Readers Insight
Publisher of open access books and journals
PJMLS OPEN ACCESS
Print ISSN: 2707-4471. Online ISSN: 2707-448X

Research Article	Pak-Euro Journal of Medical and Life Sciences
DOI: 10.31580/pjmls.v8i1.3238	Copyright © All rights are reserved by Corresponding Author
Vol. 8 No. 1, 2025: pp. 219-226	
www.readersinsight.net/pjmls	**Revised:** March 21, 2025 **Accepted:** March 26, 2025
Submission: January 10, 2025	**Published Online:** March 31, 2025

THE ROLE OF INTRALESIONAL GLUCANTIME IN TREATING CUTANEOUS LEISHMANIASIS LESIONS COMPLICATED BY SECONDARY BACTERIAL INFECTIONS

Fatima Rehman[1ǂ], Rahat Ullah Khan[2,3ǂ], Kashif-ur-Rehman[4], Jamshaida Iqbal[5], Arsalan Said[6], Arshad Ali[1], Yasir Amin[7], Momin Khan[1*]

[1]**Department of Microbiology,** Institute of Pathology and Diagnostic Medicine, Khyber Medical University, Peshawar, Khyber Pakhtunkhwa, Pakistan
[2]**CAS Key Laboratory of Pathogen Microbiology and Immunology,** Institute of Microbiology, Center for Influenza Research and Early-warning (CASCIRE), CAS-TWAS Center of Excellence for Emerging Infectious Diseases (CEEID, Chinese Academy of Sciences, 100101, Beijing, China
[3]**College of Life Sciences,** University of Chinese Academy of Sciences, 101408-Beijing, China
[4]**Department of Community Medicine,** Khyber Medical College, Khyber Pakhtunkhwa, Pakistan
[5]**Department of Dermatology,** Mian Rashid Hussain Shaheed Memorial Hospital, Pubbi, Nowshehra, Khyber Pakhtunkhwa, Pakistan
[6]**Department of Parasitology,** University of Agriculture, Faisalabad, Pakistan
[7]**Veterinary Research and Diseases Investigation Center,** Abbottabad, Pakistan

***Corresponding Author:** Dr. Momin Khan. E. mail: mominkhan.ibms@kmu.edu.pk
ǂ Shared first authorship for this work: Fatima Rehman, Rahat Ullah Khan

Abstract

Glucantime remains the primary treatment for cutaneous leishmaniasis (CL). However, the growing concern over drug resistance has raised doubts about its effectiveness, especially in cases complicated by secondary infections. This study evaluates the efficacy of intralesional Glucantime in treating cutaneous leishmaniasis lesions complicated by bacterial infections.

A total of 100 patients with confirmed CL were enrolled in the study. Lesion samples were collected, cultured on various agar media, and identified through biochemical tests. Based on the culture results, patients were divided into two groups: culture-positive and culture-negative. The culture-positive group refers to patients with bacterial infections identified through positive culture results, while the culture-negative group refers to patients whose lesion cultures did not show bacterial growth. Both groups received intralesional Glucantime therapy and were monitored until the lesions healed completely.

Of the 100 patients, 53 (53%) tested culture-positive, with Staphylococcus aureus being the predominant bacterial isolate. Among these, 20 patients (37.7%) exhibited a complete response to the treatment, while 33 patients (62.3%) showed a poor response. In contrast, 47 patients (47%) in the culture-negative group demonstrated a higher rate of complete response, with 34 patients (72%) fully recovered and 13 (28%) showing a poor response.

This study highlights that the presence of bacterial colonization in leishmaniasis lesions significantly diminishes the therapeutic efficacy of Glucantime. These findings emphasize the need to address secondary bacterial infections in the management of CL.

Keywords: *Cutaneous leishmaniasis, Glucantime efficacy, Secondary bacterial infections*

INTRODUCTION

Cutaneous leishmaniasis (CL) represents the most common clinical form of leishmaniasis, with a broad spectrum of presentations ranging from subclinical or self-limiting cutaneous ulcers to widespread disseminated infections. The disease is endemic in over 90 countries, with an estimated global incidence of 600,000 to 1 million new cases annually, disproportionately affecting individuals from low socioeconomic backgrounds (1, 2). CL is often termed the “great imitator” due to the wide diversity of its clinical manifestations. While the typical presentation involves ulcerated lesions, either solitary or multiple, affecting primarily exposed areas of the body, atypical forms have also been documented. These variations

can complicate the diagnostic process, potentially leading to misdiagnosis, inappropriate treatment, and an increased burden of morbidity (3, 4).

The skin is a critical barrier against pathogen invasion, but its protective function can be compromised by physical, chemical, or mechanical factors, leading to wound formation(5). The composition and density of bacterial populations on the skin are influenced by anatomical factors, sebum production, humidity, and hormonal fluctuations. The bacteria inhabiting the skin microbiota may engage in commensal, symbiotic, or parasitic interactions with the host, with these relationships modulated by immune-mediated responses (6). In the context of CL, the ulcers are typically painless; however, once the protective crust over the ulcer is disrupted, the lesion becomes highly susceptible to colonization by pathogenic and opportunistic microorganisms, including bacteria and fungi. This secondary microbial infection contributes to pain, a burning sensation, and delays in wound healing (7). Secondary infections are particularly common in individuals with localized CL, poor hygiene, or improper wound care. Beyond tissue destruction, these infections may also decrease the number of detectable amastigotes in microscopic samples, thereby increasing the likelihood of misdiagnosis and inappropriate treatment (8). Studies indicate that the prevalence of secondary bacterial infections in CL lesions ranges from 23.6% to 81%, with *Staphylococcus aureus*, *Streptococcus pyogenes*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* being the most frequently isolated pathogens (9). Consequently, the systematic evaluation of cutaneous lesions for bacterial infections, along with the implementation of appropriate antimicrobial therapies, is crucial prior to the administration of anti-leishmanial treatments.

Despite significant advances in understanding the pathophysiology of CL, the development of a safe and effective vaccine remains a major challenge due to the complex life cycle of the parasite, the variability in the virulence of different *Leishmania* species, and the limited commercial interest in vaccine development (10, 11). Currently, treatment options for CL include both systemic and topical therapies. Among the topical treatments, intralesional antimonials, paromomycin, cryotherapy, thermotherapy, and CO2 laser therapy have been extensively studied. These approaches are particularly important given the high costs, poor patient compliance, and suboptimal outcomes associated with systemic treatments (12,13). Despite the variety of therapeutic options available, pentavalent antimonials, particularly Meglumine antimonate (Glucantime), remain the first-line treatment for CL. Traditionally, Glucantime has been administered intramuscularly at a dosage of 20 mg/kg body weight for 20 days. However, both the World Health Organization (WHO) and the Pan American Health Organization (PAHO) now recommend local therapy for localized infections (14). Limited research has been conducted on the efficacy of Glucantime in CL lesions complicated by secondary bacterial infections, and the available findings are inconclusive. Some studies report no significant differences in drug efficacy between lesions with and without bacterial co-infections. Moreover, no studies have specifically addressed this issue in the Pakistani context. Therefore, this research was undertaken to validate the findings of prior studies and to underscore the importance of assessing bacterial infections in CL lesions before initiating antimonial therapy.

MATERIALS AND METHODS

STUDY DESIGN

This study was a six-month quasi-experimental trial conducted between March and August 2023 at the Outpatient Department (OPD) of Dermatology, Mian Rashid Hussain Shaheed Memorial Hospital, Nowshehra, Pakistan. Ethical approval for this study was granted by the Institutional Ethical Committee of the Institute of Pathology and Diagnostic Medicine (IPDM), Khyber Medical University, Peshawar, Pakistan, with approval number KMU/IPDM/IEC/2023/13. Written informed consent was obtained from all participants, or their legal guardians in the case of minors under 10 years of age. To collect comprehensive demographic data, as well as lesion characteristics and details of prior treatments, a structured questionnaire was administered to each participant. Lesion size was measured using a digital vernier caliper to ensure accurate measurement, and clinical diagnosis was confirmed through parasitological studies, including skin slit smears stained with Giemsa for microscopic examination of *Leishmania* amastigotes.

SAMPLE SIZE CALCULATION

Sample size calculations were performed using OpenEpi software, with a 95% confidence level and 80% power. Based on initial calculations, a sample size of 80 participants was estimated to be sufficient. However, to account for potential dropouts during the study, 100 patients were enrolled.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria required participants to have confirmed Leishmania infection, with the presence of Leishmania amastigotes (LT bodies) in skin slit smears, and lesions with a maximum diameter of 3 cm. Exclusion criteria included patients with multiple lesions, those who were pregnant or lactating, or individuals who had received prior treatment with antibiotics or Glucantime.

SAMPLE COLLECTION AND TRANSPORTATION

Lesion samples were collected from patients using sterile cotton swabs or scraping, ensuring aseptic technique to avoid contamination. The samples were transported in Amies transport medium to the microbiology laboratory at Khyber Medical University. In the lab, samples were cultured on blood and MacConkey agar plates to isolate any bacterial pathogens. Identification of the bacterial isolates was carried out using Gram staining and biochemical tests, which allowed for the determination of bacterial species present. Isolates were stored at -80°C for further analysis.

TREATMENT PROTOCOL AND FOLLOW-UP

Patients were divided into two groups based on culture results. Group A included patients with no secondary bacterial infection, and Group B included patients with confirmed secondary bacterial infections. Both groups were treated with intralesional Glucantime at a dose of 0.5-1 ml administered twice weekly for a duration of six weeks. Treatment progress was closely monitored with regular follow-up visits at two-week intervals throughout the treatment period, with a final assessment conducted two weeks post-treatment to evaluate the outcome.

TREATMENT OUTCOME ASSESSMENT

Treatment outcomes were classified as either a complete response, which was defined as full re-epithelialization and resolution of the lesion with no further visible ulceration, or a poor response, defined as no significant improvement in lesion size or persistent or worsened symptoms. Fig. 1 shows the methodological approach of the study, outlining the key steps involved in the research process.

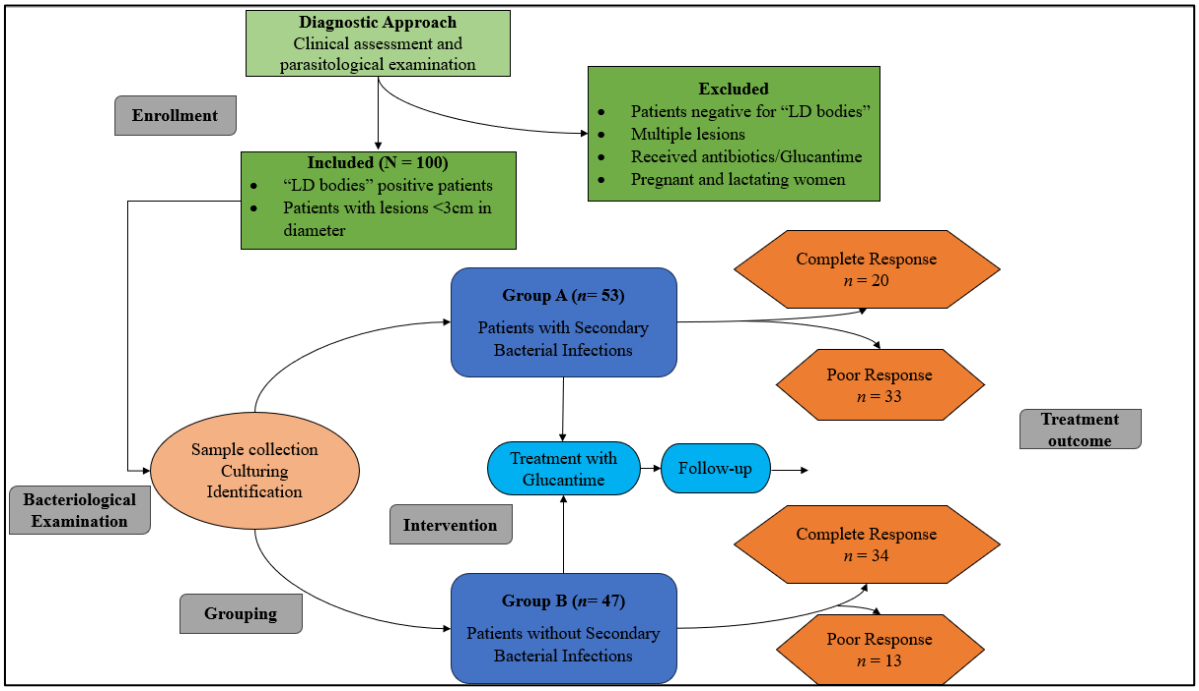

Fig. 1. The flow diagram of the research methodology

DATA ANALYSIS

Data were analyzed using SPSS version 22 (IBM, Armonk, NY). Descriptive statistics were employed to summarize demographic and clinical characteristics. The Chi-square test was used to compare the efficacy of Glucantime between culture-positive and culture-negative groups. To assess differences in age, disease duration, and lesion size between groups, an independent t-test was performed. A p-value of < 0.05 was considered statistically significant for all analyses.

RESULTS

All patients adhered strictly to the treatment protocol with Glucantime. The overall mean age of patients was 20.63 ± 17.64 years, with a mean disease duration of 4.43 ± 2.39 months and a mean lesion diameter of 2.43 ± 0.56 cm. Statistical analysis showed no significant difference in the mean disease duration (P-value = 0.875) or mean lesion diameter (P-value = 0.563) between the two groups. However, a significant difference in the mean age of patients was found between the groups (P-value = 0.022), with the group without secondary bacterial infection being older on average (24.66 ± 19.49 years) compared to the group with secondary bacterial infection (17.06 ± 15.11 years).

The disease was more prevalent in males (56%) compared to females (44%). The most frequently affected site was the face (40%), followed by the upper extremities (35%) and the lower extremities (25%). Secondary bacterial infection was more commonly observed in patients with ulcerated lesions. Table I presents the socio-demographic characteristics of patients in both groups.

Table I. Socio-demographic characteristics of patients

Characteristics	Group with secondary bacterial infection	Group without secondary bacterial infection
Gender		
Male	33 (62%)	23 (48%)
Female	20 (38%)	24 (52%)
Mean age (years)	17.06±15.11	24.66±19.49
Mean disease duration (months)	4.49±2.45	4.36±2.35
Mean lesion diameter (cm)	2.26±0.56	2.19±0.59
Lesion location		
Face	23 (43%)	17 (36%)
Upper extremity	16 30%)	19 (40%)
Lower extremity	14 (27%)	11 (23%)
Lesion type		
Papule	1 (2%)	3 (6%)
Nodule	5 (9%)	14 (30%)
Nodulo-ulcerative	17 (32%)	7 (15%)
Non-ulcerated plaque	11 (21%)	21 (45%)
Ulcer	19 (36%)	2 (4%)

CULTURE RESULTS

Of the 100 patients, 53 were culture-positive and 47 were culture-negative. A statistically significant association was found between the presence of bacterial infection and ulcerated lesions (P-value = 0.003). The most commonly isolated bacterium was *Staphylococcus aureus*, found in 15% of the cases. Polymicrobial infections, involving two bacteria, were frequently observed in patients. Common signs of bacterial infection included redness, swelling, and pus discharge. Table II summarizes the bacterial isolates recovered from the lesions.

TREATMENT AND OUTCOME

The treatment outcomes for both groups were notably different. Table III highlights the efficacy of intralesional Glucantime in treating cutaneous leishmaniasis lesions complicated by secondary bacterial infections. In the culture-positive group, 20 patients (37.7%) demonstrated a complete response, while 33 patients (62.3%) had a poor response. On the other hand, the culture-negative group showed a much higher rate of complete response, with 34 patients (72%) fully recovering and 13 (28%) showing a poor response.

These findings underscore that bacterial infections significantly hinder the therapeutic efficacy of Glucantime.

Table II. Bacteria isolated from cutaneous leishmaniasis lesions

Bacterial Isolates	Frequency	Percentage
Staphylococcus aureus	15	15.0%
Escherichia coli	4	4.0%
Staphylococcus epidermidis	2	2.0%
Streptococcus pyogenes	1	1.0%
Enterococcus faecalis	1	1.0%
Enterobacter cloaca	3	3.0%
Pseudomonas aeruginosa	1	1.0%
Bacillus subtilis	1	1.0%
Polymicrobial infections		
S.aureus+E.coli	17	17.0%
E.coli+S.epidermidis	2	2.0%
S.aureus+E.faecalis	1	1.0%
S.saprophyticus+C.koseri	1	1.0%
E.cloaca+S.aureus	3	3.0%
E.coli+S.pyogenes	1	1.0%

Table III. Treatment outcome efficacy of intralesional glucantime in cutaneous leishmaniasis lesions complicated by secondary bacterial infections

Groups	Complete response (n, %)	Poor response (n, %)	Total (n=100)
Culture- positive	20 (37.7%)	33 (62.3%)	53
Culture-negative	34 (72%)	13 (28%)	47
Overall	54 (54%)	46 (46%)	100

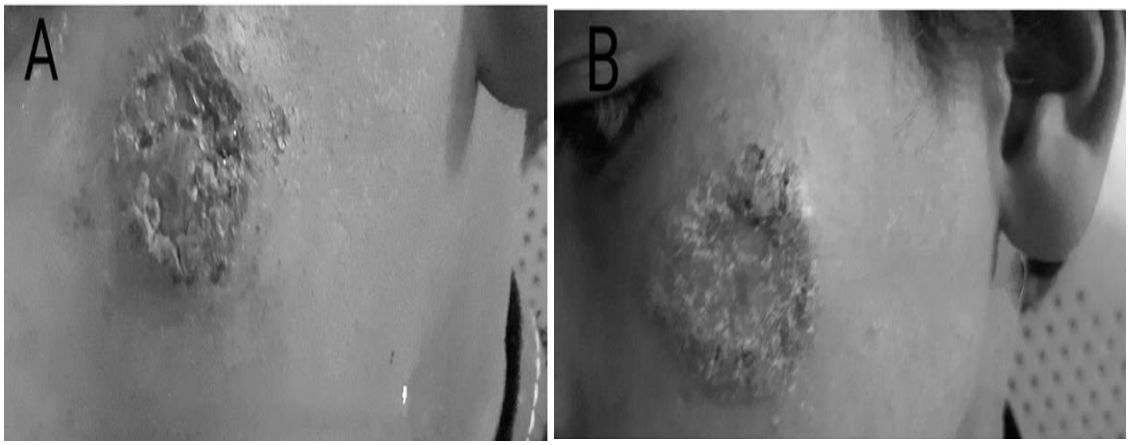

Fig. 2(A). A circular, crusted lesion with purulent discharge prior to treatment with Glucantime; **(B).** The same lesion showing no significant improvement following Glucantime treatment, complicated by a secondary bacterial infection

DISCUSSION

Cutaneous leishmaniasis continues to pose a significant challenge, especially when complicated by secondary bacterial infections. Our study confirms that secondary bacterial infections considerably diminish the therapeutic effectiveness of Glucantime, which is the first-line treatment for CL. Our results show a significant difference in treatment response between the two groups: 72% of culture-negative patients responded well to Glucantime, while only 37.7% of culture-positive patients exhibited complete healing. This finding underscores the adverse impact of bacterial colonization on lesion healing, consistent with earlier studies that have demonstrated a delay in healing when bacterial infections are present (15). The presence of bacterial infection, particularly *S. aureus*, as the most commonly isolated pathogen, correlated with poorer outcomes, leading to prolonged lesion persistence and inflammation.

Our study's results also corroborate findings from various studies that suggest the detrimental effect of secondary bacterial infections on treatment outcomes. For example, in the study by Antonio et al. (2017), no significant difference was found between culture-positive and culture-negative patients, but this contrasts with our study where a clear difference in response to Glucantime was evident. This divergence

could be due to variations in study design, the antibiotic pre-treatment in their cohort, or methodological differences in lesion assessment (16). In a similar vein, Sadeghian *et al.,* (2011) assessed the efficacy of systemic Glucantime in lesions complicated by bacterial infections. Among 38 culture-positive patients, 26 exhibited a poor response to treatment, whereas 43 of 123 culture-negative patients demonstrated a poor response (15). These results align closely with the findings of our study, indicating that bacterial infection significantly impacts treatment outcomes.

Similarly, Layegh *et al.,* (2015) conducted a study with 84 patients and observed no significant difference in the healing rates between culture-positive and culture-negative groups, which contrasts with our findings. This divergence may be attributed to differences in treatment protocols, such as the use of antibiotics (oral cephalexin) in their study, and sample size differences, which could affect statistical significance (17).

We also found polymicrobial infections, with *S. aureus* and *E. coli* being the most frequent isolates, suggesting that these patients may be exposed to unsanitary conditions that contribute to the high rate of bacterial co-infections. The presence of Escherichia coli, Enterococcus faecalis, and Enterobacter cloacae suggests possible fecal contamination, which aligns with previous literature indicating poor hygiene as a contributing factor to increased secondary bacterial infections (18-20).

The negative impact of bacterial infections on the therapeutic efficacy of Glucantime highlights the importance of considering secondary bacterial infections in the management of CL. The study strongly suggests that addressing bacterial co-infections with appropriate antibiotics before or in conjunction with antileishmanial therapy may enhance treatment outcomes and prevent complications related to poor healing.

CONCLUSION

Our study clearly demonstrates that secondary bacterial infections significantly impair the healing process and reduce the effectiveness of Glucantime in treating cutaneous leishmaniasis lesions. Patients with culture-negative lesions responded significantly better to Glucantime treatment than those with secondary bacterial infections, emphasizing the importance of managing bacterial infections in CL patients.

The findings suggest that a comprehensive treatment approach, which includes appropriate antimicrobial therapy for secondary bacterial infections, is essential before administering Glucantime. Proper wound care and infection prevention strategies should be integrated into the management plan for CL, especially in areas with poor hygiene. Moreover, a careful assessment of bacterial infections should be performed in CL lesions prior to starting antileishmanial treatment to optimize therapeutic outcomes and minimize the risk of developing drug resistance to Glucantime.

Given these results, it is essential for healthcare providers to consider both the parasitic infection and any potential bacterial co-infections in patients with CL to improve the overall treatment success and reduce the burden of the disease. Further studies exploring the role of antibiotic therapy in combination with antileishmanial drugs are warranted to enhance the efficacy of treatments for CL.

Authors' contribution:

FR, MK, RUK Conceptualization; FR, KR, JI Methodology; AA, AS Software & Formal Analysis; MK, FR, RUK Validation; FR, RUK, JI Investigation; MK, KR Resources; RUK, AS, AA Writing Review & Editing; FR, RUK Visualization; MK Project Administration.

Funding source:

This study did not receive any funding or financial support.

References:

1. Khokhar M, Shereen MA, Khan M, Khan RU, Sohail A, Khan IU. In vitro efficacy of polymer-coated miltefosine drug against Leishmania tropica. J Parasit Dis. 2022;1-11.
2. Khan R, Khan M, Sohail A, Ullah R, Iqbal A, Ahmad B. Efficacy of pentamidine-loaded chitosan nanoparticles as a novel drug delivery system for Leishmania tropica. J Pharm Sci. 2022.

3. Gurel MS, Tekin B, Uzun S. Cutaneous leishmaniasis: A great imitator. Clin Dermatol. 2020;38(2):140-51.
4. Khan RU, Khan M, Ullah Q, Khan MZ, Sohail A, Islam R, Bilal H, Ullah S, Iqbal A. In vitro and in vivo effects of conventional and chitosan nanoparticle-encapsulated miltefosine drug for treatment of cutaneous leishmaniasis. InMedical Sciences Forum. MDPI. 2023;21(1):19.
5. Lefèvre-Utile A, Braun C, Haftek M, Aubin F. Five functional aspects of the epidermal barrier. Int J Mol Sci. 2021;22(21):11676.
6. Puca V, Marulli RZ, Grande R, Vitale I, Niro A, Molinaro G. Microbial species isolated from infected wounds and antimicrobial resistance analysis: Data emerging from a three-year retrospective study. Antibiotics. 2021;10(10):1162.
7. Doro BMK. Prevalence of bacterial infections among cutaneous leishmaniasis patients. J Clin Infect Dis. 2024.
8. Sikorska K, Gesing M, Olszański R, Roszko-Wysokińska A, Szostakowska B, Van Damme-Ostapowicz K. Misdiagnosis and inappropriate treatment of cutaneous leishmaniasis: a case report. Trop Dis Travel Med Vaccines. 2022;8(1):18.
9. Ayalew G, Asmamaw A, Wolde M, Diriba R, Zerfu B. Bacterial isolates and drug susceptibility patterns in infected lesions of cutaneous leishmaniasis patients at ALERT hospital, Addis Ababa, Ethiopia. BMC Infect Dis. 2025;25(1):16.
10. Dinc R. Leishmania vaccines: the current situation with its promising aspect for the future. Korean J Parasitol. 2022;60(6):379.
11. Sohail A, Khan RU, Khan M, Khokhar M, Ullah S, Ali A. Comparative efficacy of amphotericin B-loaded chitosan nanoparticles and free amphotericin B drug against Leishmania tropica. Bull Natl Res Cent. 2021;45:1-9.
12. Azim M, Khan SA, Ullah S, Ullah S, Anjum SI. Therapeutic advances in the topical treatment of cutaneous leishmaniasis: A review. PLoS Negl Trop Dis. 2021;15(3):e0009099.
13. Ur Rahman M, Khan M, Khan SW, Khan RU, Sohail A, Zaman A. Novel Schiff bases of Vanillin: potent inhibitors of macrophage harbored Leishmania tropica. J Parasit Dis. 2023;47(3):619-29.
14. Arboleda M, Barrantes S, Úsuga LY, Robledo SM. Successful treatment of cutaneous leishmaniasis with intralesional meglumine antimoniate: A case series. Rev Soc Bras Med Trop. 2019;52:e20180211.
15. Saini I, Joshi J, Kaur S. Unwelcome prevalence of leishmaniasis with several other infectious diseases. Int Immunopharmacol. 2022;110:109059.
16. Sadeghian G, Ziaei H, Bidabadi LS, Baghbaderani AZ. Decreased effect of glucantime in cutaneous leishmaniasis complicated with secondary bacterial infection. Indian J Dermatol. 2011;56(1):37-9.
17. Antonio LdF, Lyra MR, Saheki MN, Schubach AdO, Miranda LdFC, Madeira MdF. Effect of secondary infection on epithelialisation and total healing of cutaneous leishmaniasis lesions. Mem Inst Oswaldo Cruz. 2017;112:640-6.
18. Layegh P, Ghazvini K, Moghiman T, Hadian F, Zabolinejad N, Pezeshkpour F. Bacterial contamination in cutaneous leishmaniasis: its effect on the lesions' healing course. Indian J Dermatol. 2015;60(2):211.
19. de Farias DVM, dos Santos RHM, de Oliveira SSS, de Aguiar Valentim L, de Paula Fernandes F, Quaresma TC. Evaluation of intralesional treatment in American tegumentary leishmaniasis in the Amazon region: results and perspectives. Cuad Educ Desarrol. 2024;16(3):e3635-e.
20. Yeboaa C, Odoi H, Owusu Ntim R, Boakye YD, Kwakye-Nuako G, Agyare C. Diversity and antibiograms of bacteria isolated from cutaneous leishmaniasis wounds in the Nkwanta South District of Ghana. Arch Microbiol. 2023;205(2):74.
21. Ayalew G, Asmamaw A, Wolde M, Diriba R, Zerfu B. Bacterial isolates and drug susceptibility patterns in infected lesions of cutaneous leishmaniasis patients at ALERT hospital, Addis Ababa, Ethiopia. BMC Infectious Diseases. 2025;25(1):16.