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Ameliorative effect of zinc oxide nanoparticles against cutaneous amyloidosis in rats: Histopathology and biochemical study

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Abstract

Primary Localized Cutaneous Amyloidosis (PLCA) is a relatively rare chronic condition considered by amyloid deposition in the dermis without accompanying deposits in internal organs. This study was designed to determine the role of zinc oxide nanoparticles in reducing the development of experimentally induced amyloidosis lesions in male rats. Forty male rats aged two months were used in this research, randomly divided into four groups, with 10 animals in each group. The Control group (group I) and (Group II) Rat intraperitoneally (IP) inoculated with a dose of ZnO-NPs 5 mg/kg (Group III): Rat IP inoculated with 3.0 ml of sodium caseinate solution (8%) (Group IV): Rat IP injected sodium caseinate with nano zinc oxide (ZnO-NPs). The injection protocol was four days of injection and one day of rest for 60 days. The results showed a significant increase in the level of serum amyloid A and Creative protein in Group III when compared with the group of rats, Group IV, but it did not reach its normal levels when compared with Group I. The results of the gross examination showed the presence of pathological lesions such as alopecia, skin thickening, and redness in Group III, while the pathological changes were less severe in Group IV. Histopathological examination of the skin showed infiltration of mononuclear inflammatory cells in the dermis and subcutaneous layers and around the sweat glands, with congestion of the blood vessels and the presence of edema between the muscle fibers, Zenker's necrosis, atrophy of myocytes, and the deposition of a homogeneous protein substance between the collagen fibers and the muscle fibers and around the blood vessels in G3 after 25 days of experiment lesions were more severe after 60 days of treatment. Histological sections of the skin showed a clear improvement, as represented by the slight infiltration of inflammatory cells with little protein deposition in group IV. The results of the histochemistry examination of the skin samples of the different groups showed a positive reaction to amyloid, with varying intensity depending on the treatment period and the type of substance. This study showed that zinc oxide plays a role in reducing the advance of amyloidosis lesions.

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Introduction

Cutaneous amyloidosis is a skin condition characterized by the deposition of amyloid in different layers of the skin, and it is related to chronic inflammatory conditions (1). Cutaneous amyloidosis is the most prevalent form of localized amyloidosis, recognized by extracellular amyloid deposition (2,3). Localized cutaneous amyloidosis is divided into four types: lichen amyloidosis, maculopapular amyloidosis, biphasic amyloidosis, and nodular amyloidosis (4). Cutaneous amyloidosis can be prompted experimentally by repeated injection of an inflammatory agent such as sulfur

nitrate and sodium caseinate (5,6). It can also be induced rapidly by administering amyloid fibrils, which are performed as an amyloid-enhancing factor in animals under inflammatory disorders (7). Dubernet *et al.* (8) found that giving insulin injections under the skin to diabetic patients for a long period makes them vulnerable to the occurrence of cutaneous amyloidosis. Histologically, cutaneous amyloidosis is described as a chronic condition without transformation into a malignant tumor that appears as eosinophilic amorphous deposits that are restricted to the upper dermis, particularly the papillary dermis with epidermal acanthosis and orthohyperkeratosis (9). Recently, many studies have been conducted on the use of nanoparticles in assessing the accumulation of proteins and peptides associated with amyloid-related diseases; these particles have wide-ranging applications in many disciplines, including molecular biology, physics, organic and inorganic chemistry, medicine, and materials science due to their unique chemical, optical, electrical, and magnetic properties compared to their bulk counterparts (10). There is a trend towards using nanoparticles in several fields (11-13). Despite the harmful effect of ZnO-NPs on some animals, ZnO-NPs are recorded as the safest and most environmentally friendly as they are biodegradable and non-carcinogenic, also ZnO-NPs tissue damage repair and have antioxidant activity by increasing the activities of mRNA expression of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase, glutathione reductase (GSH) and down the instruction of malondialdehyde (MDA) (14,15). ZnO-NPs enhance T-cell activity and increase the rat serum's production of antigen-specific antibodies, particularly immunoglobulin E (IgE) and immunoglobulin G (IgG) (16). However, because ZnO-NPs inhibit the growth of numerous bacteria, such as Streptococcus species, Staphylococcus species, Escherichia coli, Bacillus subtilis, and Pseudomonas fluorescens, they are regarded as a strong antibacterial agent (17,18). ZnO-NPs can reduce local skin irritation by penetrating the deep layers of allergic skin (19).

This study highlights the ability of zinc oxide nanoparticles to facilitate the development of cutaneous amyloidosis in rats.

Materials and methods

Ethical approval

Ethical approval reference number UM.VET.2024 for handling animals was awarded by the Institutional Animal Care and Use Committee at the University of Mosul, College of Veterinary Medicine.

Animals

Forty Albino male rats aged 2 months and weighing 250-300 grams were used. The Rats were housed under standard laboratory conditions, including a controlled temperature at 22±2°C and a fixed light/dark cycle (12 hours light/12 hours dark), with continuous access to food and water to ensure their well-being throughout the study.

Experimental design

Forty albino Rats were divided into four experimental groups, each consisting of ten rats. Group I: Rat IP inoculated with normal saline (control group). Group II: Rat IP inoculated with a dose of ZnO-NPs 5 mg/kg (control +I) (20). Group III: Rat IP inoculated with 3.0 ml of sodium caseinate solution (8%). (control +II) (21). Group IV: Rat IP inoculated sodium caseinate with zinc oxide. The protocol was four days of injection and one day of rest. After 25 days of the experiment, half of the animals were sacrificed; at the end of the experiment (60 days), the other half were sacrificed, and Blood samples were taken for both periods. For serum tests. Skin samples are stored in a 10% neutral buffer formalin for histopathological examination using routine stain and Congo red stain (22,23).

Biochemical examination of blood

After collecting blood samples from all groups, the serum was separated for biochemical examination (24), and then the level of both serum amyloid A (SAA) and C reactive protein (CRP) was measured via a spectrophotometer device using the diagnostic measurement kit (RAT serum amyloid A4) respectively.

Skin histopathological examination

Skin samples were fixed in 10% neutral formalin for 48 hours, washed with running water, passed through ascending concentrations of ethyl alcohol, cleared by xylene, and finally embedded in paraffin wax. Four-micron-thick tissue sections were prepared, then stained with hematoxylin-eosin and examined under a light microscope (25,26); Congo red stain was used for the detection of amyloid and the severity of lesions (27).

Statistical analysis

Statistical analysis of the numbers was performed using the SPSS program, and the standard and average error were calculated using the Duncans The significant difference for all tests was at a significance level of the $P<0.05$ (28).

Results

Measuring the level of serum amyloid A(SAA) activity in blood serum

The results of the statistical analysis of the different groups showed significant differences at the probability level $P<0.05$, as a significant increase in the level of SAA in blood serum was observed in the group of rats treated with a dose of 3 ml of 8%sodium caseinate for 25 days. The significant difference was higher when the treatment period increased to 60 days compared with the control group (G1) and the group of rats treated with nano zinc oxide (G2) at a dose of 5 mg/kg

of body weight. It was also observed that there was no significant difference in the rate of SAA activity in the group of rats treated with sodium caseinate and zinc oxide nanoparticles (G4) when compared with G1 and G2, with an arithmetic difference in G4 when compared with G3 for both periods (Table 1).

Measuring the level of serum C reactive protein (CRP) activity in blood serum

The results of the statistical analysis of the different groups after 25 days of treatment were characterized by the absence of significant differences at the probability level $P<0.05$ in the level of CRP in the blood serum between the groups, but after 60 days of treatment, the group of rats treated with sodium caseinate (G3) and at a dose of 3 ml 8% demonstrated a significant increase in CRP levels in comparison to the control group. G1 and the rats who received nano zinc oxide treatment (G2) at a dose of 5 mg/kg body white, while it was noted that when the rats were treated with sodium caseinate with nano zinc oxide (G4), it led to an arithmetic decrease in the level of CRP in the serum of rats when compared with G3 and no significant difference when compared with G1 and G2 (Table 2).

Table 1: Measuring the level of serum amyloid A(SAA) activity in blood serum

Days	Control	Zno	Nacas	Nacas+Zno
D25	0.86±24.48c	1.5±25.54 bc	2.1±29.85 ab	1.74±26.5 bc
D60	1.15±25.1 bc	1.62±26.41 bc	2.4±33.9 a	1.97±27.2 Ab

Different letters mean differences significantly at level $P\leq0.05$.

Table 2: Measuring serum C reactive protein (CRP) activity level in blood serum

Days	Control	Zno	Nacas	Nacas+Zno
D25	0.18±0.36 b	0.2±0.38 b	0.34±0.86 ab	0.25±0.4 ab
D60	0.19±0.37 b	0.25±0.4 b	2.82±1.96 a	0.27±0.45 ab

Different letters mean differences significantly at level $P\leq0.05$.

Pathological changes

The clinical changes in the group of rats treated with sodium caseinate were represented by the presence of a skin lesion in the injection area characterized by alopecia, skin thickening, and redness, which occurred after 60 days of injection, and the severity of the lesion decreased in the group treated with sodium caseinate and zinc oxide nanoparticles (Figures 1 and 2).

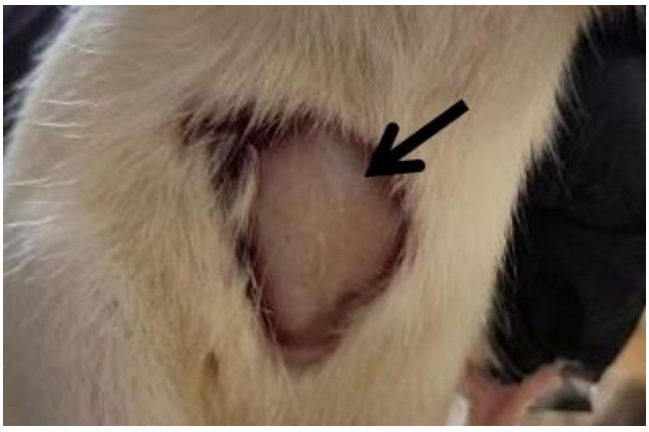

Figure 1: Macroscopic image of rats given sodium caseinate for 60 days reveals a skin lesion where the injection was made. (Black arrow).

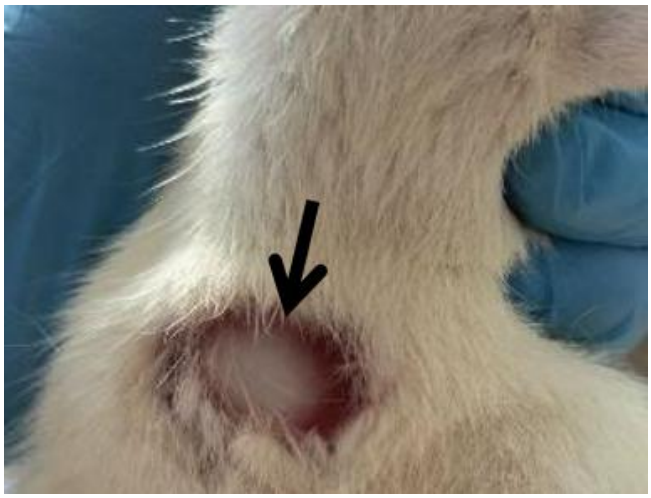

Figure 2: A macroscopic image of a rat treated with sodium caseinate and zinc oxide nanoparticles for 60 days shows a decrease in the development of the skin lesion at the injection site (Black arrow).

Histopathological changes

Histological sections of the skin of rats treated with 3 ml 8% sodium caseinate for 25 days showed infiltration of mononuclear inflammatory cells in the dermis and subcutaneous layers and around the skin glands, with congestion of the blood capillaries and the presence of edema

between the muscle fibers, muscle fiber necrosis, atrophy of myocyte and the deposition of a homogeneous protein substance between the collagen fibers and the muscle fibers and around the blood vessels (Figures 3-6). Histological sections of the skin showed a clear improvement represented by slight infiltration of mononuclear inflammatory cells with little protein deposition in rats treated with sodium caseinate and nano zinc oxide at a dose of 5 mg /kg Bwt. (Figures 7-9). After 60 days of treatment, the skin lesions of the group of rats treated with sodium caseinate were characterized by severe hyperkeratosis and acanthosis of the epidermis layer, dense infiltration of mononuclear inflammatory cells with the presence of edema between collagen fibers and muscle fibers, severe blood vessel congestion and blood clot formation, in addition to severe deposition of a homogeneous protein substance between the dermal papillae, collagen fibers, muscle fibers and around blood vessels, while the cross-sections of the group of rats treated with sodium caseinate with nano zinc oxide showed a reduction in Pathological lesions were represented by a decrease in the amount of protein deposited with a slight infiltration of inflammatory cells (Figures 10 and 11).

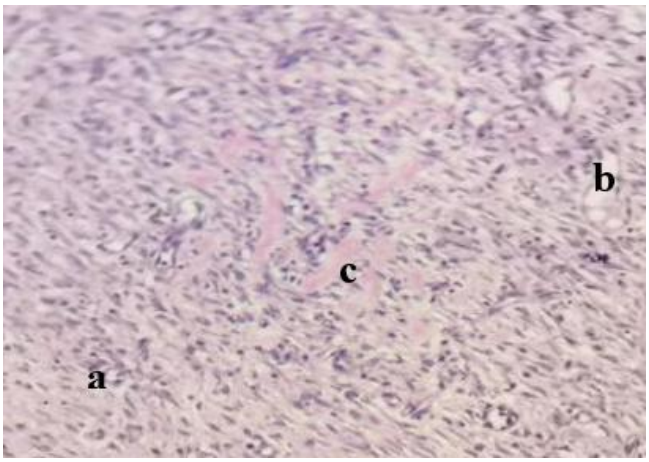

Figure 3: The histological section of the rat skin was treated with sodium caseinate for 25 days, showing the infiltration of mononuclear inflammatory cells in the dermis (a) with the presence of edema between the collagen fibers. (b) in addition to the deposition of a homogeneous protein substance between collagen fibers (c). H&E. 100x.

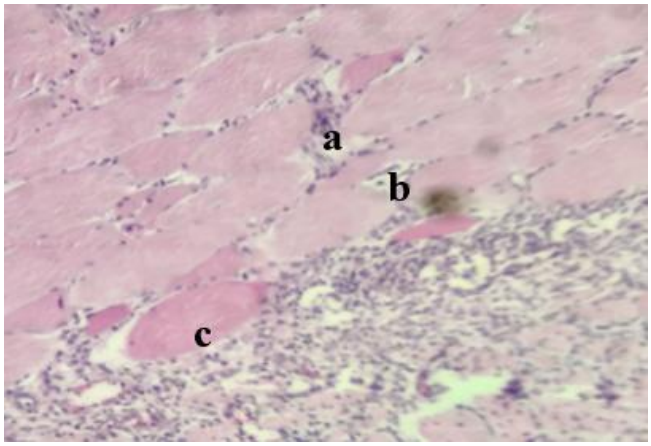

Figure 4: Histological section of rat skin treated with sodium caseinate for 25 days, showing infiltration of mononuclear inflammatory cells in the subcutaneous layer between muscle fibers, (a) with the presence of edema (b) in addition to the deposition of a homogeneous protein substance between muscle fibers (c). H&E. 100x.

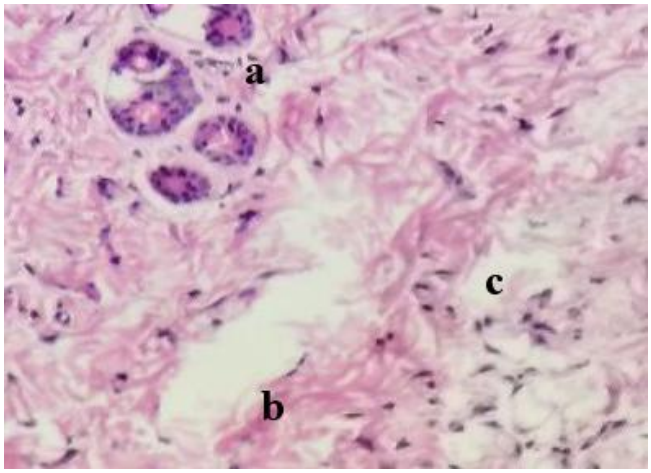

Figure 5: Histological section of skin treated with sodium caseinate for 25 days, showing infiltration of mononuclear inflammatory cells around the sweat glands(a). with deposition of protein material between the collagen fibers in the dermis layer(b) and the presence of edema (c). H&E. 100x.

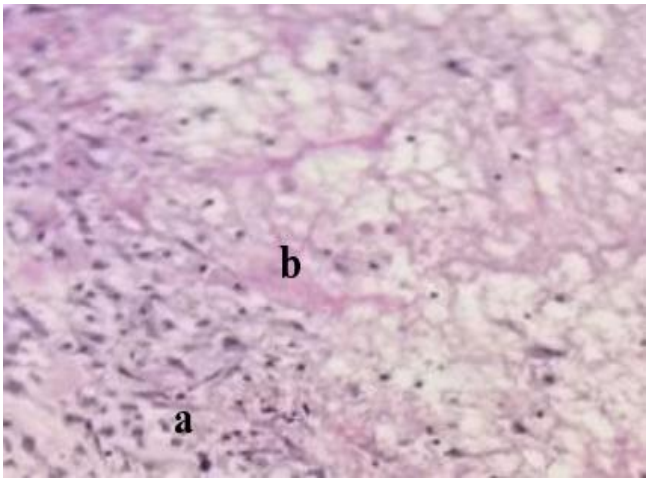

Figure 6: Histological section of rat skin treated with sodium caseinate and zinc oxide nanoparticles for 25 days, showing slight infiltration of mononuclear inflammatory cells in the dermis layer(a) with slight deposition of protein material between collagen fibers (b). H&E. 100x.

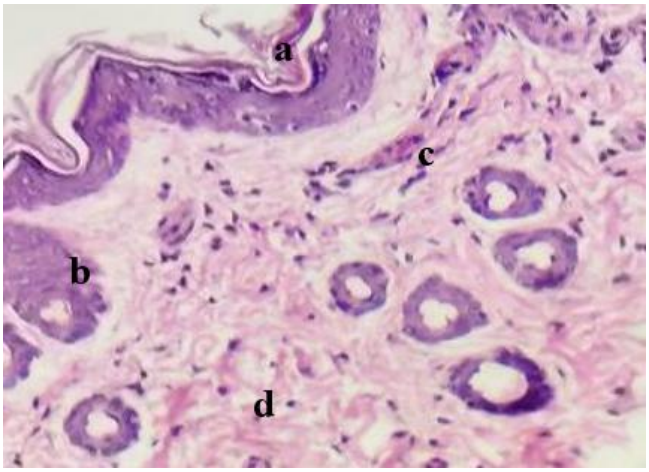

Figure 7: Histological section of skin treated with sodium caseinate for 60 days showing severe keratinization in the epidermis(a). with acanthosis (b), infiltration of mononuclear inflammatory cells between the epidermis and dermis (c), and deposition of a homogeneous protein substance between the collagen fibers (d). H&E. 100x.

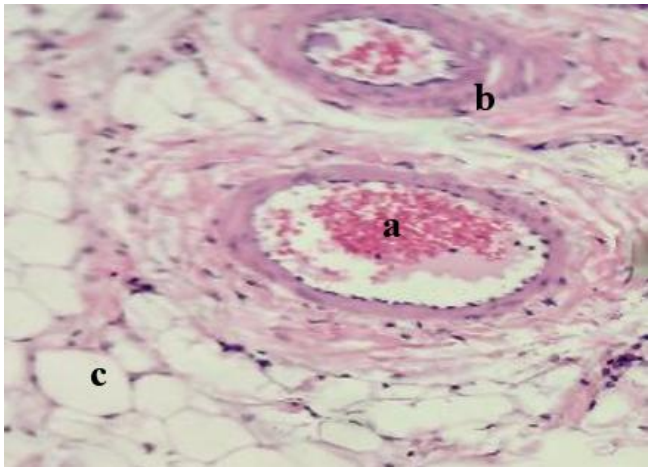

Figure 8: Histological section of skin treated with sodium caseinate for 60 days showing severe congestion of blood capillaries (a) in the subcutaneous layer with deposition of homogeneous protein material around the blood vessel (b) and between the adipocyte (c). H&E. 100x.

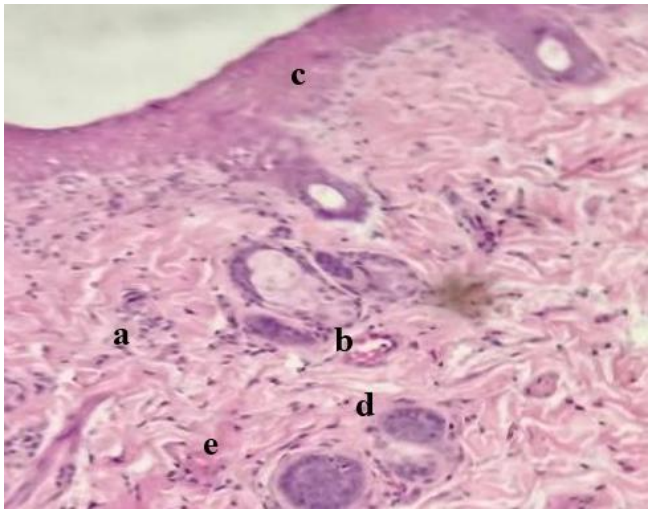

Figure 9: Histological section of rat skin treated with sodium caseinate for 60 days showing infiltration of mononuclear inflammatory cells in the epidermis and dermis layers (a) with congestion of blood capillaries (b) and deposition of homogeneous protein material between the dermal papillae (c), around the sweat glands (d), and between the collagen fibers (e). H&E. 100x.

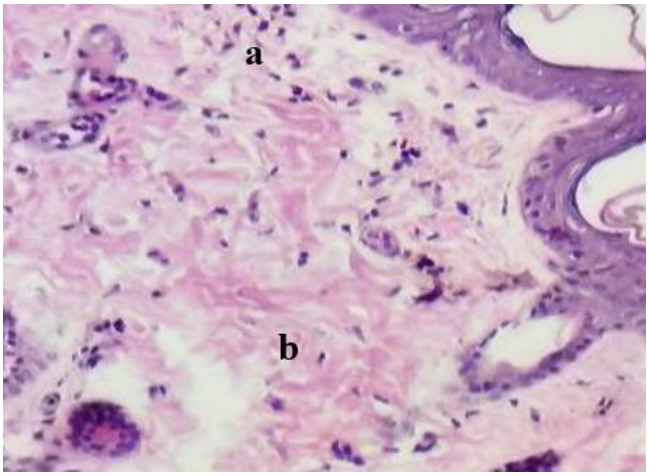

Figure 10. Histological section of rat skin treated with sodium caseinate and zinc oxide nanoparticles for 60 days, showing slight infiltration of mononuclear inflammatory cells in the epidermis and dermis layers (a), with slight deposition of protein material between collagen fibers (b). H&E. 100x.

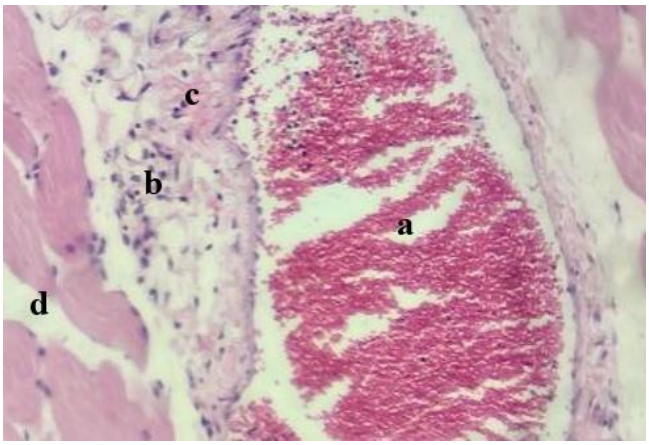

Figure 11. Histological section of rat skin treated with sodium caseinate and zinc oxide nanoparticles for 60 days showing severe congestion (a) and slight infiltration of inflammatory cells around the blood vessel (b) with slight deposition of protein material in the wall of blood vessels (c). presence of edema between muscle fibers (d). H&E. 100x.

Histochemical analysis

The results of microscopic examination of the skin layers of rats of different groups stained with Congo red stain showed a positive reaction represented by amyloid deposition with different intensity depending on the type and period of treatment, as the deposition was of medium intensity (++) in the dermis and subcutaneous layers in the group of rats treated with sodium caseinate at a dose of 3 ml 8% for 25 days (Figures 12 and 13), while the deposition was mild (+) in the dermis and subcutaneous layers in the group of rats treated with sodium caseinate and nano zinc oxide at a dose of 5mg/kg wt (Figure 14). After 60 days of treatment, the reaction was severe (+++) in all skin layers in the rats given sodium caseinate only (Figure 15), while the reaction was of medium intensity (++) in the dermis and subcutaneous layers (Figures 16 and 17) and mild (+) in the epidermis layer in the group of rats treated with sodium caseinate with nano zinc oxide (Figures 18 and 19). Table 3 shows the score and grade of amyloid deposition in the skin layers (Table 3).

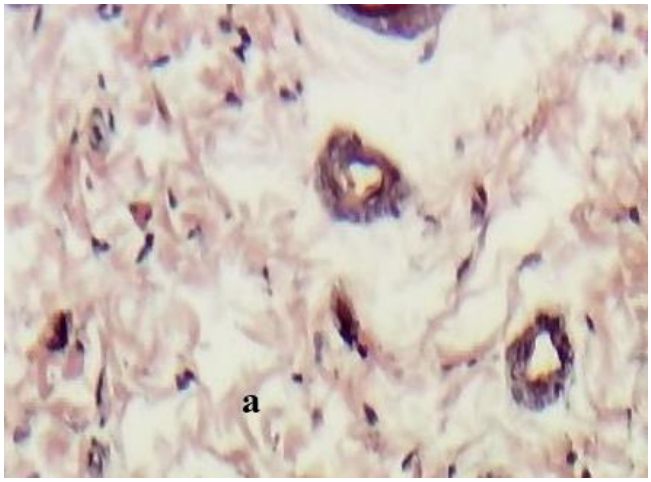

Figure 12: Histological section of rat skin treated with 3 ml 8% sodium caseinate for 25 days, showing moderate amyloid deposition in the dermis (a). Congo red, 100x.

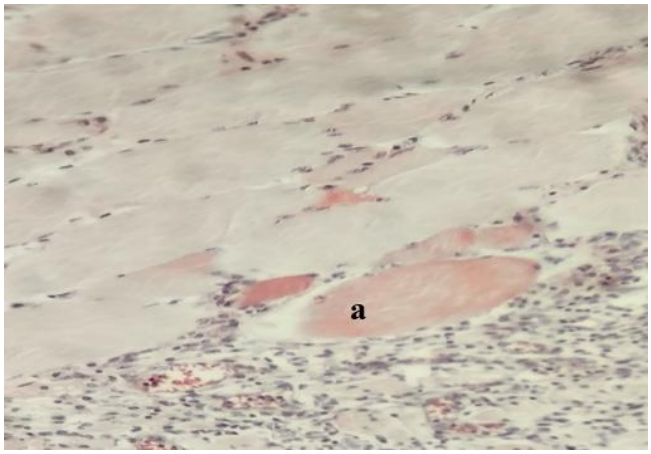

Figure 13: Histological section of rat skin treated with 3 ml 8% sodium caseinate for 25 days, showing moderate amyloid deposition in the Subcutaneous layer (a). Congo red, 100x.

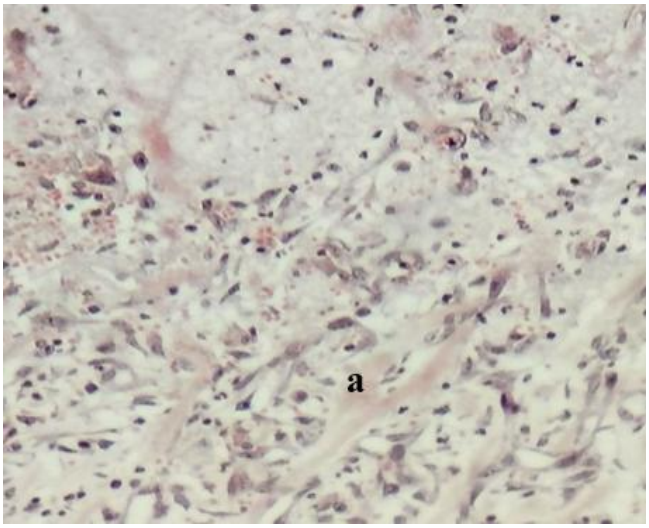

Figure 14: The histological section of the rat skin was treated with sodium caseinate and zinc oxide nanoparticles for 25 days, and mild amyloid deposition was observed in the dermis layer (a). Congo red, 100x.

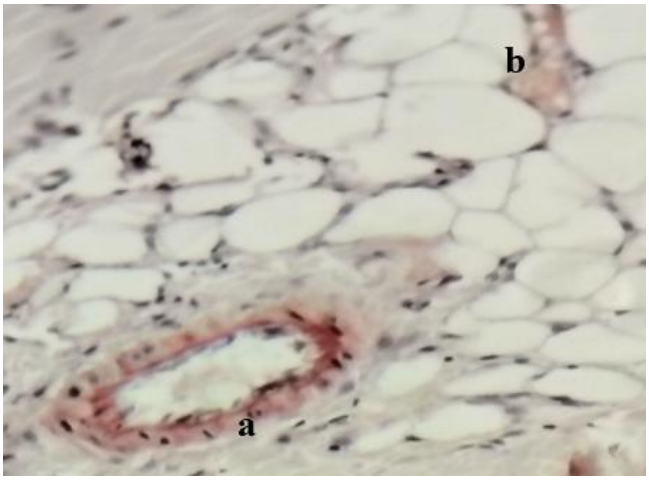

Figure 15: The histological section of the rat skin was treated with sodium caseinate and zinc oxide nanoparticles for 25 days, and mild amyloid deposition was observed in the subcutaneous layer around the blood vessels (a) and between adipose (b). Congo red, 100x.

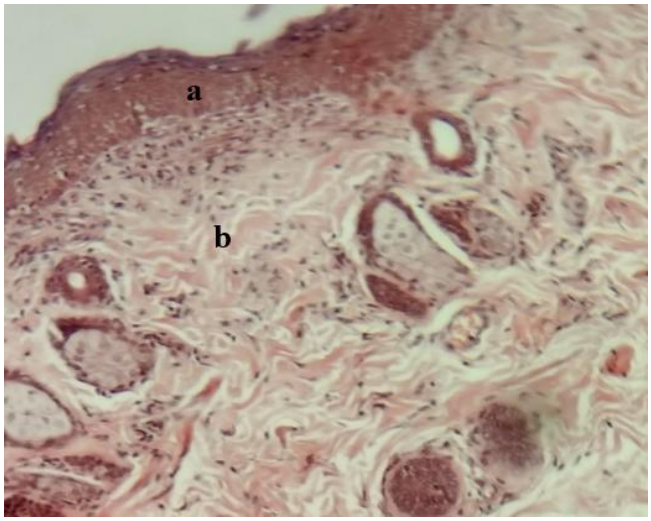

Figure 16: Histological section of rat skin treated with 3 ml 8% sodium caseinate for 60 days, showing severe amyloid deposition in the epidermis (a) and dermis layers (b). Congo red, 100x.

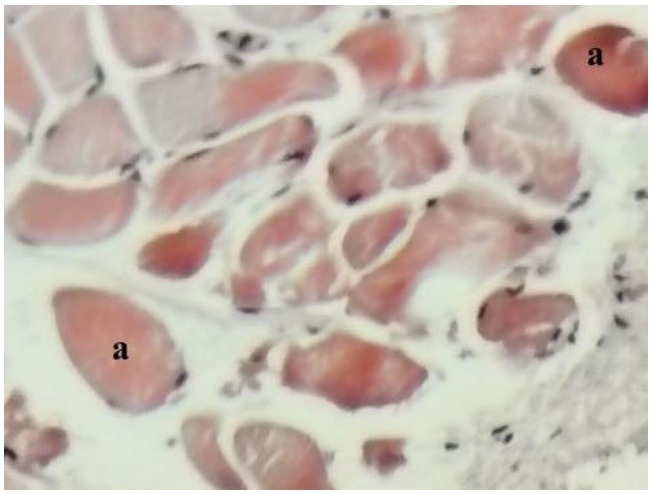

Figure 17: The histological section of rat skin was treated with 3 ml 8% sodium caseinate for 60 days, and severe amyloid deposition was observed in the subcutaneous layer (a). Congo red, 100x.

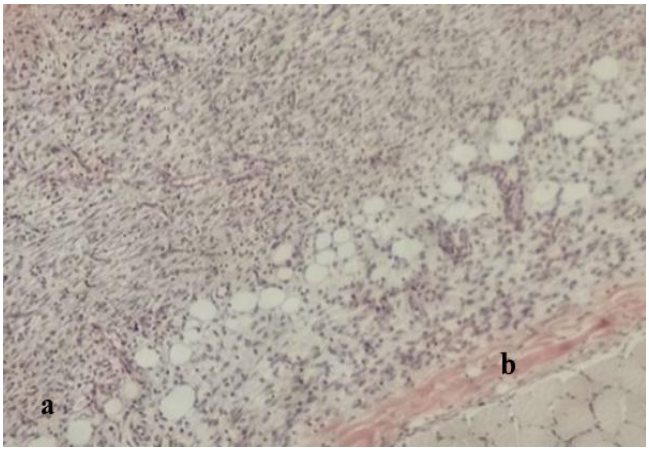

Figure 18: The histological section of the rat skin was treated with sodium caseinate and zinc oxide nanoparticles for 60 days, and moderate amyloid deposition in the dermis (a) and subcutaneous layers (b) was observed. Congo red, 100x.

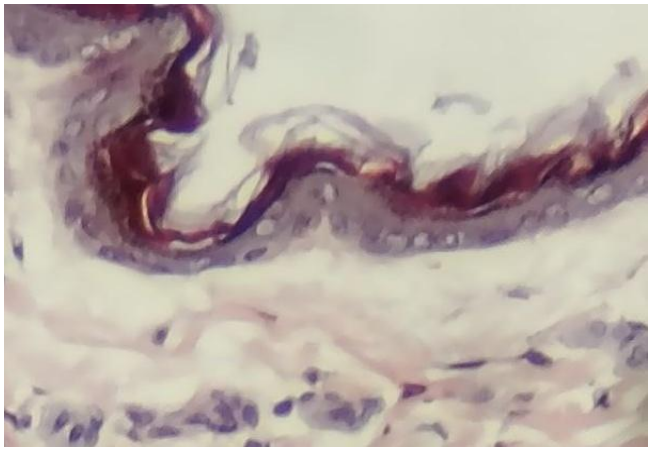

Figure 19: Histological section of rat skin treated with sodium caseinate and zinc oxide nanoparticles for 60 days showing mild amyloid deposition in the epidermis layer (a). Congo red, 100x.

Table 3: Catalog score/grade system of amyloid deposition in skin layers

Groups	After 25 days of experiment (Score/Grade)			After 60 days of experiment (Score/Grade)		
	Epidermis	Dermis	Subcutaneous	Epidermis	Dermis	Subcutaneous
G1	-/none	-/none	-/none	-/none	-/none	-/none
G2	-/none	-/none	-/none	-/none	-/none	-/none
G3	-/none	++/moderate	++/moderate	+++/sever	+++/sever	+++/sever
G4	-/none	+/mild	+/mild	+/mild	++/moderate	++/moderate

Discussion

The most dominant kind of primary localized amyloidosis of the skin is called cutaneous amyloidosis, and it is distinguished by the accumulation of localized protein fibers outside of skin cells. It is caused by repeated external stimulation, such as subcutaneous injections. Injection of casein is the most common method of inducing amyloidosis in experimental animals (28-30). Serum amyloid A is a group of apolipoproteins produced in the liver and will increase in inflammatory circumstances (31). The current study showed a significant increase in the level of serum amyloid A in the blood serum of the rats treated with sodium caseinate at a dose of 3 ml of 8% during the two experimental periods. This is consistent with what was stated by researcher Cui *et al*. (32), who found that injecting rats with casein in chelate for 35 days led to a significant rise in the level of SAA. This may be because injecting mice with this substance led to an inflammatory response in most of the 'body's tissues sodium caseinate is considered a pro-inflammatory substance (33).

The AA fibril protein that is deposited in AA amyloidosis is believed to originate from serum amyloid A (SAA) protein; the liver is where SAA is made; during inflammatory activities, the concentration of this acute-phase protein increases quickly, Interleukin (IL)-6, IL-1, and tumor necrosis factor-α (TNF-α) all-cause hepatocytes to generate SAA (34). Husby *et al.* (35) have shown that genetically modified mice with high levels of SAA make with high levels of SAA Make it more susceptible to amyloid deposition over a full and variable period. The current study also showed that treating rats with sodium caseinate with nano zinc oxide at a dose of 5 mg/kg of Bwt decreased the level of serum amyloid A when compared with Group 3. This may be because zinc oxide nanoparticles have excellent anti-inflammatory activity, as they work to inhibit the secretion of chemical mediators such as interleukin 6, interleukin 1 beta, and TNF-alpha, which are considered stimulating factors for the production of SAA from the liver (36). The current study's findings demonstrated that, compared to other groups, administering sodium caseinate to rats raised their C-reactive protein levels.

C-reactive protein and serum amyloid A are considered sensitive biological indicators of inflammation in many chronic diseases, and there is a close relationship between them, as the increase in the level of SAA is matched by an increase in the level of CRP. The decrease in CRP levels in the group of rats treated with sodium caseinate and nano zinc oxide is due to the role of zinc oxide in preventing the release of CRP from liver cells (37). The results of histological

pathological examination of skin samples of rats treated with sodium caseinate after 25 and 60 days of treatment showed a dense infiltration of inflammatory cells between the muscle fibers and collagen fibers with congestion in the blood vessels, in addition to the presence of edema between the muscle fibers with necrosis of myocyte. This is consistent with what the researcher mentioned, as he found that intraperitoneal injection of mice with sodium caseinate caused an inflammatory reaction represented by a dense infiltration of inflammatory cells in the peritoneal cavity. This may be due to the role of sodium caseinate in depleting the bone marrow reserve of mature white blood cells (38).

Injecting mice with casein into the muscle led to necrosis and atrophy of the muscle fibers with the presence of edema, as the inflammatory processes that occurred had a major role in causing the degradation of muscle protein, and the muscle atrophy was the result of the pressure caused by the edema on the muscle fibers (39). Sodium caseinate injections for 60 days resulted in hyperkeratosis and acanthosis, which may be because Chronic inflammatory skin disorders are described by these epidermal changes, where continual irritation and inflammation induce skin thickness and remodeling (40,41). The groups treated with sodium caseinate and nano zinc oxide for 25 and 60 days showed a noticeable improvement in disease lesions. This may be because ZnO-NPs can block pro-inflammatory cytokines like IL-1β and TNF-α (42,43). ZnONP with a negative surface possibly mitigated αS amyloid accumulation by repossessing the monomeric protein into a non-amyloidogenic NP-protein amorphous aggregate (44). Recent studies have shown that nanoparticles can bind to biological molecules, especially proteins, thus maintaining their stability and structure and reducing their ability to form amyloid (45,46).

The results of different groups showed the deposition of a homogeneous protein substance in the different layers of the skin, including the dermis layer, around blood vessels, sweat and sebaceous glands, and hair follicles; this amyloid deposition may be the result of an increase in the acute phase protein of chronic inflammation (SAA). This is consistent with what the researcher mentioned. It was mentioned that amyloid deposition in cutaneous amyloid is more evident in the dermis layer and around blood vessels. Per published studies, the precursor protein for amyloid, which is believed to be derived from destroyed epidermal cells, is keratin generated from apoptotic basal keratinocytes or colloid bodies. Amyloid is produced when epidermal keratinocytes' keratin tonofilaments undergo filamentous degeneration. Furthermore, it was recently suggested that the components of amyloid deposition in localized cutaneous amyloid include two β-sheet-rich proteins, actin and galectin-7 (47). The protein reacted positively when stained with Congo red. The severity of the reaction ranged between mild, moderate, and severe, depending on the type and duration of treatment. This is consistent with what the researcher mentioned, as he found that treating mice with an amyloid-promoting agent led to the deposition of amyloid in various organs of the body, such as the spleen, liver, intestines, kidneys, and heart, and the severity of the deposition varied with the length of the treatment period (48).

Conclusion

We conclude from this study that zinc oxide can reduce the development of cutaneous amyloidosis lesions, which was demonstrated through biochemical examinations, histopathological examination, and histochemistry of skin samples.

Acknowledgment

We appreciate the University of Mosul Veterinary Medicine in Mosul for supporting this study.

Conflict of interest

None.

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التأثير المحسن لجسيمات أكسيد الزنك النانوية ضد داء النشوانية الجلدي في الجرذان: دراسة نسيجية وكيميائية حيوية

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الخلاصة

داء النشواني الجلدي الموضعي الأولي هو حالة مزمنة نادرة نسبيًا حيث يترسب الأميلويد في الأدمة دون وجود رواسب مصاحبة في الأعضاء الداخلية، تم تصميم هذه الدراسة لتحديد دور أوكسيد الزنك النانوي في الحد من تطور آفات داء النشوانية الجلدي المحدث تجريبياً في ذكور الجرذان. تم استخدام اربعين ذكرا من الجرذان بعمر شهرين قسمت عشوائيًا إلى أربع مجموعات بواقع ١٠ حيوانات في كل مجموعة عدت المجموعة الأولى سيطرة وحقنت المجموعة الثانية بأوكسيد الزنك النانوية وبجرعة ٥ ملغم/كغم م وزن الجسم داخل الصفاق بينما حقنت المجموعة الثالثة بكازينات الصوديوم وبجرعة ٣مل ٨% داخل الصفاق أما المجموعة الرابعة فقد حقنت داخل الصفاق بكل من أوكسيد الزنك النانوية وكازينات الصوديوم ولمدة ٦٠ يوما. أظهرت النتائج زيادة معنوية في مستوى مصل أميلويد أ والبروتين النشط في المجموعة الثالثة عند مقارنتها بمجموعة جرذان المجموعة الرابعة، لكنها لم تصل إلى مستوياتها الطبيعية عند مقارنتها بالمجموعة الأولى. أظهرت نتائج الفحص العياني للجلد وجود آفات مرضية مثل فقدان الشعر وسماكة الجلد والاحمرار في المجموعة الثالثة، بينما كانت الآفة المرضية أقل حدة في المجموعة الرابعة. تميز الفحص النسيجي للجلد بارتشاح الخلايا الالتهابية وحيدة النواة في الأدمة والطبقات تحت الجلد وحول الغدد العرقية، مع احتقان الأوعية الدموية ووجود وذمة بين ألياف العضلات ونخر وضمور الخلايا العضلية وترسب مادة بروتينية متجانسة بين ألياف الكولاجين وألياف العضلات وحول الأوعية الدموية في المجموعة الثالثة بعد ٢٥ يومًا من المعاملة بينما كانت الآفات أكثر حدة عند نهاية التجربة (٦٠يوما). وأظهرت المقاطع النسيجية تحسناً واضحاً تمثل في ارتشاح طفيف للخلايا الالتهابية مع ترسب قليل للبروتين في المجموعة الرابعة. وتميزت نتائج فحص كيمياء النسيج لعينات الجلد من المجموعات المختلفة تفاعل موجب للامايلود، بشدة متفاوتة اعتمادا على فترة المعاملة ونوع المادة. نستنتج أن أوكسيد الزنك النانوية يلعب دورا مهما في الحد من تطور آفات داء النشوانية الجلدي.

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