and 24-week outcomes.

Within-group analysis demonstrated a significant reduction from baseline to 24 weeks in the chromium group ($p< 0.001$). Between-group comparisons at 24 weeks showed significantly lower Burke scores in the chromium group (mean difference = −2.60, $p< 0.001$) (Table 3). Furthermore, the magnitude of improvement (baseline–24 weeks) was substantially greater with chromium supplementation (3.5 ± 0.83 vs 1.05 ± 0.66; $p< 0.001$).

Table 3: Outcomes and groups

Variables	Group	Mean±SD	Median	Mann-Whitney U	
				Difference	*p*-value
Burke at 24-week	I	5.45±2.137	5.10	-2.60	<0.001
	II	7.996±1.883	8.00		
HOMA IR at 24-week	I	2.75±0.893	2.72	-0.90	<0.001
	II	3.624±0.85	3.70		
Burke change (Baseline-24 week)	I	3.50±0.83	3.60	2.50	<0.001
	II	1.049±0.656	1.00		
HOMA change (Baseline-24 week)	I	1.35±0.346	1.28	1.00	<0.001
	II	0.331±0.24	0.29		

Group I: Chromium treated; Group II: Placebo treated.

HOMA-IR values over time are shown in Table 2. The chromium group showed a reduction from 4.1 ± 0.92 at baseline to 2.75 ± 0.98 in 24 weeks, whereas the placebo group showed a reduction from 3.96 ± 0.840 at baseline to 3.62 ± 0.85 at 24 weeks. During the 24th week, HOMA-IR was significantly lower in the chromium group compared with the placebo (mean difference = −0.90, $p< 0.001$). Similarly, change-from-baseline analysis revealed greater improvement with chromium (1.35 ± 0.35 *vs*. 0.33 ± 0.24; $p< 0.001$) (Table 3). A strong

positive association was found between changes in HOMA-IR and changes in Burke score using Spearman correlation analysis with r= 0.749, and p<0.001 (Figure 3).

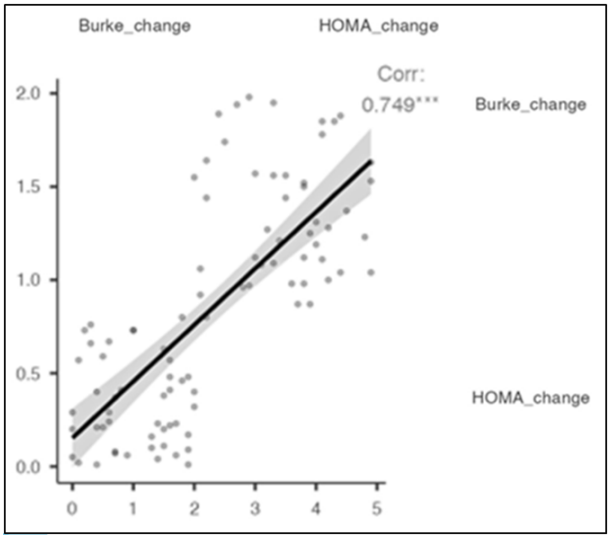

Figure 3: Spearman's Correlation between HOMA-IR change and Burke change (r= 0.749; p< 0.01).

Repeated-measures ANOVA revealed a highly significant main effect of time (F= 830, p< 0.001, partial η^2= 0.904). A significant time × group interaction was observed (F= 241, p< 0.001, partial η^2= 0.733), demonstrating that chromium produced significantly greater improvement over time compared with placebo. The between-group main effect was also significant (p= 0.003). The Greenhouse–Geisser correction was applied due to violation of sphericity (ε= 0.336). Bonferroni-adjusted post-hoc analyses confirmed significant reductions between all consecutive time points (Table 4).

Table 4: Bonferroni-adjusted pairwise comparisons for Burke score and HOMA-IR (Across all participants) (Post hoc analysis)

Comparison	Mean±SE	p-value
Burke Score		
Baseline *vs*. 8 weeks	0.684±0.024	<0.001
Baseline *vs.* 16 weeks	1.364±0.047	<0.001
Baseline *vs.* 24 weeks	2.277±0.079	<0.001
8 *vs*. 16 weeks	0.68±0.024	<0.001
8 *vs*. 24 weeks	1.592±0.056	<0.001
16 *vs*. 24 weeks	0.912±0.032	<0.001
HOMA-IR		
Baseline *vs*. 8 weeks	0.252±0.009	<0.001
Baseline *vs*. 16 weeks	0.506±0.019	<0.001
Baseline *vs*. 24 weeks	0.842±0.031	<0.001
8 *vs*. 16 weeks	0.253±0.009	<0.001
8 *vs*. 24 weeks	0.59±0.022	<0.001
16 *vs*. 24 weeks	0.337±0.013	<0.001

Similarly, HOMA-IR showed a strong main effect of time (F= 722, p< 0.001, partial η^2= 0.891) and a significant time × group interaction (F= 266, p< 0.001, partial η^2= 0.751). The between-group main effect did not reach statistical significance (p= 0.066). The Greenhouse–Geisser correction was applied (ε≈ 0.333). Post-hoc comparisons demonstrated significant reductions between all follow-up intervals (Table 4). Adverse events were mild and comparable between groups (Table 5). Headache and mild gastrointestinal upset were the most commonly reported symptoms, with no statistically significant association between chromium and placebo (p= 0.863).

Table 5: Adverse events by groups

Adverse Event	Group		Total	p-value
	I	II		
None	29(51.8)	27(48.2)	56(100)	0.863*
Headache	8(44.4)	10(55.6)	18(100)	
Mild GI upset	8(50)	8(50)	16(100)	
Total	45(50)	45(50)	90(100)	

Values are presented as frequency and percentage. Group I: Chromium treated; Group II: Placebo treated. *Chi-square test.

DISCUSSION

In the current RCT, supplementation with chromium picolinate capsule 200 mcg once daily led to significant improvements in both HOMA-IR and Burke acanthosis nigricans scores over 24 weeks, with pronounced time versus group interactions in both clinical outcomes. These findings potentially suggest that chromium picolinate supplementation can produce clinically meaningful reductions in insulin resistance and its dermatological manifestation (acanthosis nigricans), particularly in adolescent and young adult populations, specifically those at risk for metabolic dysfunctions. Chromium has been shown to improve glycemic control primarily by enhancing insulin sensitivity through multiple molecular pathways. Under insulin-resistant conditions, chromium potentiates insulin receptor signaling by increasing tyrosine phosphorylation of insulin receptor substrates and activating downstream PI3K/Akt pathways. Thus, promoting GLUT4 translocation and facilitating cellular glucose uptake in skeletal muscle and adipose tissue [21]. In addition, chromium suppresses key negative regulators of insulin signaling, including Jun N-terminal kinase (JNK)–mediated serine phosphorylation of IRS-1 and protein tyrosine phosphatase-1B, thereby preserving insulin signal propagation [22]. Emerging evidence also indicates that chromium alleviates endoplasmic reticulum stress, a central contributor to insulin resistance, and reduces oxidative stress and inflammatory cytokine production, further supporting metabolic homeostasis effects of chromium [23]. Beyond insulin-dependent mechanisms, chromium activates AMP-activated protein kinase (AMPK), promoting insulin-independent glucose uptake and enhancing cellular energy metabolism [22]. Collectively, these actions restore impaired insulin signaling, improve glucose transport, and attenuate metabolic stress, with clinical relevance appearing most pronounced in individuals with established insulin resistance rather than metabolically normal subjects. Our results demonstrate a progressive

and statistically significant reduction in HOMA-IR among participants receiving chromium compared with those on placebo reaching significance by 24 weeks. This aligns with broader evidence supporting the metabolic effects of chromium on glycemic control [24]. A recent systematic review and meta-analysis of randomized trials in patients with type 2 diabetes mellitus by Asbaghi *et al*. in 2020 [24] found that chromium supplementation was associated with significant reductions in HOMA-IR, fasting glucose, and insulin levels compared with control interventions. They reported a weighted mean difference for HOMA-IR of −1.53 with $p< 0.001$, supporting our findings of improved insulin sensitivity with chromium treatment. In the context of insulin resistance beyond frank diabetes, studies have also documented beneficial effects of chromium. For instance, Aghdassi *et al*.'s [25] study (2010) on patients with HIV-associated metabolic abnormalities reported that chromium supplementation resulted in a significant decrease in HOMA-IR and fasting insulin, consistent with improved insulin signaling. Similarly, studies in women with polycystic ovary syndrome (PCOS), which is a condition often characterized by insulin resistance, Ashoush *et al*. [26] reported significant reductions in insulin resistance indices with chromium picolinate supplementation. Together, these data support the biological and clinical relevance of chromium's effect on insulin resistance as measured by HOMA-IR. Acanthosis nigricans is a well-recognized clinical sign of insulin resistance, likely related to growth factor levels and insulin-mediated activation of insulin-like growth factor (IGF) on keratinocytes and increased growth factor levels [24,1]. Other mediators that have been identified include fibroblast growth factor and tyrosine kinase receptors (epidermal growth factor receptor) [1]. The pathophysiological process behind acanthosis nigricans appears to be related to the proliferation of fibroblasts and the enhanced stimulation of epidermal keratinocytes. In this study, participants receiving chromium picolinate exhibited profound and progressive reductions in Burke AN scores compared with placebo, which closely mirror the observed improvements in insulin resistance. The strong correlation between changes in HOMA-IR and changes in AN severity further supports the concept that amelioration of systemic insulin resistance may drive improvement in acanthosis nigricans; however, this association should be interpreted with caution, as chromium may also exert direct effects on keratinocytes through alternative pathways. Although studies on chromium's impact on AN are scarce in the literature, these findings are consistent with observational data showing that interventions improving insulin sensitivity, such as weight loss, lifestyle modification, or insulin-sensitizing drugs like metformin, can lead to improvements in acanthosis nigricans [27]. The concurrent improvement in both HOMA-IR and AN severity in this clinical trial indicates that greater reductions in insulin resistance were associated with greater improvement in acanthosis nigricans severity. These findings fill an important gap in human clinical evidence, linking a well-defined nutritional intervention to both metabolic and dermatologic favorable outcomes. Insulin resistance and its cutaneous manifestations, such as acanthosis nigricans, are key early markers for metabolic syndrome and future risk of type 2 diabetes [28]. The current study adds to a growing body of evidence indicating that targeted micronutrient supplementation may serve as a low-cost adjunctive strategy in populations at high metabolic risk. Importantly, the progressive improvements observed over repeated assessments at 8, 16, and 24 weeks suggest that chromium's metabolic effects are cumulative over time, highlighting the value of longer intervention periods in clinical trials and potential real-world use. Future studies should focus on evaluating the long-term effects of chromium supplementation on both dermatological and metabolic outcomes, as well as assessing the persistence of these effects following discontinuation of therapy.

Limitations and Recommendations

Several limitations must be acknowledged. While the data strongly support improvements in insulin resistance and AN severity, the broader clinical significance of these changes—particularly in relation to downstream outcomes, such as diabetes incidence or cardiovascular risk— remains to be determined. Furthermore, heterogeneity in chromium formulations, dosages, and baseline metabolic risk across studies complicates direct comparisons. Well-designed trials in diverse populations will help clarify the generalizability of our results. Another limitation of this study is the lack of pubertal assessment in the inclusion criteria, systematic assessment of weight changes, and formal monitoring of diet and physical activity during the intervention period, which may act as a confounding factor influencing insulin resistance and acanthosis nigricans severity. Despite these limitations, the randomized controlled design strengthens the internal validity of the findings.

Conclusion

Chromium picolinate capsule 200 mcg once daily supplementation significantly improved both insulin resistance (HOMA-IR) and acanthosis nigricans severity over 24 weeks. These results support the potential utility of chromium as a safe and effective adjunctive intervention in metabolically at-risk populations.

Conflict of interests

The author declares no conflict of interest.

Funding source

The author did not receive any source of funds.

Data sharing statement

Supplementary data can be viewed at Zenodo: Effect of Chromium Picolinate on Clinical Severity of Acanthosis Nigricans and Insulin Resistance. https://doi.org/10.5281/zenodo.18723325. Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

REFERENCES

1. Hughes EK, Brady MF and Rawla P, (Eds.), Acanthosis Nigricans. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2025, StatPearls Publishing LLC., 2025.
2. Das S, Sett A, Saha A, Patra S and Gharami RCH. Clinico-demographic study of patients with acanthosis nigricans- A menace for cardiovascular disease. *Asian J Pharm Clin Res*. 2023;16:26-30. doi: 10.22159/ajpcr.2023.v16i12.47987.
3. Freeman AM, Acevedo LA, Pennings N, (Eds.), Insulin Resistance. StatPearls. Treasure Island (FL): StatPearls Publishing LLC., 2025. Copyright © 2025.
4. Shiana, Parmar S, Guleria P, Jindal S, Ashawat MS, Kumar P. A comprehensive review of acanthosis nigricans: Pathogenesis, clinical manifestation and management. *Recent Adv Inflamm Allergy Drug Discov*. 2025;19:135-45. doi: 10.2174/0127722708314530240919054410.
5. Liu Z, Cao W. Malignant acanthosis nigricans with oral manifestations in a young female: A case report and literature review. *Front Oncol*. 2024;14:2024. doi: 10.3389/fonc.2024.1459148.
6. Svoboda SA, Shields BE. Cutaneous manifestations of nutritional excess: Pathophysiologic effects of hyperglycemia and hyperinsulinemia on the skin. *Cutis*. 2021;107:74-78. doi: 10.12788/cutis.0173.
7. WHO. Infertility [Internet]. [cited 2023 Feb 3]. Available from: https://www.who.int/health-topics/infertility#tab=tab_1.
8. Brickman WJ, Binns HJ, Jovanovic BD, Kolesky S, Mancini AJ, Metzger BE. Acanthosis nigricans: a common finding in overweight youth. *Pediatr Dermatol*. 2007;24:601-606. doi: 10.1111/j.1525-1470.2007.00547.x.
9. Alkhalidi F. A comparative study to assess the use of chromium in type 2 diabetes mellitus. *J Med Life*. 2023;16:1178-1182. doi: 10.25122/jml-2023-0081.
10. Argano C, Mirarchi L, Amodeo S, Orlando V, Torres A, Corrao S. The role of vitamin D and its molecular bases in insulin resistance, diabetes, metabolic syndrome, and cardiovascular disease: State of the art. *Int J Mol Sci*. 2023;24:20231023. doi: 10.3390/ijms242015485.
11. Herman R, Kravos NA, Jensterle M, Janež A, Dolžan V. Metformin and insulin resistance: A review of the underlying mechanisms behind changes in GLUT4-mediated glucose transport. *Int J Mol Sci*. 2022;23:20220123. doi: 10.3390/ijms23031264.
12. Fatahi M, Aghajani S, Javaheri H, Toqroljerdi M. The effect of chromium supplements on insulin resistance: A systematic review and meta-analysis of randomized controlled trials. *J Health Med Sci*. 2025;8:13-42. doi: 10.31014/aior.1994.08.04.245.
13. Vajdi M, Khajeh M, Safaei E, Moeinolsadat S, Mousavi S, Seyedhosseini-Ghaheh H, et al. Effects of chromium supplementation on body composition in patients with type 2 diabetes: A dose-response systematic review and meta-analysis of randomized controlled trials. *J Trace Elem Med Biol*. 2024;81:127338. doi: 10.1016/j.jtemb.2023.127338.
14. Food and Drug Administration, HHS. Food Labeling: Revision of the Nutrition and Supplement Facts Labels. Final rule. *Fed Regist*. 2016;81(103):33741-999.
15. Henriksen C, Bügel S. Chromium - a scoping review for Nordic Nutrition Recommendations 2023. *Food Nutr Res*. 2023;67:20231206. doi: 10.29219/fnr.v67.10325.
16. Choudhary SV, Saoji V, Singh A, Mane S. Acanthosis nigricans: a clinical marker of insulin resistance. *Int J Res Dermatol*. 2017;3:161-167. doi: 10.18203/issn.2455-4529.IntJResDermatol20171497.
17. Burke JP, Hale DE, Hazuda HP, Stern MP. A quantitative scale of acanthosis nigricans. *Diabetes Care*. 1999;22:1655-1659. doi: 10.2337/diacare.22.10.1655.
18. Diniz M, Beleigoli AMR, Schmidt MI, Duncan BB, Ribeiro ALP, Vidigal PG, et al. Homeostasis model assessment of insulin resistance (HOMA-IR) and metabolic syndrome at baseline of a multicentric Brazilian cohort: ELSA-Brasil study. *Cad Saude Publica*. 2020;36:e00072120. doi: 10.1590/0102-311x00072120.
19. Zhong B. How to calculate sample size in randomized controlled trial? *J Thorac Dis*. 2009;1:51-54. PMID: 22263004.
20. Talab AT, Abdollahzad H, Nachvak SM, Pasdar Y, Eghtesadi S, Izadi A, et al. Effects of chromium picolinate supplementation on cardiometabolic biomarkers in patients with type 2 diabetes mellitus: A randomized clinical trial. *Clin Nutr Res*. 2020;9:97-106. doi: 10.7762/cnr.2020.9.2.97.
21. Chen WY, Chen CJ, Liu CH, Mao FC. Chromium supplementation enhances insulin signalling in skeletal muscle of obese KK/HlJ diabetic mice. *Diabetes Obes Metab.* 2009;11:293-303. doi: 10.1111/j.1463-1326.2008.00936.x.
22. Hua Y, Clark S, Ren J, Sreejayan N. Molecular mechanisms of chromium in alleviating insulin resistance. *J Nutr Biochem*. 2012;23:313-9. doi: 10.1016/j.jnutbio.2011.11.001.
23. Nakatani Y, Kaneto H, Kawamori D, Yoshiuchi K, Hatazaki M, Matsuoka TA, et al. Involvement of endoplasmic reticulum stress in insulin resistance and diabetes. *J Biol Chem*. 2005;280:847-851. doi: 10.1074/jbc.M411860200.
24. Asbaghi O, Fatemeh N, Mahnaz RK, Ehsan G, Elham E, Behzad N, et al. Effects of chromium supplementation on glycemic control in patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *Pharmacol Res*. 2020;161:105098. doi: 10.1016/j.phrs.2020.105098.
25. Aghdassi E, Arendt BM, Salit IE, Mohammed SS, Jalali P, Bondar H, et al. In patients with HIV-infection, chromium supplementation improves insulin resistance and other metabolic abnormalities: a randomized, double-blind, placebo controlled trial. *Curr HIV Res*. 2010;8:113-120. doi: 10.2174/157016210790442687.
26. Ashoush S, Abou-Gamrah A, Bayoumy H, Othman N. Chromium picolinate reduces insulin resistance in polycystic ovary syndrome: Randomized controlled trial. *J Obstet Gynaecol Res*. 2016;42:279-285. doi: 10.1111/jog.12907.
27. Patel NU, Roach C, Alinia H, Huang WW, Feldman SR. Current treatment options for acanthosis nigricans. *Clin Cosmet Investig Dermatol*. 2018;11:407-413. doi: 10.2147/ccid.S137527.
28. Nithun TM, Ranugha PSS, Betkerur JB, Shastry V. Association of acanthosis nigricans and insulin resistance in Indian children and youth - A HOMA2-IR based cross-sectional study. *Indian Dermatol Online J*. 2019;10:272-278. doi: 10.4103/idoj.IDOJ_303_18.