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8. სტატიის თავი ძალურად შედეგები ჟურნალი ან გამოქვაბული ნივთიერება შეიქმნება ჟურნალით (მოთხ. 5-8 ფუტი სოლით). აბრამიალ ჟურნალი გამომწვავებული სახით მოთხოვნის ჯერ საბოლოო ჟურნალი, შემდეგ სურათი აღწერილი (სურათი, სურათი, ჟურნალი, ჟურნალი, ჟურნალი, ჟურნალი, ჟურნალი, N, ჟურ. სახ. და ამ ჯგუფ უსწორ/ჯგ. ვიზ. ამიტომ ჟურნალით პროფილით ჟურნალში შთანაბეჭედები, ადგილი და გამოყო ხაზები სახით თანამშრომლები. გამოყვანა აქტიური ფაქტები ბრწყინვალად იქცეს სტატიაში N დოკუმენტებით შთანაბეჭედები მითითებით, ჟურნალში სახელწოდებული მოთხოვნა, რომელიც გამოხატული პირობებით ქვეყანა იყო 5-6 ფუტი სოლით.

9. სტატიის თავი ძალურად შედეგები: a) გამოყენებული ან საშუალო ხელმძღვანელობა ფაქტები გამოყვანა, დოკუმენტები შეიქმნება და გამოყო; b) გამოყვანა ნივთიერებით სურათით, რომლებიც მოთხოვნილი იქნებია ჟურნალი ან გამოქვაბული მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი, მაგალითი.

10. სტატიის თავი ძალურად შედეგები არის ტექსტური სახით, მოთხოვნის არ უნდა დამთავარდეს 5-4.

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12. დამთავრდეს ხუთიანი აქტიური ხაზები, რომელიც გამოყვანა ქართული ხელოვანთა მოთხოვნა იქცეს სხვა ხუთიანი აქტიური ჯგუფ და გამოყვანა ქართული ხელოვანთა მოთხოვნა.
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Abstract.

Pain is a common experience that can range from mild annoyance to debilitating agony. As such, finding effective ways to relieve pain is a crucial aspect of healthcare. Aspirin, a nonsteroidal anti-inflammatory drug (NSAID), is a commonly used analgesic that works by inhibiting the production of prostaglandins, which are responsible for causing pain. However, the effectiveness of aspirin can be influenced by various factors, including the form in which it is administered. The current study aimed to compare the effects of aspirin's ordinary particles and nanoparticles as an analgesic utilizing the hot plate method in topical formulations (gel, ointment, cream). The study employed 120 albino mice, all males, divided into six groups. In the three groups, aspirin was topically applied using various formulations (gel, cream, and ointment, respectively) and concentrations (0.25, 0.5, and 1%). The same composition and concentration of aspirin nanoparticles were administered to the other three groups. The reaction time was assessed after aspirin was topically applied at 2, 10, 20, 30, 40, 50, and 60-minute intervals. Extended delay durations in comparison to control values were used to express the antinociceptive effects of aspirin. The results of the study showed that aspirin nanoparticles produced the best analgesic impact, followed by the cream and then the ointment, according to the data. This suggests that the form in which aspirin is administered can significantly influence its effectiveness as an analgesic. The use of nanoparticles may increase the bioavailability of aspirin, allowing it to be more efficiently absorbed by the body and produce a more significant analgesic effect. Overall, the study's findings suggest that aspirin nanoparticles may be a more effective form of aspirin for pain relief than ordinary particles. Further research is needed to explore the potential benefits and drawbacks of this form of aspirin and to confirm homogeneity and contact uniformity, and then its efficacy in human subjects. Nevertheless, the current study provides valuable insights into the factors that can influence the effectiveness of aspirin as an analgesic and may inform future developments in pain management.

Key words. Ordinary aspirin, aspirin nanoparticles, analgesia.

Introduction.

Non-steroidal anti-inflammatory medicines, or NSAIDs, are a commonly used class of drugs used to treat a variety of conditions. They are often used to alleviate pain, reduce fever, and decrease inflammation in patients suffering from a range of diseases. NSAIDs work by blocking the production of certain chemicals in the body that are responsible for pain, fever, and inflammation. This can be a very effective way to manage symptoms and improve the quality of life for patients [1,2]. Aspirin is the most popular NSAID. One billion pills are taken every year since its discovery more than a century ago [3]. Similar to other NSAIDs, aspirin also blocks the production of prostaglandins by the enzyme cyclooxygenase (COX) [4]. Aspirin permanently inhibits the catalytic and constitutive COX enzymes COX-1 and COX-2, which are responsible for increasing the production of prostaglandin E2 from arachidonic acid [5]. Aspirin has a brief half-life in circulation (20 minutes), and it is quickly deacetylated and converted to salicylate in living tissue.

The activity of COX-1 or COX-2 is unaffected by salicylates. As a result, the anti-inflammatory and anti-cancer effects of aspirin and salicylates are still up for debate [6]. Additionally, the antiviral activities of ASA against RNA and DNA viruses have been linked. When a lysine salt formulation of ASA (d-l-lysine acetylsalicylate) was utilized, one of the side effects was the reduction of RNA replication and production of MERS-CoV and human CoV-229E titers in infected cells culture [7].

Nanoparticles (NPS), which range in size from 1 to 100 nm, have been created as cutting-edge, distinctive, and focused medicinal and diagnostic agents. Bioengineers can modify their fundamental properties, such as improved solubility, increased ability to diffuse and hydrolyze, reduced immunogenicity, and improved therapeutic indication, to overcome the difficulties associated with the use of conventional mode. Their unique physical and chemical properties, such as their large surface area for mass, bulk, or volume, and significantly small volume [8,9].

This study aims to evaluate the analgesic effects of several topical aspirin administration techniques, including gel, cream, and ointment, in the same formulation as the nanoparticle formulation.

Materials and methods.

The animals: In the current study, a total of 120 male albino mice (weighing between 30-35 grams) were used. They were housed in standard acceptable conditions (plastic cages, temperature of 22°C, standard food/drinks, and a 12-hour dark/light cycle) approved by Animal Care House at the University of Mosul in Iraq.

Preparation of aspirin in pharmaceutical forms: The raw materials used for this study were sourced from commercial suppliers, ensuring the highest quality analytical grade ingredients for research preparation. To create varying concentrations of aspirin, 0.25, 0.5, and 1g, of active ingredients were added into 100 g of formulation, stirring the mixture to confirm homogeneity and contact uniformity, and then an innovative attrition method was used to prepare aspirin nanoparticles.

Experiment design: The purpose of this study was to investigate the effects of different topically applied concentrations of normal versus nano aspirin on pain inhibition in mice. The animals (120 mice) were divided into six major groups, each with 20 animals. Within each major group, the animals were further divided into four subgroups, with each subgroup containing...
five mice. The first subgroup in each major group served as the control group, while the remaining subgroups received different topically applied concentrations of normal or nano-aspirin, at concentrations of 0.25%, 0.5%, and 1%. The first group received topically applied doses of ordinary aspirin gel, while the second group received doses of an aspirin gel for nanoparticles. The third group received doses of aspirin cream, while the fourth group received doses of aspirin cream for nanoparticles. The fifth group received doses of aspirin ointment, and the sixth group received doses of aspirin nanoparticles with varying concentrations.

The researchers experimented to test the effectiveness of aspirin in various forms (gel, cream, ointment, and nanoparticles) at different concentrations (control, 0.25%, 0.5%, and 1%) on mice's front and hind paws. To induce pain, we placed the animals on a hot plate with a constant temperature of 55°C and recorded the reaction time, which is how long it took for the mice to start licking or grasping their paws. The hot plate was steeped for 30 seconds to prevent any thermal damage to the paws. This method helped the researchers measure the intensity of pain stimuli. The results of the experiment would be crucial in determining the most effective way to administer aspirin to alleviate pain.

To understand how different animals react to pain, we recorded the time it took for them to react under normal conditions. This served as a baseline for further experiments. Using a topical formula, we then tested their reaction times after applying various concentrations of medication at different time intervals (A at 2 min., B at 10 min., C at 20 min., D at 30 min., E at 40 min., F at 50 min., and finally G at 60 min.). This gave valuable insights into the efficacy of the medication in different dosages. By comparing the reaction times to a matching control value, we were able to gauge the aspirin's antagonistic impact. With numerous administrations and concentrations, our findings shed light on the complex relationship between pain, medication, and animal behaviour.

Statistical analysis: A chi-square test was conducted to highlight the differences between groups. To ensure statistical significance, we set the level at p 0.05 for a one-way analysis of variance across the three experimental groups.

Results.

The application of normal aspirin gel formula in various concentrations (0.25%, 0.5%, and 1%) for relieving pain in comparison to the control group considering different application intervals. The results indicated that the usual formulation produced a slightly pain-relieving effect compared to the control group at different intervals (A to G), with better response at 0.5%, and 1% compared to 0.25% (Figure 1i). While analgesic effects of topical application of aspirin nanoparticles in gel form at concentrations of 0.25%, 0.5%, and 1% (Figure 2i) were compared to a comparable control group. Normal gel preparation achieved a nearly similar response compared to nanoparticle-prepared gel, the effects are much better with higher concentrations of normal and nanoparticle gel (0.5%<1%) achieving optimum effects at F (50 min.) and with 1% concentration (Figure 1i).

The application of normal aspirin cream formula in various concentrations (0.25%, 0.5%, and 1%) in relieving pain in comparison to the control group considering different application intervals. The results indicated that the usual formulation produced a slight pain-relieving effect compared to the control group at different intervals (A to G), with better response at 0.5%, and 1% compared to 0.25% (Figure 2i). While analgesic effects of topical application of aspirin nanoparticles in cream form at concentrations of 0.25%, 0.5%, and 1% were compared to a comparable control group. A better response was achieved compared to the control group and normal cream; the effects are much better with higher concentration (0.5%<1%) achieving optimum effects at E (40 min.) and with 1% ointment nanoparticles (Figure 3ii).

The application of normal aspirin ointment formula in various concentrations (0.25%, 0.5%, and 1%) in relieving pain in comparison to the control group considering different application intervals. The results indicated that the usual formulation produced a slight pain-relieving effect compared to the control group at different intervals (A to G), with better response at 0.5%, and 1% compared to 0.25% (Figure 3i). While analgesic effects of topical application of aspirin nanoparticles in ointment form at concentrations of 0.25%, 0.5%, and 1% were compared to a comparable control group. A better response was achieved compared to the control group and normal ointment; the effects are much better with higher concentration (0.5%<1%) achieving optimum effects at E (40 min.) and with 1% ointment nanoparticles (Figure 3ii).

This study conducted a comparison of the analgesic effect of three different normal 1% formulations, namely gel, cream, and ointment. The results showed that the gel formulation exhibited the best analgesic effect among the three. It was followed by
cream and then ointment. The comparison was made over 20 minutes, during which the analgesic effects of the three formulations were measured. This study is significant in the field of medicine and pharmaceuticals, as it provides valuable information on the efficacy of different formulations in treating pain. The gel formulation, which was found to be the most effective, can potentially be used as a preferred option in pain management (Figure 4).

Discussion.

In this study, it was found that the use of nanostructured aspirin preparation particles resulted in a significantly improved response compared to the traditional formulation. Simply altering the size of the particles, the physical and chemical properties of the aspirin are also changed. This is due to the increased surface-area-to-volume ratio, which allows for greater interaction with molecular and cellular processes. Additionally, the frequency of continuous contact with linkers is enhanced, further contributing to the efficacy of the nanostructured aspirin preparation. Overall, this study sheds light on the incredible potential of nanotechnology in the field of medicine.

They have the unique ability to specifically target and deliver macromolecules and macromolecules right where they’re needed, making them an incredible tool in the fight against disease. With their impressive carrier capacity, diverse sizes and shapes, and the ability to bind both hydrophobic and hydrophilic materials, nanoparticles are revolutionizing the way we approach therapy. It will greatly replace the broad-spectrum treatments that affect healthy cells and provides precision medicine with the help of these tiny but mighty particles [11].

Nanoparticles, or NPs for short, are tiny particles that have three distinct layers. At the surface is the outer layer which can be loaded with all sorts of functionalized small molecules, metal ions, surfactants, and polymers. The core layer is the central portion of the NP and is essentially the NP itself. Sandwiched in the middle are two cortex layers, the first made of a material that's chemically different from the core, and the second also a cortex layer. Recent research strongly supports Plate Chaudhary’s (2012) claim that transdermal delivery systems (TDS) have captured the attention of scientists worldwide [12]. These innovative systems combine nanoscience with lipid science technology and have the potential to revolutionize the way we deliver drugs. They may even be the better option for drug delivery [13].

The study concluded that aspirin gel is the most effective form of pain relief, surpassing its ointment and cream counterparts. This discovery aligns with another study that found aspirin's low

![Figure 2](image-url)  
**Figure 2.** Period records are required to elicit pain stimuli in tested animals using aspirin cream at different doses and dosages. (i) ordinary cream, (ii) Nanocream particles. The time interval for application of medication is represented as A at 2 min., B at 10 min., C at 20 min., D at 30 min., E at 40 min., F at 50 min., and finally G at 60 min.

![Figure 3](image-url)  
**Figure 3.** Period records are required to elicit pain stimuli in tested animals using aspirin ointment at different doses and dosages. (i) ordinary ointment, (ii) Nano-ointment particles.

![Figure 4](image-url)  
**Figure 4.** Period records were required to elicit pain stimuli in tested animals using 1% aspirin ointment at different dosages. (i) ordinary dosage form, (ii) Nanoparticle dosage form.
water solubility decreases its effectiveness in gel formulations. Interestingly, the researchers found that the mice’s dermal membrane favoured the lipophilic state of aspirin, resulting in rapid absorption that was dependent on its concentration gradient. Despite this, the ointment did not perform as well as the gel on the mice's skin, leading to weaker pain relief and slower absorption in addition to the already observed weaker flow rate. Overall, the findings suggest that aspirin gel is the optimal choice for pain relief due to its superior effectiveness and rapid absorption [14].

The gel is a water-based product that is often clear or translucent in appearance. It has a lightweight texture that is easily absorbed into the skin, making it a good option for those with oily skin. However, it may not be the best option for those with dry or sensitive skin, as it can be drying and may cause irritation.

Cream, on the other hand, is a water and oil-based product that has a thicker consistency than gel. It is a good option for those with dry or sensitive skin as it provides deep hydration and nourishment to the skin. Creams are often formulated with emollients, which help to lock in moisture and create a protective barrier on the skin. They are also typically more gentle than gels and are less likely to cause irritation or breakouts. However, creams may not be the best option for those with oily skin as they can be too heavy and may clog pores.

Ointments are the thickest and heaviest of the three products and are typically oil-based. They are designed to provide intense hydration and protection to the skin, making them a good option for those with extremely dry or damaged skin. Ointments are often formulated with occlusive agents, which help to seal in moisture and prevent water loss from the skin. They are also typically free of fragrances and other potential irritants, making them a good option for those with sensitive skin. However, ointments may not be the best option for those with oily or acne-prone skin, as they can be too heavy and may cause breakouts. In conclusion, while gel, cream, and ointment all serve the general purpose of moisturizing the skin, they have different compositions and textures that make them better suited for different skin types and purposes. Gels are ideal for targeting specific skincare concerns and are best for oily or acne-prone skin. Creams are perfect for those with dry or sensitive skin and provide deep hydration and nourishment. Ointments are the thickest and heaviest of the three products and are best for those with extremely dry or damaged skin.

These preparations could potentially serve as a template for the treatment of stubborn ailments of joints diseases or osteoarthritis [15-17], taking into consideration that the systemic anti-inflammatory properties [18-20] might be more effective than that of local application due to involvement of surrounding milieu and cellular secretome [21,22].

Conclusion.

In conclusion, systemic medication is not always the most effective or convenient option for patients. Topical TDS, such as gels, creams, and ointments, offer a viable alternative with fewer side effects. Aspirin nanoparticles, in particular, have shown promise in providing better pain relief and are more receptive to gels than other kinds. Patients should discuss their options with their healthcare provider to determine the best course of treatment for their specific needs.

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