Journal of Pioneering Medical Sciences
Received April 15, 2024 Accept July 08, 2024 Publish July 30, 2024.
Volume 13, Issue 4, Pages 138-140

DOI https://doi.org/10.61091/jpms202413421

Formulation and Characterization of Sodium Fusidate Loaded-Silver Nanoparticles as Gel for Topical Applications

Omar Saleh Abdulkader[1,*], Abdulkareem Hameed Abd[2] and Ahmed Najim Abood[3]
[1]Department of Pharmacology, Basrah University College of Science and Technology, Basra, Iraq.
[2]Department of Pharmacology, College of Medicine, Al-Nahrain University, Baghdad, Iraq.
[3]Department of Pharmaceutics, College of Pharmacy, University of Basra, Basra, Iraq.

Corresponding author: Omar Saleh Abdulkader (e-mail: omar.saleh@basra-college.edu.iq).

Abstract **Background:** The application of topical medications to facilitate the healing process and prevent infection continues to be an essential component of treatment for all types of wounds. **Methods:** Silver nanoparticles loaded with sodium fusidate and produced through chemical reduction using trisodium citrate as the reducing agent to produce silver nanoparticles firstly. Then the gel prepared by using carbomer 940 and triethanolamine. sodium fusidate loaded-silver nanoparticles was characterized by by pH, polydispersity index (PDI), and globular diameter. **Results:** The novel formula had (668.2±0.2nm) globular diameter, normal homogeneous dispersion (PDI, 0.567±0.002) and pH (6.2±0.05). **Conclusions:** To our knowledge, this is the first sodium fusidate loaded-silver nanoparticles nano-drug delivery system. Its preclinical and clinical applications seem promising.

Key Words sodium fusidate, silver nanoparticles, gel, topical, nanoformulation

1. Background

The application of topical medications to facilitate the healing process and prevent infection continues to be an essential component of treatment for all types of wounds. Therefore, there is still a significant need to investigate new medicinal substances for the treatment of wounds on the surface of the skin [1]. New treatment strategies utilizing Nanotechnology have been developed to address many ailments, specifically burn wounds and burn infections [2].

Nanotechnology has brought to the utilization of particles composed of diverse materials, yet its shared characteristic is their size range of 10–1000 nm [3]. Nanomedicine has the potential to enhance therapy for infected burns and promote superior skin recovery. Nanotechnology has demonstrated remarkable antibacterial efficacy against drug-resistant germs and can help expedite the regeneration of skin damaged by wounds or burns [4].

Platforms with silver at the nano-scale, such as silver nanoparticles (AgNPs), and hydrogels containing silver, have been used in the treatment of burn wounds. AgNPs were utilized as an antibacterial substance for the treatment of skin wounds. They demonstrated a significant antimicrobial activity and the potential to be employed in wound dressings [5].

Nanotechnology is a discipline that concentrates on manipulating the structure of materials at the nanoscale scale to produce new properties and benefits [6]. The field also focuses on the advancement of nanotechnology to facilitate the creation of novel treatments for diverse ailments [7].

Antimicrobial resistance is widely recognized as a significant public health issue, necessitating the development of innovative approaches to either create new antibiotics or improve the efficacy of current medicines. Consequently, numerous research offer a comprehensive analysis of the management of microbial illness and antibiotic resistance [8].

Nanostructured materials are being developed as a strategy to combat certain types of bacterial resistance. Hence, Nanoparticles present a potential answer as they possess the ability to not only directly attack bacteria, but also serve as carriers for antibiotics, bypassing bacterial drug resistance processes and aiding in the administration of new medications. [9].

Although sodium fusidate (SF) is used in different bacterial skin infections therapy, it has limitations like drug resistance, poor skin penetration, local irritation, and suboptimal efficacy. For this reason, several innovative drug delivery techniques have been developed to promote patient compliance, reduce resistance, increase SF administration, and get beyond conventional formulation constraints. So, various novel SF preparations have been established, such as dressings made of hydrogel, liposomes, nanofibers, nanocapsules and lipid carriers with nanostructured [10].

In this study, we utilized sodium fusidate and AgNPs to create a gel dosage form. To the best of our knowledge, this is the first report on the impact of topically applied sodium fusidate loaded-silver nanoparticles in gel form for dermatological uses.

2. Materials and Methods

Joyang Laboratories supplied SF powder (China). Unilong Industry Co., Ltd., supplied carbomer 940 polymer (China). Sliver Nitrate supplied by Thermo Fisher Scientific (India). while Nice Chemicals supplied Triethanolamine and Trisodium Citrate (India).

A. Formulation of sodium fusidate loaded-silver nanoparticles gel

Using trisodium citrate (TSC) as the reducing agent, silver nanoparticles were created using the chemical reduction process. Silver Ag+ ions are reduced by trisodium citrate to generate metallic silver, which then clumps together to form oligomeric clusters. In the end, these clusters produce metallic colloidal silver particles [11]. Trisodium citrate and silver nitrate (AgNO3) were utilized as raw materials to create silver nanoparticles. All of the reactive material solutions were made with distilled water. 0.001 M AgNO3 in 50 ml was brought to a boil. Drop by drop, 5 milliliters of 1% trisodium citrate were added to this mixture. The solutions were heated and vigorously blended throughout the process until a discernible color shift—more precisely, a pale yellow—took place. The material was then taken out of the heating device and stirred until room temperature was achieved [12].

A 10 ml of sodium fusidate 2% solution was added to 10 ml of silver nanoparticles solution (previously prepared) to produce a diluted 20 ml solution of sodium fusidate 1% loaded-silver nanoparticles.

A 0.5% (0.1g) of carbomer 940 was added to 20 ml of drug loaded-silver nanoparticles solution. the mixture was stirred by mechanical stirrer until homogeneous dispersion occur then drops of 98% triethanolamine were added to this dispersion till get viscous or thick appearance gel [13].

B. Particle Size and Polydispersity Index Analysis

Sodium fusidate Loaded Silver Nanoparticles' particle size and polydispersity index (PDI) were assessed by photon correlation spectroscopy, utilizing Zetasizer NanoZS (Malvern Instrument, UK), which examines variations in light scattering based on Brownian particle movements and light scatter [14].

The particle size analysis was conducted at a temperature of 25°C using an angle of detection of 173° [15]. The diameter and polydispersity index of Sodium fusidate Loaded Silver Nanoparticles were obtained directly from the device.

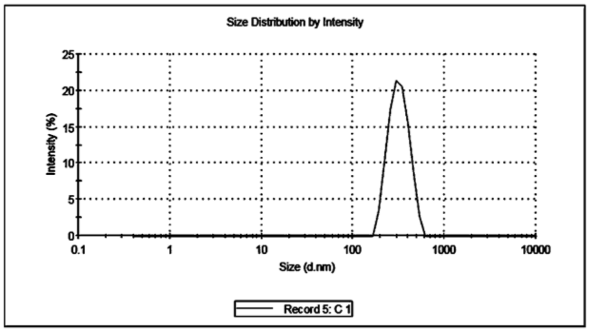

Figure 1: Globular Diameter (nm) of sodium fusidate loaded silver nanoparticle

C. Measurement of pH

The pH readings of the samples were determined using a pH meter. Prior to each usage, the pH meter was calibrated using a buffer solution with a pH value of 4, 7, and 9. The samples were analyzed directly on the electrode. The formulation's pH was measured at 25ºC, and mean values were calculated [16].

3. Results

A. Particle Size and Polydispersity Index Analysis

The particle size and polydispersity index (PDI) of sodium fusidate loaded silver nanoparticles were examined by Zetasizer. Findings showed that the formula was regarded within the nano-size range. the formula had a typical uniform dispersion (PDI; 0.567±0.002) and globular diameter (668.2±0.2nm).

B. Sodium Fusidate Loaded Silver Nanoparticles pH

The sodium fusidate loaded silver nanoparticles was analyzed directly on the probe of the pH meter. The mean value of the final formula pH is (6.2±0.05), making it suitable for topical skin application.

4. Discussion

A. Evaluation of the Sodium Fusidate Loaded- Nanoparticles

The most valuable test to distinguish the micro from nanoparticles is determining its globular size, which should be in the nano range [17]. Variable particle size may be used for nanoparticle delivery; however, the smaller particle is easier to uptaken by the cell and shows a larger surface area. Consequently, a smaller particle is related to faster drug release [18]. The resulting nano-sized particle (668.2 ±0.2nm) revealed a significant reduction in particle size, less than 1 μm.

Polydispersity index (PDI) is a measure of heterogeneity based on the size of nanoparticles. The small PDI value yielded in the formulation (0.567 ±0.002) may lead to better stability.

For successful wound healing, several endogenous and exogenous elements that participate in the regeneration process are required. The pH values are essential elements that can influence wound metabolism. The keratinocyte secretions of fatty and amino acids often cause the intact skin to state an acidic milieu. This pH is acidic and varies; it is typically stated to range between 4 and 6 [19].

The prepared formula of sodium fusidate loaded silver nanoparticles shows acidic pH (6.2 ±0.05) that complies with topical skin formulation pH conditions. If the pH value of the wound area becomes alkaline, thus its healing process decreases, pathogenic bacteria can colonize, and antibiotic therapy may be altered [20]. On the other hand, SF's Antibacterial effectiveness depends on pH. At acidic pH, SF increased antibacterial activity in vitro. Thus, the skin's low pH creates an ideal environment for effective treatment [21].

5. Conclusions

The developed formula of sodium fusidate loaded silver nanoparticles has unique physicochemical properties characterized by an excellent nanoparticle size with typical uniform dispersion that gave a dramatic penetration of the formula deep to skin dermis tissue. Also, sodium fusidate loaded silver nanoparticles formula potentiated the antibacterial effect of sodium fusidate.

6. Abbreviations

PDI, polydispersity index; AgNO3, Silver Nitrate; SF, Sodium Fusidate; AgNPs, Silver Nanoparticles; TSC, Trisodium Citrate

Conflict of interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

All authors contributed equally in this paper.

References

[1] Na, R., & Wei, T. (2021). Recent perspectives of nanotechnology in burn wounds management: a review. *Journal of Wound Care, 30*(5), 350-370.

[2] Karimi, M., Zare, H., Bakhshian Nik, A., Yazdani, N., Hamrang, M., Mohamed, E., ... & Hamblin, M. R. (2016). Nanotechnology in diagnosis and treatment of coronary artery disease. *Nanomedicine, 11*(5), 513-530.

[3] Malekzad, H., Mirshekari, H., Sahandi Zangabad, P., Moosavi Basri, S. M., Baniasadi, F., Sharifi Aghdam, M., ... & Hamblin, M. R. (2018). Plant protein-based hydrophobic fine and ultrafine carrier particles in drug delivery systems. *Critical Reviews in Biotechnology, 38*(1), 47-67.

[4] Zhu, X., Radovic-Moreno, A. F., Wu, J., Langer, R., & Shi, J. (2014). Nanomedicine in the management of microbial infection–overview and perspectives. *Nano today, 9*(4), 478-498.

[5] Konop, M., Damps, T., Misicka, A., & Rudnicka, L. (2016). Certain aspects of silver and silver nanoparticles in wound care: a minireview. *Journal of Nanomaterials, 2016*(1), 7614753.

[6] DeLouise, L. A. (2012). Applications of nanotechnology in dermatology. *Journal of Investigative Dermatology, 132*(3), 964-975.

[7] Saini, R., Saini, S., & Sharma, S. (2010). Nanotechnology: the future medicine. *Journal of Cutaneous and Aesthetic Surgery, 3*(1), 32-33.

[8] Michael, C. A., Dominey-Howes, D., & Labbate, M. (2014). The antimicrobial resistance crisis: causes, consequences, and management. *Frontiers in Public Health, 2,* 110657.

[9] Baptista, P. V., McCusker, M. P., Carvalho, A., Ferreira, D. A., Mohan, N. M., Martins, M., & Fernandes, A. R. (2018). Nano-strategies to fight multidrug resistant bacteria—"A Battle of the Titans". *Frontiers in microbiology, 9,* 381070.

[10] Williamson, D. A., Carter, G. P., & Howden, B. P. (2017). Current and emerging topical antibacterials and antiseptics: agents, action, and resistance patterns. *Clinical Microbiology Reviews, 30*(3), 827-860.

[11] Wiley, B., Sun, Y., Mayers, B., & Xia, Y. (2005). Shape-controlled synthesis of metal nanostructures: the case of silver. *Chemistry–A European Journal, 11*(2), 454-463.

[12] Vashishth, V., & Kaushik, D. (2017). Mupirocin amalgamated inorganic nanoparticles for augmenting drug delivery in resistant microbial strains. *World J Pharm Pharm Sci*, 1214-29.

[13] Islam, M. T., Rodríguez-Hornedo, N., Ciotti, S., & Ackermann, C. (2004). Fourier transform infrared spectroscopy for the analysis of neutralizer-carbomer and surfactant-carbomer interactions in aqueous, hydroalcoholic, and anhydrous gel formulations. *The AAPS journal, 6*, 61-67.

[14] Eid, A. M., Istateyeh, I., Salhi, N., & Istateyeh, T. (2019). Antibacterial activity of Fusidic acid and sodium Fusidate nanoparticles incorporated in pine oil Nanoemulgel. *International Journal of Nanomedicine,* 9411-9421.

[15] Sanad, R. A., AbdelMalak, N. S., Elbayoomy, T. S., & Badawi, A. A. (2010). Formulation of a novel oxybenzone-loaded nanostructured lipid carriers (NLCs). *Aaps Pharmscitech, 11*, 1684-1694.

[16] Rubenick, J. B., Rubim, A. M., Bellé, F., Nogueira-Librelotto, D. R., & Rolim, C. M. B. (2017). Preparation of mupirocin-loaded polymeric nanocapsules using essential oil of rosemary. *Brazilian Journal of Pharmaceutical Sciences, 53*, e16101.

[17] Parveen, R., Baboota, S., Ali, J., Ahuja, A., Vasudev, S. S., & Ahmad, S. (2011). Oil based nanocarrier for improved oral delivery of silymarin: in vitro and in vivo studies. *International Journal of Pharmaceutics, 413*(1-2), 245-253.

[18] Singh, R., & Lillard Jr, J. W. (2009). Nanoparticle-based targeted drug delivery. *Experimental and Molecular Pathology, 86*(3), 215-223.

[19] Schneider, L. A., Korber, A., Grabbe, S., & Dissemond, J. (2007). Influence of pH on wound-healing: a new perspective for wound-therapy?. *Archives of Dermatological Research, 298*(9), 413-420.

[20] Pourali, P., Razavianzadeh, N., Khojasteh, L., & Yahyaei, B. (2018). Assessment of the cutaneous wound healing efficiency of acidic, neutral and alkaline bacterial cellulose membrane in rat. *Journal of Materials Science: Materials in Medicine, 29*, 1-9.

[21] Lemaire, S., Van Bambeke, F., Pierard, D., Appelbaum, P. C., & Tulkens, P. M. (2011). Activity of fusidic acid against extracellular and intracellular Staphylococcus aureus: influence of pH and comparison with linezolid and clindamycin. *Clinical Infectious Diseases, 52*(suppl_7), S493-S503.