

OPTIMASI DAN KARAKTERISASI *NANOSTRUCTURED LIPID CARRIER* DARI L-DOPA-ASAM LAURAT-MINYAK KEDELAI (NLC-DSL) SEBAGAI KANDIDAT OBAT PARKINSON

SKRIPSI

Diajukan untuk memenuhi sebagian syarat memperoleh Sarjana Sains pada
Fakultas Pendidikan Matematika dan Ilmu Pengetahuan Alam



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**OPTIMASI DAN KARAKTERISASI *NANOSTRUCTURED LIPID*
CARRRIER DARI L-DOPA-ASAM LAURAT-MINYAK KEDELAI (NLC-
DSL) SEBAGAI KANDIDAT OBAT PARKINSON**

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Skripsi ini diajukan untuk memenuhi salah satu syarat memperoleh gelar Sarjana
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LEMBAR PENGESAHAN

**OPTIMASI DAN KARAKTERISASI *NANOSTRUCTURED LIPID*
CARRIER DARI L-DOPA-ASAM LAURAT-MINYAK KEDELAI
(NLC-DSL) SEBAGAI KANDIDAT OBAT PARKINSON**

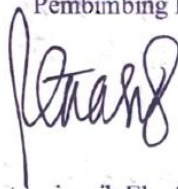
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PERNYATAAN

Dengan ini saya menyatakan bahwa skripsi dengan judul “**Optimasi dan Karakterisasi *Nanostructured Lipid Carrier* dari L-Dopa-Asam Laurat-Minyak Kedelai (NLC-DSL) Sebagai Kandidat Obat Parkinson**” beserta seluruh isinya adalah benar-benar karya saya sendiri. Saya tidak melakukan pengutipan atau penjiplakan dengan cara-cara yang tidak sesuai dengan etika keilmuan yang berlaku dalam masyarakat keilmuan. Atas pernyataan ini saya siap menerima risiko atau sanksi apabila kemudian hari ditemukan adanya pelanggaran etika keilmuan atau ada klaim dari pihak lain terhadap keaslian karya saya.

Bandung, 2024

Yang membuat pernyataan,



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Penulis berharap dengan skripsi ini pembaca, penulis, dan peneliti dalam bidang kimia dapat meningkatkan wawasan dan berkontribusi lebih banyak. Penulis menyadari terdapat banyak kekurangan selama proses pelaksanaan maupun penyusunan skripsi. Oleh karena itu, sangat diharapkan kritik dan saran yang bersifat membangun dalam proses penyempurnaan penelitian maupun penyusunan skripsi. Akhir kata, penulis berharap semoga penyusunan skripsi ini dapat bermanfaat khususnya bagi penulis dan umumnya bagi pembaca.

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ABSTRAK

L-Dopa menjadi pilihan utama dalam pengobatan penyakit parkinson yang mempunyai keterbatasan bioavailabilitas dan stabilitas sehingga diperlukan enkapsulasi menggunakan sistem *Nanostructured Lipid Carrier* (NLC). Penelitian ini bertujuan untuk mendapatkan formulasi optimum, karakteristik, nilai *entrapment efficiency* dan profil *drug release* dari produk L-Dopa berbasis asam laurat dan minyak kedelai (NLC-DSL). Pembuatan NLC-DSL dilakukan menggunakan homogenisasi panas dan ultrasonikasi dengan variabel optimasi meliputi perbandingan lipid, konsentrasi surfaktan, dan waktu ultrasonikasi. Karakterisasi NLC-DSL meliputi penentuan ukuran partikel, *polydispersity indeks*, dan zeta potensial menggunakan PSA, morfologi menggunakan TEM, gugus fungsi menggunakan FTIR. Penentuan nilai *entrapment efficiency* dan profil *drug release* dilakukan menggunakan spektrofotometri UV-Vis. Hasil penelitian menunjukkan kondisi optimum pembuatan NLC-DSL diperoleh pada perbandingan asam laurat terhadap minyak kedelai 1:9, konsentrasi surfaktan 2,5% dan waktu ultrasonikasi 40 menit. Produk NLC-DSL yang diperoleh memiliki ukuran partikel $49,4 \pm 0,07$ nm dengan *polydispersity indeks* 0,451 serta zeta potensial -44,3 mV. Analisis dengan FTIR menunjukkan adanya pergeseran puncak serapan gugus C=O, O-H dan N-H yang mengidentifikasi adanya interaksi antara senyawa L-Dopa dengan asam laurat dan minyak kedelai. Sementara itu hasil TEM menunjukkan bentuk *spherical* dengan ukuran kisaran 49,73 nm. Persentase *entrapment efficiency* dari NLC-DSL diperoleh sebesar 78,05% dan profil *drug release* NLC-DSL menunjukkan kemampuan melepaskan L-Dopa secara lambat dan terkontrol hingga 6 jam dan mencapai 51,20% pada pH 1,2 dengan mengikuti model kinetika korsmeyer-peppas dan 72,87% pada pH 7,4 dengan mengikuti model kinetika orde nol setelah 24 jam. Berdasarkan hasil yang diperoleh, produk NLC-DSL memiliki potensi sebagai kandidat obat parkinson.

Kata Kunci : L-Dopa, *Nanostructured Lipid Carrier*, Asam Laurat, Minyak Kedelai, Parkinson

ABSTRACT

L-Dopa is the primary choice in the treatment of Parkinson's disease, which has limited bioavailability and stability, requiring encapsulation using the nanostructured lipid carrier system (NLC). The research aims to obtain optimum formulation, characteristics, entrapment efficiency values, and drug release profiles of L-Dopa lauric acid and soy oil-based products. (NLC-DSL). The production of NLC-DSL is done using heat homogenization and ultrasonication with optimization variables covering lipid ratio, surface agent concentration, and ultrasound time. NLC-DSL characterization includes particle size determination, polydispersity index, and zeta potential using PSA, morphology using TEM, and function clustering using FTIR. The determination of entrapment efficiency values and drug release profile is done using UV-Vis spectroscopic photometry. The results show the optimum condition of production of NLC-DSL is obtained at a comparison of lauric acid to soy oil 1:9, a surface agent concentration of 2.5%, and an ultrasound time of 40 minutes. The resulting NLC-DSL product has a particulate size of $49,4 \pm 0,07$ nm with a polydispersibility index of 0,451 and a potential zeta of -44,3 mV. Analysis with FTIR shows a peak shift in the cluster of C=O, O-H and N-H that identifies the interaction between L-Dopa compounds with lauric acid and soybean oil. Meanwhile, TEM results showed a spherical shape with an average size of 49.73 nm. The percentage entrapment efficiency of NLC-DSL was obtained at 78.05%, and the NLC/DSL drug release profile showed the ability to release L-Dopa slowly and controlled for up to 6 hours and reach 51.20% at pH 1.2 following the Korsmeyer-Peppas kinetic model and 72.87% at pH 7.4 following the zero-order kinetics model after 24 hours. Based on the results obtained, the NLC-DSL product has potential as a candidate drug for Parkinson's disease.

Keywords: L-Dopa, Nanostructured Lipid Carrier, Lauric Acid, Soybean Oil, Parkinson's disease.

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DAFTAR PUSTAKA

- Agrawal, M., Saraf, S., Pradhan, M., Patel, R. J., Singhvi, G., Ajazuddin, & Alexander, A. (2021). Design and optimization of curcumin loaded nano lipid carrier system using Box-Behnken design. *Biomedicine and Pharmacotherapy*, 141. <https://doi.org/10.1016/j.biopha.2021.111919>
- Aisiyah, S., Harjanti, R., & Nopiyanti, V. (2019a). Pengaruh Panjang Rantai Karbon Lipid Padat terhadap Karakteristik Nanostructured Lipid Carrier Resveratrol. *JPSCR : Journal of Pharmaceutical Science and Clinical Research*, 4(2), 69. <https://doi.org/10.20961/jpscr.v4i2.34408>
- Aisiyah, S., Harjanti, R., & Nopiyanti, V. (2019b). Pengaruh Panjang Rantai Karbon Lipid Padat terhadap Karakteristik Nanostructured Lipid Carrier Resveratrol. *JPSCR : Journal of Pharmaceutical Science and Clinical Research*, 4(2), 69. <https://doi.org/10.20961/jpscr.v4i2.34408>
- Aisiyah, S., Harjanti, R., & Nopiyanti, V. (2019c). Pengaruh Panjang Rantai Karbon Lipid Padat terhadap Karakteristik Nanostructured Lipid Carrier Resveratrol. *JPSCR : Journal of Pharmaceutical Science and Clinical Research*, 4(2), 69. <https://doi.org/10.20961/jpscr.v4i2.34408>
- Akanda, M., Getti, G., & Douroumis, D. (2021). *In Vivo Evaluation of Nanostructured Lipid Carrier Systems (NLCs) in Mice Bearing Prostate Cancer Tumours*. <https://doi.org/10.21203/rs.3.rs-884461/v1>
- Alam, M., Ahmed, S., Nikita, Moon, G., Aqil, M., & Sultana, Y. (2018). Chemical engineering of a lipid nano-scaffold for the solubility enhancement of an antihyperlipidaemic drug, simvastatin; preparation, optimization, physicochemical characterization and pharmacodynamic study. *Artificial Cells, Nanomedicine, and Biotechnology*, 46(8), 1908–1919.
- Alia, S., Hidayati, H. B., Hamdan, M., Nugraha, P., Fahmi, A., Turchan, A., & Haryono, Y. (2021). *Penyakit Parkinson: Tinjauan Tentang Salah Satu Penyakit Neurodegeneratif yang Paling Umum* (Vol. 1, Issue 2).
- Amyliana, N. A., & Agustini, R. (2021). FORMULATION AND CHARACTERIZATION OF NANOENCAPSULATION YEAST BLACK RICE BY SONICATION METHOD WITH POLOXAMER. In *UNESA Journal of Chemistry* (Vol. 10, Issue 2).
- Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. *JAMA*, 323(6), 548–560. <https://doi.org/10.1001/JAMA.2019.22360>
- Ayuningrum, F. Tri. (2023). *Proyeksi penduduk Indonesia 2020-2050 : hasil sensus penduduk 2020*. Badan Pusat Statistik.

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- Borrelle, S. B., Ringma, J., Lavender Law, K., Monnahan, C. C., Lebreton, L., McGivern, A., Murphy, E., Jambeck, J., Leonard, G. H., Hilleary, M. A., Eriksen, M., Possingham, H. P., De Frond, H., Gerber, L. R., Polidoro, B., Tahir, A., Bernard, M., Mallos, N., Barnes, M., & Rochman, C. M. (2020). Predicted growth in plastic waste exceeds efforts to mitigate plastic pollution. *Science*, *369*(6509), 1515–1518. https://doi.org/10.1126/SCIENCE.ABA3656/SUPPL_FILE/ABA3656-BORRELLE-SM-DATA-S4.CSV
- Cao, C., Wang, Q., & Liu, Y. (2019). Lung cancer combination therapy: doxorubicin and β -elemene co-loaded, pH-sensitive nanostructured lipid carriers. *Drug Design, Development and Therapy*, 1087–1098.
- Castro, S. R., Ribeiro, L. N. M., Breikreitz, M. C., Guilherme, V. A., Rodrigues da Silva, G. H., Mitsutake, H., Alcântara, A. C. S., Yokaichiya, F., Franco, M. K. K. D., Clemens, D., Kent, B., Lancellotti, M., de Araújo, D. R., & de Paula, E. (2021). A pre-formulation study of tetracaine loaded in optimized nanostructured lipid carriers. *Scientific Reports*, *11*(1), 1–15. <https://doi.org/10.1038/s41598-021-99743-6>
- Cerri, S., & Blandini, F. (2020). An update on the use of non-ergot dopamine agonists for the treatment of Parkinson's disease. *Expert Opinion on Pharmacotherapy*, *21*(18), 2279–2291. <https://doi.org/10.1080/14656566.2020.1805432>
- Chauhan, I., Yasir, M., Verma, M., & Singh, A. P. (2020). Nanostructured lipid carriers: A groundbreaking approach for transdermal drug delivery. *Advanced Pharmaceutical Bulletin*, *10*(2), 150.
- Cirri, M., Bragagni, M., Mennini, N., & Mura, P. (2012). Development of a new delivery system consisting in “drug--in cyclodextrin--in nanostructured lipid carriers” for ketoprofen topical delivery. *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Fur Pharmazeutische Verfahrenstechnik e.V.*, *80*(1), 46–53. <https://doi.org/10.1016/J.EJPB.2011.07.015>
- Cunha, S., Costa, C. P., Loureiro, J. A., Alves, J., Peixoto, A. F., Forbes, B., Lobo, J. M. S., & Silva, A. C. (2020). Double optimization of rivastigmine-loaded nanostructured lipid carriers (NLC) for nose-to-brain delivery using the quality by design (QbD) approach: Formulation variables and instrumental parameters. *Pharmaceutics*, *12*(7), 1–27. <https://doi.org/10.3390/pharmaceutics12070599>
- Dahan, A., & González-álvarez, I. (2021). Regional intestinal drug absorption: Biopharmaceutics and drug formulation. In *Pharmaceutics* (Vol. 13, Issue 2, pp. 1–5). MDPI AG. <https://doi.org/10.3390/pharmaceutics13020272>

- 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.
- David R. Lide. (2006). CRC Handbook of Chemistry and Physics, 86th Edition Edited. In *Journal of the American Chemical Society* (86 th, Vol. 128, Issue 16). American Chemical Society. <https://doi.org/10.1021/ja0598681>
- DeMaagd, G., & Philip, A. (2015). Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. *P & T: A Peer-Reviewed Journal for Formulary Management*, *40*, 504–532.
- Dhanya, C. S., Paul, W., Rekha, M. R., & Joseph, R. (2023). Solid lipid nanoparticles of lauric Acid: A prospective drug carrier for oral drug delivery. *Journal of Molecular Liquids*, *380*, 121738. <https://doi.org/10.1016/J.MOLLIQ.2023.121738>
- Ding, S., Khan, A. I., Cai, X., Song, Y., Lyu, Z., Du, D., Dutta, P., & Lin, Y. (2020). Overcoming blood–brain barrier transport: Advances in nanoparticle-based drug delivery strategies. *Materials Today*, *37*, 112–125.
- Du, J., & Li, L. (2016). Which one performs better for targeted lung cancer combination therapy: pre- or post-bombesin-decorated nanostructured lipid carriers? *Drug Delivery*, *23*(5), 1799–1809. <https://doi.org/10.3109/10717544.2015.1099058>
- Eh Suk, V. R., Mohd. Latif, F., Teo, Y. Y., & Misran, M. (2020a). 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*, 3259–3266.
- Eh Suk, V. R., Mohd. Latif, F., Teo, Y. Y., & Misran, M. (2020b). 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>
- Ellis, J. M., & Fell, M. J. (2017). Current approaches to the treatment of Parkinson's Disease. *Bioorganic & Medicinal Chemistry Letters*, *27*(18), 4247–4255. <https://doi.org/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*, *29*(9), 999–1012. <https://doi.org/10.1016/j.jsps.2021.07.015>

- Fathi, H. A., Allam, A., Elsabahy, M., Fetih, G., & El-Badry, M. (2018). Nanostructured lipid carriers for improved oral delivery and prolonged antihyperlipidemic effect of simvastatin. *Colloids and Surfaces B: Biointerfaces*, 162, 236–245. <https://doi.org/https://doi.org/10.1016/j.colsurfb.2017.11.064>
- Fitzhugh, O. G., Schouboe, P. J., & Nelson, A. A. (1960). Oral toxicities of lauric acid and certain lauric acid derivatives. *Toxicology and Applied Pharmacology*, 2(1), 59–67.
- Fu, Y., & Kao, W. J. (2010). Drug release kinetics and transport mechanisms of non-degradable and degradable polymeric delivery systems. *Expert Opinion on Drug Delivery*, 7, 429–444. <https://api.semanticscholar.org/CorpusID:23420304>
- Gomaa, E., Fathi, H. A., Eissa, N. G., & Elsabahy, M. (2022). Methods for preparation of nanostructured lipid carriers. *Methods*, 199, 3–8. <https://doi.org/https://doi.org/10.1016/j.ymeth.2021.05.003>
- Haddad, F., Sawalha, M., Khawaja, Y., Najjar, A., & Karaman, R. (2018). Dopamine and levodopa prodrugs for the treatment of Parkinson's disease. In *Molecules* (Vol. 23, Issue 1). MDPI AG. <https://doi.org/10.3390/molecules23010040>
- Haqie, N. U. (2010). *Profil Pelepasan Atenolol Dari Matriks Eksiipien Koproses Kitosan-Ssg*. 1–81.
- Hayes, M. T. (2019). Parkinson's Disease and Parkinsonism. In *American Journal of Medicine* (Vol. 132, Issue 7, pp. 802–807). Elsevier Inc. <https://doi.org/10.1016/j.amjmed.2019.03.001>
- Herbianto, A. S. (2018). PENGARUH PERBEDAAN KONSENTRASI SURFAKTAN TERHADAP KARAKTER FISIK DAN pH NANOEMULSI PENCERAH KULIT. *CALYPTRA*, 7(1), 736–746.
- Honary, S., & Zahir, F. (2013). Effect of zeta potential on the properties of nano-drug delivery systems - A review (Part 1). *Tropical Journal of Pharmaceutical Research*, 12(2), 255–264. <https://doi.org/10.4314/tjpr.v12i2.19>
- Hung, L. C., Basri, M., Tejo, B. A., Ismail, R., Nang, H. L. L., Hassan, H. A., & May, C. Y. (2011). An improved method for the preparations of nanostructured lipid carriers containing heat-sensitive bioactives. *Colloids and Surfaces B: Biointerfaces*, 87(1), 180–186. <https://doi.org/https://doi.org/10.1016/j.colsurfb.2011.05.019>
- Ivanov, D., Levi, J. D., & Sredanovi, S. A. (2011). *FATTY ACID COMPOSITION OF VARIOUS SOYBEAN PRODUCTS*. <https://api.semanticscholar.org/CorpusID:87626312>

- Javed, S., Mangla, B., Almoshari, Y., Sultan, M. H., & Ahsan, W. (2022). Nanostructured lipid carrier system: A compendium of their formulation development approaches, optimization strategies by quality by design, and recent applications in drug delivery. *Nanotechnology Reviews*, *11*(1), 1744–1777. https://doi.org/10.1515/NTREV-2022-0109/ASSET/GRAPHIC/J_NTREV-2022-0109_FIG_004.JPG
- Joshi, M., & Patravale, V. (2006). Formulation and Evaluation of Nanostructured Lipid Carrier (NLC)-based Gel of Valdecoxib. *Drug Development and Industrial Pharmacy*, *32*(8), 911–918. <https://doi.org/10.1080/03639040600814676>
- Kakoty, M., & Gogoi, S. (2019). *Evaluation of Surfactant Formulation for EOR in Some Depleted Oil Fields of Upper Assam: Proceedings of the 2nd GeoMEast International Congress and Exhibition on Sustainable Civil Infrastructures, Egypt 2018 – The Official International Congress of the Soil-Structure Interaction Group in Egypt (SSIGE)* (pp. 57–75). https://doi.org/10.1007/978-3-030-01929-7_5
- Kelidari, H. R., Saeedi, M., Akbari, J., Morteza-semnani, K., Valizadeh, H., Maniruzzaman, M., Farmoudeh, A., & Nokhodchi, A. (2017). Development and Optimisation of Spironolactone Nanoparticles for Enhanced Dissolution Rates and Stability. *AAPS PharmSciTech*, *18*(5), 1469–1474. <https://doi.org/10.1208/s12249-016-0621-0>
- Khan, H. U., Aamir, K., Jusuf, P. R., Sethi, G., Sisinthy, S. P., Ghildyal, R., & Arya, A. (2021). Lauric acid ameliorates lipopolysaccharide (LPS)-induced liver inflammation by mediating TLR4/MyD88 pathway in Sprague Dawley (SD) rats. *Life Sciences*, *265*, 118750.
- Khosa, A., Reddi, S., & Saha, R. N. (2018). Nanostructured lipid carriers for site-specific drug delivery. *Biomedicine & Pharmacotherapy*, *103*, 598–613. <https://doi.org/10.1016/J.BIOPHA.2018.04.055>
- Lewitt, P. A. (2015a). Levodopa therapy for Parkinson's disease: Pharmacokinetics and pharmacodynamics. *Movement Disorders: Official Journal of the Movement Disorder Society*, *30*(1), 64–72. <https://doi.org/10.1002/MDS.26082>
- Lewitt, P. A. (2015b). Levodopa therapy for Parkinson's disease: Pharmacokinetics and pharmacodynamics. *Movement Disorders: Official Journal of the Movement Disorder Society*, *30*(1), 64–72. <https://doi.org/10.1002/MDS.26082>
- Li, P.-H., & Chiang, B.-H. (2012). Process optimization and stability of d-limonene-in-water nanoemulsions prepared by ultrasonic emulsification using response

- surface methodology. *Ultrasonics Sonochemistry*, 19(1), 192–197. <https://doi.org/https://doi.org/10.1016/j.ultsonch.2011.05.017>
- Li, Y., Li, C., Feng, F., Wei, W., & Zhang, H. (2021). Synthesis of medium and long-chain triacylglycerols by enzymatic acidolysis of algal oil and lauric acid. *LWT*, 136. <https://doi.org/10.1016/j.lwt.2020.110309>
- Lockman, P. R., Koziara, J. M., Mumper, R. J., & Allen, D. D. (2004). Nanoparticle surface charges alter blood–brain barrier integrity and permeability. *Journal of Drug Targeting*, 12(9–10), 635–641.
- Lu, Z.-H., Yang, M., Pan, C.-H., Zheng, P.-Y., & Zhang, S.-X. (2022). Multi-modal deep learning based on multi-dimensional and multi-level temporal data can enhance the prognostic prediction for multi-drug resistant pulmonary tuberculosis patients. *Science in One Health*, 1, 100004. <https://doi.org/10.1016/J.SOH.2022.100004>
- 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 Wwww.Jocpr.Com Journal of Chemical and Pharmaceutical Research*, 8(2), 627–643. www.jocpr.com
- Martien, R., Adhyatmika, A., Irianto, I. D. K., Farida, V., & Sari, D. P. (2012). Perkembangan teknologi nanopartikel sebagai sistem penghantaran obat. *Majalah Farmaseutik*, 8(1), 133–144.
- Martinez-Felipe, A., Cook, A. G., Abberley, J. P., Walker, R., Storey, J. M. D., & Imrie, C. T. (2016). An FT-IR spectroscopic study of the role of hydrogen bonding in the formation of liquid crystallinity for mixtures containing bipyridines and 4-pentoxybenzoic acid. *Rsc Advances*, 6(110), 108164–108179.
- Mary Ann Liebert, Inc. (1987). *Publishers Final Report on the Safety Assessment of Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid*.
- Mohanraj, V. J., & Chen, Y. (2006). Nanoparticles-A Review. In *Tropical Journal of Pharmaceutical Research* (Vol. 5, Issue 1). <http://www.tjpr.freehosting.net>
- Mollaei, F., Shiller, D. M., Baum, S. R., & Gracco, V. L. (2019). The relationship between speech perceptual discrimination and speech production in Parkinson's disease. *Journal of Speech, Language, and Hearing Research*, 62(12), 4256–4268.
- 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(October 2020), 102212. <https://doi.org/10.1016/j.jddst.2020.102212>

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- Müller, R. H., Radtke, M., & Wissing, S. A. (2002). Nanostructured lipid matrices for improved microencapsulation of drugs. *International Journal of Pharmaceutics*, 242(1–2), 121–128. [https://doi.org/10.1016/S0378-5173\(02\)00180-1](https://doi.org/10.1016/S0378-5173(02)00180-1)
- Nakayama, H., Nakahara, M., Matsugi, E., Soda, M., Hattoki, T., Hara, K., Usami, A., Kusumoto, C., Higashiyama, S., & Kitaichi, K. (2021). *Protective Effect of Ferulic Acid against Hydrogen Peroxide Induced Apoptosis in PC12 Cells*. 1–9. <https://doi.org/https://doi.org/10.3390/molecules26010090>
- Nallasamy, K., Gupta, S., Bansal, A., Biswal, M., Jayashree, M., Zaman, K., Williams, V., & Kumar, A. (2020). Clinical profile and predictors of intensive care unit admission in pediatric scrub typhus: A retrospective observational study from north India. *Indian Journal of Critical Care Medicine*, 24(6), 445–450. <https://doi.org/10.5005/jp-journals-10071-23445>
- Naseri, N., Valizadeh, H., & Zakeri-Milani, P. (2015). Solid Lipid Nanoparticles and Nanostructured Lipid Carriers: Structure, Preparation and Application. *Advanced Pharmaceutical Bulletin*, 5(3), 305–313. <https://doi.org/10.15171/APB.2015.043>
- Oktariza, Y., Amalia, L., Sobaryati, S., & Kurniawati, M. Y. (2019). Evaluasi Kualitas Hidup Pasien Parkinson Berdasarkan Terapi Berbasis Levodopa. *Indonesian Journal of Clinical Pharmacy*, 8(4), 246. <https://doi.org/10.15416/ijcp.2019.8.4.246>
- 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>
- Pandey, P. K., Sharma, A. K., & Gupta, U. (2016). Blood brain barrier: An overview on strategies in drug delivery, realistic in vitro modeling and in vivo live tracking. *Tissue Barriers*, 4(1). <https://doi.org/10.1080/21688370.2015.1129476>
- Pardeike, J., Hommoss, A., & Müller, R. H. (2009). Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *International Journal of Pharmaceutics*, 366(1–2), 170–184. <https://doi.org/10.1016/J.IJPHARM.2008.10.003>
- Pertiwi, H. (2015). Evaluasi Profil Disolusi Tablet Lepas Lambat Teofilin yang Beredar di Masyarakat. *Universitas Islam Negeri Syarif Hidayatullah*.
- Poerwanto, S., Hidayat, C., & Supriyadi, S. (2010). SINTESIS LIPIDA TERSTRUKTUR DARI ASAM LAURAT DAN GLISEROL DALAM

PELARUT ISOOKTANA DENGAN BIOKATALIS LIPASE *Candida rugosa*.
Reaktor, 13. <https://doi.org/10.14710/reaktor.13.1.44-50>

- Pokharkar, V., Patil-Gadhe, A., & Kaur, G. (2018a). Physicochemical and pharmacokinetic evaluation of rosuvastatin loaded nanostructured lipid carriers: influence of long- and medium-chain fatty acid mixture. *Journal of Pharmaceutical Investigation*, 48(4), 465–476. <https://doi.org/10.1007/s40005-017-0342-8>
- Pokharkar, V., Patil-Gadhe, A., & Kaur, G. (2018b). Physicochemical and pharmacokinetic evaluation of rosuvastatin loaded nanostructured lipid carriers: influence of long- and medium-chain fatty acid mixture. *Journal of Pharmaceutical Investigation*, 48(4), 465–476. <https://doi.org/10.1007/s40005-017-0342-8>
- Pratap-Singh, A., Guo, Y., Lara Ochoa, S., Fathordoobady, F., & Singh, A. (2021). Optimal ultrasonication process time remains constant for a specific nanoemulsion size reduction system. *Scientific Reports*, 11(1). <https://doi.org/10.1038/s41598-021-87642-9>
- Prieto, C., & Calvo, L. (2013). Performance of the Biocompatible Surfactant Tween 80, for the Formation of Microemulsions Suitable for New Pharmaceutical Processing. *Journal of Applied Chemistry*, 2013, 1–10. <https://doi.org/10.1155/2013/930356>
- Prihantini, M., Zulfa, E., Prastiwi, L. D., & Yulianti, I. D. (2020). PENGARUH WAKTU ULTRASONIKASI TERHADAP KARAKTERISTIK FISIKA NANOPARTIKEL KITOSAN EKSTRAK ETANOL DAUN SUJI (*Pleomele angustifolia*) DAN UJI STABILITAS FISIKA MENGGUNAKAN METODE CYCLING TEST. *Jurnal Ilmu Farmasi Dan Farmasi Klinik*, 16(02), 125. <https://doi.org/10.31942/jiffk.v16i02.3237>
- Rabima, R., & Saru Purnama, M. (2019). Entrapment efficiency and drug loading of curcumin nanostructured lipid carrier (NLC) formula. *Pharmaciana*, 9(2), 299–306.
- Rahmadanti, S. (2023). *ESTD UPI*. Universitas Pendidikan Indonesia.
- Rochman, M. F., Darmawan, A., & Wardhana, P. (2022a). Nanostructured Lipid Carriers System Solid Lipid Poloxamer and Stearic Acid with Liquid Lipid Soybean Oil. *Jurnal Ilmiah Medicamento*, 8(1), 1–7. <https://doi.org/10.36733/medicamento.v8i1.3161>
- Rochman, M. F., Darmawan, A., & Wardhana, P. (2022b). Nanostructured Lipid Carriers System Solid Lipid Poloxamer and Stearic Acid with Liquid Lipid Soybean Oil. *Jurnal Ilmiah Medicamento*, 8(1), 1–7. <https://doi.org/10.36733/medicamento.v8i1.3161>

Ai Susanti, 2024

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Universitas Pendidikan Indonesia | repository.upi.edu | perpustakaan.upi.edu

- Rustan, A. Chr., & Drevon, C. A. (2020). Fatty Acids: Structures and Properties. *ELS*. <https://api.semanticscholar.org/CorpusID:11335130>
- Saedi, A., Rostamizadeh, K., Parsa, M., Dalali, N., & Ahmadi, N. (2018). Preparation and characterization of nanostructured lipid carriers as drug delivery system: Influence of liquid lipid types on loading and cytotoxicity. *Chemistry and Physics of Lipids*, 216, 65–72. <https://doi.org/https://doi.org/10.1016/j.chemphyslip.2018.09.007>
- Saghafi, Z., Mohammadi, M., Mahboobian, M. M., & Derakhshandeh, K. (2021). Preparation, characterization, and in vivo evaluation of perphenazine-loaded nanostructured lipid carriers for oral bioavailability improvement. *Drug Development and Industrial Pharmacy*, 47(3), 509–520. <https://doi.org/10.1080/03639045.2021.1892745>
- Saifullah, Md., Ahsan, A., & Shishir, M. R. I. (2016). 12 - Production, stability and application of micro- and nanoemulsion in food production and the food processing industry. In A. M. Grumezescu (Ed.), *Emulsions* (pp. 405–442). Academic Press. <https://doi.org/https://doi.org/10.1016/B978-0-12-804306-6.00012-X>
- Salih, R. O. (2023). Parkinson Disease: review. *Journal of Multidisciplinary Research, Biology, Chemistry and Medicine*, 5, 84–95. <https://doi.org/https://doi.org/10.47577/biochemmed.v5i.8847>
- Salvi, V. R., & Pawar, P. (2019). Nanostructured lipid carriers (NLC) system: A novel drug targeting carrier. In *Journal of Drug Delivery Science and Technology* (Vol. 51, pp. 255–267). Editions de Sante. <https://doi.org/10.1016/j.jddst.2019.02.017>
- Seyfoddin, A., Sherwin, T., V Patel, D., N McGhee, C., D Rupenthal, I., A Taylor, J., & Al-Kassas, R. (2016a). Ex vivo and in vivo evaluation of chitosan coated nanostructured lipid carriers for ocular delivery of acyclovir. *Current Drug Delivery*, 13(6), 923–934.
- Seyfoddin, A., Sherwin, T., V Patel, D., N McGhee, C., D Rupenthal, I., A Taylor, J., & Al-Kassas, R. (2016b). Ex vivo and in vivo evaluation of chitosan coated nanostructured lipid carriers for ocular delivery of acyclovir. *Current Drug Delivery*, 13(6), 923–934.
- Shah, N. V., Seth, A. K., Balaraman, R., Aundhia, C. J., Maheshwari, R. A., & Parmar, G. R. (2016). Nanostructured lipid carriers for oral bioavailability enhancement of raloxifene: Design and in vivo study. *Journal of Advanced Research*, 7(3), 423–434. <https://doi.org/10.1016/J.JARE.2016.03.002>
- Soeratri, W., Hidayah, R., & Rosita, N. (2019a). Effect of Combination Soy Bean Oil and Oleic Acid to Characteristic, Penetration, Physical Stability of

- Nanostructure Lipid Carrier Resveratrol. *Folia Medica Indonesiana*, 55(3), 213. <https://doi.org/10.20473/fmi.v55i3.15505>
- Soeratri, W., Hidayah, R., & Rosita, N. (2019b). Effect of Combination Soy Bean Oil and Oleic Acid to Characteristic, Penetration, Physical Stability of Nanostructure Lipid Carrier Resveratrol. *Folia Medica Indonesiana*, 55(3), 213. <https://doi.org/10.20473/fmi.v55i3.15505>
- Solikah, A. (2021). Box-Behnken Design for Optimization of Nanostructured Lipid Carrier Sonication Conditions from Mixtures of Palm Stearin and Palm Olein. In *RESEARCH ARTICLE 522 Indonesian Journal of Pharmacy Indonesian J Pharm* (Vol. 32, Issue 4).
- Song, A., Zhang, X., Li, Y., Mao, X., & Han, F. (2016). Effect of liquid-to-solid lipid ratio on characterizations of flurbiprofen-loaded solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) for transdermal administration. *Drug Development and Industrial Pharmacy*, 42(8), 1308–1314.
- Subramaniam, B., Siddik, Z. H., & Nagoor, N. H. (2020). Optimization of nanostructured lipid carriers: understanding the types, designs, and parameters in the process of formulations. *Journal of Nanoparticle Research*, 22(6), 141. <https://doi.org/10.1007/s11051-020-04848-0>
- Sukondari, B., Tunjung Sari, D., Hutagalung, H. S., Raisa, N., & Marisdina, S. (2024). *Perhimpunan Dokter Spesialis Neurologi Indonesia 2024 Panduan Tatalaksana*.
- Tamjidi, F., Shahedi, M., Varshosaz, J., & Nasirpour, A. (2013a). Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. *Innovative Food Science & Emerging Technologies*, 19, 29–43. <https://doi.org/https://doi.org/10.1016/j.ifset.2013.03.002>
- Tamjidi, F., Shahedi, M., Varshosaz, J., & Nasirpour, A. (2013b). Nanostructured lipid carriers (NLC): A potential delivery system for bioactive food molecules. *Innovative Food Science & Emerging Technologies*, 19, 29–43.
- Thomas, S., Thomas, R., Zachariah, A., & Mishra, R. (2017). Spectroscopic Methods for Nanomaterials Characterization. In *Spectroscopic Methods for Nanomaterials Characterization*. <https://doi.org/10.1016/B978-0-323-46140-5.01001-3>
- Tsamarah, D. F., Izzaturrahmi, A. S., & Sopyan, I. (2023). Sistem Penghantaran Obat Limfatik: Peningkatan Bioavailabilitas Obat dengan Nanopartikel. *Majalah Farmasetika*, 8(5), 475. <https://doi.org/10.24198/MFARMASETIKA.V8I5.47852>

- Turana, Y., Tenglawan, J., Suswanti, I., Suharya, D. Y., Riyadina, W., & Pradono, J. (2019). Primary Prevention of Alzheimer's Disease in Indonesia. *International Journal of Aging Research*. <https://doi.org/10.28933/ijoar-2019-06-2506>
- Wang, M., Jin, Y., Yang, Y., Zhao, C., Yang, H., Xu, X., Qin, X., Wang, Z., Zhang, Z., & Jian, Y. (2010). In vivo biodistribution, anti-inflammatory, and hepatoprotective effects of liver targeting dexamethasone acetate loaded nanostructured lipid carrier system. *International Journal of Nanomedicine*, 487–497.
- Witayaudom, P., & Klinkesorn, U. (2017). Effect of surfactant concentration and solidification temperature on the characteristics and stability of nanostructured lipid carrier (NLC) prepared from rambutan (*Nephelium lappaceum* L.) kernel fat. *Journal of Colloid and Interface Science*, 505, 1082–1092. <https://doi.org/10.1016/J.JCIS.2017.07.008>
- Yue-Xing, C., Fei-Fei, Y., Han, W., Tao-Tao, F., Chun-Yu, L., Li-Hui, Q., & Yong-Hong, L. (2018). The effect of l-leucine on the stabilization and inhalability of spray-dried solid lipid nanoparticles for pulmonary drug delivery. *Journal of Drug Delivery Science and Technology*, 46, 474–481. <https://doi.org/https://doi.org/10.1016/j.jddst.2018.06.011>
- Zhang, X., Gan, Y., Gan, L., Nie, S., & Pan, W. (2008). PEGylated nanostructured lipid carriers loaded with 10-hydroxycamptothecin: an efficient carrier with enhanced anti-tumour effects against lung cancer. *Journal of Pharmacy and Pharmacology*, 60(8), 1077–1087. <https://doi.org/10.1211/jpp.60.8.0014>
- Zhang, Z., Chen, Y., Klausen, L. H., Skaanvik, S. A., Wang, D., Chen, J., & Dong, M. (2023). The Rational Design and Development of Microalgae-Based Biohybrid Materials for Biomedical Applications. *Engineering*, 24, 102–113. <https://doi.org/10.1016/j.eng.2022.09.016>