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# Effect of Tinidazole Treatment on Experimental Giardia Infection in Male Rats

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## Abstract

This study investigated the effect of tinidazole treatment in eliminating Giardia parasite in experimentally infected male rats. The study included some parameters targeted by Giardia in glucose metabolism, insulin values, liver enzymes, and albumin in the serum of male rats after four weeks of infection. Results using tinidazole showed that some parameters approached normal levels. Glucose levels showed the lowest value in the fourth week post-infection (131.±14.30) mg/dL as shown in Table (1), with a recovery rate of 68.67%, indicating the efficacy of tinidazole in reducing the parasite's effect on glucose pathways and enhancing insulin secretion and glucose absorption. Insulin resistance HOMA-IR approached the normal limit in all infected groups, with the lowest value in the second and third weeks, then returning to the normal limit (14.87±1.63) in the fourth week compared to the control group, with an insulin recovery rate of 73.09%. In contrast, insulin sensitivity values decreased, with the lowest value (0.199±0.034) in the third week post-infection compared to the control group. Results also showed tinidazole's effectiveness in indirectly reducing the parasite's effect on liver enzymes, with a slight effect on ALT(GPT), AST(GOT) levels. Albumin levels were close to the control group in weeks 2, 3, and 4, with the best value (2.23±0.38) g/dL and a recovery rate of 90.00% in the second week post-infection.

**Keywords:** *Giardia, HOMA-IR, Tinidazole, Glucose, Insulin.*

## Introduction:

Giardiasis is an infectious intestinal disease caused by the Giardia lamblia parasite, also known as *Giardia duodenalis* (Giardia intestinalis), which is associated with poor personal hygiene and inadequate sanitation (Minetti *et al*.,2016). Giardia is one of the most common primary intestinal diseases worldwide, including Iraq (Speich *et al*.,2016). It is prevalent in most poor communities that lack adequate economic and social levels (Nabaw *et al*.,2008). Symptoms appear as diarrhea, abdominal pain, nausea, dehydration,

and weight loss. Although giardiasis is rarely fatal, the World Health Organization has confirmed it can become chronic if untreated, highlighting the importance of effective treatment in controlling infection and its transmission from person to person (Harizonov *et al*.,2020). Giardia is considered the only intestinal protozoan that colonizes the human digestive tract (Torgerson *et al*., 2015), and Giardia infection contributes to approximately one million deaths due to recurrent diarrhea (Deng *et al*.,2021). Infection usually occurs through transmission of infectious agents via water or food contaminated due to lack of hygiene, and due to the persistence of cysts in humid environments for a long time (Upcroft&Upcroft.,2001).The current optimal treatment for giardiasis is Tinidazole (TIN), which is considered an appropriate option for eliminating infection because its short treatment duration is one of its most important advantages (Yitageasu *et al*.,2026;Dixon.,2021)A study showed that the efficacy of tinidazole treatment is similar to metronidazole, as response rates in treating giardiasis did not differ (Rossignol.,2010) Tinidazole is a compound from second-generation Nitroimidazole-5 derivatives used as an antimicrobial to treat anaerobic bacterial infections and primary parasitic infections in humans, and less commonly in veterinary medicine (Pasupuleti *et al*.,2014).It works by penetrating the parasitic cell, causing DNA damage, and inhibiting nucleic acid synthesis, leading to parasite death (Tournade *et al*.,2021).Despite advances in diagnostic methods for parasitic diseases and treatment approaches, they remain widely prevalent (Sartori *et al*.,2025).Recent studies have shown that Giardia has effects on metabolic pathways including glucose, insulin, and liver enzymes ALT, AST (Dabrowska.,2024).The parasite adheres to the intestinal wall and reduces villous cells(Klimczak et al.,2024; Inge *et al*.,1988).

## Materials and Methods:

### 2.1 Experimental Design:

This experiment was designed to verify the effect of tinidazole on inhibiting Giardia infection experimentally and its effect on glucose, insulin, and liver enzyme levels. The current study included 26 male white Albino Swiss strain rats divided into four groups, each consisting of five experimentally infected rats injected using a feeding tube with Giardia parasites, plus 6 rats as an uninfected control group. Blood samples were collected and examined after 1, 2, 3, and 4 weeks post-experimental infection.

### 2.2 Sample Collection and Source:

Stool samples were collected from patients with diarrhea at Al-Salam Teaching Hospital in Mosul. Samples were preserved in clean, sterile containers until reaching the laboratory of the College of Education for Girls at the University of Mosul for use in injecting laboratory animals.

### 2.3 Microscopic Examination:

Microscopic examination was performed to confirm the presence of infectious parasite cysts in all samples using the sedimentation method with physiological saline, using a light microscope at 40X magnification then 100X magnification (Ritchie *et al*.,1960).

### 2.4 Isolation of Giardia Parasite and Preparation of Injection Dose:

To isolate Giardia from stool samples, centrifugation was performed at 3000 rpm for 5 minutes three times. Parasites were identified microscopically using Giemsa stain. For dose preparation, 20 microliters

of the stool sample solution were placed on a glass slide, and a dose containing 150 cysts per animal was taken (Carl craft.,1982).

**2.5 Preparation of Tinidazole Treatment Dose:**

The injection dose was prepared by taking one Tinidazole tablet (500 mg each), dissolving it in 5 mL of distilled water, and administering 2 mL orally via a metal feeding tube to each rat weighing 200 g. If the rat weighed 150 g, it received 1.5 mL; if it weighed 250 g, it received 2.5 mL, and so on, according to drug administration methods in laboratory animals (Turner et al.,2011;Tournade et al.,2021).

**2.6 Laboratory Animals:**

White Swiss Albino strain rats aged one and a half to two months, weighing between 175 and 200 g, were used. Animals were orally gavaged with parasite cysts using a metal feeding tube at a dose containing approximately 150 cysts. After confirming infection, animals were treated with tinidazole after 1, 2, 3, and 4 weeks, then re-examined to confirm recovery by the absence of Giardia cysts in stool samples. Blood samples were then collected from the heart in test tubes containing anticoagulant gel, centrifuged at 3000X for 15 minutes, and stored at -20°C for biochemical analysis using a Chemistry Analyzer and immunological analysis using the ELISA technique (Parasurman *et al*.,2015;Greenfield.,2017).

**2.7 Laboratory Examination:**

**2.7.1 Serum Glucose Measurement:**

Glucose levels were measured using photochemical analysis technology (Smart-120, USA), which relies on enzymatic color change, with results obtained automatically on the computer screen.

**2.7.2 Serum Insulin Measurement:**

The ELISA technique was used with the Rat Insulin (INS) ELISA Kit (Product No. ADL-ELRT00483, China) using the double antibody sandwich method.

**2.7.3 Assessment of Insulin Resistance HOMA-IR:**

Insulin resistance was assessed using the HOMA-IR index calculated after fasting laboratory animals for 12 hours.

HOMA-IR = Fasting Insulin (U/mL) × Fasting Glucose (mmol/L) / 22.5

(Er *et al*.,2016;Minh *et al*.,2021).HOMA-IR values indicate return to normal levels; week 1 shows a significant difference $P<0.01$ with a lower elevation than the control group, while weeks 2, 3, and 4 show non-significant values approaching control, indicating decreased insulin resistance.

**2.7.4 Quantitative Insulin Sensitivity Check Index QUICKI:**

QUICKI was used to assess insulin sensitivity:

QUICKI = 1 / (log fasting insulin (U/mL) + log fasting glucose (mmol/L))

(Gutch *et al*.,2015;Minh *et al*.,2021).Elevated QUICKI values indicate decreased insulin resistance.

### 2.8 Statistical Analysis:

The SPSS statistical analysis program was used between groups. To find differences between groups, One-Way Analysis of Variance (ANOVA) was used. Insulin resistance was calculated using the HOMA-IR formula and insulin sensitivity was calculated using QUICKI.

## Results:

### 3.1 Blood Glucose Levels:

Results showed that serum glucose levels in rats treated with tinidazole and experimentally infected with Giardia showed a non-significant elevation in glucose levels in weeks 1, 2, and 3, time-correlated with post-infection, with a significant decrease in week 4 reaching (131.79±14.30) mg/dL as shown in Table (1).

**Table (2): Effect of Tinidazole Treatment on Mean Glucose Measurement in Infected Male Rats at Different Time Periods Post-Infection**

| Mean Control Glucose | Mean Treatment Glucose | Time |
|---|---|---|
| 105.6667 | 188.79±26.50 b | 1 Week |
| 105.6667 | 180.67±19.08 b | 2 Weeks |
| 105.6667 | 172.08±24.33 b | 3 Weeks |
| 105.6667 | 131.79±14.30 a | 4 Weeks |

*Results showed a clear decrease in mean glucose in week 4 (a), being lower or higher than the statistical significance $P<0.05$

### 3.2 Insulin Levels, Insulin Resistance, and Insulin Sensitivity:

Results of this study showed a slight decrease in insulin levels in weeks 1 and 4 post-infection (4.723±3.92)(4.739±3.31), approaching normal levels of the control group as shown in Table (2). The HOMA-IR index in all infected groups decreased compared to the control group. HOMA-IR was calculated using serum insulin and glucose levels during fasting as described in section 2.7.3. A slight decrease in insulin resistance was noted, with the lowest value in weeks 2 and 3. In contrast, insulin sensitivity showed a decrease in week 3 (0.199±0.034) followed by (0.203±0.032) in week 4 as shown in Table (2).

**Table (1): Effect of Tinidazole Treatment on Mean Insulin Measurement at Different Time Periods**

| Control | Treatment Insulin Sensitivity | Control | Treatment Insulin Resistance Mean | Control | Treatment Insulin Mean | Time |
|---|---|---|---|---|---|---|
| 0.292 | 0.204±0.056 a | 15.31% | 14.61±1.53 a | 6.66 | 3.92±4.723 a | 1 Week |
| 0.292 | 0.210±0.113 b | 15.31% | 12.30±2.90 b | 6.66 | 3.511±2.309 b | 2 Weeks |
| 0.292 | 0.199±0.034 b | 15.31% | 10.33±2.76 b | 6.66 | 2.144±1.496 b | 3 Weeks |
| 0.292 | 0.203±0.032 a | 15.31% | 14.87±1.63 a | 6.66 | 4.739±3.31 a | 4 Weeks |

### 3.3 Effect of Tinidazole Treatment on ALT(GPT), AST(GOT) Levels:

According to results, serum ALT, AST levels showed a notable increase over four weeks, which was statistically significant $P<0.05$ compared to the control group, with a clear decrease in both ALT and AST. The lowest ALT value was in week 3 (57.0±8.71) U/L as shown in Table (3). Similarly, AST decreased in the same direction, reaching (172.58±10.29) U/L as shown in Table (4).

**Table (3): Effect of Tinidazole Treatment on Mean ALT(GPT) at Different Time Periods Post-Infection**

| Mean ALT GPT Control Group | Mean ALT GPT Treated Group U/L | Time |
|---|---|---|
| 62.254 | 67.03±4.21 a | 1 Week |
| 65.224 | 80.33±6.16 a | 2 Weeks |
| 63.225 | 57.0±8.71 b | 3 Weeks |
| 61.255 | 68.5±4.86 a | 4 Weeks |

**Table (4): Effect of Tinidazole Treatment on Mean AST(GOT) in Male Rats at Different Time Periods:**

| Mean AST GOT Control Group | Mean AST(GOT) Treated Group U/L | Time |
|---|---|---|
| 227 | 289.66±15.37 a | 1 Week |
| 229 | 257.38±16.50 a | 2 Weeks |

| | | |
|---|---|---|
| 222 | 172.58±10.29 b | 3 Weeks |
| 225 | 233.77±16.96 a | 4 Weeks |

### 3.4 Effect of Tinidazole Treatment on Mean Serum Albumin:

According to results in Table (5), albumin levels showed that all values were non-significant, indicating minor changes within normal variation with no clear disease effect. There was a slight significant difference in week 4 (2.15±0.49) g/dL.

**Table (5): Effect of Tinidazole Treatment on Mean Albumin in Male Rats at Different Time Periods Post-Infection**

| Mean Albumin Control Group (g/dL) | Mean Albumin Treated Group (g/dL) | Time |
|---|---|---|
| 2.27 | 2.67±0.55 a | 1 Week |
| 2.27 | 2.23±0.38 a | 2 Weeks |
| 2.27 | 2.37±0.25 a | 3 Weeks |
| 2.27 | 2.15±0.49 b | 4 Weeks |

### 3.5 Table Showing Recovery Rates for Glucose, Insulin, AST, ALT, and Albumin at Different Time Periods:

| Time Period | Treatment Glucose Mean | Glucose Recovery Rate | Treatment Insulin Mean | Insulin Recovery Rate |
|---|---|---|---|---|
| 1 Week | 188 | 0.00% | 4.72 | 70.88% |
| 2 Weeks | 180 | 9.64% | 3.51 | 52.73% |
| 3 Weeks | 172 | 23.38% | 2.14 | 32.35% |
| 4 Weeks | 131 | 68.67% | 4.39 | 73.09% |

### 3.6 Table Showing Recovery Rates for ALT, AST, and Albumin:

| Time Period | ALT(GPT) Mean | Recovery Rate | AST(GOT) Mean | Recovery Rate | Albumin Mean | Recovery Rate |
|---|---|---|---|---|---|---|
| 1 Week | 67.03 | 86.67% | 289 | 41.18% | 2.67 | 0.00% |
| 2 Weeks | 80 | 0.00% | 257 | 72.55% | 2.23 | 90.0% |
| 3 Weeks | 57.0 | 90.0% | 127 | 0.00% | 2.37 | 75.0% |
| 4 Weeks | 68 | 89.00% | 233 | 96.08% | 2.15 | 70.0% |

## Discussion:

Results of the current study showed that tinidazole treatment in experimentally Giardia-infected male rats had a clear effect on recovery and parasite elimination. Serum glucose levels in tinidazole-treated experimentally infected rats showed a slight non-significant elevation in weeks 1, 2, and 3, time-correlated post-infection, with a notable significant decrease in week 4 reaching (131.79±14.30) mg/dL as shown in Table (1), with a recovery rate of 68.67% compared to the control group. Experimental results in various animal models indicate oscillations in glucose levels during the first weeks of infection, then gradually returning to normal with treatment. This pattern is consistent with a study showing that parasitic infection causes malabsorption of carbohydrates and fats, leading to a temporary blood sugar disturbance (Adam.,2001).Elevated glucose levels are known to result from impaired glucose absorption in intestinal cells, where Giardia trophozoite stages adhere to intestinal villi and interfere with glucose transport via SGLT-I(Yu *et al*.,2008). The rates shown by tinidazole treatment results for insulin values were close to the normal limit of the control group. Results showed a slight decrease in insulin levels in weeks 1 and 4 post-infection (4.723±3.92)(4.739±3.31) U/mL as shown in Table (2). Normal insulin levels in all groups indicate that parasitic infection has weakened and beta cells began enhancing insulin clearance, contributing to relative insulin increase due to a decrease in inflammatory cytokines (Solymani-Mohammadi.,2022; Demichele et al.,2025).The HOMA-IR index in all treated groups decreased compared to the control group, with the lowest value recorded in week 1 post-infection (14.61±1.53), then week 4 (14.87±1.63) close to the normal limit. Glucose remained slightly elevated, possibly due to delayed metabolic recovery, residual inflammatory effects, or microbiome reorganization (Becattini *et al*.,2016;Sommer & Backhed.,2013). Elevated insulin resistance in week 1 resulted from a chronic inflammatory response leading to cytokine secretion (TNF-α, IL-6); these cytokines reduce insulin sensitivity and raise insulin resistance (Gusev *et al*.,2026;UI Islam Hashmi.,2025). Results also showed the effectiveness of tinidazole treatment on returning ALT, AST levels to normal throughout the post-infection period. A low increase was noted over four weeks of infection, with the lowest ALT value in week 3 (57.0±8.71) U/L as shown in Table (3), with a recovery rate of 89.00% in week 4 post-infection. Similarly, AST decreased in the same direction, with the lowest value in week 3 post-infection (172.58±10.29) U/L, then returning to normal in week 4 (233.77±16.96) U/L, with a recovery rate of 96.08% in week 4. This is consistent with a study indicating that tinidazole typically does not cause liver toxicity at therapeutic doses, although some minor and temporary changes did not cause a significant difference in AST, ALT levels (Tox.,2020).The oscillation in enzyme values during the infection period is due to the parasite's own effect on absorption and nutrition, not a direct result of the drug (Petry *et al*.,2010).According to results in Table (5), albumin levels showed that all values were non-significant, indicating minor changes within normal variation with no clear disease effect, suggesting that treatment is effective in returning levels to normal, with the least slight significant difference in week 4 (2.15±0.49) g/dL. Previous studies showed that tinidazole treatment leads to gradual improvement in albumin levels with restoration of normal intestinal functions; however, some fluctuations may appear due to differences in infection severity or individual responses to treatment (Farthing.,1996).All results indicate that tinidazole treatment led to gradual improvement in metabolic indicators related to insulin resistance and other indicators towards levels close to the normal limit, although most of these changes were not

statistically significant, indicating that the treatment effect was limited or affected by individual variation among animals.

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