# Formulation, Characterization, and Optimization of Lauric acid and Tea Tree Oil-loaded Solid Lipid Nanoparticles

Fezile Motsoene, Heidi Abrahamse, Sathish Sundar Dhilip Kumar*
Laser Research Centre, Faculty of Health Sciences, University of Johannesburg, P.O. Box: 17011, Johannesburg 2028, South Africa.
*E-mail: sathishd@uj.ac.za

## ABSTRACT

**Background**

Over the past few decades, Solid Lipid Nanoparticles (SLNs) have demonstrated their potential as an alternative drug delivery system by overcoming the limitations of polymeric micro and nanoparticles, liposomes, and emulsions [1]. Solid lipid nanoparticles are site-specific and sub-colloidal lipid-based nanoparticles composed solid lipid core (within which the drug is located depending on its hydrophobicity or hydrophilicity) surrounded by a surfactant, which increases the drug stability, the stability and entrapment efficacy of the drug-loaded system. These particles have numerous benefits, including safeguarding sensitive compounds from harmful environmental factors like moisture, light, and pH [2,3]. Biological activity would be greatly diminished if this protection were not provided for the compounds [4]. In addition, SLNs have also enhanced the biocompatibility and delivery of lipophilic and hydrophobic drug molecules with natural active ingredients such as Tea tree oil and lauric acid in various medical applications. Therefore, the present study aimed to formulate, characterise, and determine the antibacterial effect of the Lauric acid (LA) and Tea Tree oil (TTO)-loaded Solid Lipid Nanoparticles (LT-SLNs).

Lauric acid and TTO are hydrophobic drug molecules that have difficulty penetrating the skin's epithelial tissue. Lauric acid is a carbon-12 saturated fatty acid commonly found in palm kernel and coconut oil [5]. Lauric acid possesses good thermal, antibacterial and anti-inflammatory properties that effectively combat both Gram-negative and Gram-positive bacteria. Additionally, it facilitates cell migration and preserves the sterility of the wound bed. On the other hand, TTO contains several compounds, including p-cymene, 1,8-cineole, terpinen-4-ol, and γ-terpinene. These compounds are known to possess antiseptic, antibacterial, and anti-inflammatory properties that work against both gram-negative and gram-positive bacteria [6,7]. Therefore, using Stearic acid Solid Lipid Nanoparticles to deliver these drugs to the site of the wound is advantageous. This is because SLNs containing stearic acid have a high entrapment efficiency and are uniform in size, making them a potentially effective targeted preparation for epidermal delivery [8]. Furthermore, the usage of Tween 80 to stabilize SA-SLN results in a reduction of surface energy and prevents crystal growth. This ultimately leads to the production of smaller nanoparticles [9].

**Methodology**

The LT-SLNs were prepared by homogenization method at 17,500 rpm for 30 minutes. The prepared LT-SLNs were then cooled at room temperature to allow the SLN formation. Following this, the LT-SLNs were then filtered using a 200 nm sterile syringe and stored at 2°C. The LT-SLNs formulation surface charge, composition, and appearance were analyzed using techniques such as Zeta potential and size, HR-TEM, XRD, and FTIR. To determine its efficacy against bacterial cells, *Pseudomonas aeruginosa* was used. Evaluation methods included bacterial Growth Kinetics, Kirby-Bauer Disk Diffusion, Live/dead cell analysis using flow cytometry, and bacterial membrane damage study.

**Results**

Stearic acid, lauric acid and Tea tree oil were dissolved in 99% ethanol and the LT-SLNs were prepared by homogenization at 17,500 rpm for 30 minutes. Table 1 represents the polydisperse index (PDI), average particle size, and surface charge (Zp) of the SLN and LT-SLN formulations. In addition, an XRD experiment was also performed to demonstrate the crystallographic structure and chemical composition for all SLN and LT-SLN formulations compared to the standard lauric acid and stearic acid standard XRD readings. In addition, the minimum inhibition concentration results are shown in Figure 1.

Table 1: Surface charge (Zeta potential) Particle size distribution of SLN and LT-SLN

| Formulation | Average Particle size Distribution (PSD) (d.nm) | Zeta Potential (mV) | Particle density Index |
|---|---|---|---|
| F1 | 239.58 ± 7.96 | -9.36 ± 3.89 | 1.000 |
| F2 | 284.7± 17.74 | -13.2 ± 5.30 | 1.000 |
| F3 | 212.4 ± 13.20 | -12.1 ± 4.53 | 1.000 |
| F4 | 344.7 ± 16.13 | -9.05 ± 5.20 | 1.000 |
| F5 | 270.1 ± 0.931 | -12.3 ± 3.78 | 1.000 |

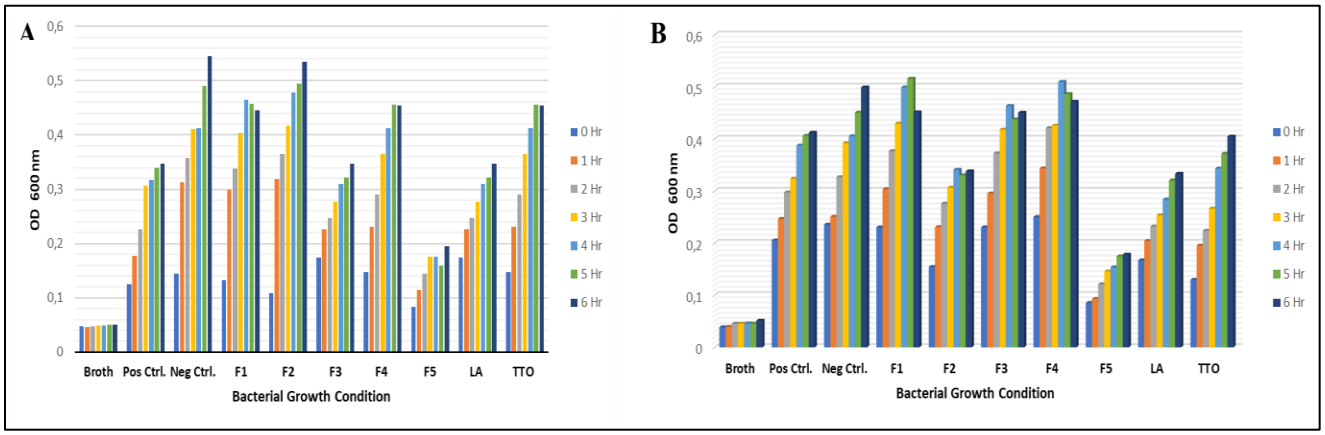


Figure 1: Growth Kinetic study for the formulated SLN and LT-SLNs using P aeruginosa A) MIC 12,5 Trial 1 and B) 12,5mg/ml Trial 2 for *P aeruginosa* bacterial study.

**Conclusion**

This study discussed the potential process of preparing, characterisation, and antibacterial effect of SLNs and LT-SLNs and it may be useful for the treatment of pathogen-infected wounds. The SLNs and LT-SLNs were well-designed with good physicochemical properties and biocompatibility, which allowed them to penetrate deep into the bacterial membrane of *P. aeruginosa* displaying their antibacterial effect. This makes them suitable for the treatment of pathogen-infected wounds.

## References


1. K.H. Ramteke, S.A. Joshi, S.N. Dhole, Solid Lipid Nanoparticle: A Review Ramteke K.H, IOSR Journal of Pharmacy. 6, 34–44. 2012

2. P. Ekambaram, A. Abdul hasansathali, K. Priyanka, Solid Lipid Nanoparticles: A Review, Scientific Reviews & Chemical Communications. 2 (2011) 80–102.

3. N.K. Rajendran, S.S.D. Kumar, N.N. Houreld, H. Abrahamse, A review on nanoparticle-based treatment for wound healing, J. Drug Deliv. Sci. Technol. 44, 421–430, 2018 https://doi.org/10.1016/j.jddst.2018.01.009.

4. Y. Duan, A. Dhar, C. Patel, M. Khimani, S. Neogi, P. Sharma, N. Siva Kumar, R.L. Vekariya, A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems, RSC Adv. 10, 26777–26791, 2020 https://doi.org/10.1039/d0ra03491f.

5. M.S. Lerata, S. D'Souza, N.R.S. Sibuyi, A. Dube, M. Meyer, T. Samaai, E.M. Antunes, D.R. Beukes, Encapsulation of variabilin in stearic acid solid lipid nanoparticles enhances its anticancer activity in vitro, Molecules. 25, 830, 2020 https://doi.org/10.3390/molecules25040830.

6. F.O. Nitbani, Jumina, D. Siswanta, E.N. Solikhah, Isolation and antibacterial activity test of lauric acid from crude coconut oil (cocos nucifera L.), Procedia Chem. 18,132–140,2016 https://doi.org/10.1016/j.proche.2016.01.021.

7. R.C.V. Santos, L.Q.S. Lopes, C.F. dos S. Alves, V.P. Fausto, K. Pizzutti, V. Barboza, M.E. de Souza, R.P. Raffin, P. Gomes, D. Takamatsu, Y. Morinaga, A.A. Boligon, M.L. Athayde, C.C. Felippi, R. de Almeida Vaucher, Antimicrobial activity of tea tree oil nanoparticles against American and European foulbrood diseases agents, J. Asia. Pac. Entomol. 17, 343–347, 2014 https://doi.org/10.1016/j.aspen.2014.02.003.

8. Xie F.-M., Zeng K., Li G.-F., Lin Z.-F., Sun L.-D., Preparation of stearic acid solid lipid nanoparticles containing podophyllotoxin, Di Yi Jun Yi Da Xue Xue Bao. 25, 99–101, 2005

9. A. Sukmawati, W. Utami, R. Yuliani, M. Da'i, A. Nafarin, Effect of tween 80 on nanoparticle preparation of modified chitosan for targeted delivery of combination doxorubicin and curcumin analogue, IOP Conf. Ser. Mater. Sci. Eng. 311, 012024., 2011 https://doi.org/10.1088/1757-899x/311/1/012024.

**List of Journals (Journals I'm interested in are marked in green)**

- **Journal of Biomedical Photonics & Engineering (impact factor: 1.04)**
- **Quantum Electronics (Russian/English), (impact factor: 2.52)**
- **Optics and Spectroscopy (Russian/English) (impact factor: 0.74)**
- **Nonlinear Applied Physics (Russian/English) (impact factor: 1.934)**
- **Optics and Spectroscopy (Russian/English) (impact factor: 0.74)**
- **Journal of Technical Physics (Russian/English) (impact factor: 0.489)**
- **Journal of Biomedical Optics (impact factor: 3.582)**
- **Journal of Biophotonics (impact factor: 3.39)**
- **Journal Innovative Optical Health Science (impact factor: 1.352)**
- **Optical Engineering (impact factor: 1.352)**
- **MDPI Materials (impact factor: 3.748)**
- **MDPI Diagnostics (impact factor: 3.6)**
- **MDPI Applied Sciences (impact factor: 2.7)**