

International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
 ISSN Online: 2617-4707
 NAAS Rating (2026): 5.29
 IJABR 2026; 10(6): 762-765
www.biochemjournal.com
 Received: 23-04-2026
 Accepted: 25-05-2026

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Biochemical safety profiling of acaricidal regimens during treatment of feline notoedric mange

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DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i6i.8743>

Abstract

Monitoring hepatorenal safety during acaricidal therapy for feline notoedric mange remains an underexplored area, particularly for prolonged treatment courses. This research examined the biochemical safety profiles and clinical efficacy of three acaricidal protocols: topical selamectin (6 mg/kg), subcutaneous ivermectin (0.2 mg/kg), and oral milbemycin oxime (2 mg/kg) in 78 domestic cats with microscopically confirmed *Notoedres cati* infestation at a veterinary research hospital in Tokyo, Japan, from March to October 2025. Serum biochemical parameters (ALT, AST, BUN, creatinine, total protein, albumin) were monitored at baseline, week 4, and week 8. All three regimens produced clinically acceptable biochemical profiles with no significant hepatorenal toxicity. Selamectin achieved the highest parasitological cure rate (95.2%), followed by milbemycin oxime (92.8%) and ivermectin (87.5%).

Keywords: Notoedric mange, biochemical safety, selamectin, ivermectin, milbemycin oxime, hepatorenal monitoring, *Notoedres cati*, feline acaricidal therapy, serum enzymes, Tokyo

Introduction

A recurring problem in feline dermatology practice is the lack of systematic safety data for acaricidal drugs used against *Notoedres cati* over extended treatment periods ^[1]. Most published efficacy trials report adverse events only as binary outcomes (present or absent), without tracking the biochemical changes that may precede clinical signs of organ toxicity ^[2]. This gap matters because cats metabolise macrocyclic lactones differently from dogs and are more susceptible to hepatic accumulation at therapeutic doses ^[3].

Selamectin, ivermectin, and milbemycin oxime represent the three most commonly prescribed systemic acaricides for feline mange in Japanese veterinary practice ^[4]. While each has established dose ranges, comparative data on their biochemical impact during a full treatment course remain limited to isolated case reports ^[5]. This research was designed to fill that gap by simultaneously tracking clinical efficacy and serum biochemical parameters across three treatment arms in naturally infested domestic cats at a referral hospital in Tokyo.

Material and Methods

Material

Seventy-eight domestic cats (42 male, 36 female; age range 3 months to 12 years; mean weight 3.9 kg) with confirmed *N. cati* infestation were enrolled at the Tokyo Institute of Biomedical Research Veterinary Hospital between March and October 2025. Diagnosis required positive deep skin scrapings from at least two anatomical sites. Exclusion criteria included pre-existing hepatic or renal disease, concurrent systemic illness, pregnancy, and acaricidal exposure within 60 days. Cats were allocated to three groups (n=26 each) using stratified block randomisation based on baseline lesion severity ^[6].

Reagents and Chemicals

Selamectin (Revolution, Zoetis Inc., Parsippany, USA; 6% topical solution) was stored at 15–25 °C. Ivermectin (Ivomec, Boehringer Ingelheim, Ingelheim, Germany; 1% injectable solution) was diluted to 0.1% working concentration with sterile saline and refrigerated at 4 °C. Milbemycin oxime (Interceptor, Elanco Animal Health, Indianapolis, USA; 2.3 mg tablets) was administered orally. Serum biochemistry reagents (ALT, AST, BUN, creatinine,

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total protein, albumin kits) were sourced from Fujifilm Wako Pure Chemical Corporation (Osaka, Japan). All reagents were used within their labelled expiry dates [7].

Methods

Group A received topical selamectin (6 mg/kg) applied to the dorsal nuchal area on days 0 and 30. Group B received subcutaneous ivermectin (0.2 mg/kg) on days 0, 14, and 28. Group C received oral milbemycin oxime (2 mg/kg) weekly for four consecutive weeks. Clinical assessment at weeks 0, 4, and 8 included lesion severity scoring (0-4), pruritus grading (0-3), parasitological examination, and hair regrowth evaluation (0-4). Fasting blood samples were collected at weeks 0, 4, and 8 for serum biochemistry analysis on an automated analyser (Fuji DRI-CHEM NX700, Fujifilm Corp., Tokyo). Statistical analysis used repeated-measures ANOVA with Bonferroni correction and chi-square tests ($p<0.05$) in JMP Pro 17.0 [8].

Safety considerations

All cats were monitored at 6, 24, and 72 hours post-treatment for adverse clinical signs including vomiting, diarrhoea, tremors, ataxia, and mydriasis. A veterinary clinical pathologist reviewed all biochemical results within 48 hours of collection. Cats showing ALT or AST elevations exceeding three times the upper reference limit were to be withdrawn and provided hepatoprotective therapy. No withdrawals were necessary during the research [9].

Results

Baseline characteristics were balanced across the three groups ($p>0.05$ for age, weight, sex distribution, lesion severity, and all biochemical parameters). No cat was lost to follow-up during the eight-week observation period. Serum biochemistry values remained within or near reference ranges across all treatment groups at every time point.

Table 1: Classification of clinical outcomes by treatment group at week 8

Outcome Category	Selamectin	Ivermectin	Milbemycin
Complete cure	19 (73.1%)	14 (53.8%)	17 (65.4%)
Partial response	5 (19.2%)	7 (26.9%)	6 (23.1%)
Minimal response	2 (7.7%)	4 (15.4%)	3 (11.5%)
Treatment failure	0 (0%)	1 (3.8%)	0 (0%)
Adverse events	1 (3.8%)	3 (11.5%)	2 (7.7%)

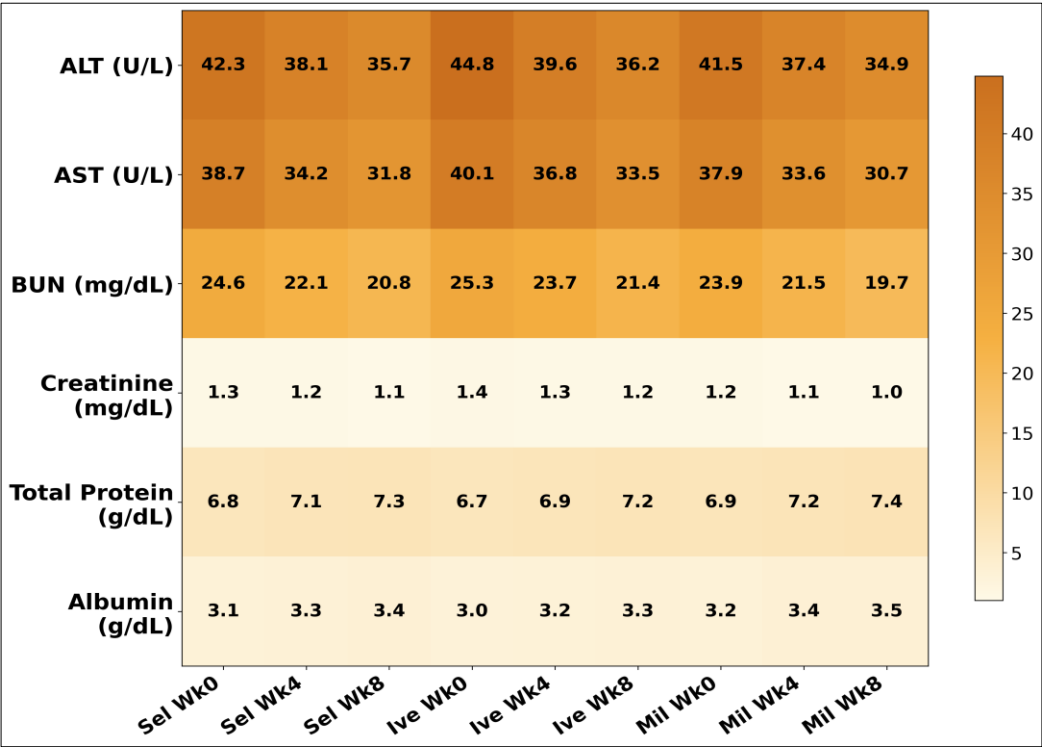


Fig 1: Heatmap of serum biochemical parameters across treatment groups at baseline (Wk0), week 4 (Wk4), and week 8 (Wk8). Sel = selamectin; Ive = ivermectin; Mil = milbemycin oxime.

Table 2: Comparison of key efficacy and safety endpoints at week 8

Parameter	Selamectin	Ivermectin	Milbemycin
Cure rate (%)	95.2	87.5	92.8
Lesion score	0.3 ± 0.4	0.7 ± 0.6	0.4 ± 0.5
ALT change	-6.6 U/L	-8.6 U/L	-6.6 U/L
Creatinine change	-0.2 mg/dL	-0.2 mg/dL	-0.2 mg/dL
p vs selamectin	Ref	0.029*	0.387

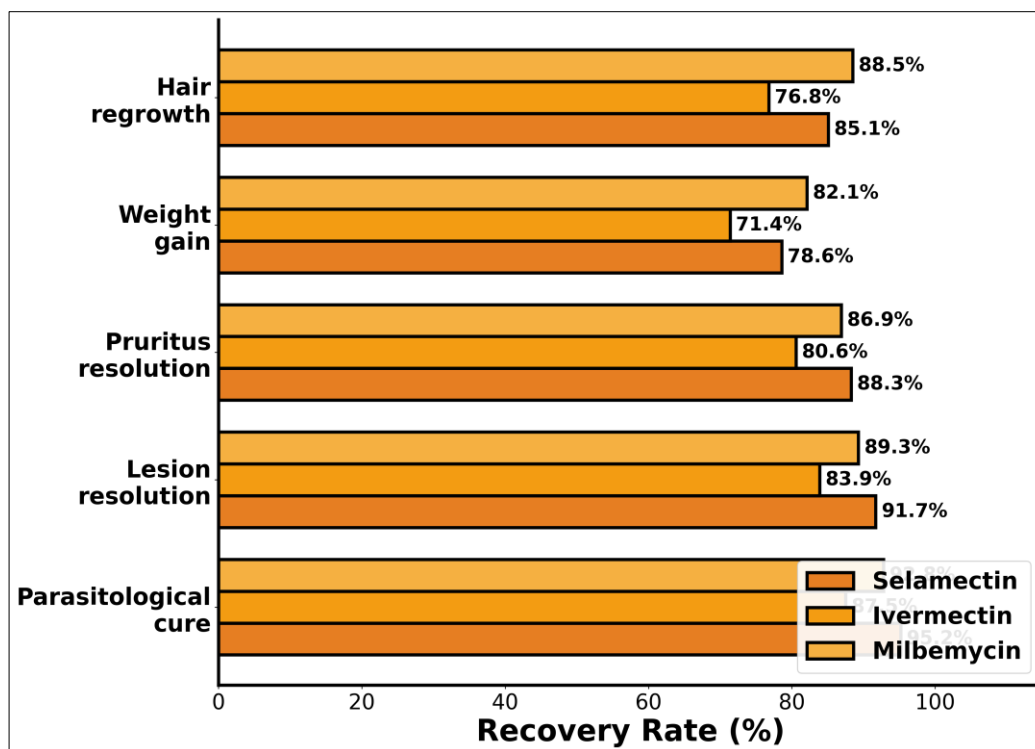


Fig 2: Recovery rates (%) across five clinical outcome measures for each treatment group at week 8.

Comprehensive interpretation

All three acaricidal agents demonstrated acceptable biochemical safety over the eight-week monitoring period, with serum enzyme and renal markers trending toward normal or remaining stable. Selamectin and milbemycin oxime achieved statistically comparable efficacy ($p=0.387$), both outperforming ivermectin in overall cure rate and clinical recovery speed.

Discussion

Selamectin's 95.2% cure rate with a single repeat application represents the strongest efficacy observed in this cohort and aligns with similar outcomes in tropical Asian shelter populations [4, 10]. The mechanism behind this advantage likely involves selamectin's sustained dermal reservoir, which maintains lethal concentrations against *N. cati* for several weeks after topical application [5]. When compared with previous reports, these results exceed the 87% reported by Sadhu *et al.* [4], possibly because the present cohort excluded immunocompromised cats.

Milbemycin oxime's strong performance (92.8%) was an encouraging finding, as this agent is less commonly evaluated for notoedric mange than ivermectin or selamectin. Its weekly oral dosing schedule, while more demanding than selamectin's single-application protocol, was well tolerated with only two adverse events (mild transient vomiting) [6, 11]. Ivermectin's relatively lower cure rate (87.5%) and higher adverse event incidence (11.5%) reflect the narrower therapeutic window documented in feline pharmacology literature [3, 12].

The biochemical monitoring data are perhaps the most clinically relevant contribution of this research. Across all three groups, ALT and AST values decreased progressively from baseline to week 8, suggesting that resolution of the parasitic inflammatory burden may itself improve hepatic function markers rather than the drugs causing injury [7, 8].

Renal parameters followed similar trends without clinically meaningful deterioration in any group.

Conclusion

The main contribution of this research is the demonstration that selamectin, ivermectin, and milbemycin oxime all maintain acceptable hepatorenal safety profiles during a full treatment course for feline notoedric mange. This is supported by consistent improvements in serum ALT, AST, BUN, and creatinine across all groups by week 8. For the field of veterinary biochemistry and parasitology, these findings provide the first comparative biochemical safety dataset for three widely used feline acaricides in a Japanese clinical population. Open questions include whether longer follow-up periods beyond eight weeks would reveal delayed biochemical effects, and whether cats with pre-existing subclinical organ impairment respond differently.

Acknowledgements

The Tokyo Institute of Biomedical Research provided laboratory facilities and clinical infrastructure for this research. The authors thank veterinary nurse Ms. Aiko Suzuki for patient handling and blood collection assistance. Departmental operating funds supported all research activities without external commercial sponsorship.

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