

- Ahmad, J., Mir, S.R., Kohli, K., Chuttani, K., Mishra, A.K., Panda, A.K., dan Amin, S., 2014. Solid-Nanoemulsion Preconcentrate for Oral Delivery of Paclitaxel: Formulation Design, Biodistribution, and γ Scintigraphy Imaging. *BioMed Research International*, 1–12.
- Ahmad, N., Fazal, H., Abbasi, B.H., Farooq, S., Ali, M., dan Khan, M.A., 2012. Biological role of Piper nigrum L. (Black pepper): A review. *Asian Pacific Journal of Tropical Biomedicine*, **2**: S1945–S1953.
- Al-Khattawi, A., Koner, J., Rue, P., Kirby, D., Perrie, Y., Rajabi-Siahboomi, A., dan Mohammed, A.R., 2015. A pragmatic approach for engineering porous mannitol and mechanistic evaluation of particle performance. *European Journal of Pharmaceutics and Biopharmaceutics*, **94**: 1–10.
- Alves, F.S., Rodrigues Do Rego, J. de A., Da Costa, M.L., Lobato Da Silva, L.F., Da Costa, R.A., Cruz, J.N., dan Brasil, D.D.S.B., 2019. Spectroscopic methods and in silico analyses using density functional theory to characterize and identify piperine alkaloid crystals isolated from pepper (Piper Nigrum L.). *Journal of Biomolecular Structure and Dynamics*, **38**: 2792–2799.
- Ameeduzzafar, Z., El-Bagory, I., Alruwaili, N.K., Elkomy, M.H., Ahmad, J., Afzal, M., Ahmad, N., Elmowafy, M., Alharbi, K.S., dan Md, S.A., 2019. Development of novel dapagliflozin loaded solid self-nanoemulsifying oral delivery system: Physiochemical characterization and in vivo antidiabetic activity. *Journal of Drug Delivery Science and Technology*, **54**: 1–12.
- An, Y., Yan, X., Li, B., dan Li, Y., 2014. Microencapsulation of capsanthin by self-emulsifying nanoemulsions and stability evaluation. *European food research & technology*, **239**: 1077–1085.
- Anton, N., Benoit, J.-P., dan Saulnier, P., 2008. Design and production of nanoparticles formulated from nano-emulsion templates-a review. *Journal of Controlled Release: Official Journal of the Controlled Release Society*, **128**: 185–199.
- Anton, N. dan Vandamme, T.F., 2009. The universality of low-energy nano-emulsification. *International Journal of Pharmaceutics*, **377**: 142–147.
- Ashour, E.A., Majumdar, S., Alsheteli, A., Alshehri, S., Alsulays, B., Feng, X., Gryczke, A., Kolter, K., Langley, N., dan Repka, M.A., 2016. Hot melt extrusion as an approach to improve solubility, permeability and oral absorption of a

psychoactive natural product, piperine. *Journal of Pharmacy and Pharmacology*, **68**: 989–998.

- Atef, E. dan Belmonte, A.A., 2008. Formulation and in vitro and in vivo characterization of a phenytoin self-emulsifying drug delivery system (SEDDS). *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **35**: 257–263.
- Aukunuru, J.V. dan Bonepally, C.R., 2017. Optimization of Encapsulation Efficiency of Piperine in Soya- Lecithin Multilamellar Vesicles. *International Journal of ChemTech Research*, **10**: 723–729.
- Badran, M.M., Taha, E.I., Tayel, M.M., dan Al-Suwayeh, S.A., 2014. Ultra-fine self nanoemulsifying drug delivery system for transdermal delivery of meloxicam: Dependency on the type of surfactants. *Journal of Molecular Liquids*, **190**: 16–22.
- Balakrishnan, P., Lee, B.-J., Oh, D.H., Kim, J.O., Hong, M.J., Jee, J.-P., Kim, J.A., Yoo, B.K., Woo, J.S., Yong, C.S., dan Choi, H.-G., 2009a. Enhanced oral bioavailability of dexibuprofen by a novel solid self-emulsifying drug delivery system (SEDDS). *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Fur Pharmazeutische Verfahrenstechnik e.V.*, **72**: 539–545.
- Balakrishnan, P., Lee, B.-J., Oh, D.H., Kim, J.O., Lee, Y.-I., Kim, D.-D., Jee, J.-P., Lee, Y.-B., Woo, J.S., Yong, C.S., dan Choi, H.-G., 2009b. Enhanced oral bioavailability of Coenzyme Q10 by self-emulsifying drug delivery systems. *International journal of pharmaceutics*, **374**: 66–72.
- Bandyopadhyay, S., Katare, O.P., dan Singh, B., 2012. Optimized self nano-emulsifying systems of ezetimibe with enhanced bioavailability potential using long chain and medium chain triglycerides. *Colloids and Surfaces. B, Biointerfaces*, **100**: 50–61.
- Bang, J.S., Oh, D.H., Choi, H.M., Sur, B.J., Lim, S.J., Yeon, J.Y., Yang, H.I., Chul, M.C., Hahm, D.H., dan Kim, K.S., 2009. Anti-inflammatory and antiarthritic effects of piperine in human interleukin 1 β -stimulated fibroblast-like synoviocytes and in rat arthritis models. *Arthritis Research and Therapy*, **11**: 1–9.
- Bari, A., Chella, N., Sanka, K., Shastri, N.R., dan Diwan, P.V., 2015. Improved anti-diabetic activity of glibenclamide using oral self nano emulsifying powder. *Journal of Microencapsulation*, **32**: 54–60.

Basalious, E.B., Shawky, N., dan Badr-Eldin, S.M., 2010. SNEDDS containing bioenhancers for improvement of dissolution and oral absorption of lacidipine. I: development and optimization. *International Journal of Pharmaceutics*, **391**: 203–211.

Bäumler, E.R., Carrín, M.E., dan Carelli, A.A., 2016. Extraction of sunflower oil using ethanol as solvent. *Journal of Food Engineering*, **178**: 190–197.

Bhalekar, M.R., Madgulkar, A.R., Desale, P.S., dan Marium, G., 2017. Formulation of piperine solid lipid nanoparticles (SLN) for treatment of rheumatoid arthritis. *Drug Development and Industrial Pharmacy*, **43**: 1003–1010.

Brittain, H.G., 2001. X-ray Diffraction III: Pharmaceutical Applications. *Spectroscopy*, **16**: 1–5.

Burger, A., Henck, J.O., Hetz, S., Rollinger, J.M., Weissnicht, A.A., dan Stöttner, H., 2000. Energy/temperature diagram and compression behavior of the polymorphs of D-mannitol. *Journal of Pharmaceutical Sciences*, **89**: 457–468.

Carosso, S. dan Miller, M.J., 2014. Nitroso Diels–Alder (NDA) reaction as an efficient tool for the functionalization of diene-containing natural products. *Organic & Biomolecular Chemistry*, **12**: 7445–7468.

Cavallari, C., Rodriguez, L., Albertini, B., Passerini, N., Rosetti, F., dan Fini, A., 2005. Thermal and fractal analysis of diclofenac/Gelucire 50/13 microparticles obtained by ultrasound-assisted atomization. *Journal of Pharmaceutical Sciences*, **94**: 1124–1134.

Cerpnjak, K., Zvonar, A., Gašperlin, M., dan Vrečer, F., 2013. Lipid-based systems as a promising approach for enhancing the bioavailability of poorly water-soluble drugs. *Acta Pharmaceutica (Zagreb, Croatia)*, **63**: 427–445.

Chan, C.C., Lee, Y.C., Lam, H., dan Zhang, X.-M. (Editor), 2004. *Analytical Method Validation and Instrument Performance Verification*. John Wiley & Sons, Hoboken, N.J.

Chatterjee, B., Hamed Almurisi, S., Ahmed Mahdi Dukhan, A., Mandal, U.K., dan Sengupta, P., 2016. Controversies with self-emulsifying drug delivery system from pharmacokinetic point of view. *Drug Delivery*, **23**: 3639–3652.

Chaudhri, V.K., 2017. Isolation and Evaluation of Piperine from Black Pepper and White Pepper. *World Journal of Pharmacy and Pharmaceutical Sciences*, **6**: 1424–1430.

- Cherniakov, I., Domb, A.J., dan Hoffman, A., 2015. Self-nano-emulsifying drug delivery systems: an update of the biopharmaceutical aspects. *Expert Opinion on Drug Delivery*, **12**: 1121–1133.
- Cole, E.T., Cadé, D., dan Benameur, H., 2008. Challenges and opportunities in the encapsulation of liquid and semi-solid formulations into capsules for oral administration. *Advanced Drug Delivery Reviews*, **60**: 747–756.
- Cornell, J.A., 2002. The Analysis of Mixture Data, dalam: *Experiments with Mixtures: Designs, Models, and the Analysis of Mixture Data, Third Edition*. John Wiley & Sons, Ltd, hal. 223–285.
- Dash, S., Kumar, A., Mandal, B.N., Lal, K., dan Kumar, D., 2018. Experiments with mixtures. *Bhartiya Krishi Anusandhan Patrika*, **33**: 181–184.
- Date, A.A., Desai, N., Dixit, R., dan Nagarsenker, M., 2010. Self-nanoemulsifying drug delivery systems: formulation insights, applications and advances. *Nanomedicine (London, England)*, **5**: 1595–1616.
- Date, A.A. dan Nagarsenker, M.S., 2007. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for cefpodoxime proxetil. *International Journal of Pharmaceutics*, **329**: 166–172.
- Depkes RI, 2008. *Farmakope Herbal Indonesia*, Edisi I. Departemen Kesehatan RI, Jakarta.
- Dewan, I., Shahriar, M., dan Islam, A., 2011. Study of Differential Scanning Calorimetry of Atorvastatin in Solid Solution. *Bangladesh Pharmaceutical Journal*, **14**: 141–146.
- Do, Q.D., Angkawijaya, A.E., Tran-Nguyen, P.L., Huynh, L.H., Soetaredjo, F.E., Ismadji, S., dan Ju, Y.-H., 2014. Effect of extraction solvent on total phenol content, total flavonoid content, and antioxidant activity of *Limnophila aromatica*. *Journal of Food and Drug Analysis*, **22**: 296–302.
- Du, X. dan He, J., 2010. Fine-tuning of silica nanosphere structure by simple regulation of the volume ratio of cosolvents. *Langmuir: the ACS journal of surfaces and colloids*, **26**: 10057–10062.
- Dutta, S. dan Bhattacharjee, P., 2016. Modeling of supercritical carbon dioxide extraction of piperine from Malabar black pepper. *Materials Today: Proceedings*, **3**: 3238–3252.

- Dutta, S. dan Bhattacharjee, P., 2017. Nanoliposomal encapsulates of piperine-rich black pepper extract obtained by enzyme-assisted supercritical carbon dioxide extraction. *Journal of Food Engineering*, **201**: 49–56.
- Ebrahimi, A., Saffari, M., dan Langrish, T., 2015a. Spray Drying and Post-Processing Production of Highly-Porous Lactose Particles Using Sugars as Templating Agents. *Powder Technology*, **283**: 171–177.
- Ebrahimi, A., Saffari, M., dan Langrish, T., 2015b. Developing a new production process for high-porosity lactose particles with high degrees of crystallinity. *Powder Technology*, **272**: 45–53.
- Ee, G.C.L., Lim, C.M., Rahmani, M., Shaari, K., dan Bong, C.F.J., 2010. Pellitorine, a potential anti-cancer lead compound against HL6 and MCT-7 cell lines and microbial transformation of piperine from Piper Nigrum. *Molecules (Basel, Switzerland)*, **15**: 2398–2404.
- Elnaggar, Y.S.R., Etman, S.M., Abdelmonsif, D.A., dan Abdallah, O.Y., 2015. Novel piperine-loaded Tween-integrated monoolein cubosomes as brain-targeted oral nanomedicine in Alzheimer's disease: pharmaceutical, biological, and toxicological studies. *International Journal of Nanomedicine*, **10**: 5459–5473.
- El-Sherif, D.M. dan Wheatley, M.A., 2003. Development of a novel method for synthesis of a polymeric ultrasound contrast agent. *Journal of Biomedical Materials Research. Part A*, **66**: 347–355.
- Emmanuelawati, I., Yang, J., Zhang, J., Zhang, H., Zhou, L., dan Yu, C., 2013. Low-cost and large-scale synthesis of functional porous materials for phosphate removal with high performance. *Nanoscale*, **5**: 6173–6180.
- Escorsim, A.M., da Rocha, G., Vargas, J.V.C., Mariano, A.B., Ramos, L.P., Corazza, M.L., dan Cordeiro, C.S., 2018. Extraction of *Acutodesmus obliquus* lipids using a mixture of ethanol and hexane as solvent. *Biomass and Bioenergy*, **108**: 470–478.
- Etman, S.M., Elnaggar, Y.S.R., Abdelmonsif, D.A., dan Abdallah, O.Y., 2018. Oral Brain-Targeted Microemulsion for Enhanced Piperine Delivery in Alzheimer's Disease Therapy: In Vitro Appraisal, In Vivo Activity, and Nanotoxicity. *AAPS PharmSciTech*, **19**: 3698–3711.
- Ezawa, T., Inoue, Y., Murata, I., Takao, K., Sugita, Y., dan Kanamoto, I., 2018. Characterization of the Dissolution Behavior of Piperine/Cyclodextrins Inclusion Complexes. *AAPS PharmSciTech*, **19**: 923–933.

- Fauzi, S.H.M., Rashid, N.A., dan Omar, Z., 2013. Effects of chemical interesterification on the physicochemical, microstructural and thermal properties of palm stearin, palm kernel oil and soybean oil blends. *Food Chemistry*, **137**: 8–17.
- Fernandez-Tarrio, M., Yañez, F., Immesoete, K., Alvarez-Lorenzo, C., dan Concheiro, A., 2008. Pluronic and tetronic copolymers with polyglycolized oils as self-emulsifying drug delivery systems. *AAPS PharmSciTech*, **9**: 471–479.
- Galvan, D., Effting, L., Cremasco, H., dan Conte-Junior, C.A., 2021. Recent Applications of Mixture Designs in Beverages, Foods, and Pharmaceutical Health: A Systematic Review and Meta-Analysis. *Foods*, **10**: 1941.
- Gershanik, T. dan Benita, S., 2000. Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs. *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Fur Pharmazeutische Verfahrenstechnik e.V*, **50**: 179–188.
- Gervelas, C., Serandour, A.-L., Geiger, S., Grillon, G., Fritsch, P., Taulelle, C., Le Gall, B., Benech, H., Deverre, J.-R., Fattal, E., dan Tsapis, N., 2007. Direct lung delivery of a dry powder formulation of DTPA with improved aerosolization properties: effect on lung and systemic decorporation of plutonium. *Journal of controlled release*, **118**: 78–86.
- Gu, F., Huang, F., Wu, G., dan Zhu, H., 2018. Contribution of Polyphenol Oxidation, Chlorophyll and Vitamin C Degradation to the Blackening of Piper nigrum L. *Molecules : A Journal of Synthetic Chemistry and Natural Product Chemistry*, **23**: 370.
- Gustavo González, A. dan Ángeles Herrador, M., 2007. A practical guide to analytical method validation, including measurement uncertainty and accuracy profiles. *TrAC Trends in Analytical Chemistry*, **26**: 227–238.
- Han, Y., Chin Tan, T.M., dan Lim, L.-Y., 2008. In vitro and in vivo evaluation of the effects of piperine on P-gp function and expression. *Toxicology and Applied Pharmacology*, **230**: 283–289.
- Hanus, M.J. dan Langrish, T.G., 2007. Re-entrainment of wall deposits from a laboratory-scale spray dryer. *Asia-Pacific Journal of Chemical Engineering*, **2**: 90–107.
- Hauss, D.J., 2007. Oral lipid-based formulations. *Advanced Drug Delivery Reviews*, **59**: 667–676.

- Hill, T. dan Lewicki, P., 2006. *Statistics: Methods and Applications: A Comprehensive Reference for Science, Industry, and Data Mining, 1st Ed.* StatSoft, Inc, Tusla, OK, USA.
- Holm, R., Jensen, I.H.M., dan Sonnergaard, J., 2006. Optimization of self-microemulsifying drug delivery systems (SMEDDS) using a D-optimal design and the desirability function. *Drug Development and Industrial Pharmacy*, **32**: 1025–1032.
- Hooda, A., Nanda, A., Jain, M., Kumar, V., dan Rathee, P., 2012. Optimization and evaluation of gastroretentive ranitidine HCl microspheres by using design expert software. *International Journal of Biological Macromolecules*, **51**: 691–700.
- Hu, X., Lin, C., Chen, D., Zhang, J., Liu, Z., Wu, W., dan Song, H., 2012. Sirolimus solid self-microemulsifying pellets: formulation development, characterization and bioavailability evaluation. *International Journal of Pharmaceutics*, **438**: 123–133.
- Hulse, W.L., Forbes, R.T., Bonner, M.C., dan Getrost, M., 2009. The characterization and comparison of spray-dried mannitol samples. *Drug Development and Industrial Pharmacy*, **35**: 712–718.
- ICH, 2005. *Q2 (R1), "Validation of Analytical Procedures: Text and Methodology" ICH Harmonised Tripartite Guideline*. International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use, Chicago, USA.
- Ikan, R., 2013. *Natural Products: A Laboratory Guide*. Elsevier.
- Inugala, S., Eedara, B.B., Sunkavalli, S., Dhurke, R., Kandadi, P., Jukanti, R., dan Bandari, S., 2015. Solid self-nanoemulsifying drug delivery system (S-SNEDDS) of darunavir for improved dissolution and oral bioavailability: In vitro and in vivo evaluation. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **74**: 1–10.
- Jain, A., Hurkat, P., dan Jain, S.K., 2019. Development of liposomes using formulation by design: Basics to recent advances. *Chemistry and Physics of Lipids*, **224**: 104764.
- Kadu, P.J., Kushare, S.S., Thacker, D.D., dan Gattani, S.G., 2011. Enhancement of oral bioavailability of atorvastatin calcium by self-emulsifying drug delivery systems (SEDDS). *Pharmaceutical Development and Technology*, **16**: 65–74.

- Kang, J.H., Oh, D.H., Oh, Y.-K., Yong, C.S., dan Choi, H.-G., 2012. Effects of solid carriers on the crystalline properties, dissolution and bioavailability of flurbiprofen in solid self-nanoemulsifying drug delivery system (solid SNEDDS). *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Fur Pharmazeutische Verfahrenstechnik e.V*, **80**: 289–297.
- Karehill, P.G., Glazer, M., dan Nyström, C., 1990. Studies on direct compression of tablets. XXIII. The importance of surface roughness for the compactability of some directly compressible materials with different bonding and volume reduction properties. *International Journal of Pharmaceutics*, **64**: 35–43.
- Kathavarayan dan Yoo, Y.J., 2017. Enhanced solubility of piperine using hydrophilic carrier-based potent solid dispersion systems. *Drug Development and Industrial Pharmacy*, **43**: 1501–1509.
- Kerns, E.H. dan Di, L., 2008. *Drug-like Properties: Concepts, Structure Design and Methods; from ADME to Toxicity Optimization; [Metabolism, Solubility, Pharmacokinetics, Permeability, CYP Inhibition, Toxicity, Prodrugs]*. Elsevier, Acad. Press, Amsterdam.
- Khajuria, A., Thusu, N., dan Zutshi, U., 2002. Piperine modulates permeability characteristics of intestine by inducing alterations in membrane dynamics: influence on brush border membrane fluidity, ultrastructure and enzyme kinetics. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology*, **9**: 224–231.
- Khan, A.W., Kotta, S., Ansari, S.H., Sharma, R.K., dan Ali, J., 2012. Potentials and challenges in self-nanoemulsifying drug delivery systems. *Expert Opinion on Drug Delivery*, **9**: 1305–1317.
- Khan, A.W., Kotta, S., Ansari, S.H., Sharma, R.K., dan Ali, J., 2015. Self-nanoemulsifying drug delivery system (SNEDDS) of the poorly water-soluble grapefruit flavonoid Naringenin: design, characterization, *in vitro* and *in vivo* evaluation. *Drug Delivery*, **22**: 552–561.
- Khan, S., Mirza, K.J., Anwar, F., dan Abidin, M.Z., 2010. Development of RAPD markers for authentication of *Piper nigrum* (L.). *Environment & We An International Journal of Science & Technology*, **5**: 47–56.
- Khan, Z., Moni, F., Sharmin, S., Al-Mansur, M., Gafur, A., Rahman, O., dan Afroz, F., 2017. Isolation of Bulk Amount of Piperine as Active Pharmaceutical Ingredient

- Khanolkar, A., Thorat, V., Raut, P., dan Samanta, G., 2017. Application of Quality by Design: Development to Manufacturing of Diclofenac Sodium Topical Gel. *AAPS PharmSciTech*, **18**: 2754–2763.
- Kibbe, A.H., 2000. *Handbook of Pharmaceutical Excipients*. American Pharmaceutical Association, Washington, D.C.
- Kim, D.S., Cho, J.H., Park, J.H., Kim, J.S., Song, E.S., Kwon, J., Giri, B.R., Jin, S.G., Kim, K.S., Choi, H.-G., dan Kim, D.W., 2019. Self-microemulsifying drug delivery system (SMEDDS) for improved oral delivery and photostability of methotrexate. *International Journal of Nanomedicine*, **14**: 4949–4960.
- Kim, K.S., Yang, E.S., Kim, D.S., Kim, D.W., Yoo, H.H., Yong, C.S., Youn, Y.S., Oh, K.T., Jee, J.P., Kim, J.O., Jin, S.G., dan Choi, H.G., 2017. A novel solid self-nanoemulsifying drug delivery system (S-SNEDDS) for improved stability and oral bioavailability of an oily drug, 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol. *Drug Delivery*, **24**: 1018–1025.
- Koga, K., Kawashima, S., dan Murakami, M., 2002. In vitro and in situ evidence for the contribution of Labrasol and Gelucire 44/14 on transport of cephalexin and cefoperazone by rat intestine. *European journal of pharmaceutics and biopharmaceutics*, **54**: 311–318.
- Kotte, S.C.B., Dubey, P.K., dan Murali, P.M., 2014. Identification and characterization of stress degradation products of piperine and profiling of a black pepper (*Piper nigrum* L.) extract using LC/Q-TOF-dual ESI-MS. *Analytical Methods*, **6**: 8022–8029.
- Koul, I.B. dan Kapil, A., 1993. Evaluation of the liver protective potential of piperine, an active principle of black and long peppers. *Planta Medica*, **59**: 413–417.
- Kozukue, N., Park, M.-S., Choi, S.-H., Lee, S.-U., Ohnishi-Kameyama, M., Levin, C.E., dan Friedman, M., 2007. Kinetics of light-induced cis-trans isomerization of four piperines and their levels in ground black peppers as determined by HPLC and LC/MS. *Journal of Agricultural and Food Chemistry*, **55**: 7131–7139.
- Krstić, M., Medarević, Đ., Đuriš, J., dan Ibrić, S., 2018. Chapter 12 - Self-nanoemulsifying drug delivery systems (SNEDDS) and self-microemulsifying drug delivery systems (SMEDDS) as lipid nanocarriers for improving dissolution rate and bioavailability of poorly soluble drugs, dalam: Grumezescu, A.M.

- Kuncahyo, I., Choiri, S., Fudholi, A., Rohman, A., dan Martien, R., 2019. Understanding the effect of lipid formulation loading and ethanol as a diluent on solidification of pitavastatin super-saturable SNEDDS using factorial design approach. *Research in Pharmaceutical Sciences*, **14**: 378–390.
- Lee, D.W., Marasini, N., Poudel, B.K., Kim, J.H., Cho, H.J., Moon, B.K., Choi, H.-G., Yong, C.S., dan Kim, J.O., 2014. Application of Box-Behnken design in the preparation and optimization of fenofibrate-loaded self-microemulsifying drug delivery system (SMEDDS). *Journal of Microencapsulation*, **31**: 31–40.
- Li, L., Liu, Haiqing, Shi, W., Liu, Hai, Yang, J., Xu, D., Huang, H., dan Wu, L., 2017. Insights into the Action Mechanisms of Traditional Chinese Medicine in Osteoarthritis. *Evidence-based Complementary and Alternative Medicine*, 1–13.
- Li, S., Wang, C., Wang, M., Li, W., Matsumoto, K., dan Tang, Y., 2007. Antidepressant like effects of piperine in chronic mild stress treated mice and its possible mechanisms. *Life Sciences*, **80**: 1373–1381.
- Littringer, E.M., Mescher, A., Schroettner, H., Achelis, L., Walzel, P., dan Urbanetz, N.A., 2012. Spray dried mannitol carrier particles with tailored surface properties-the influence of carrier surface roughness and shape. *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Fur Pharmazeutische Verfahrenstechnik e.V*, **82**: 194–204.
- Liu, H., Luo, R., Chen, X., Liu, J., Bi, Y., Zheng, L., dan Wu, X., 2013. Tissue distribution profiles of three antiparkinsonian alkaloids from *Piper longum* L. in rats determined by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences*, **928**: 78–82.
- Mahmoud, E.A., Bendas, E.R., dan Mohamed, M.I., 2009. Preparation and evaluation of self-nanoemulsifying tablets of carvedilol. *AAPS PharmSciTech*, **10**: 183–192.
- Malakar, J., Sen, S.O., Nayak, A.K., dan Sen, K.K., 2012. Formulation, optimization and evaluation of transferosomal gel for transdermal insulin delivery. *Saudi Pharmaceutical Journal*, **20**: 355–363.
- Marasini, N., Yan, Y.D., Poudel, B.K., Choi, H.-G., Yong, C.S., dan Kim, J.O., 2012. Development and optimization of self-nanoemulsifying drug delivery system with

- Massart, D.L., Vandeginste, B.G.M., Buydens, L.M.C., De Jong, S., Lewi, P.J., dan Smeyers-Verbeke, J. (Editor), 1998. Chapter 24 Multi-level designs, dalam: *Data Handling in Science and Technology, Handbook of Chemometrics and Qualimetrics: Part A*. Elsevier, hal. 701–738.
- Mathieu, R., Baghdadi, I., Briat, O., Gyan, P., dan Vinassa, J.-M., 2017. D-optimal design of experiments applied to lithium battery for ageing model calibration. *Energy*, **141**: 2108–2119.
- Mazyed, E.A. dan Abdelaziz, A.E., 2020. Fabrication of Transgelosomes for Enhancing the Ocular Delivery of Acetazolamide: Statistical Optimization, In Vitro Characterization, and In Vivo Study. *Pharmaceutics*, **12**: 465.
- Mohd, A.B., Sanka, K., Bandi, S., Diwan, P.V., dan Shastri, N., 2015. Solid self-nanoemulsifying drug delivery system (S-SNEDDS) for oral delivery of glimepiride: development and antidiabetic activity in albino rabbits. *Drug Delivery*, **22**: 499–508.
- Mokale, V., Rajput, R., Patil, J., Yadava, S., dan Naik, J., 2016. Formulation of metformin hydrochloride nanoparticles by using spray drying technique and in vitro evaluation of sustained release with 32-level factorial design approach. *Drying Technology*, **34**: 1455–1461.
- Montgomery, D.C., 2017. *Design and Analysis of Experiments*.
- Morais, J.M., dos Santos, O.D.H., Delicato, T., dan da Rocha-Filho, P.A., 2006. Characterization and Evaluation of Electrolyte Influence on Canola Oil/Water Nano-Emulsion. *Journal of Dispersion Science and Technology*, **27**: 1009–1014.
- Mujumdar, A.M., Dhuley, J.N., Deshmukh, V.K., Raman, P.H., dan Naik, S.R., 1990. Anti-inflammatory activity of piperine. *Japanese Journal of Medical Science & Biology*, **43**: 95–100.
- Mukherjee, T. dan Plakogiannis, F.M., 2010. Development and oral bioavailability assessment of a supersaturated self-microemulsifying drug delivery system (SMEDDS) of albendazole. *The Journal of Pharmacy and Pharmacology*, **62**: 1112–1120.
- Myers, R.H., Montgomery, D.C., dan Anderson-Cook, C.M., 2009. *Other Mixture Design and Analysis Techniques. In: Response Surface Methodology: Process and Product Optimization Using Designed Experiments*. John Wiley & Sons.

- Nahak, G. dan Sahu, R.K., 2011. Phytochemical Evaluation and Antioxidant activity of Piper cubeba and Piper nigrum. *Journal of Applied Pharmaceutical Science*, **08**: 153–157.
- Nazzal, S. dan Khan, M.A., 2006. Controlled release of a self-emulsifying formulation from a tablet dosage form: stability assessment and optimization of some processing parameters. *International Journal of Pharmaceutics*, **315**: 110–121.
- Niamprem, P., Rujivipat, S., dan Tiyafoonchai, W., 2014. Development and characterization of lutein-loaded SNEDDS for enhanced absorption in Caco-2 cells. *Pharmaceutical Development and Technology*, **19**: 735–742.
- Oh, D.H., Kang, J.H., Kim, D.W., Lee, B.-J., Kim, J.O., Yong, C.S., dan Choi, H.-G., 2011. Comparison of solid self-microemulsifying drug delivery system (solid SMEDDS) prepared with hydrophilic and hydrophobic solid carrier. *International Journal of Pharmaceutics*, **420**: 412–418.
- Ohrem, H.L., Schornick, E., Kalivoda, A., dan Ognibene, R., 2014. Why is mannitol becoming more and more popular as a pharmaceutical excipient in solid dosage forms? *Pharmaceutical Development and Technology*, **19**: 257–262.
- Pachauri, M., Gupta, E.D., dan Ghosh, P.C., 2015. Piperine loaded PEG-PLGA nanoparticles: Preparation, characterization and targeted delivery for adjuvant breast cancer chemotherapy. *Journal of Drug Delivery Science and Technology*, **29**: 269–282.
- Park, H.M., Kim, J.H., dan Kim, D.K., 2019. Anti-oxidative Effect of Piperine from Piper nigrum L. in *Caenorhabditis elegans*. *Natural Product Sciences*, **25**: 255–260.
- Parmar, N., Singla, N., Amin, S., dan Kohli, K., 2011. Study of cosurfactant effect on nanoemulsifying area and development of lercanidipine loaded (SNEDDS) self nanoemulsifying drug delivery system. *Colloids and Surfaces B: Biointerfaces*, **86**: 327–338.
- Parthasarathy, V.A., Chempakam, B., dan Zachariah, T.J., 2008. *Chemistry of Spices*. CABI.
- Passerini, N., Albertini, B., Perissutti, B., dan Rodriguez, L., 2006. Evaluation of melt granulation and ultrasonic spray congealing as techniques to enhance the dissolution of praziquantel. *International Journal of Pharmaceutics*, **318**: 92–102.
- Patel, A., Shelat, P., dan Lalwani, A., 2015. Development and Optimization of Solid Self Nanoemulsifying Drug Delivery (S-SNEDDS) Using D-Optimal Design for

Improvement of Oral Bioavailability of Amiodarone Hydrochloride. *Current Drug Delivery*, **12**: 745–760.

- Patel, S.K., 2016. CONVENTIONAL AND ALTERNATIVE PHARMACEUTICAL METHODS TO IMPROVE ORAL BIOAVAILABILITY OF LIPOPHILIC DRUGS. *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm*, **1**: 1–8.
- Peng, T., Zhang, X., Huang, Y., Zhao, Z., Liao, Q., Xu, J., Huang, Z., Zhang, J., Wu, C.Y., Pan, X., dan Wu, C., 2017. Nanoporous mannitol carrier prepared by non-organic solvent spray drying technique to enhance the aerosolization performance for dry powder inhalation. *Scientific Reports*, **7**: 1–11.
- Pentak, D., 2016. In vitro spectroscopic study of piperine-encapsulated nanosize liposomes. *European Biophysics Journal*, **45**: 175–186.
- Pouton, C.W., 2006. Formulation of poorly water-soluble drugs for oral administration: physicochemical and physiological issues and the lipid formulation classification system. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **29**: 278–287.
- Pouton, C.W. dan Porter, C.J.H., 2008. Formulation of lipid-based delivery systems for oral administration: materials, methods and strategies. *Advanced Drug Delivery Reviews*, **60**: 625–637.
- Priprem, A., Chonpathompikunlert, P., Sutthiparinyanont, S., dan Wattanathorn, J., 2011. Antidepressant and cognitive activities of intranasal piperine-encapsulated liposomes. *Advances in Bioscience and Biotechnology*, **02**: 108–116.
- Qi, X., Qin, J., Ma, N., Chou, X., dan Wu, Z., 2014. Solid self-microemulsifying dispersible tablets of celastrol: formulation development, characterization and bioavailability evaluation. *International Journal of Pharmaceutics*, **472**: 40–47.
- Raay, B., Medda, S., Mukhopadhyay, S., dan Basu, M.K., 1999. Targeting of piperine intercalated in mannose-coated liposomes in experimental leishmaniasis. *Indian Journal of Biochemistry & Biophysics*, **36**: 248–251.
- Rahman, A., Chakma, J.S., Islam, S., dan Uddin, N., 2011. Evaluation of antioxidant, antibacterial, antifungal and cytotoxic effects of *Clausena suffruticosa* ethanolic root extract. *Journal of Applied Pharmaceutical Science*, **01**: 90–95.
- Rang, M.-J. dan Miller, C.A., 1999. Spontaneous Emulsification of Oils Containing Hydrocarbon, Nonionic Surfactant, and Oleyl Alcohol. *Journal of Colloid and Interface Science*, **209**: 179–192.

- Rao, S.V.R., Yajurvedi, K., dan Shao, J., 2008. Self-nanoemulsifying drug delivery system (SNEDDS) for oral delivery of protein drugs: III. In vivo oral absorption study. *International Journal of Pharmaceutics*, **362**: 16–19.
- Ravindran, P.N. dan Kallapurackal, J.A., 2012. Black pepper, dalam: *Handbook of Herbs and Spices*. Elsevier, hal. 86–115.
- Ren, S., Park, M.-J., Kim, A., dan Lee, B.-J., 2008. In vitro metabolic stability of moisture-sensitive rabeprazole in human liver microsomes and its modulation by pharmaceutical excipients. *Archives of Pharmacal Research*, **31**: 406–413.
- Riepma, K.A., Lerk, C.F., de Boer, A.H., Bolhuis, G.K., dan Kussendrager, K.D., 1990. Consolidation and compaction of powder mixtures. I. Binary mixtures of same particle size fractions of different types of crystalline lactose. *International Journal of Pharmaceutics*, **66**: 47–52.
- Sadurní, N., Solans, C., Azemar, N., dan García-Celma, M.J., 2005. Studies on the formation of O/W nano-emulsions, by low-energy emulsification methods, suitable for pharmaceutical applications. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **26**: 438–445.
- Saffari, M., Ebrahimi, A., dan Langrish, T., 2015a. Highly-porous mannitol particle production using a new templating approach. *Food Research International*, **67**: 44–51.
- Saffari, M., Ebrahimi, A., dan Langrish, T., 2015b. The Role of Acidity in Crystallization of Lactose and Templating Approach for Highly-Porous Lactose Production. *Journal of Food Engineering*, **164**: 1–9.
- Saffari, M., Ebrahimi, A., dan Langrish, T., 2016. A novel formulation for solubility and content uniformity enhancement of poorly water-soluble drugs using highly-porous mannitol. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **83**: 52–61.
- Saha, K., Seal, H., dan Noor, M., 2014. Isolation and characterization of piperine from the fruits of black pepper (*Piper nigrum*). *Journal of the Bangladesh Agricultural University*, **11**: 11–16.
- Sahin, Y.B., Demirtaş, E.A., dan Burnak, N., 2016. Mixture design: A review of recent applications in the food industry. *Pamukkale University Journal of Engineering Sciences*, **22**: 297–304.

- Sahu, P., Sharma, A., dan Rayees, 2014. Pharmacokinetic study of piperine in Wistar rats after oral and intravenous administration. *International Journal Drug Delivery*, **6**: 82–88.
- Salem, H.F., Kharshoum, R.M., Sayed, O.M., dan Abdel Hakim, L.F., 2019. Formulation development of self-nanoemulsifying drug delivery system of celecoxib for the management of oral cavity inflammation. *Journal of Liposome Research*, **29**: 195–205.
- Satyendra, P., Arun, P., Shailendra, P., Neelesh, D., dan Neeraj, K., 2018. Formulation and Evaluation of Topical Cream of Piperine for Vitiligo. *World Journal of Pharmaceutical Research*, **7**: 11.
- Scheffé, H., 1958. *Experiments with Mixtures*. J. Royal Statist.Soc., B20.
- Schulz, H., Baranska, M., Quilitzsch, R., Schütze, W., dan Lösing, G., 2005. Characterization of peppercorn, pepper oil, and pepper oleoresin by vibrational spectroscopy methods. *Journal of Agricultural and Food Chemistry*, **53**: 3358–3363.
- Seo, Y.G., Kim, D.H., Ramasamy, T., Kim, J.H., Marasini, N., Oh, Y.-K., Kim, D.-W., Kim, J.K., Yong, C.S., Kim, J.O., dan Choi, H.-G., 2013. Development of docetaxel-loaded solid self-nanoemulsifying drug delivery system (SNEDDS) for enhanced chemotherapeutic effect. *International Journal of Pharmaceutics*, **452**: 412–420.
- Seo, Y.G., Kim, D.W., Yousaf, A.M., Park, J.H., Chang, P.-S., Baek, H.H., Lim, S.-J., Yong, C.S., dan Choi, H.-G., 2015. Solid self-nanoemulsifying drug delivery system (SNEDDS) for enhanced oral bioavailability of poorly water-soluble tacrolimus: physicochemical characterisation and pharmacokinetics. *Journal of Microencapsulation*, **32**: 503–510.
- Shabir, G.A., 2003. Validation of high-performance liquid chromatography methods for pharmaceutical analysis Understanding the differences and similarities between validation requirements of the US Food and Drug Administration, the US Pharmacopeia and the International Conference on Harmonization. *J. Chromatogr. A*, 57–66.
- Shao, B., Cui, C., Ji, H., Tang, J., Wang, Z., Liu, H., Qin, M., Li, X., dan Wu, L., 2015. Enhanced oral bioavailability of piperine by self-emulsifying drug delivery systems: *in vitro*, *in vivo* and *in situ* intestinal permeability studies. *Drug Delivery*, **22**: 740–747.

- Sharma, S., Sher, P., Badve, S., dan Pawar, A.P., 2005. Adsorption of meloxicam on porous calcium silicate: Characterization and tablet formulation. *AAPS PharmSciTech*, **6**: E618–E625.
- Sher, P., Ingavle, G., Ponrathnam, S., dan Pawar, A.P., 2007. Low density porous carrier drug adsorption and release study by response surface methodology using different solvents. *International Journal of Pharmaceutics*, **331**: 72–83.
- Shingate, P.N., Dongre, P.P., dan Kannur, D.M., 2013. New Method Development For Extraction and Isolation of Piperine From Black Pepper. *International journal of pharmaceutical sciences and research*, **4**: 3165–3170.
- Silverstein, R.M. dan Bassler, G.C., 1962. Spectrometric identification of organic compounds. *Journal of Chemical Education*, **39**: 546.
- Singh, B., Bandopadhyay, S., Kapil, R., Singh, R., dan Katare, O., 2009. Self-emulsifying drug delivery systems (SEDDS): formulation development, characterization, and applications. *Critical Reviews in Therapeutic Drug Carrier Systems*, **26**: 427–521.
- Singh, G., Kapoor, I.P.S., Singh, P., de Heluani, C.S., de Lampasona, M.P., dan Catalan, C.A.N., 2013. Chemistry and Antioxidant Properties of Essential Oil and Oleoresins Extracted from the Seeds of Tomer (*Zanthoxylum armatum* DC)*. *International Journal of Food Properties*, **16**: 288–300.
- Singh, G., Marimuthu, P., Catalan, C., dan de Lampasona, M., 2004. Chemical, antioxidant and antifungal activities of volatile oil of black pepper and its acetone extract. *Journal of the Science of Food and Agriculture*, **84**: 1878–1884.
- Singh, S.K., Verma, P.R.P., dan Razdan, B., 2010. Glibenclamide-loaded self-nanoemulsifying drug delivery system: development and characterization. *Drug Development and Industrial Pharmacy*, **36**: 933–945.
- Snyder, L.R., Kirkland, J.J., dan Glajch, J.L., 1997. *Practical HPLC Method Development. 2nd Edition*. John Wiley & Sons, Inc., Hoboken.
- Srinivasan, K., 2007. Black pepper and its pungent principle-piperine: a review of diverse physiological effects. *Critical Reviews in Food Science and Nutrition*, **47**: 735–748.
- Srivastava, A.K. dan Singh, V.K., 2017. Biological Action Of Piper Nigrum - The King Of Spices. *European Journal of Biological Research*, **7**: 223–233.

- Taha, E.I., Al-Saidan, S., Samy, A.M., dan Khan, M.A., 2004. Preparation and in vitro characterization of self-nanoemulsified drug delivery system (SNEDDS) of all-trans-retinol acetate. *International Journal of Pharmaceutics*, **285**: 109–119.
- Tang, B., Cheng, G., Gu, J.-C., dan Xu, C.-H., 2008. Development of solid self-emulsifying drug delivery systems: preparation techniques and dosage forms. *Drug Discovery Today*, **13**: 606–612.
- Telang, C., Suryanarayanan, R., dan Yu, L., 2003. Crystallization of D-Mannitol in Binary Mixtures with NaCl: Phase Diagram and Polymorphism. *Pharmaceutical Research*, **20**: 1939–1945.
- Thomas, N., Müllertz, A., Graf, A., dan Rades, T., 2012. Influence of lipid composition and drug load on the In Vitro performance of self-nanoemulsifying drug delivery systems. *Journal of Pharmaceutical Sciences*, **101**: 1721–1731.
- Tije, A.J., Verweij, J., Loos, W.J., dan Sparreboom, A., 2003. Pharmacological effects of formulation vehicles: implications for cancer chemotherapy. *Clinical Pharmacokinetics*, **42**: 665–685.
- Trivedi, M., Khemani, A., Vachhani, U., Shah, C., dan Santani, D., 2011. Pharmacognostic, phytochemical analysis and antimicrobial activity of two piper species. *Int. J. Comp. Pharm.*, **7**: .
- Umar, S., Golam Sarwar, A.H.M., Umar, K., Ahmad, N., Sajad, M., Ahmad, S., Katiyar, C.K., dan Khan, H.A., 2013. Piperine ameliorates oxidative stress, inflammation and histological outcome in collagen induced arthritis. *Cellular Immunology*, **284**: 51–59.
- Vasavirama, K. dan Upender, M., 2014. Piperine: a valuable alkaloid from piper species. *Int J Pharm Pharm Sci*, **6**: 34–8.
- Vehring, R., 2008. Pharmaceutical Particle Engineering via Spray Drying. *Pharmaceutical Research*, **25**: 999–1022.
- Vicente, J., Pinto, J., Menezes, J., dan Gaspar, F., 2013. Fundamental analysis of particle formation in spray drying. *Powder technology*, **247**: 1–7.
- Wang, L., Dong, J., Chen, J., Eastoe, J., dan Li, X., 2009. Design and optimization of a new self-nanoemulsifying drug delivery system. *Journal of Colloid and Interface Science*, **330**: 443–448.
- Wattanathorn, J., Chonpathompikunlert, P., Muchimapura, S., Priprem, A., dan Tankamnerdthai, O., 2008. Piperine, the potential functional food for mood and cognitive disorders. *Food and Chemical Toxicology: An International Journal*

3110.

- Wei, L., Sun, P., Nie, S., dan Pan, W., 2005. Preparation and evaluation of SEDDS and SMEDDS containing carvedilol. *Drug Development and Industrial Pharmacy*, **31**: 785–794.
- Westesen, K. dan Bunjes, H., 1995. Do nanoparticles prepared from lipids solid at room temperature always possess a solid lipid matrix? *International Journal of Pharmaceutics*, **115**: 129–131.
- Wu, Z., Xia, X., dan Huang, X., 2012. Determination of equilibrium solubility and apparent oil/water partition coefficient of piperine. *J Jinan Univ*, **33**: 473–6.
- Yeom, D.W., Song, Y.S., Kim, S.R., Lee, S.G., Kang, M.H., Lee, S., dan Choi, Y.W., 2015. Development and optimization of a self-microemulsifying drug delivery system for atorvastatin calcium by using D-optimal mixture design. *International Journal of Nanomedicine*, **10**: 3865–3877.
- Ying, X., Chen, X., Cheng, S., Shen, Y., Peng, L., dan Xu, H., 2013. Piperine inhibits IL- β induced expression of inflammatory mediators in human osteoarthritis chondrocyte. *International Immunopharmacology*, **17**: 293–299.
- Zellnitz, S., Redlinger-Pohn, J.D., Kappl, M., Schroettner, H., dan Urbanetz, N.A., 2013. Preparation and characterization of physically modified glass beads used as model carriers in dry powder inhalers. *International Journal of Pharmaceutics*, **447**: 132–138.
- Zhou, Q.T. dan Morton, D.A.V., 2012. Drug-lactose binding aspects in adhesive mixtures: controlling performance in dry powder inhaler formulations by altering lactose carrier surfaces. *Advanced Drug Delivery Reviews*, **64**: 275–284.