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ACUTE DERMAL TOXICITY ASSESSMENT OF "NANOZINC" GEL (TASHPHARMI, UZBEKISTAN)

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ABSTRACT

This study investigated the acute dermal toxicity of "Nanozinc" gel (TashPharmi, Uzbekistan) following topical administration in laboratory animals. The aim of the study was to evaluate the safety and tolerability of a zinc oxide nanoparticle-based gel intended for future use in dermatological formulations. The experiment was performed on sexually mature white mice of both sexes following a single topical application of the gel at different dose levels. The animals were observed continuously during the first hours after administration and subsequently for 14 consecutive days. Clinical observations included general appearance, behavioral changes, locomotor activity, respiration, cardiac activity, food and water intake, body weight, and other indicators of systemic toxicity. No mortality, signs of acute intoxication, behavioral abnormalities, or pathological alterations were observed in any experimental group throughout the observation period. The obtained findings indicate that "Nanozinc" gel does not produce acute toxic effects after topical administration under the experimental conditions employed.These results confirm the safety of topical application of "Nanozinc" gel (TashPharmi, Uzbekistan) and support its further preclinical evaluation as a promising dermatological formulation.

Introduction. The rapid development of nanotechnology over the past decades has opened new opportunities for the design of advanced pharmaceutical and biomedical products. Nanoparticle-based drug delivery systems have attracted considerable attention because of their improved bioavailability, controlled release characteristics, and enhanced therapeutic efficacy compared with conventional formulations [1]. Among various nanomaterials, **zinc oxide nanoparticles (ZnO NPs)** are

considered one of the most promising candidates for pharmaceutical applications due to their broad-spectrum antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties [2]. Their high surface-to-volume ratio, photocatalytic activity, and ability to interact with biological membranes have resulted in widespread application in topical formulations, including creams, ointments, hydrogels, and wound dressings designed for the treatment of burns, skin injuries, and infectious diseases [3].

Despite these therapeutic advantages, the biological safety of nanoparticles remains an important issue. Owing to their nanoscale dimensions and unique physicochemical characteristics, nanoparticles may exhibit biological behaviors different from those of their bulk counterparts. Previous studies have demonstrated that ZnO nanoparticles may penetrate damaged skin, accumulate within tissues, interact with cellular membranes, and induce oxidative stress through the release of zinc ions under certain experimental conditions [4,5]. Therefore, comprehensive toxicological evaluation is an essential prerequisite for the development of safe nanoparticle-containing pharmaceutical products.

The present investigation focuses on an experimental **"Nanozinc" gel (TashPharmi, Uzbekistan)** formulated with zinc oxide nanoparticles. A hydrogel dosage form was selected because of its excellent biocompatibility, ease of topical administration, favorable patient compliance, and ability to ensure uniform distribution of the active ingredient across the wound surface. To evaluate the safety profile of the formulation, an acute dermal toxicity study was performed using laboratory mice. Topical administration was selected because it reflects the intended clinical route of application in humans. White mice were chosen as the experimental model because of their high sensitivity to toxic agents and their extensive use in regulatory toxicological studies. Previous investigations have demonstrated that topical administration of ZnO nanoparticles at doses up to 1000 mg/kg did not produce mortality or clinically significant adverse effects in mice [6]. The working hypothesis of the present study was that topical administration of **"Nanozinc" gel** would not induce signs of acute toxicity and could therefore be classified as a low-toxicity pharmaceutical preparation suitable for further preclinical investigations. Evaluation of acute toxicity represents an important stage in the development of novel zinc nanoparticle-based pharmaceutical products intended for dermatological and cosmetic applications. The objective of this study was to evaluate the acute dermal toxicity and safety profile of **"Nanozinc" gel (TashPharmi, Uzbekistan)** containing zinc oxide nanoparticles following topical administration in laboratory animals.

Materials and Methods

All experimental procedures were performed using healthy laboratory animals that had undergone a quarantine and acclimatization period of **10–14 days** before the beginning of the study [7–9].

Acute dermal toxicity was evaluated according to standard toxicological

protocols using healthy outbred white mice of both sexes weighing **18–22 g**. Six animals were included in each experimental group, resulting in a total of **18 mice**.

Twenty-four hours before treatment, the hair on the dorsal region of each animal was carefully removed from an area measuring approximately **1 × 1 cm** to facilitate uniform topical application [10].

"Nanozinc" gel (0.02%) was administered topically at doses of **1, 3, and 5 mg/kg**, corresponding to application volumes of **0.1, 0.3, and 0.5 mL per 20 g body weight**, respectively. The applied volume did not exceed the maximum recommended volume for dermal administration [11].

Following treatment, animals were housed individually and monitored continuously during the first hour. Subsequently, clinical observations were performed every hour during the first 24 hours and once daily for the following **13 days**, giving a total observation period of **14 days**.

The following parameters were evaluated throughout the study: general appearance, behavior, locomotor activity, muscle tone, coordination, occurrence of tremors or convulsions, response to external stimuli, respiratory and cardiovascular function, condition of the skin, hair coat and mucous membranes, food and water consumption, body weight changes, and other clinical signs indicative of systemic toxicity. The onset of intoxication symptoms and mortality, if any, were also recorded [7,8].

Throughout the experiment, all animals were maintained under standard vivarium conditions with unrestricted access to food and drinking water.

Results and Discussion

No mortality or clinical signs of acute intoxication were observed following topical administration of **"Nanozinc" gel (TashPharmi, Uzbekistan)** at doses ranging from **1 to 5 mg/kg**. Throughout the 14-day observation period, the treated animals maintained normal behavior, locomotor activity, respiration, food and water consumption, and body weight, without evidence of skin irritation or other pathological changes.

Because no deaths occurred in any experimental group, calculation of conventional acute toxicity parameters, including the median lethal dose (LD_{50}), was not possible. The absence of mortality at the highest tested dose indicates that the **LD_{50} exceeds 5 mg/kg** following dermal administration of **"Nanozinc" gel (TashPharmi, Uzbekistan)** (Tables 1–2).

The obtained results demonstrate that the investigated formulation possesses a favorable safety profile after single topical administration. These findings are consistent with previously published studies reporting the low dermal toxicity of zinc oxide nanoparticle-based topical formulations [4–6].

Overall, the absence of toxic manifestations under the experimental conditions confirms the good tolerability of **"Nanozinc" gel** and supports its further preclinical pharmacological evaluation as a promising topical nanopharmaceutical for dermatological applications.

Table 1. Results of the acute dermal toxicity assessment of "Nanozinc" gel (TashPharmi, Uzbekistan)

Dose	Observation
1 mg/kg	No clinical signs of intoxication or mortality were observed following topical application of the gel.
3 mg/kg	No clinical signs of intoxication or mortality were observed following topical application of the gel.
5 mg/kg	Four mice developed small scars at the sites of gel application. However, no mortality or systemic signs of acute toxicity were observed during the 14-day observation period.

Table note: *Animals were observed for 14 days after a single topical administration of "Nanozinc" gel.*

Table 2. Acute dermal toxicity parameters of "Nanozinc" gel (TashPharmi, Uzbekistan)

Dose	Number of dead animals/Total
1 mg/kg	0/6
3 mg/kg	0/6
5 mg/kg	0/6

Estimated LD_{50}: > 5 mg/kg (topical administration)

Table 3. Clinical observations following topical administration of "Nanozinc" gel (TashPharmi, Uzbekistan)

Dose	Clinical observations
1 mg/kg	No clinical signs of intoxication or mortality were observed following topical administration.
3 mg/kg	No clinical signs of intoxication or mortality were observed following topical administration.
5 mg/kg	Mild local scab formation was observed at the application site in four mice. However, no mortality or systemic signs of acute toxicity were detected during the observation period.

Table 4. Body weight of experimental animals used for the acute dermal toxicity study

Animal No.	1 mg/kg	3 mg/kg	5 mg/kg
1	18	21	22
2	19	22	18
3	21	19	19
4	22	18	21

Animal No.	1 mg/kg	3 mg/kg	5 mg/kg
5	20	22	22
6	19	21	19

Values are expressed as body weight (g) before treatment.

Discussion

The acute dermal toxicity assessment demonstrated that **"Nanozinc" gel (TashPharmi, Uzbekistan)** possesses a favorable toxicological profile after a single topical administration. Throughout the study, no mortality was recorded in any treatment group receiving doses ranging from **1 to 5 mg/kg**. Likewise, no clinically significant manifestations of acute intoxication, including behavioral abnormalities, impaired locomotor activity, respiratory distress, or cardiovascular dysfunction, were observed.

A mild localized dermal reaction characterized by scab formation was detected in four animals receiving the highest tested dose (**5 mg/kg**). However, this local response was transient and was not associated with systemic toxicity or mortality. Such findings suggest that the observed skin changes were limited to the application site and did not indicate generalized toxic effects.

Because no deaths occurred during the experimental period, determination of the median lethal dose ($\mathbf{LD_{50}}$) was not possible. Therefore, the $\mathbf{LD_{50}}$ of **"Nanozinc" gel** following topical administration can be considered to be **greater than 5 mg/kg**, indicating a low acute toxicity profile under the experimental conditions.

The obtained findings are consistent with previous reports demonstrating that topical zinc oxide nanoparticle formulations exhibit excellent dermal biocompatibility with minimal systemic absorption and low toxicological risk [2–6]. Collectively, these results support the safety of the developed formulation for topical use and provide a scientific basis for further preclinical investigations.

Conclusion

The present study represents an important stage in the preclinical safety evaluation of the experimental **"Nanozinc" gel (TashPharmi, Uzbekistan)**.

The results demonstrated that single topical administration of the formulation at doses ranging from **1 to 5 mg/kg** did not produce mortality or clinically significant signs of acute systemic toxicity in laboratory mice. Although mild local scab formation was observed in several animals receiving the highest dose, no severe dermal reactions or systemic adverse effects were detected throughout the 14-day observation period.

The estimated $\mathbf{LD_{50}}$ exceeded **5 mg/kg**, indicating that the investigated formulation may be classified as a **low-toxicity topical preparation** according to accepted toxicological criteria.

Overall, the favorable safety profile observed in this study supports the continued preclinical development of **"Nanozinc" gel**. Further investigations should include repeated-dose toxicity, chronic toxicity, local tolerance, reproductive toxicity, and pharmacological efficacy studies to

establish its therapeutic potential as a safe and effective zinc oxide nanoparticle-based dermatological formulation.

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