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**ORIGINAL ARTICLE / ÖZGÜN MAKALE**

# *IN VITRO* EVALUATION OF THE ANTIBACTERIAL EFFECT OF CHITOSAN COATED TEICOPLANIN-LOADED LIPID NANOPARTICLES AGAINST *STAPHYLOCOCCUS AUREUS*

## *KİTOSAN KAPLI TEİKOPLANİN YÜKLÜ LİPİD NANOPARTİKÜLLERİN STAPHYLOCOCCUS AUREUS'A KARŞI ANTİBAKTERİYEL ETKİSİNİN İN VİTRO DEĞERLENDİRİLMESİ*

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## ABSTRACT

**Objective:** *The aim of this research is to formulate teicoplanin-loaded solid lipid nanoparticles (SLN) coated with chitosan to sustain teicoplanin release for effective antibacterial therapy.*
**Material and Method:** *"Double emulsion-solvent evaporation technique was used for the production of SLNs. The nanoparticles were characterised in terms of morphology, size, encapsulation efficacy, in-vitro drug release and antibacterial activity studies after optimization of process and formulation parameters.*
**Result and Discussion:** *Transmission electron microscopy images confirmed the formation of spherical SLNs. With chitosan coating, the size increased (from 80 nm to 106 nm) and the negative value of zeta potential (- 11.29) changed to positive (+34.41). The in-vitro release data showed prolonged release of teicoplanin from optimized SLN and chitosan-coated SLN (c-SLN) formulations over 1 week. The antibacterial activity study (S. aureus and Methicillin-resistant S. aureus) showed the activity of the teicoplanin loaded SLN formulations. In conclusion, this study demonstrated the potential of c-SLN for effective delivery of teicoplanin.*
**Keywords:** *Chitosan, coating, lipid nanoparticle, precirol ATO 5, teicoplanin*

## ÖZ

**Amaç:** *Bu araştırmanın amacı, etkili antibakteriyel tedavi için teikoplanin salımını uzatmak üzere kitosanla kaplanmış teikoplanin yüklü katı lipit nanopartiküllerinin (SLN) formüle edilmesidir.*
**Gereç ve Yöntem:** *SLN'ler çift emülsifikasyon-solvent buharlaştırma tekniği ile hazırlanmıştır. Proses ve formülasyon parametrelerinin optimizasyonu sonrasında nanopartiküller morfoloji, boyut, enkapsülasyon etkinliği, in vitro etken madde salımı ve antibakteriyel aktivite çalışmaları açısından karakterize edilmiştir.*
**Sonuç ve Tartışma:** *Geçirimli elektron mikroskobu görüntüleri küresel SLN'lerin oluşumunu doğrulamıştır. Kitosan kaplama ile boyut artmış (80 nm'den 106 nm'ye) ve zeta potansiyelinin negatif değeri (-11.29) pozitife (+34.41) dönüşmüştür. İn vitro salım verileri, optimize edilmiş SLN ve kitosan kaplı SLN (c-SLN) formülasyonlarından teikoplaninin 1 hafta boyunca uzun süreli salınımını göstermiştir. Antibakteriyel aktivite çalışması (S. aureus ve Metisiline dirençli S. aureus),*

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*teikoplanin yüklü SLN formülasyonlarının aktivitesini göstermiştir. Sonuç olarak, bu çalışma c-SLN'nin teikoplaninin etkin verilişi için potansiyelini ortaya koymuştur.*
**Anahtar Kelimeler:** *Kaplama, kitosan, lipit nanopartikül, precirol ATO 5, teikoplanin*

## INTRODUCTION

Antibiotics constitute the primary treatment step in pathogenic bacterial infections. However, in recent years, due to the uncontrolled or incorrect use, antibiotic-sensitive bacteria are constantly mutating, which triggers the emergence of bacterial drug resistance [1]. Against antibiotic resistance, the use of drug delivery systems that can deliver high doses of antibiotics that cannot be administered systemically or cause side effects directly to the site of infection has improved the therapeutic index while minimizing side effects [2]. However, antibiotics may be sensitive to production conditions such as temperature increase, sonication, use of organic solvents, etc., which are common in preparation methods of nanoparticles. For these reasons, conditions to which antibiotics are sensitive, such as temperature, should be optimized, especially during the preparation and encapsulation steps.

SLNs have great potential as nanocarriers for antibiotic encapsulation due to their industrial scale-up capability and minimal toxicity [3]. Their biodegradability, biosafety, long-term release behavior, and ability to hold both lipophilic and hydrophilic medicines make them appealing for improving drug targeting capabilities [4]. The most utilized methods for preparing SLNs are high-pressure/high shear homogenization [5] and microemulsion-based approaches [6]. When combined with the solvent evaporation approach, the double emulsion method (w/o/w), is more mild and prevents temperature or pressure stress on the trapped molecules [7].

The surface of SLNs can be modified for various purposes, such as preventing the removal of nanoparticles from the circulation by the reticuloendothelial system, increasing the half-life of the active molecule loaded into the particulate system, improving the stability of nanoparticles, reducing toxicity, increasing biocompatibility, and increasing mucosal penetration. Surface modification of nanoparticles with chitosan, a natural cationic polysaccharide derived from chitin, is a strategy used to increase the penetration of encapsulated molecules through mucosal surfaces. This biopolymer is preferred due to its antimicrobial and mucoadhesive properties, as well as being biocompatible, biodegradable, and low toxicity [8].

Teicoplanin is a glycopeptide antibiotic produced by Actinoplanes teichomiceticus that acts through inhibition of bacterial cell wall biosynthesis, is effective against Gram-positive bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA). Compared to other glycopeptide antibiotics such as vancomycin, teicoplanin is significantly more surface active with multiple, unique, functional groups. Another advantage of teicoplanin is that it can be sterilized with γ-irradiation [9]. There are few studies in the literature on nano systems containing teicoplanin. In this paper, we investigated the synthesis and efficiency of teicoplanin-bearing SLNs as an innovative system for glycopeptide formulation.

The goal of this research was to produce teicoplanin-loaded SLN formulation by using double emulsion and solvent evaporation technique to achieve small particle size and high teicoplanin encapsulation. The surface of SLN formulations was coated with chitosan polymer, which has adhesive and antimicrobial properties. The developed SLN and chitosan-coated SLN formulations were characterized *in vitro*.

## MATERIAL AND METHOD

### Materials

Precirol ATO 5 was gifted from Gattefossé (France), teicoplanin, chitosan (low molecular weight), Pluronic F68 and dichloromethane were purchased from Sigma-Aldrich Co (USA). All other analytical grade reagents were used as received without further purification.

### Preparation of Solid Lipid Nanoparticles and Coating with Chitosan

Double emulsion solvent evaporation method was used for the preparation of SLN [7,10]. First, Pluronic F68 (2%) was mixed with the cold water and kept in the refrigerator overnight for a clear

solution. 40 mg of Precirol ATO 5 was dissolved in 1 ml dichloromethane. Teicoplanin was dissolved in 0.5 ml of Pluronic F68 solution and added to the lipid phase and sonicated for 1 min (Bandelin Sonopuls HD2070 (Germany), 90% amplitude). The resulting emulsion was then immediately added to 10 ml of Pluronic F68 solution and sonicated 10 mins while cooling in an ice bath. Dichloromethane was evaporated by magnetic stirring and teicoplanin-loaded solid lipid nanoparticles were obtained with a Vivaspin® 20 centrifugal concentrator. To coat the solid lipid nanoparticles, chitosan (1%) was dissolved in acetic acid solution (1%). Lipid nanoparticles and chitosan solution (1:1, v/v) were magnetically stirred for 90 minutes, and chitosan-coated nanoparticles were obtained with a Vivaspin® 20 centrifugal concentrator.

**Particle Size and Size Distribution**

SLN aliquots were diluted tenfold with ultrapure water. The particle size and distribution of SLN formulations were measured at ambient conditions using Malvern Zetasizer Ultra (Malvern Instruments, UK) and each sample was analyzed in triplicate [11].

**Encapsulation Efficiency (EE)**

The EE of teicoplanin was determined by the indirect method [12]. In the end of the nanoparticle preparation process, nanoparticles were collected with the Vivaspin® 20 centrifugal concentrator. The amount of teicoplanin in the supernatant phase was analyzed by the microBCA analysis method and the EE was calculated by the following equation. All measurements were carried out in triplicate and results were expressed as mean values with a standard deviation (SD).

$$\text{EE } \% = \frac{\text{Total amount of Teicoplanin} - \text{Free Teicoplanin}}{\text{Total amount of Teicoplanin}} * 100$$

***In Vitro* Release**

Dialysis membrane method was used to determine the *in vitro* release of teicoplanin from the F8 and c-F8 SLN formulations [11]. SLN formulations were placed in the dialysis bag (12000-14000 Da MWCO), the dialysis bag was placed in pH 7.4 phosphate buffer (20 ml) at 37±0.5°C and shaken at 50 rpm in an incubated shaker. A volume of 0.5 ml was withdrawn at each specified time, replaced with the same amount of fresh pH 7.4 phosphate buffer and teicoplanin concentrations were measured by microBCA analysis. The cumulative drug release percentage was calculated, and *in vitro* release graphs were created. All experiments were performed in triplicate.

**Transmission Electron Microscopy (TEM) Analysis**

The morphology of the c-F8 formulation was determined by TEM (FEI Tecnai G2, the Netherlands). Briefly, a drop of the c-F8 SLN formulation was placed on 200-mesh copper grid, excess formulation was removed using filter paper, dried at room temperature and imaged by TEM (120 kV) [13].

**DSC Analysis**

The thermal properties of teicoplanin, Precirol ATO 5, plain SLN, teicoplanin loaded SLN and chitosan-coated teicoplanin-loaded SLN were analyzed with a Shimadzu DSC-60 device. Approximately 5 mg of samples were placed in an aluminum pan and compressed. Nitrogen gas (50 ml/min), heating rate of 10°C/min, temperature range 30-300°C were used in the analysis of the samples [11].

**Antibacterial Activity**

Antibacterial activity of the teicoplanin, F8 and c-F8 formulations were tested against *Staphylococcus aureus* (ATCC 29213) and methicillin resistant *Staphylococcus aureus* (MRSA) (ATCC 43300). Antibacterial activity test was evaluated by broth microdilution method as a minimal inhibition concentration (MIC) according to European Committee on Antimicrobial Susceptibility Testing standards (ISO 20776-1:2019) [14]. In the broth microdilution test, 100 µl of cation-adjusted Mueller-Hinton broth (MHB) was added to each well of a sterile U-bottom microplate. The same volume of SLN

formulations (teicoplanin concentrations from 0.0625 μg $\mu l^{-1}$ to 32 μg $\mu l^{-1}$) [15] and controls was added to the first well and diluted. Then, a 1:100 dilution of bacterial suspension made in 0.9% NaCl from fresh bacterial culture to a density of 0.5% McFarland turbidity was added to the wells. Following the incubation of microplates at 35 ± 1°C for 18 ± 2 hours, MIC was defined as the lowest concentration of formulations that inhibited the visible growth of bacteria.

## RESULT AND DISCUSSION

### Particle Size, PDI and Zeta Potential

Different drug/lipid ratios and sonication times were tested to optimize the particle size of SLN formulations (Table 1). All formulations were prepared with fixed concentration of drug (2 mg) and surfactant (2%), varying only lipid ratios (10-40 mg). When the sonication time was kept constant, the particle size clearly decreased as the drug/lipid ratio increased. In the opposite case, when the drug/lipid ratio was kept constant, the particle size clearly decreased as the sonication time increased. The formulation coded F8, where the drug/lipid ratio was 20:1 and the sonication time was 10 minutes, was found to have a significantly smaller particle size than the others. It was observed that PDI values increased significantly as the particle size decreased. Although the zeta potential value of the F8 formulation is lower than other formulations, it was decided to proceed to the next stage by choosing the F8 formulation since it is significantly smaller than the other formulations, considering that the chitosan coating planned to be applied afterwards will increase the stability and taking into account that the particle size will increase after coating. In the c-F8 formulation coated with chitosan, it was observed that the particle size increased slightly to 106.8 nm and the zeta potential turned positive as expected. The zeta potential of the c-F8 formulation was found to be +34.41 mV and was classified as highly stable according to the literature [13]. The coating mechanism of SLN is based on the electrostatic interaction of positively charged chitosan with the negatively charged SLN surface. The method was found to be advantageous as it preserves the structure and functionality of teicoplanin because it does not involve heat or chemical functionalization [8].

**Table 1.** Composition and characterization results of formulations (Data are expressed as mean ± SD of triplicate measurements)

| | Lipid:Drug (w/w) | Sonication (min) | Particle size (nm) | PDI | Zeta potential (mV) |
|---|---|---|---|---|---|
| **F1** | 10:1 | 2 | 512.8±3.67 | 0.284±0.014 | -25.16±1.59 |
| **F2** | 20:1 | 5 | 545.5±41.8 | 0.454±0.092 | -23.65±0.75 |
| **F3** | 5:1 | 5 | 309.8±11.3 | 0.421±0.026 | -25.15±0.60 |
| **F4** | 10:1 | 10 | 273.1±90.4 | 0.357±0.026 | -33.67±0.78 |
| **F5** | 10:1 | 5 | 445.1±22.4 | 0.402±0.044 | -19.78±0.09 |
| **F6** | 5:1 | 2 | 375.2±7.66 | 0.315±0.080 | -22.80±0.38 |
| **F7** | 5:1 | 10 | 249.4±19.1 | 0.324±0.022 | -27.92±1.19 |
| **F8** | 20:1 | 10 | 80.69±1.06 | 0.594±0.033 | -11.29±0.90 |
| **c-F8** | 20:1 | 10 | 106.8±4.41 | 0.681±0.048 | +34.41±2.05 |

### Encapsulation Efficiency (EE%)

Encapsulation efficiency of F8 and c-F8 formulations were found 58.23% ±1.18 and 54.47% ±7.94, respectively (Table 2). It was observed that the encapsulation efficiency decreased slightly in the c-F8 formulation coated with chitosan. This decrease may be due to a small loss of active ingredient on the surface of the nanoparticles during the 90 mins mixing time in the coating process.

**Table 2.** Encapsulation efficiency (%) results of F8 and c-F8 formulations (Data are expressed as mean ± SD of triplicate measurements)

| | F8 | c-F8 |
|---|---|---|
| **Encapsulation Efficiency (%)** | 58.23 ±1.18 | 54.47±7.94 |

### *In Vitro* Release

The *in vitro* release of teicoplanin from F8 and c-F8 formulations were compared (Figure 1). It was observed that the *in vitro* release of free teicoplanin was completed in 8 hours. With F8 and c-F8 formulations, the *in vitro* release time of teicoplanin was extended to over 1 week. The *in vitro* release of teicoplanin from the c-F8 formulation is slower than that from the F8 formulation. This is an expected result since the c-F8 formulation is coated with chitosan. Similar results have been seen in the literature for nanoparticle systems coated with chitosan [16]. These data obtained as a result of *in vitro* release are preliminary indicators of advantageous features such as providing a long-term antibacterial effect in the in vivo environment, stable protection of the active substance in nanoparticle structure, and extending its half-life by not being eliminated immediately.

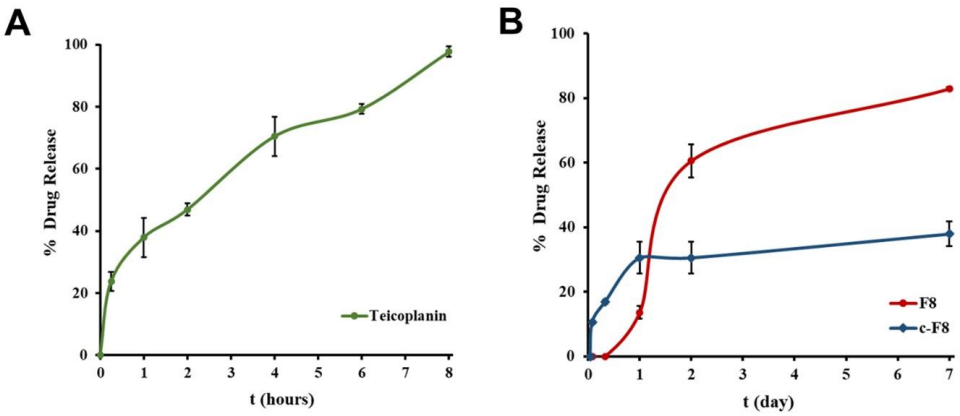


**Figure 1.** *In vitro* release of free teicoplanin (A) and *in vitro* release of teicoplanin from F8 and c-F8 formulations (B)

### TEM Analysis

TEM analysis was performed to examine nanoparticle morphology. Figure 2 is the TEM image of the c-F8 formulation, and the particles observed to be smaller than 100 nm in spherical shape are consistent with the particle size analysis data.

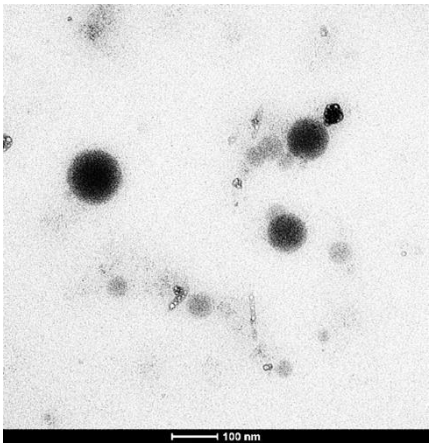


**Figure 2.** TEM image (scale: 100 nm) of c-F8 formulation

### DSC Analysis

DSC analysis revealed an endothermic peak belonging to teicoplanin at 55.31°C, which is consistent with the literature [2]. Characteristic peak of Precirol ATO 5 observed at 55.18°C [17]. DSC

thermogram of drug-free SLN, F8 and c-F8 formulations exhibited similar peak around 47-48°C (Figure 3). It was observed that the peak of teicoplanin-loaded SLN formulations had similar pattern, location, and intensity as the blank formulation and this result confirmed incorporation of antibiotic in the SLNs.

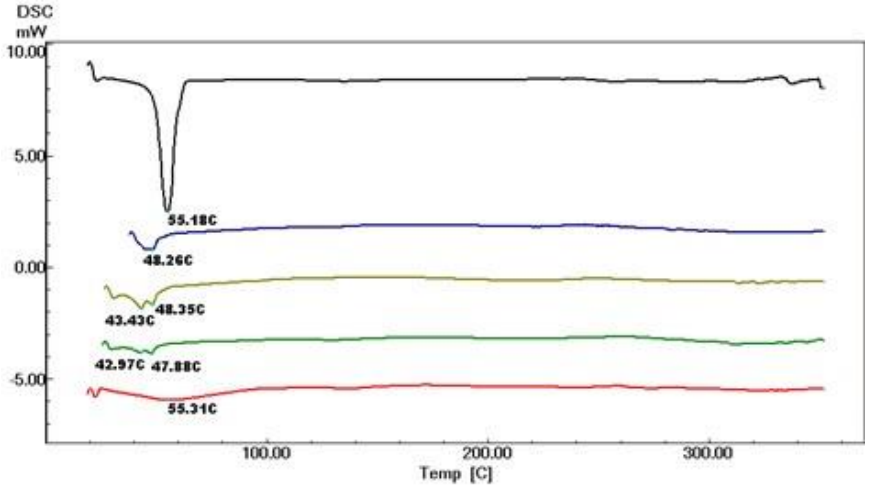


**Figure 3.** DSC thermograms of teicoplanin (red), F8 (green), drug-free SLN (khaki), c-F8 (blue), Precirol ATO 5 (black)

## Antibacterial Activity

Antibacterial activity of teicoplanin loaded F8 and c-F8 formulations were investigated by broth microdilution method. MIC results for all formulations were listed at Table 3. Free teicoplanin application on both *S. aureus* and MRSA strains resulted in MIC of 0.061 µg $ml^{-1}$. An MIC value of 0.0625 µg $ml^{-1}$ was obtained with the F8 and c-F8 formulations, similar to teicoplanin. This result may be due to the prolonged release of teicoplanin for up to 1 week, as seen in the *in vitro* release test. Therefore, the release rate may increase the inhibitory effect of teicoplanin over time. The MIC value of the c-F8 formulation was found to be 1 µg $ml^{-1}$. Chitosan's antimicrobial activity against a variety of bacteria is well known. Therefore, it was evaluated that this result was achieved due to the chitosan coating in the c-F8 formulation. Similar MIC values of different chitosan types against *S. aureus* strains are available in the literature [18].

**Table 3.** MIC values of the teicoplanin and formulations against *S. aureus* strains

| Bacteria | Minimal inhibition concentration (µg/ml) | | | | |
|---|---|---|---|---|---|
| | F8 | c-F8 | Drug-free F8 | Drug-free c-F8 | Teicoplanin |
| ***Staphylococcus aureus* ATCC 29213** | 0.0625 | 0.0625 | 0 | 1 | 0.061 |
| **Methicillin-resistant *Staphylococcus aureus* ATCC 43300** | 0.0625 | 0.0625 | 0 | 1 | 0.061 |

In this research, a teicoplanin-loaded chitosan-coated SLN formulation was developed and its potential for application as an antibacterial drug delivery system was evaluated. The double emulsion-solvent evaporation method was used to produce nanoparticles. It was concluded that the optimized teicoplanin-loaded c-SLN formulation consisted of spherical-shaped particles, the particle size was 106.8 nm, the encapsulation efficiency was 54.47%, and it was effective on both *S. aureus* and MRSA. These observations indicate that the developed nanoparticulate carrier system is promising for antibiotic delivery.

## AUTHOR CONTRIBUTIONS

Concept: B.K.; Design: B.K.; Control: B.K., M.E.K.; Sources: B.K., M.E.K.; Materials: B.K., M.E.K.; Data Collection and/or Processing: B.K., M.E.K.; Analysis and/or Interpretation: B.K., M.E.K.; Literature Review: B.K., M.E.K.; Manuscript Writing: B.K., M.E.K.; Critical Review: B.K., M.E.K.; Other: -

## CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflicts of interest for this article.

## ETHICS COMMITTEE APPROVAL

The authors declare that ethical committee approval is not required for this study.

## REFERENCES

1. Li, B., Wang, W., Zhao, L., Yan, D., Li, X., Gao, Q., Zheng, J., Zhou, S., Lai, S., Feng, Y., Zhang J., Jiang, H., Long, C., Gan, W., Chen, X., Wang, D., Tang, B.Z., Liao, Y. (2023). Multifunctional AIE nanosphere-based "nanobomb" for trimodal imaging-guided photothermal/photodynamic/pharmacological therapy of drug-resistant bacterial infections. ACS Nano, 17(5), 4601-4618. [CrossRef]
2. Gonzalez Gomez, A., Xu, C., Hosseinidoust, Z. (2019). Preserving the efficacy of glycopeptide antibiotics during nanoencapsulation in liposomes. ACS Infectious Diseases, 5(10), 1794-1801. [CrossRef]
3. Radaic, A., Malone, E., Kamarajan, P., Kapila, Y.L. (2022). Solid lipid nanoparticles loaded with nisin (sln-nisin) are more effective than free nisin as antimicrobial, antibiofilm, and anticancer agents. Journal of Biomedical Nanotechnology, 18(4), 1227-1235. [CrossRef]
4. Mohammed, M., Ibrahim, U.H., Aljoundi, A., Omolo, C.A., Devnarain, N., Gafar, M.A., Mocktar, C., Govender, T. (2023). Enzyme-responsive biomimetic solid lipid nanoparticles for antibiotic delivery against hyaluronidase-secreting bacteria. International Journal of Pharmaceutics, 640, 122967. [CrossRef]
5. Singh, M., Schiavone, N., Papucci, L., Maan, P., Kaur, J., Singh, G., Nandi, U., Nosi, D., Tani, A., Khuller, G.K., Priya, M., Singh, R., Kaur, I.P. (2021). Streptomycin sulphate loaded solid lipid nanoparticles show enhanced uptake in macrophage, lower MIC in Mycobacterium and improved oral bioavailability. European Journal of Pharmaceutics and Biopharmaceutics, 160, 100-124. [CrossRef]
6. Moez, N.M., Hosseini, S.M., Kalhori, F., Shokoohizadeh, L., Arabestani, M.R. (2023). Co-delivery of streptomycin and hydroxychloroquine by labeled solid lipid nanoparticles to treat brucellosis: An animal study. Scientific Reports, 13(1), 14012. [CrossRef]
7. Qi, C., Chen, Y., Jing, Q.Z., Wang, X.G. (2011). Preparation and characterization of catalase-loaded solid lipid nanoparticles protecting enzyme against proteolysis. International Journal of Molecular Sciences, 12(7), 4282-4293. [CrossRef]
8. Fonte, P., Andrade, F., Araújo, F., Andrade, C., Neves, J.D., Sarmento, B. (2012). Chitosan-coated solid lipid nanoparticles for insulin delivery. Methods in Enzymology, 508, 295-314. [CrossRef]
9. Britton, S., Lee, K., Azizova, L., Shaw, G., Ayre, W.N., Mansell, J.P. (2022). Immobilised teicoplanin does not demonstrate antimicrobial activity against Staphylococcus aureus. Scientific Reports, 12(1), 16661. [CrossRef]
10. Yousry, C., Fahmy, R.H., Essam, T., El-Laithy, H.M., Elkheshen, S.A. (2016) Nanoparticles as tool for enhanced ophthalmic delivery of vancomycin: A multidistrict-based microbiological study, solid lipid nanoparticles formulation and evaluation. Drug Development and Industrial Pharmacy, 42(11), 1752-62. [CrossRef]
11. Küçüktürkmen, B., Devrim, B., Saka, O.M., Yilmaz, Ş., Arsoy, T., Bozkir, A. (2016). Co-delivery of pemetrexed and miR-21 antisense oligonucleotide by lipid-polymer hybrid nanoparticles and effects on glioblastoma cells. Drug Development and Industrial Pharmacy, 43(1), 12-21. [CrossRef]
12. Woo, J.O., Misran, M., Lee, P.F., Tan, L.P. (2014). Development of a controlled release of salicylic acid loaded stearic acid-oleic acid nanoparticles in cream for topical delivery. The Scientific World Journal, 205703. [CrossRef]
13. Küçüktürkmen, B., Öz, U.C., Er, E., Gómez, I.J., Tekneci, S.İ., Eşim, Ö., Özköse U.U., Gülyüz, S., Üstündağ, A., Yılmaz, Ö., Zajíčková, L., Bozkır, A. (2024). Design of polymeric nanoparticles for theranostic delivery of capsaicin as anti-cancer drug and fluorescent nitrogen-doped graphene quantum dots. Macromolecular Bioscience, 2400149. [CrossRef]

14. Bielec, F., Brauncajs, M., Pastuszak-Lewandoska, D. (2023). Comparison of substance sources in experimental antimicrobial susceptibility testing. Scientia Pharmaceutica, 91(1), 10. [CrossRef]
15. Ucak, S., Sudagidan, M., Borsa, B.A., Mansuroglu, B., Ozalp, V.C. (2020). Inhibitory effects of aptamer targeted teicoplanin encapsulated PLGA nanoparticles for Staphylococcus aureus strains. World Journal of Microbiology and Biotechnology, 36(5), 69. [CrossRef]
16. Luo, Y., Teng, Z., Li, Y., Wang, Q. (2015). Solid lipid nanoparticles for oral drug delivery: Chitosan coating improves stability, controlled delivery, mucoadhesion and cellular uptake. Carbohydrate Polymers, 122, 221-229. [CrossRef]
17. Fang, J.Y., Fang, C.L., Liu, C.H., Su, Y.H. (2008). Lipid nanoparticles as vehicles for topical psoralen delivery: Solid lipid nanoparticles (SLN) versus nanostructured lipid carriers (NLC). European Journal of Pharmaceutics and Biopharmaceutics, 70(2), 633-640. [CrossRef]
18. Asli, A., Brouillette, E., Ster, C., Ghinet, M.G., Brzezinski, R., Lacasse, P., Jackues, M., Malouin, F. (2017). Antibiofilm and antibacterial effects of specific chitosan molecules on Staphylococcus aureus isolates associated with bovine mastitis. PLoS One, 12(5), e0176988. [CrossRef]