

**OPTIMASI DAN KARAKTERISASI FORMULASI *NANOSTRUCTURED*
LIPID CARRIER DARI L-DOPA-SETIL PALMITAT-ASAM LINOLEAT
(NLC-DCL) SEBAGAI KANDIDAT OBAT PARKINSON**

SKRIPSI

Diajukan untuk memenuhi sebagian syarat memperoleh gelar sarjana sains pada
Fakultas Pendidikan Matematika dan Ilmu Pengetahuan Alam



Disusun oleh

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2009887

PROGRAM STUDI KIMIA

FAKULTAS PENDIDIKAN MATEMATIKA DAN ILMU PENGETAHUAN ALAM

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**OPTIMASI FORMULASI NANOSTRUCTURED LIPID CARRIER (NLC)
DARI L-DOPA-SETIL PALMITAT-ASAM LINOLEAT SEBAGAI
KANDIDAT OBAT PARKINSON**

oleh,

Salsabila Fitri Pratami

Sebuah skripsi yang diajukan untuk memenuhi salah satu syarat memperoleh gelar Sarjana Sains pada Fakultas Pendidikan Matematika dan Ilmu Pengetahuan Alam

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OPTIMASI DAN KARAKTERISASI FORMULASI *NANOSTRUCTURED LIPID CARRIER* DARI L-DOPA-SETIL PALMITAT-ASAM LINOLEAT (NLC-DCL) SEBAGAI KANDIDAT OBAT PARKINSON

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PERNYATAAN KEASLIAN SKRIPSI

Saya menyatakan bahwa skripsi yang berjudul “**Optimasi dan Karakterisasi Formulasi Nanostructured Lipid Carrier dari L-DOPA-Setil Palmitat-Asam Linoleat (NLC-DCL) sebagai Kandidat Obat Parkinson**” ini sepenuhnya adalah karya saya sendiri. Tidak ada di dalamnya yang merupakan plagiat dari karya orang lain dan saya tidak melakukan penjiplakan atau pengutipan dengan cara-cara yang tidak sesuai dengan etika keilmuan yang berlaku dalam masyarakat keilmuan. Atas pernyataan ini, saya siap menanggung risiko/sanksi yang dijatuhkan kepada saya apabila kemudian ditemukan adanya pelanggaran terhadap etika keilmuan dalam karya saya ini, atau klaim dari pihak lain terhadap keaslian karya saya ini.

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Yang membuat pernyataan,

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KATA PENGANTAR

Puji serta syukur penulis haturkan ke hadirat Tuhan Yang Maha Esa yang telah dilimpahkan rahmat serta karunia-Nya sehingga penulis dapat menyelesaikan skripsi yang berjudul “Optimasi dan Karakterisasi Formulasi Nanostructured Lipid Carrier Dari L-DOPA-Setil Palmitat-Asam Linoleat (NLC-DCL) sebagai Kandidat Obat Parkinson” Skripsi ini disusun untuk memenuhi salah satu syarat untuk menerima gelar Sarjana Sains di Departemen Pendidikan Kimia, Fakultas Pendidikan Matematika dan Ilmu Pengetahuan Alam, Universitas Pendidikan Indonesia.

Penelitian ini dilakukan untuk mengeksplorasi pengembangan sistem penghantaran obat, yang memungkinkan L-DOPA termuat dalam partikel-partikel kecil yang stabil dan mudah diserap oleh tubuh. Dalam penelitian ini, penulis menggunakan sistem *Nanostructured Lipid Carrier* (NLC) berbasis setil palmitat dan asam linoleat sebagai matriks untuk menyalut L-DOPA.

Penulis berharap skripsi penelitian ini dapat meningkatkan wawasan serta kontribusi bagi penulis, pembaca, dan peneliti selanjutnya dalam bidang kimia. Penulis menyadari bahwa masih terdapat kekurangan pada skripsi ini. Oleh karena itu, sangat diperlukan kritik serta saran yang bersifat membangun dari berbagai pihak untuk perbaikan dan penyempurnaan di kemudian hari.

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ABSTRAK

L-DOPA yang merupakan obat penyakit Parkinson memiliki keterbatasan bioavailabilitas dan stabilitas, sehingga perlu dilakukan enkapsulasi L-DOPA menggunakan *sistem Nanostructured Lipid Carrier* (NLC). Penelitian ini bertujuan memperoleh formulasi optimum, karakteristik, dan nilai *entrapment efficiency* dan profil *drug release* dari produk nanoenkapsulasi L-DOPA menggunakan NLC berbasis setil palmitat dan asam linoleat (NLC-DCL). Sintesis sistem NLC untuk L-DOPA dilakukan dengan menggunakan metode homogenisasi panas dan ultrasonikasi, serta optimasi berdasarkan 2 variabel, yaitu perbandingan komposisi lipid dan massa surfaktan. Karakterisasi NLC-DCL meliputi penentuan ukuran partikel, indeks polidispersitas, dan zeta potensial menggunakan PSA, morfologi partikel menggunakan TEM, gugus fungsi menggunakan FTIR. Penentuan *entrapment efficiency* dan profil *drug release* dilakukan menggunakan spektrofotometer UV-Vis. Hasil penelitian menunjukkan, formulasi terbaik NLC-DCL terjadi pada komposisi setil palmitat dan asam linoleat 4:6 dengan massa surfaktan sebesar 1,25 gram. Produk NLC-DCL yang diperoleh memiliki ukuran partikel rata-rata sebesar 87,9 nm dengan indeks polidispersitas sebesar 0,185, dan zeta potensial yang terukur sebesar -28,3 mV. Hasil karakterisasi FTIR menunjukkan terjadinya pergeseran pada serapan gugus O-H, N-H, C=O, dan C-O yang mengindikasikan adanya interaksi antara L-DOPA dengan setil palmitat dan asam linoleat. Hasil analisis menggunakan TEM menunjukkan bentuk NLC-DCL spherical dengan kisaran ukuran sebesar 87,5 nm. Persentase *entrapment efficiency* dari NLC-DCL diperoleh sebesar 75,49%. Profil *drug release* NLC-DCL menunjukkan pelepasan L-DOPA pada 7 jam pertama mengikuti model Korsmeyer-Peppars. Setelah 24 jam, L-DOPA dilepaskan sebanyak 26,68% pada pH 1,2 dan 36,49% pada pH 7,4.

Kata kunci: L-DOPA, *Nanostructured Lipid Carrier*, Setil Palmitat, Asam Linoleat, Penyakit Parkinson

ABSTRACT

L-DOPA, a drug used for Parkinson's disease, has limitations in bioavailability and stability, necessitating its encapsulation using the Nanostructured Lipid Carrier (NLC) system. This study aims to obtain the optimum formulation, characteristics, entrapment efficiency, and drug release profile of L-DOPA nanoencapsulation products using NLC based on cetyl palmitate and linoleic acid (NLC-DCL). The NLC system synthesis for L-DOPA was carried out using the hot homogenization and ultrasonication method, with optimization based on two variables: the lipid composition ratio and the surfactant mass. NLC-DCL characterization includes determining particle size, polydispersity index, and zeta potential using PSA, particle morphology using TEM, and functional groups using FTIR. Entrapment efficiency and drug release profiles were determined using a UV-Vis spectrophotometer. The results showed that the best NLC-DCL formulation occurred at a cetyl palmitate and linoleic acid composition ratio of 4:6 with a surfactant mass of 1.25 grams. The obtained NLC-DCL product had an average particle size of 87.9 nm with a polydispersity index of 0.185, and a measured zeta potential of -28.3 mV. FTIR characterization results showed shifts in the absorption of O-H, N-H, C=O, and C-O groups, indicating interactions between L-DOPA and cetyl palmitate and linoleic acid. TEM analysis results showed that NLC-DCL had a spherical shape with a size range of 87.5 nm. The entrapment efficiency percentage of NLC-DCL was 75.49%. The drug release profile of NLC-DCL showed that L-DOPA release in the first 7 hours followed the Korsmeyer-Peppas model. After 24 hours, 26.68% of L-DOPA was released at pH 1.2 and 36.49% at pH 7.4.

Keywords: *L-DOPA, Nanostructured Lipid Carrier, Cetyl Palmitate, Linoleic Acid, Parkinson's Disease*

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DAFTAR PUSTAKA

- Abdulloh Suyuti, Esti Hendradi, & Tutiek Purwanti. (2023). Effect of Different Lipid Ratios on Physicochemical Stability and Drug Release of Nanostructured Lipid Carriers Loaded Coenzyme Q10. *JURNAL FARMASI DAN ILMU KEFARMASIAN INDONESIA*, 10(1), 44–53. <https://doi.org/10.20473/jfiki.v10i12023.44-53>
- Abourehab, M. A. S., Khames, A., Genedy, S., Mostafa, S., Khaleel, M. A., Omar, M. M., & El Sisi, A. M. (2021). Sesame oil-based nanostructured lipid carriers of nicergoline, intranasal delivery system for brain targeting of synergistic cerebrovascular protection. *Pharmaceutics*, 13(4). <https://doi.org/10.3390/pharmaceutics13040581>
- Ajiboye, A. L., Nandi, U., Galli, M., & Trivedi, V. (2021). Olanzapine loaded nanostructured lipid carriers via high shear homogenization and ultrasonication. *Scientia Pharmaceutica*, 89(2). <https://doi.org/10.3390/scipharm89020025>
- Arief Al Rasyid, R., Mardiana, D., Firmansyah, R., & Ningsih, Z. (2023). Effects of Preparation Temperature and Liquid-Solid Lipid Composition to Curcumin-Nanostructured Lipid Carrier Characteristics Fabricated by Microfluidic Technique. *The Journal of Pure and Applied Chemistry Research*, 12(2), 104–116. <https://doi.org/10.21776/ub.jpacr.2023.012.02.3317>
- Apostolou, M., Assi, S., Fatokun, A. A., & Khan, I. (2021). The Effects of Solid and Liquid Lipids on the Physicochemical Properties of Nanostructured Lipid Carriers. *Journal of Pharmaceutical Sciences*, 110(8), 2859–2872. [10.1016_j.xphs.2021.04.012](https://doi.org/10.1016/j.xphs.2021.04.012)
- Avadi, M. R., Sadeghi, A. M. M., Mohammadpour, N., Abedin, S., Atyabi, F., Dinarvand, R., & Rafiee-Tehrani, M. (2010). Preparation and characterization of insulin nanoparticles using chitosan and Arabic gum with ionic gelation method. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 6(1), 58–63. <https://doi.org/10.1016/j.nano.2009.04.007>
- Chauhan, I., Yasir, M., Verma, M., & Singh, A. P. (2020). Nanostructured lipid carriers: A groundbreaking approach for transdermal drug delivery. In *Advanced Pharmaceutical Bulletin* (Vol. 10, Issue 2, pp. 150–165). Tabriz University of Medical Sciences. <https://doi.org/10.34172/apb.2020.021>
- Cooley, M., Sarode, A., Hoore, M., Fedosov, D. A., Mitragotri, S., & Sen Gupta, A. (2018). Influence of particle size and shape on their margination and wall-adhesion: implications in drug delivery vehicle design across nano-to-micro scale. *Nanoscale*, 10(32), 15350–15364. <https://doi.org/10.1039/c8nr04042g>
- Danaei, M., Dehghankhold, M., Ataei, S., Hasanzadeh Davarani, F., Javanmard, R., Dokhani, A., Khorasani, S., & Mozafari, M. R. (2018). Impact of Particle Size and Polydispersity Index on the Clinical Applications of Lipidic Nanocarrier

- Systems. *Pharmaceutics*, 10(2), 57.
<https://doi.org/10.3390/pharmaceutics10020057>
- Dai, F., Zhuang, Q., Huang, G., Deng, H., & Zhang, X. (2023). Infrared Spectrum Characteristics and Quantification of OH Groups in Coal. *ACS omega*, 8(19), 17064–17076. <https://doi.org/10.1021/acsomega.3c01336>
- Dash, S., Murthy, P. N., Nath, L., & Chowdhury, P. (2010). Kinetic modeling on drug release from controlled drug delivery systems. *Acta poloniae pharmaceutica*, 67(3), 217–223.
- Decuzzi, P., & Ferrari, M. (2008). The receptor-mediated endocytosis of nonspherical particles. *Biophysical journal*, 94(10), 3790–3797. <https://doi.org/10.1529/biophysj.107.120238>
- Demissie, H., & Duraisamy, R. (2016). Effects of electrolytes on the surface and micellar characteristics of Sodium dodecyl sulphate surfactant solution. *Journal of Scientific and Innovative Research*, 5(6), 208–214. www.jsirjournal.com
- Eh Suk, V. R., Mohd Latif, F., Teo, Y. Y., & Misran, M. (2020). Development of nanostructured lipid carrier (NLC) assisted with polysorbate nonionic surfactants as a carrier for l-ascorbic acid and Gold Tri.E 30. *Journal of food science and technology*, 57(9), 3259–3266. <https://doi.org/10.1007/s13197-020-04357-x>
- Eleraky, N., M Omar, M., A Mahmoud, H., & A Abou-Taleb, H. (2020). Nanostructured Lipid Carriers to Mediate Brain Delivery of Temazepam: Design and In Vivo Study. *Pharmaceutics*, 12(5), 451. <https://doi.org/10.3390/pharmaceutics12050451>
- Ellis, J. M., & Fell, M. J. (2017). Current approaches to the treatment of Parkinson's Disease. In *Bioorganic and Medicinal Chemistry Letters* (Vol. 27, Issue 18, pp. 4247–4255). Elsevier Ltd. <https://doi.org/10.1016/j.bmcl.2017.07.075>
- Elmowafy, M., & Al-Sanea, M. M. (2021). Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. *Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society*, 29(9), 999–1012. <https://doi.org/10.1016/j.jsps.2021.07.015>
- Emamzadeh, F. N., & Surguchov, A. (2018). Parkinson's disease: Biomarkers, treatment, and risk factors. In *Frontiers in Neuroscience* (Vol. 12, Issue AUG). Frontiers Media S.A. <https://doi.org/10.3389/fnins.2018.00612>
- Fadlelmoula, A., Pinho, D., Carvalho, V. H., Catarino, S. O., & Minas, G. (2022). Fourier Transform Infrared (FTIR) Spectroscopy to Analyse Human Blood over the Last 20 Years: A Review towards Lab-on-a-Chip Devices. In *Micromachines* (Vol. 13, Issue 2). MDPI. <https://doi.org/10.3390/mi13020187>
- Feng, S., Sheng, J., Yu, J., Lin, Y., & Shao, P. (2023). Encapsulation and release of citral using nanostructured lipid carriers: A study on the impact of different

preparation methods. *Food Bioscience*, 56.
<https://doi.org/10.1016/j.fbio.2023.103185>

- Frihart C. R. (2023). Chemistry of Dimer Acid Production from Fatty Acids and the Structure-Property Relationships of Polyamides Made from These Dimer Acids. *Polymers*, 15(16), 3345. <https://doi.org/10.3390/polym15163345>
- Gerasimov, Andrei & Eremina, O & Cherkasova, M. & Dmitriev, S. (2021). Application of particle-size analysis in various industries. *Journal of Physics: Conference Series*. 1728. 012003. 10.1088/1742-6596/1728/1/012003.
- Gilani, S. J., Jumah, M. N. B., Zafar, A., Imam, S. S., Yasir, M., Khalid, M., Alshehri, S., Ghuneim, M. M., & Albohairy, F. M. (2022). Formulation and Evaluation of Nano Lipid Carrier-Based Ocular Gel System: Optimization to Antibacterial Activity. *Gels (Basel, Switzerland)*, 8(5), 255. <https://doi.org/10.3390/gels8050255>
- Gross-Rother, J., Blech, M., Preis, E., Bakowsky, U., & Garidel, P. (2020). Particle Detection and Characterization for Biopharmaceutical Applications: Current Principles of Established and Alternative Techniques. *Pharmaceutics*, 12(11), 1112. <https://doi.org/10.3390/pharmaceutics12111112>
- Hashemi, F. S., Farzadnia, F., Aghajani, A., Ahmadzadeh NobariAzar, F., & Pezeshki, A. (2020). Conjugated linoleic acid loaded nanostructured lipid carrier as a potential antioxidant nanocarrier for food applications. *Food Science and Nutrition*, 8(8), 4185–4195. <https://doi.org/10.1002/fsn3.1712>
- Honary, S., & Zahir, F. (2013). Effect of zeta potential on the properties of nano-drug delivery systems - A review (Part 2). *Tropical Journal of Pharmaceutical Research*, 12(2), 265–273. <https://doi.org/10.4314/tjpr.v12i2.20>
- Houacine, C., Adams, D., & Singh, K. K. (2020). Impact of liquid lipid on development and stability of trimyristin nanostructured lipid carriers for oral delivery of resveratrol. *Journal of Molecular Liquids*, 316. <https://doi.org/10.1016/j.molliq.2020.113734>
- Iarkov, A., Barreto, G. E., Grizzell, J. A., & Echeverria, V. (2020). Strategies for the Treatment of Parkinson's Disease: Beyond Dopamine. In *Frontiers in Aging Neuroscience* (Vol. 12). Frontiers Media S.A. <https://doi.org/10.3389/fnagi.2020.00004>
- Izza, N., Suga, K., Okamoto, Y., Watanabe, N., Bui, T. T., Wibisono, Y., Fadila, C. R., & Umakoshi, H. (2021). Systematic Characterization of Nanostructured Lipid Carriers from Cetyl Palmitate/Caprylic Triglyceride/Tween 80 Mixtures in an Aqueous Environment. *Langmuir*, 37(14), 4284–4293. <https://doi.org/10.1021/acs.langmuir.1c00270>
- Jain, K., Sood, S., & Gowthamarajan, K. (2015). Optimization of artemether-loaded NLC for intranasal delivery using central composite design. *Drug delivery*, 22(7), 940–954. <https://doi.org/10.3109/10717544.2014.885999>
- Jelvehgari, M., Salatin, S., Barar, J., Barzegar-Jalali, M., Adibkia, K., Kiafar, F., & Jelvehgari, M. (2017). Development of a nanoprecipitation method for the

entrapment of a very water soluble drug into Eudragit RL nanoparticles. In *Research in Pharmaceutical Sciences* (Vol. 12, Issue 1).

- Karn-Orachai, K., Smith, S. M., Phunpee, S., Treethong, A., Puttipipatkachorn, S., Pratontep, S., & Ruktanonchai, U. R. (2014). The effect of surfactant composition on the chemical and structural properties of nanostructured lipid carriers. *Journal of microencapsulation*, 31(6), 609–618. <https://doi.org/10.3109/02652048.2014.911374>
- Khan, S., Sharma, A., & Jain, V. (2023). An overview of nanostructured lipid carriers and its application in drug delivery through different routes. In *Advanced Pharmaceutical Bulletin* (Vol. 13, Issue 3, pp. 446–460). Tabriz University of Medical Sciences. <https://doi.org/10.34172/apb.2023.056>
- Khasanah, U., & Fatchur Rochman, M. (2021). STABILITAS NANOSTRUCTURED LIPID CARRIER COENZYME Q10 DENGAN VARIASI WAKTU PENGADUKAN. *Jurnal Ilmu Farmasi Dan Farmasi Klinik (JIFFK)*, 18(2), 55–63. www.unwahas.ac.id/publikasiilmiah/index.php/ilmufarmasidanfarmasiklinik
- Kobylecki, C. (2020). Update on the diagnosis and management of Parkinson's disease. *Clinical Medicine, Journal of the Royal College of Physicians of London*, 20(4), 393–398. <https://doi.org/10.7861/CLINMED.2020-0220>
- Krambeck, K., Silva, V., Silva, R., Fernandes, C., Cagide, F., Borges, F., Santos, D., Otero-Espinar, F., Lobo, J. M. S., & Amaral, M. H. (2021). Design and characterization of Nanostructured lipid carriers (NLC) and Nanostructured lipid carrier-based hydrogels containing *Passiflora edulis* seeds oil. *International journal of pharmaceutics*, 600, 120444. <https://doi.org/10.1016/j.ijpharm.2021.120444>
- Kushwaha, Krishna & Mishra, Manoj & Srivastava, Rajat. (2019). Fabrication and Characterization of Pluronic F68 and Phospholipon 90g Embedded Nanoformulation for Sertraline Delivery: An Optimized Factorial Design Approach and In Vivo Study. *Asian Journal of Pharmaceutical Research and Development*. 7. 59-66. [10.22270/ajprd.v7i3.505](https://doi.org/10.22270/ajprd.v7i3.505).
- Kwon, D. K., Kwatra, M., Wang, J., & Ko, H. S. (2022). Levodopa-Induced Dyskinesia in Parkinson's Disease: Pathogenesis and Emerging Treatment Strategies. In *Cells* (Vol. 11, Issue 23). MDPI. <https://doi.org/10.3390/cells11233736>
- Lasoń, E., Sikora, E., & Ogonowski, J. (2013). Influence of process parameters on properties of Nanostructured Lipid Carriers (NLC) formulation. *Acta biochimica Polonica*, 60(4), 773–777.
- Li, Q., Cai, T., Huang, Y., Xia, X., Cole, S. P. C., & Cai, Y. (2017). A Review of the Structure, Preparation, and Application of NLCs, PNPs, and PLNs. *Nanomaterials (Basel, Switzerland)*, 7(6), 122. <https://doi.org/10.3390/nano7060122>

- Loo, C. H., Basri, M., Ismail, R., Lau, H. L. N., Tejo, B. A., Kanthimathi, M. S., Hassan, H. A., & Choo, Y. M. (2013). Effect of compositions in nanostructured lipid carriers (NLC) on skin hydration and occlusion. *International Journal of Nanomedicine*, 8, 13–22. <https://doi.org/10.2147/IJN.S35648>
- Malatesta, M. (2021). Transmission electron microscopy as a powerful tool to investigate the interaction of nanoparticles with subcellular structures. In *International Journal of Molecular Sciences* (Vol. 22, Issue 23). MDPI. <https://doi.org/10.3390/ijms222312789>
- Malekmohammadi, M., Ghanbarzadeh, B., Hanifian, S., Samadi Kafil, H., Gharekhani, M., & Falcone, P. M. (2023). The Gelatin-Coated Nanostructured Lipid Carrier (NLC) Containing *Salvia officinalis* Extract: Optimization by Combined D-Optimal Design and Its Application to Improve the Quality Parameters of Beef Burger. *Foods*, 12(20). <https://doi.org/10.3390/foods12203737>
- Mateos, H., Valentini, A., Robles, E., Brooker, A., Cioffi, N., & Palazzo, G. (2019). Measurement of the zeta-potential of solid surfaces through Laser Doppler Electrophoresis of colloid tracer in a dip-cell: Survey of the effect of ionic strength, pH, tracer chemical nature and size. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 576, 82–90. <https://doi.org/10.1016/j.colsurfa.2019.05.006>
- Midekessa, G., Godakumara, K., Ord, J., Viil, J., Lättekivi, F., Dissanayake, K., Kopanchuk, S., Rinke, A., Andronowska, A., Bhattacharjee, S., Rinke, T., & Fazeli, A. (2020). Zeta Potential of Extracellular Vesicles: Toward Understanding the Attributes that Determine Colloidal Stability. *ACS Omega*, 5(27), 16701–16710. <https://doi.org/10.1021/acsomega.0c01582>
- Mozaffar, S., Radi, M., Amiri, S., & McClements, D. J. (2021). A new approach for drying of nanostructured lipid carriers (NLC) by spray-drying and using sodium chloride as the excipient. *Journal of Drug Delivery Science and Technology*, 61. <https://doi.org/10.1016/j.jddst.2020.102212>
- M Surya Tej, K. V, Moin, A., Gowda, D. V, Karunakar, G., Patel, N. P., & Sai Kamal, S. (2016). Nano structured lipid carrier based drug delivery system. Available Online *Www.Jocpr.Com Journal of Chemical and Pharmaceutical Research*, 8(2), 627–643. www.jocpr.com
- Muhimatul Hasanah, Y., & Raharjo, S. (2024). APLIKASI NANO-SIZE LIPID CARRIER (NLC) MINYAK BEKATUL (RBO) PADA MINUMAN SARI BUAH APEL DAN JERUK KOMERSIAL. 13, 38–48. <http://ejournal3.undip.ac.id/index.php/jnc/>
- Nair, Sreeja & Vinayan, Kollencheri & Mangalathillam, Sabitha. (2021). Nose to Brain Delivery of Phenytoin Sodium Loaded Nano Lipid Carriers: Formulation, Drug Release, Permeation and In Vivo Pharmacokinetic Studies. *Pharmaceutics*. 13. 1640. [10.3390/pharmaceutics13101640](https://doi.org/10.3390/pharmaceutics13101640).

- Ortiz, A. C., Yañez, O., Salas-Huenuleo, E., & Morales, J. O. (2021). Development of a nanostructured lipid carrier (NLC) by a low-energy method, comparison of release kinetics and molecular dynamics simulation. *Pharmaceutics*, *13*(4). <https://doi.org/10.3390/pharmaceutics13040531>
- Pertiwi, H. (2015). Evaluasi Profil Disolusi Tablet Lepas Lambat Teofilin yang Beredar di Masyarakat. Universitas Islam Negeri Syarif Hidayatullah
- Perinelli, D. R., Cespi, M., Lorusso, N., Palmieri, G. F., Bonacucina, G., & Blasi, P. (2020). Surfactant Self-Assembling and Critical Micelle Concentration: One Approach Fits All?. *Langmuir : the ACS journal of surfaces and colloids*, *36*(21), 5745–5753. <https://doi.org/10.1021/acs.langmuir.0c00420>
- Pezeshki, A., Ghanbarzadeh, B., Mohammadi, M., Fathollahi, I., & Hamishehkar, H. (2014). Encapsulation of Vitamin A Palmitate in Nanostructured Lipid Carrier (NLC)-Effect of Surfactant Concentration on the Formulation Properties. *Advanced pharmaceutical bulletin*, *4*(Suppl 2), 563–568. <https://doi.org/10.5681/apb.2014.083>
- Rabima, R., & Sari, M. P. (2019). Entrapment efficiency and drug loading of curcumin nanostructured lipid carrier (NLC) formula. *Pharmaciana*, *9*(2), 299. <https://doi.org/10.12928/pharmaciana.v9i2.13070>
- Rahmasari, D., Rosita, N., & Soeratri, W. (2022). Physicochemical Characteristics, Stability, and Irritability of Nanostructured Lipid Carrier System Stabilized with Different Surfactant Ratios. *JURNAL FARMASI DAN ILMU KEFARMASIAN INDONESIA*, *9*(1), 8–16. <https://doi.org/10.20473/jfiki.v9i12022.8-16>
- Rohmah, M., Rahmadi, A., & Raharjo, S. (2022). Bioaccessibility and antioxidant activity of β -carotene loaded nanostructured lipid carrier (NLC) from binary mixtures of palm stearin and palm olein. *Heliyon*, *8*(2). <https://doi.org/10.1016/j.heliyon.2022.e08913>
- Sahraee, S., Ghanbarzadeh, B., Maryam mohammadi, Pezeshki, A., & hoseini, M. (2022). Development of heat-stable gelatin-coated nanostructured lipid carriers (NLC): Colloidal and stability properties. *LWT*, *160*. <https://doi.org/10.1016/j.lwt.2022.113265>
- Silva, S., Almeida, A. J., & Vale, N. (2021). Importance of nanoparticles for the delivery of antiparkinsonian drugs. *Pharmaceutics*, *13*(4). <https://doi.org/10.3390/pharmaceutics13040508>
- Sultana, Rajia & Khatun, Ambia & Hossen, Md. Farhad. (2024). A comprehensive review of particle size analysis techniques. *International Journal of Pharmaceutical Research and Development*. *6*. 01-05. [10.33545/26646862.2024.v6.i1a.37](https://doi.org/10.33545/26646862.2024.v6.i1a.37).
- Syed Azhar, S. N. A., Ashari, S. E., Zainuddin, N., & Hassan, M. (2022). Nanostructured Lipid Carriers-Hydrogels System for Drug Delivery: Nanohybrid Technology Perspective. *Molecules (Basel, Switzerland)*, *27*(1), 289. <https://doi.org/10.3390/molecules27010289>

- Tan, J. M., Saifullah, B., Kura, A. U., Fakurazi, S., & Hussein, M. Z. (2018). Incorporation of levodopa into biopolymer coatings based on carboxylated carbon nanotubes for ph-dependent sustained release drug delivery. *Nanomaterials*, 8(6). <https://doi.org/10.3390/nano8060389>
- Unagolla, J. M., & Jayasuriya, A. C. (2018). Drug transport mechanisms and in vitro release kinetics of vancomycin encapsulated chitosan-alginate polyelectrolyte microparticles as a controlled drug delivery system. *European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences*, 114, 199–209. <https://doi.org/10.1016/j.ejps.2017.12.012>
- Viegas, C., Patrício, A. B., Prata, J. M., Nadhman, A., Chintamaneni, P. K., & Fonte, P. (2023). Solid Lipid Nanoparticles vs. Nanostructured Lipid Carriers: A Comparative Review. In *Pharmaceutics* (Vol. 15, Issue 6). Multidisciplinary Digital Publishing Institute (MDPI). <https://doi.org/10.3390/pharmaceutics15061593>
- Wanjari, S. P. (2019). *NOVATEUR PUBLICATIONS INTERNATIONAL JOURNAL OF INNOVATIONS IN ENGINEERING RESEARCH AND TECHNOLOGY [IJIERT] STUDY OF PHARMACEUTICAL DRUGS ENCAPSULATION WITHIN SURFACTANT MICELLES BY MOLECULAR COMPUTATIONS*.
- Wei, Z., Jiao, D., & Xu, J. (2015). Using Fourier transform infrared spectroscopy to study effects of magnetic field treatment on wheat (*Triticum aestivum* L.) seedlings. *Journal of Spectroscopy*, 2015. <https://doi.org/10.1155/2015/570190>
- Wirawan, W. (2023). Formulation and Characteristics of Nanostuctured Lipid Carrier (NLC) Red Palm Oil (RPO) Prepared by High-Pressure Homogenization and Its Applications in Orange Juice. *Indonesian Food and Nutrition Progress*, 19(1), 31. <https://doi.org/10.22146/ifnp.70924>
- Xia, D., Shrestha, N., van de Streek, J., Mu, H., & Yang, M. (2016). Spray drying of fenofibrate loaded nanostructured lipid carriers. *Asian Journal of Pharmaceutical Sciences*, 11(4), 507–515. <https://doi.org/10.1016/j.ajps.2016.01.001>
- Yao, Z., Nie, P., Zhang, X., Chen, C., An, Z., Wei, K., Zhao, J., Lv, H., Niu, K., Yang, Y., Zou, W., & Yang, L. (2023). Establishment and Validation of Fourier Transform Infrared Spectroscopy (FT–MIR) Methodology for the Detection of Linoleic Acid in Buffalo Milk. *Foods*, 12(6). <https://doi.org/10.3390/foods12061199>
- Yusuf, A., Almotairy, A. R. Z., Henidi, H., Alshehri, O. Y., & Aldughaim, M. S. (2023). Nanoparticles as Drug Delivery Systems: A Review of the Implication of Nanoparticles' Physicochemical Properties on Responses in Biological Systems. *Polymers*, 15(7), 1596. <https://doi.org/10.3390/polym15071596>
- Zhang, T., Yang, R., Pan, J., & Huang, S. (2023). Parkinson's disease related depression and anxiety: A 22-year bibliometric analysis (2000-2022). In

Neuropsychiatric Disease and Treatment (Vol. 19, pp. 1477–1489). Dove Medical Press Ltd. <https://doi.org/10.2147/NDT.S403002>

Zhou, Z. D., Yi, L. X., Wang, D. Q., Lim, T. M., & Tan, E. K. (2023). Role of dopamine in the pathophysiology of Parkinson's disease. In *Translational Neurodegeneration* (Vol. 12, Issue 1). BioMed Central Ltd. <https://doi.org/10.1186/s40035-023-00378-6>

Zirak, M. B., & Pezeshki, A. (2015). Effect of Surfactant Concentration on the Particle Size, Stability and Potential Zeta of Beta carotene Nano Lipid Carrier. In *Int.J.Curr.Microbiol.App.Sci* (Vol. 4, Issue 9). <http://www.ijemas.com>

Zwain, T., Alder, J. E., Sabagh, B., Shaw, A., Burrow, A. J., & Singh, K. K. (2021). Tailoring functional nanostructured lipid carriers for glioblastoma treatment with enhanced permeability through in-vitro 3D BBB/BBTB models. *Materials Science and Engineering C*, 121. <https://doi.org/10.1016/j.msec.2020.111774>