UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

DAFTAR PUSTAKA

Adewole, S.O., Caxton-Martins, E.A., dan Ojewole, J.A., 2006. Protective effect of quercetin on the morphology of pancreatic beta-cells of streptozotocin-treated diabetic rats. *African Journal of Traditional, Complementary and Alternative Medicines*, **4**:64-74.

Agarwal, V. dan Khan, M., 2001. *Current status of the oral delivery of insulin pharmaceutical technology*, www.pharmtech.com (diakses tanggal 10 November 2014).

Almeida, A.J. dan Souto, E., 2007. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advanced Drug Delivery Reviews*, **59**: 478–490.

Amidon, G., Lennernas, H., Shah, V., dan Crison, J., 1995. A Theoritical basis for a biopharmaceutic drug classification: the correlation of *in vitro* drug product dissolution and *in-vivo* bioavailability. *Pharmaceutical Research*, **12**(3):413-20.

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.

Aryal, S., 2017. *Enzyme-linked immunosorbent assay (ELISA).* http://www.immunologynotes.com. [diakses 10 Maret 2018].

Asada, H., Douen, T., Mizokoshi, Y., Fujita, T., Murakami, M., Yamamoto, A., dkk., 1994. Stability of acyl derivatives of insulin in the small intestine:relative importance of insulin association characteristics in aqueous solution. *Pharmaceutical Research*, **11**(8):1115-20.

Avdeef, A., 2003. *Absorption and drug development:solubility, permeability, and charge state*. John Wiley & Sons, Inc.

Aydin, S., 2015. A short history, principles, and types of ELISA, and our laboratory experience with peptide/protein analyses using ELISA. Peptides, **72**:4-15.

Babchin, A.J. dan Schramm, L.L., 2012. Osmotic repulsion force due to adsorbed surfactants. *Colloids Surf B Biointerfaces*, **91**:137-43.

Barham, D., dan Trinder, P., 1972. An improved colour reagent for the determination of blood glucose by the oxidase system. *Analyst*, **97**(151):142-5

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Bai, J. dan Chang, L., 1995. Transepithelial transport of insulin I. Insulin degradation by insulin-degrading enzyme in small intestinal epithelium. *Pharmaceutical Research*, **12**(8):1171-5.

Bai, J., Chang, L., dan Guo, J., 1996. Effects of polyacrylic polymers on the degradation of insulin and peptides drugs by chymotrypsin and trypsin. *Journal of Pharmacy and pharmacology*, **48**(1):17-21.

Baid, A., 2016. ELISA- A Mini Review. *Research and Reviews: Journal of Pharmaceutical Analysis*, 118-125.e-ISSN: 2320-0812 p-ISSN: 2347-2340.

Balakumar, K., Raghavan, C.V., Selvan, N.T., Prasad, R.H., dan Abdu, S., 2013. Self nanoemulsifying drug delivery system (SNEDDS) of rosuvastatin calcium: design, formulation, bioavailability and pharmacokinetic evaluation. *Colloids surfaces B Biointerfaces*, **112**:337-43.

Balakumar, Rajkumar, Raghavan, V., Selvan, T., dan Prasad, H., 2014. Enabling the development and life cycle management of oral poorly soluble drugs using lipid-based drug delivery systems. *Pharmaceutica Analytica Acta*, 4th International Conference and Exhibition on Pharmaceutics & Novel Drug Delivery Systems, March 24-26, Hilton San Antonio Airport, USA

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.

Behera, S., Ghanty, S., Ahmad, F., Santra, S., dan Banerjee, S., 2012. UV-Visible spectrophotometric method development and validation of assay of paracetamol tablet formulation. *Journal of Analytical & Bioanalytical Techniques*, **3**:1-6.

Bell, G., Pictet, R., Rutter, W., Cordell, B., Tischer, E., dan Goodman, H., 1980. Sequence of the human insulin gene. *Nature*, **6**:284(5751):26-32.

Belmin, J. dan Valensi, P., 2003. Novel drug delivery systems for insulin clinical potential for use in the elderly. *Drugs Aging*, **20**:303-12.

Bendayan, M. dan Rasio, E., 1996. Transport of insulin and albumin by the microvascular endothelium of the rete mirabile. *Journal of Cell Science*, **109**(Pt 7):1857-64.

Bergeron, J., Paiment, J., Khan, M., dan Smith, C., 1985. Terminal glycosylation in rat hepatic Golgi fractions: heterogeneous locations for sialic acid and galactose acceptors and their transferases. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, **821**:393-403.

Bernkop-Schnürch, A. dan Scerbe-Saiko, A., 1998. Synthesis and *in vitro* evaluation of chitosan-EDTA-protease-inhibitor conjugates which might be useful in oral delivery of peptides and proteins. *Pharmaceutical Research*, **15**:263-9.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Binder, C., Lauritzen, T., Faber, O., dan Pramming, S., 1984. Insulin pharmacokinetics. *Diabetes Care*, **7**:188-99.

Bonner-Weir, S., Trent, D.F., Honey, R.N., dan Weir, G.C., 1981. Responses of neonatal rat islets to streptozotocin:limited B-cell regeneration and hyperglycemia. *Diabetes*, **30**:64-9.

Bradford, M.M., 1976. A rapid and sensitives method for the quantitation of micogram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*, **72**:248-254.

Burcelin, R., Eddouks, M., Maury, J., Kande, J., Assan, R., dan Girard, J., 1995. Excessive glucose production, rather than insulin resistance, accounts for hyperglycaemia in recent-onset streptozotocin-diabetic rats. *Diabetologia*, **38**: 283–290.

Camenisch, G., Alsenz, J., van de Waterbeemd, H., dan Folkers, G., 1998. Estimation of permeability by passive diffusion through Caco-2 cell monolayers using the drugs' lipophilicity and molecular weight. *European Journal of Pharmaceutical Sciences*, **6**: 313–319.

Carleton, H.M. dan Drury, R.A.B., 1957. *Histological Technique for normal and patological tissues and the identification of parasites*. third edition, Oxford University Press, London, 11-30.

Chalasani, K.B., Russell-Jones, G.J., Yandrapu, S.K., Diwan, P.V., dan Jain, S.K., 2007. A novel vitamin B12-nanosphere conjugate carrier system for peroral delivery of insulin. *Journal of Controlled Release*, **117**: 421–429.

Chime, S.A., Kenechukwu, F.C., dan Attama, A.A., 2014. Nanoemulsions — Advances in Formulation, Characterization and Applications in Drug Delivery, dalam: Sezer, A.D. (Ed.), *Application of Nanotechnology in Drug Delivery*. InTech. ISBN 978-953-51-1628-8.

Chinwong, S, Chinwong, D, dan Mangklabruks, A, 2012. 'The Effect of Daily Consumption of Virgin Coconut Oil on Plasma Lipoproteins Levels in Healthy Thai Volunteers' *Geneva Health Forum*. URL: http://ghf.globalhealthforum.net/2012/01/06/the-effect-of-daily-consumption-of-virgin-coconut-oil-on-plasma-lipoproteins-levels-in-healthy-thai-volunteers/#.U3MY4nYzeeo (diakses tanggal 14/5/2014).

Chudasama, A., Patel, V., Nivsarkar, M., Vasu, K., dan Shishoo, C., 2011. A novel lipid-based oral drug delivery system of nevirapine. *International Journal of PharmTech Research*, **3**:1159-1168.

Çilek, A., Çelebi, N., Tırnaksız, F., dan Tay, A., 2005. A lecithin-based microemulsion of rh-insulin with aprotinin for oral administration: Investigation of hypoglycemic effects in non-diabetic and STZ-induced diabetic rats. *International Journal of Pharmaceutics*, **298**: 176–185.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Clark, B.J., Frost, T., dan Russell, M.A., 1993. *UV spectroscopy:tecniques, instrumentation, data handling*. London; New York: Chapman & Hall, 6-13.

Clement, S., Braithwaite, S., Ahmann, A., Smith, E., Schafer, R., dan Hirsch, I., 2004. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*, **27**:553-591.

Constantinides, P.P., Scalart, J.P., Lancaster, C., Marcello, J., Marks, G., Ellens, H., dkk., 1994. Formulation and intestinal absorption enhancement evaluation of water-in-oil microemulsions incorporating medium-chain glycerides. *Pharmaceutical Research*, **11**: 1385–1390.

Constantinides, P.P., 1995. Lipid microemulsions for improving drug dissolution and oral absorption: physical and biopharmaceutical aspects. *Pharmaceutical Research*, **12**: 1561–1572.

Cooke, A.R., 1975. Control of gastric emptying and motility. *Gastro-enterology*, 68:804-16.

Costa, J.A., Lucas, E.F., Queirós, Y.G.C., dan Mansur, C.R.E., 2012. Evaluation of nanoemulsions in the cleaning of polymeric resins. *Colloibradfordds and Surfaces A: Physicochemical and Engineering Aspects*, **415**: 112–118.

Cui, F., Shi, K., Zhang, L., Tao, A., dan Kawashima, Y., 2006. Biodegradable nanoparticles loaded with insulin–phospholipid complex for oral delivery: Preparation, *in vitro* characterization and *in vivo* evaluation. *Journal of Controlled Release*, **114**: 242–250.

Croda, 2010. *Tween and Span*. Croda Europe Ltd Cowick Hall Snaith Goole East Yorkshire DN14 9AA England. www.Croda.com/Europe.Accessed 2 February 2016.

Date, A.A. dan Nagarsesadeghinker, M.S., 2007. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for cefpodoxime proxetil. *International Journal of Pharmaceutics*, **329**: 166–172.

Date, A.A., Desai, N., Dixit, R., dan Nagarsenker, M., 2010. Self-nanoemulsifying drug delivery systems:formulation insights, applications and advances. *Nanomedicine*, **5**:1595-1616.

Dave, N., Hazra, P., Khedkar, A., Manjunath, H., Iyer, H., dan Suryanarayanan, S., 2007. Process and purification for manufacture of a modified insulin intended for oral delivery. *Journal of Chromatography A*, **11**:282-6.

Debnath, S., Satayanarayana, dan Kumar, G., 2011. Nanoemulsion-a method to improve the solubility. *PHARMANEST*, ISSN 0976-8090 (Print), 2231-0541 (online), Vol **2**(2-3).

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Deeds, M.C., Anderson, J.M., Amstrong, A.S., Gastineau, D.A., Hidding, H.J., Jahangir, A., dkk., 2011. Single dose streptozotocin-induced diabetes:considerations for study design in islet transplantation models. *Laboratory Animals*, **45**:131-40.

Denis, J. dan Farah, N., 2000. *Orally Administrable Composition Capable of Providing Enhanced Bioavailability When Ingested*. Google Patents. US 6312704 B1.

Desmukh, A. dan Kulkarni, S., 2014. Solid self-microemulsifying drug delivery system of ritonavir. *Drug dev Ind Pharm*, **40**:477-87.

Dixit, R.P. dan Nagarsenker, M.S., 2008. Self-nanoemulsifying granules of ezetimibe: design, optimization and evaluation. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **35**: 183–192.

Donovan, M.D., Flynn, G.L., dan Amidon, G.L., 1990. Absorption of polyethylene glycols 600 through 2000: the molecular weight dependence of gastrointestinal and nasal absorption. *Pharmaceutical Research*, **7**: 863–868.

Duckworth, W.C., Bennett, R.G., dan Hamel, F.G., 1998. Insulin degradation:progress and potential 1. *Endocrine Reviews*, **19**:608-624.

Dunn, M., 2005. Zinc-ligand interactions modulate assembly and stability of the insulin hexamer-a review. *Biometals*, **18**:295-303.

El Kadi, N., Taulier, N., Le Huérou, J.Y., Gindre, M., Urbach, W., Nwigwe, I., dkk., 2006. Unfolding and refolding of bovine serum albumin at acid pH: ultrasound and structural studies. *Biophysical Journal*, **91**: 3397–3404.

Eleazu, C.O., Eleazu, K.C., Chukwuma, S., dan Essien, U.N., 2013. Review of the mechanism of cell death resulting from streptozotocin challenge in experimental animals, its practical use and potential risk to humans. *Journal of Diabetes & Metabolic Disorders*, **12**:1-7.

Elnaggar, Y.S.R., El-Massik, M.A., dan Abdallah, O.Y., 2009. Self-nanoemulsifying drug delivery systems of tamoxifen citrate: design and optimization. *International Journal of Pharmaceutics*, **380**: 133–141.

Engvall, E., 2010. The ELISA enzyme-linked immunosorbent assay. *Clinical Chemistry*, **56**:319-320.

Fasano, A. dan Uzzau, S., 1997. Modulation of intestinal tight junctions by Zonula occludens toxin permits enteral administration of insulin and other macromolecules in an animal model. *Journal of Clinical Investigation*, **99**: 1158–1164.

Federer, W.T., 1977. *Experimental Design Theory and Application*. 3rd edition, New Delhi Bombay Calcuta:Oxford and IBH Publishing Co.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Fei, Y., Kostewicz, E.S., Sheu, M.-T., dan Dressman, J.B., 2013. Analysis of the enhanced oral bioavailability of fenofibrate lipid formulations in fasted humans using an *in vitro*-in silico-*in vivo* approach. *European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Für Pharmazeutische Verfahrenstechnik e.V*, **85**: 1274–1284.

Fernandez, P., André, V., Rieger, J., dan Kühnle, A., 2004. Nano-emulsion formation by emulsion phase inversion. *Colloids Surface: A Physicochemical and Engineering Aspects*, **251**:53-58.

Flanagan, J. dan Singh, H., 2006. Microemulsions: a potential delivery system for bioactives in food. *Critical Reviews in Food Science and Nutrition*, **46**: 221–237.

Foss, A.C. dan Peppas, N.A., 2004. Investigation of the cytotoxicity and insulin transport of acrylic-based copolymer protein delivery systems in contact with Caco-2 cultures. *Eropean Journal Of Pharmaceutics and Biopharmaceutics*, **57**:447-55.

Fujii, S., Yokoyama, T., Ikegaya, K., Sato, F., dan Yokoo, N., 1985. Promoting effect of the new chymotrypsin inhibitor FK-448 on the intestinal absorption of insulin in rats and dogs. *Journal of Pharmacy and Pharmacology*, **37**(8):545-9.

Gan, S. dan Patel, K.R., 2013. Enzyme Immunoassay and Enzyme-Linked Immunosorbent. *Journal of Investigative Dermatology*, **133**:1-3.

Ge, W., Sui, Y.-F., Wu, D.-C., Sun, Y.-J., Chen, G.-S., Li, Z.-S., dkk., 2006. MAGE-1/Heat shock protein 70/MAGE-3 fusion protein vaccine in nanoemulsion enhances cellular and humoral immune responses to MAGE-1 or MAGE-3 in vivo. *Cancer immunology, immunotherapy: CII*, **55**: 841–849.

Georgakopoulos, E., Farah, N., dan Vergnault, G., 1992. Oral anhydrous non-ionic nanoemulsions administered in soft gel capsules. *Bulletin Technology Gattefosse*, 11-19.

Gerhardt, N.I. dan Dungan, S.R., 2002. Time-dependent solubilization of IgG in AOT-brine-isooctane microemulsions: role of cluster formation. *Biotechnology and Bioengineering*, **78**: 60–72.

Ginsburg, A. dan Schachman, H., 1960. Studies on the enzymatic breakdown of proteins. I. Action of chymotrypsin on insulin. *Journal of Biological Chemistry*, **235**:108-14.

Glyk, A., Heinisch, S.L., Scheper, T., dan Beutel, S., 2005. Comparison of colorimetric methods for the quantification of model proteins in aqueous two- phase systems. *Analytical Biochemistry*, **477**:35-7

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Grant, R.W., O'Brien, K.E., Waxler, J.L., Vassy, J.L., Delahanty, L.M., Bissett, L.G., dkk., 2012. Personalized generic risk counseling to motivate diabetes prevention. *Diabetes Care*, **36**:13-9.

Gribble, F. dan Remann, F., 2003. Differential selectivity of insulin secretagogues mechanisms, clinical implications, and drug interactions. *Journal of Diabetes Complications*, **17**(2 Suppl):11-5.

Groves, M.J. dan de Galindez, D.A., 1976. The self-emulsifying action of mixed surfactants in oil. *Acta Pharmaceutica Suecica*, **13**: 361–372.

Gunawan dan Gan, S., 2009. *Farmakologi dan Terapi*. Edisi 5. Departemen Farmakologi dan Terapetik Fakultas Kedokteran Universitas Indonesia, Jakarta.

Gursoy, R., N. dan Benita, S., 2004. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. *Biomedicine & Pharmacotherapy*, **58**: 173–182.

Hakim, L., 2017. *Farmakokinetik*. Edisi 2. Bursa Ilmu, Yogyakarta.

Hamman, J., Enslin, G., dan Kotze, A., 2005. Oral delivery of peptide drugs barriers and developments. *BioDrugs*, **19**(3):165-77.

Hansen, J., 1991. The self-association of zinc-free human insulin and insulin analogue B13-glutamine. *Biophysical Chemistry*, **39**(1):107-10.

Harmita, 2004. Petunjuk pelaksanaan validasi metode dan cara perhitungannya. *Majalah Ilmu kefarmasian*, **1**:117-135.

Hodgins, G., 1999. Investigating methods of identifying pre-renesaince artists paints and glues. *PhD Thesis*.University of Oxford, UK.

Hoffman, A. dan Ziv, E., 1997. Pharmacokinetic considerations of new insulin formulations and routes of administration. *Clinical Pharmacokinetic*, **33**(4):285-301.

Houen, G., Svaerke, C., dan Barkholt, V., 1999. The Solubilities of Denatured Proteins in Different Organic Solvents. Acta.Chem.Scand. **53**:1122-1126

Hugger, E.D., Audus, K.L., dan Borchardt, R.T., 2002. Effects of poly(ethylene glycol) on efflux transporter activity in Caco-2 cell monolayers. *Journal of Pharmaceutical Sciences*, **91**: 1980–1990.

Hutton, J., 1994. Insulin secretory granule biogenesis and the proinsulin-processing endopeptidases. *Diabetologia*, 37 Suppl **2**:S48-56.

ICH, 2005. *Validation of analytical procedures:text and methodology Q2(R1).* ICH Harmonised Tripartite Guideline.

Ihlo, C., Lauritzen, T., Sturis, J., Skyggebjerg, O., Christiansen, J., dan Laursen, T., 2011. Pharmacokinetics and pharmacodynamics of different modes of insulin pump delivery. A randomized, controlled study comparing subcutaneous and intravenous administration of insulin aspart. *Diabetic Medicine*, **28**(2):230-6.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Imada, C., Takahashi, T., Kuramoto, M., Masuda, K., Ogawara, K., Sato, A., dkk., 2015. Improvement of oral bioavailability of N-251, a novel antimalarial drug, by increasing lymphatic transport with long-chain fatty acid-based self-nanoemulsifying drug delivery system. *Pharmaceutical Research*, **32**:2595-608.

Ittiqo, D.H., Pramono, S., dan Martien, R., 2016. Optimasi formula SNEDDS ekstrak terpurifikasi kombinasi temulawak (Curcuma xanthorrhiza) dan sambiloto (Andrographis paniculata (Burm.f.) Nees) menggunakan Miglyol 812N sebagai fase minyak dan uji absorbsi secara *in vitro*. *Tesis*, M.Sc., Fakultas Farmasi Universitas Gadjah Mada, Yogyakarta.

Iyer, H., Khedkar, A., dan Verma, M., 2010. Oral insulin - a review of current status. *Diabetes, Obesity & Metabolism*, **12**: 179–185.

Jain, A.K., Thanki, K., dan Jain, S., 2014. Novel self-nanoemulsifying formulation of quercetin: Implications of pro-oxidant activity on the anticancer efficacy. *Nanomedicine: Nanotechnology, Biology, and Medicine*, **10**: 959–969.

Jain, S., Kambam, S., Thanki, K., dan Jain, A.K., 2015. Cyclosphorine A loaded self-nanoemulsifying drug delivery system (SNEDDS):implication of a functional excipient based co-encapsulation strategy on oral bioavailability and nephrotoxicity. *RSC Adv*, **5**:49633-42.

Jehle, P., Micheler, C., Jehle, D., Breitig, D., dan Boehm, B., 1999. Inadequate suspension of neutral protamine Hagendorn (NPH) insulin in pens. *Lancet*, **6**;354(9190):1604-7.

Joshi, S., Parikh, R., dan Das, A., 2007. Insulin-History, Biochemistry, Physiology and Pharmacology. *Journal of The Association of Physicians of India*, **55** Suppl:19-25.

Jung, H.H., Yang, S.-T., Sim, J.-Y., Lee, S., Lee, J.Y., Kim, H.H., dkk., 2010. Analysis of the solution structure of the human antibiotic peptide dermcidin and its interaction with phospholipid vesicles. *BMB reports*, **43**: 362–368.

Kadowaki, H., Nishitoh, H., Urano, F., Sadamitsu, C., Matsuzawa, A., Takeda, K., dkk., 2005. Amyloid beta induces neuronal cell death through ROS-mediated ASK1 activation. *Cell Death and Differentiation*, **12**:19-24.

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 Für Pharmazeutische Verfahrenstechnik e.V*, **80**: 289–297.

Katayama, K. dan Fujita, T., 1972. Studies on biotransformation of elastase II. Intestinal absorption of 131 I-labelled elastase in vivo. *Biochimica et Biophysica Acta*, **288**:181-9.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Kato, K., Hamaguchi, Y., Okawa, S., Ishikawa, E., dan Kobayashi, K., 1977. Use of rabbit antibody IgG bound onto plain and aminoalkysilyl glass surface for the enzyme-linked sandwich immunoassay. *Journal of Biochemistry*, **82**:261-266.

Kaukonen, A.M., Boyd, B.J., dan Porter, C.J.H., 2004. Influence of the intermediate digestion phases of common formulation lipids on the absorption of a poorly water-soluble drug. *Journal of Pharmaceutical Sciences*, **94**:481-492.

Kaur, G. dan Harikumar, S.L., 2013. Formulation Development Of Self Nanoemulsifying Drug Delivery Systems (SNEDDS) Of Celecoxib For Improvement Of Oral Bioavailability. *Pharmacophore*, **4**: 120–133.

Kawakami, K., Yoshikawa, T., Moroto, Y., Kanaoka, E., Takahashi, K., Nishihara, Y., dkk., 2002. Microemulsion formulation for enhanced absorption of poorly soluble drugs.I. Prescription design. *Journal of Controlled Release*, **81**:65-74.

Ke, W.T., Lin, S.Y., Ho, H.O., dan Sheu, M.T., 2005. Physical characterization of microemulsion systems using tocopheryl polyethylene glycol 1000 succinate (TPGS) as a surfactant for the oral delivery of protein drugs. *Journal Controlled Release*, **102**;489-507.

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 Deliv*, **22**(4):552-61.

Khattab, A., Hassanin, L., dan Zaki, N., 2016. Self-Nanoemulsifying drug delivery system of Coenzyme (Q10) with improved dissolution, bioavailability, and protective efficiency on liver fibrosis. *AAPSJ*, **18**:180-6.

Khedekar, K. dan Mittal, S., 2013. Self emulsifying drug delivery system: A review. *International Journal of Parmaceutical Sciences and Research*, **4**:4494-4507.

Kiernan, J.A., 1990. *Histological & Histochemical Methods: Theory and Practice*. Pergamon Press.

Ko, D.H., Won, D., Jeong, T.D., Lee, W., Chun, S., dan Min, W.K., 2015. Comparison of red blood cell hemolysisi using plasma and serum separation tubes for outpatient specimens. *Annals of Laboratory Medicine*, **35**:194.

Kommuru, T.R., Gurley, B., Khan, M.A., dan Reddy, I.K., 2001. Self-emulsifying drug delivery systems (SEDDS) of coenzyme Q10: formulation development and bioavailability assessment. *International Journal of Pharmaceutics*, **212**: 233–246.

Kramer, W., Muller, G., Girbig, F., Gutjahr, U., Kowalewski, S., Hartz, D., dkk., 1995. The molecular interaction of sulfonylureas with beta-cell ATP-sensitive. *Diabetes Research and Clinical Practice*, Suppl:S67-80.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Kumar, V., Sharma, V.K., dan Kalonia, D.S., 2009a. Effect of polyols on polyethylene glycol (PEG)-induced precipitation of proteins: impact on solubility, stability and conformation. *International Journal of Pharmacy*, **366**:38-43.

Kumar, R., Patil, M.B., Patil, S.R., dan Paschapur, M.S., 2009b, Polysaccharides based colon spesific drug delivery: a review. *International Journal of PharmTech Reserach*, **1**:334-346.

Larsen, A.T., Ogbonna, A., Abu-Rmaileh, R., Abrahamsson, B., Østergaard, J., dan Müllertz, A., 2012. SNEDDS containing poorly water soluble cinnarizine; development and *in vitro* characterization of dispersion, digestion and solubilization. *Pharmaceutics*, **4**:641-665.

Laskowski, M. dan Qasim, M., 2000. What can the structures of enzyme-inhibitor complexes tell us about the structures of enzyme substrate complexes? *Biochimica et Biophysica Acta*, **7**:1477(1-2):324-37.

Lee, H.K., Song, J.H., Shin, C.S., Park, D.J., Park, K.S., Lee, K.U., dkk., 1998. Decreased mitochondrial DNA content in peripheral blood precedes the development of non-insulin-dependent diabetes mellitus. *Diabetes Res Clin Pract*, **42**(3):161-7.

Leonard, T.W., Lynch, J., McKenna, M.J., dan Brayden, D.J., 2006. Promoting absorption of drugs in humans using medium chain fatty acid based solid dosage forms:GIPET. *Expert Opinion on Drug Delivery*, **3**:685-92.

Li, P., Tan, A., Prestidge, C.A., Nielsen, H.M., dan Müllertz, A., 2014. Self-nanoemulsifying drug delivery systems for oral insulin delivery: *In vitro* and in vivo evaluations of enteric coating and drug loading. *International Journal of Pharmaceutics*, **477**: 390–398.

Li, P., Nielsen, H.M., dan Müllertz, A., 2016. Impact of Lipid-Based Drug Delivery Systems on the Transport and Uptake of Insulin Across Caco-2 Cell Monolayers. *Journal of Pharmaceutical Sciences*, **105**:2743-51.

Lian, J. dan Yang, V., 2005. Insulin-cell penetrating peptide hybrids with improved intestinal absorption efficiency. *Biochemical and Biophysical Research communications*, **30**;335(3):734-8.

Lin, Y.M., Wu, J.Y., Chen, Y.C., Su, Y.D., Ke, W.T., Ho, H.O., dkk., 2011. In situ formation of nanocrystals from a self-microemulsifying drug delivery system to enhance oral bioavailability of fenofibrate. *International Journal of Nanomedicine*, **6**:2445–2457.

Lindmark, T., Nikkilä, T., dan Artursson, P., 1995. Mechanisms of absorption enhancement by medium chain fatty acids in intestinal epithelial Caco-2 cell monolayers. *The Journal of Pharmacology and Experimental Therapeutics*, **275**: 958–964.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Liu, Y., Zhang, P., Feng, N., Zhang, X., Wu, S., dan Zhao, J., 2009. Preparation and evaluation of self-nanoemulsifying tablets of carvedilol. *AAPS PharmSciTech*, **365**:136-142.

Ma, H., Liu, Z., dan Zheng, C., 2006. *In vitro* and *in vivo* evaluation of a novel oral insulin formulation1. *Acta pharmacologica sinica*, **27**: 1382–1388.

Madigan, M., Martinko, J., dan Parker, J., 2001. *Brock Biology of Microorganisms*. edisi 10. Prentice Hall.

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.

Makadia, H.A., Bhatt, A.Y., Parmar, R.B., Paun, J.S., dan Tank, H.M., 2013. Self-nano Emulsifying Drug Delivery System (SNEDDS): Future Aspects. *Asian Journal of Pharmaceutical Research*, **3**: 21–27.

Markussen, J., Damgaard, U., Jorgensen, K., Sorensen, E., dan Thim, L., 1983. Human monocomponent insulin. Chemistry and characteristics. *Acta Medica Scandinavica*, **671**:99-105.

Mathieu, C. dan Gale, E.A.M., 2007. Inhaled insulin: gone with the wind? *Diabetologia*, **51**: 1–5.

May, A.J. dan Whaler, B.C., 1958. The absorption of Clostridium botulinum Type A toxin from the alimentary canal. *British Journal of Experimental Pathology*, **39**:307-316.

McClements, D.J., 2012. Nanoemulsions versus microemulsions: terminology, differences, and similarities. *Soft Mattterials*, **8**:1719.

McMahon, G.T. dan Arky, R.A., 2007. Inhaled insulin for diabetes mellitus. *New England Journal of Medicine*, **356**: 497–502.

Michaelsen, M.H., Wasan, K.M., Sivak, O., Müllertz, A., dan Rades, T., 2016. The Effect of Digestion and Drug Load on Halofantrine Absorption from Self-nanoemulsifying Drug Delivery System (SNEDDS). *AAPSJ*, 15:219-27.

Miller, J.N. dan Miller, J.C., 2010. Statistics and Chemometrics for Analytical Chemistry. Sixth Edition, Ashford Colour Press Ltd., Gosport, UK, hal.112.

Morais, J.M., Santos, O., dan Delicato, T., 2006. Characterization and evaluation of electrolyte influence on canola oil/water nano-emulsion. *Journal of Dispersion Science and Technology*, **27**:1009-1014.

Morishita, M., Morimoto, F., Kitamura, K., Koga, T., Fukui, Y., Maekawa, H., Yamashita, I., dan Shimoda, C., 2002. Phosphatidylinositol 3-phosphate 5-kinase is required for the cellular response to nutritional starvation and mating pheromone signals in Schizosaccharomyces pombe. *Genes to Cells*, **7**:199-215.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Mudie, D.M., Murray, K., Hoad, C.L., Pritchard, S.E., Garnett, M.C., Amidon, G.L., dkk., 2014. Quantification of Gastrointestinal liquid volumes and distribution following a 240 mL dose of water in the fasted state. *Molecular Pharmaceutics*, **11**:3039-47.

Mueller, E.J., Meyer, E., Rudolph, J., Davisson, V.J., Stubbe, J., 1994. N5-carboxyaminoimidazole ribonucleotide:evidence for a new intermediate and two new enzymatic activities in the de novo purine biosynthetic pathway of Eschericia coli. *Biochemistry*, **33**:2269-78.

Muranishi, S., 1990. Absorption enhancers. *Critical reviews in therapeutic drug carrier systems*, **7**:1-33.

Nasr, A., Gardouh, A. dan Ghorab, M., 2016. Novel solid self-nanoemulsifying drug delivery system (S-SNEDDS) for oral delivery of olmesartan medoxomil:design,formulation, pharmacokinetic and bioavailability evaluation. *Pharmaceutics*, **8**(20):1-29.

Nazzal, S., Smalyukh, I.I., Lavrentovich, O.D., dan Khan, M.A., 2002. Preparation and *in vitro* characterization of a eutectic based semisolid self-nanoemulsified drug delivery system (SNEDDS) of ubiquinone: mechanism and progress of emulsion formation. *International journal of pharmaceutics*, **235**: 247–265.

Nielsen, D.R., Leonard, E., Yoon, S.-H., Tseng, H.-C., Yuan, C., dan Prather, K.L.J., 2009. Engineering alternative butanol production platforms in heterologous bacteria. *Metabolic Engineering*, **11**: 262–273.

Noble, J.E. dan Bailey, J.A., 2009. Quantitation of Protein. *Methods Enzymology*, **463**:73-95.

Notari, R.E., 1986. *Pharmacokinetic Application in Clinical Practice: Biopharmaceutics and Clinical Pharmacokinetics*, 4th ed, Marcel Dekker Inc, New York.

Oddoze, C., Lombard, E., dan Portugal, H., 2012. Stability study of 81 analytes in human whole blood, in serum and in plasma. *Clinical Biochemistry*, **45**:464-469.

Onuki, Y., Morishita, M., Takayama, K., Tokiwa, S., Chiba, Y., Isowa, K., dkk., 2000. In vivo effects of highly purified docosahexaenoic acid on rectal insulin absorption. *International Journal of Pharmacy*, **198**(2):147-56.

Park, K., Kwon, I.C., dan Park, K., 2011. Oral protein delivery: Current status and future prospect. *Reactive and Functional Polymers*, **71**: 280–287.

Patel, P.A., Chaulang, G.M., dan Akolkotkar, A., 2008. Self emulsifying drug delivery system. *Research Journal of Pharmacy and Technology*, **1**:313-319.

Patel, J., Patel, A., Raval, M., dan Sheth, N., 2011. Formulation and development of a self-nanoemulsifying drug delivery system of irbesartan. *Journal of Advanced Pharmaceutical Technology & Research*, **2**: 9–16.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Patel, H., Santwani, P., Patel, P., Akshay, K., Ranch, K., dan Shah, D., 2013. A review on solid self-emulsification - tecniques, dosage forms development and pharmaceutical applications. J*ournal of Biomedical and Pharmaceutical Reserach*, **2**(4):52-56.

Patil, P., Jpateloshi, P., dan Paradkar, A., 2004. Effect of formulation variables on preparation and evaluation of gelled self-emulsifying drug delivery system (SEDDS) of ketoprofen. *AAPS PharmSciTech*, **5**: 43–50.

Peniche, C., Arguelles-Monal, W., Peniche, H., dan Acosta, N., 2003. Chitosan An Attractive Biocompatible Polymer for Microencapsulation - Peniche - 2003 - *Macromolecular Bioscience* - Wiley Online Library.html.

Peppas, N.A. dan Kavimandan, N.J., 2006. Nanoscale analysis of protein and peptide absorption: insulin absorption using complexation and pH-sensitive hydrogels as delivery vehicles. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **29**: 183–197.

Ponchel dan Irache, null, 1998. Specific and non-specific bioadhesive particulate systems for oral delivery to the gastrointestinal tract. *Advanced Drug Delivery Reviews*, **34**: 191–219.

Porter, C.J.H. dan Charman, W.N., 2001. Transport and absorption of drugs via the lymphatic system. *Advance Drug Delivery Review*, **50**:1-2.

Porter, C.J.H. dan Kaukonen, A.M., Taillardat-Bertschinger, A., Boyd, B.J., O'Connor, J.M., Edwards, G.A., dkk., 2004. Use of *in vitro* lipid digestion data to explain the in vivo performance of triglyceride-based oral lipid formulations of poorly water-soluble drugs: studies with halofantrine. *Journal of Pharmaceutical Sciences*, **93**: 1110–1121.

Pouton, C.W., 1985. Self-emulsifying drug delivery systems: assessment of the efficiency of emulsification. *International Journal of Pharmaceutics*, **27**: 335–348.

Pouton, C.W., 2000. Lipid formulation for oral administration of drugs:non-emulsifying, self-emulsifying and self-microemulsifying drug delivery systems. *European Journal of Pahrmaceutical Science*, **11**:S93-S98.

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.

Pringels, E., Callens, C., Vervaet, C., Dumont, F., Slegers, G., Foreman, P., dkk., 2006. Influence of deposition and spray pattern of nasal powders on insulin bioavailability. *International Journal of Pharmaceutics*, **310**: 1–7.

Pujara, N.D., 2012. Self-emulsifying drug delivery system: a novel approach. *Internatioanl Journal of Current Pharmaceutical Research*, **4**: 18–23.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Rachmawati, H., Rasaputri, D., Susilowidodo, R., Darijanto, S., dan Sumirtapura, Y., 2008. The influence of oils and surfactants on the formation of self-nanoemul sifying drug delivery systems (SNEDDS) containing therapeutic protein. *Materials Science and Technology*. Institute Teknologi Bandung.digilib.batan.go.id.

Rachmawati, H., Haryadi, B.M., Anggadiredja, K., dan Suendo, V., 2014. Intraoral Film Containing Insulin-Phospholipid Microemulsion: Formulation and In Vivo Hypoglycemic Activity Study. AAPS PharmSciTech, 16:692-703.

Raj, N. dan Sharma, C., 2003. Oral insulin--a perspective. *Journal of Biomaterials Application*., **17**(3):183-96.

Rao, S.V.R., Agarwal, P., dan Shao, J., 2008a. Self-nanoemulsifying drug delivery systems (SNEDDS) for oral delivery of protein drugs. I. Formulation design. *International Journal of Pharmaceutics*, **362**: 10–15.

Rao, S.V.R., Yajurvedi, K., dan Shao, J., 2008b. Self-nanoemulsifying drug delivery system (SNEDDS) for oral delivery of protein drugs. II. *In Vitro* transport study. *International Journal of Pharmaceutics*, **362**: 16–19.

Rao, V., R. dan Shao, J., 2008. Self-nanoemulsifying drug delivery systems (SNEDDS) for oral delivery of protein drugs. III. In vivo oral absorption study. *International Journal of Pharmaceutics*, **362**: 2–9.

Reddy, L.H. dan Murthy, R.S., 2002. Lympatic transport orally administered drugs. *Indian Journal of Experimental Biology*, **40**:1097-1109.

Reddy, S., Reddy, M.S., Reddy, N.S., dan Reddy, O.M., 2014. Formulation and evaluation of novel lipid based solid self nano emulsifying drug delivery system of repaglinide. *International Journal of Pharmacy & Pharmaceutical Sciences*, **6**(4):106-110.

Reddy, S. dan Sowjanya, N., 2015. Formulation and *in vitro* characterization of solid self-nanoemulsifying drug delivery system (s-SNEDDS) of simvastatin. *Journal Pharmaceutical Science and Research*, **7**:40-48.

Rees, D.A., dan Alcolado, J.C., 2005. Animal models of diabetes mellitus. *Diabetic Medicine*, **22**:359-370.

Rege, B.D., Kao, J.P.Y., dan Polli, J.E., 2002. Effects of nonionic surfactants on membrane transporters in Caco-2 cell monolayers. *European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences*, **16**: 237–246.

Remy, I. dan Michnick, S.W., 2006. A highly sensitive protein-protein interaction assay based on Gaussia luciferase. *Nature Methods*, **3**: 977–979.

Ren, C., Fang, L., Li, T., Wang, M., Zhao, L., dan He, Z., 2008. Effect of permeation enhancers and organic acids on the skin permeation of indapamide. *International Journal of Pharmaceutics*, **350**: 43–47.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Roda, E., Lonati, D., Buscaglia, E., Papa, P., Rocchi, L., Locatelli, C.A., dkk., 2016. Evaluation of Two Different Screening ELISA Assays for Synthetic Cathinones (Mephedrone/Methcathinone and MDPV) with LC-MS Method in Intoxicatedrees Patients. *Journal of Clinical Toxicology*, **6**:1-9.

Rohloff, C.M., Shimek, J.W., dan Dungan, S.R., 2003. Effect of added alpha-lactalbumin protein on the phase behavior of AOT-brine-isooctane systems. *Journal of Colloid and Interface Science*, **261**: 514–523.

Rosenbaum, S., 2012. *Basic Pharmacokinetics and Pharmacodynamics: An integrated textbook and computer simulations*. John Wiley & Sons.

Rowe, R.C., Sheskey, P.J., dan Quinn, M.E., 2009. *Handbook Of Pharmaceutical Exipients*, 6th ed. Pharmaceutical Press and American Pharmacists Association, London,UK.

Rowland, M. dan Tozer, T.N., 1995. *Clinical Pharmacokinetics*. Lea & Febiger, 600 Washington Square.

Ruan, J., Liu, J., Zhu, D., Gong, T., Yang, F., Hao, X., dkk., 2010. Preparation and evaluation of self-nanoemulsified drug delivery systems (SNEDDSs) of matrine based on drug-phospholipid complex technique. *Int J Pharm*, **386**:282-90.

Sadeghi, A.M., Ayadi, M.R., Ejtemaimehr, S.H., Abashzadeh, S.H., Partoazar, A., Dorkoosh, F., dkk., 2009. Development of a gas empowered drug delivery system for peptide delivery in the small intestine. *Journal of Controlled Release*, **134**:11-7.

Sadrzadeh, N., Glembourtt, M., dan Stevenson, C., 2007. Peptide drug delivery strategies for the treatment of diabetes. *Journal of Pharmaceutical Science*, **96**:1925-54.

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.

Sagar, K., Kendre, P., Pande, V., dan Chaudhari, V., 2014. Design, development and characterization of self-nanoemulsifying drug delivery system (SNEDDS) of Nateglinide. *World Journal of Pharmacy and Pharmaceutical Sciences*, **3**:794-811.

Sakai, K., Takesawa, S., Mimura, R., dan Ohashi, H., 1987. Structural analysis of hollow fiber dialysis membranes for clinical use. *Journal of Chemical Engineering of Japan*, **20**:351-356.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Sakloetsakun, D., Dünnhaupt, S., Barthelmes, J., Perera, G., dan Bernkop-Schnürch, A., 2013. Combining two technologies: Multifunctional polymers and self-nanoemulsifying drug delivery system (SNEDDS) for oral insulin administration. *International Journal of Biological Macromolecules*, **61**: 363–372.

Sakthi, U., Lobo, J.R., dan Uppuluri, K.B., 2013. Self Nano Emulsifying Drug Delivery Systems for Oral Delivery of Hydrophobic Drugs. *Biomedical & Pharmacology Journal*, **6**: 355–362.

Salentinig, S., Sagalowicz, L., dan Glatter, O., 2010. Self-Assembled Structures and pKa Value of Oleic Acid in Systems of Biological Relevance. *Langmuir*, **26**:11670-11679.

Sanchez, M.C., Berjano, M., Guerrero, A., dan Gallegos, C., 2001. Emulsification rheokinetics of nonionic surfactant-stabilized oil in water emulsions. *Langmuir*, **17**:5410-5416.

Sanford, B., 1997. *Pharmaceutical Statistics Practical And Clinical Applications, Third Edition*. Taylor & Francis.

Sanjeewani, N.A. dan Sakeena, M.H.F., 2013. Formulation and Characterization of Virgin Coconut Oil (VCO) Based Emulsion. *International Journal of Scientific and Research Publications*, Vol 3(12), ISSN 2250-3153.

Selvam, R.P., Kulkarni, P.K., dan Dixit, M., 2013. Preparation and evaluation of self-nanoemulsifying formulation of efavirenz. *Indian Journal of Pharmaceutical Education & Research*, **47**:47-54.

Serajuddin, A.T.M., Sheen, P.-C., Mufson, D., Bernstein, D.F., dan Augustine, M.A., 1988. Effect of vehicle amphiphilicity on the dissolution and bioavailability of a poorly water-soluble drug from solid dispersions. *Journal of Pharmaceutical Sciences*, **77**: 414–417.

Shafiq-un-Nabi, S., Shakeel, F., Talegaonkar, S., Ali, J., Baboota, S., Ahuja, A., dkk., 2007. Formulation development and optimization using nanoemulsion technique: A technical note. *AAPS PharmSciTech*, **8**: E12–E17.

Shah, S., Joshi, S., dan Parmar, D., 1997. History of insulin. *Journal Association of Physicians of India*, Suppl **1**:4-9.

Shargel, L. dan Yu, A.B.C., 2005. *Biofarmasetika dan Farmakokinetika Terapan*. Edisi 2. Airlangga University Press, Surabaya.

Sharma, G., Wilson, K., van der Walle, C.F., Sattar, N., Petrie, J.R., dan Ravi Kumar, M.N.V., 2010. Microemulsions for oral delivery of insulin: Design, development and evaluation in streptozotocin induced diabetic rats. *European Journal of Pharmaceutics and Biopharmaceutics*, **76**: 159–169.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Shi, K., Cui, F., Yu, Y., Zhang, L., Tao, A., dan Cun, D., 2006. Preparation and characterization of a novel insulin-phospholipid complex. *Journal of Asian Pharmaceutical Science*, **1**: 168–174.

Shintov, A.C., Shapiro, L., 2004. New microemulsions vehicle facilitates percutaneous penetration *in vitro* and cutaneous drug bioavailability in vivo. *Journal Controlled Release*, **95**:173-183.

Sintov, A., Krymberk, I., Daniel, D., Hannan, T., Sohn, Z., dan Levin, G., 2007. Radiofrequency-driven skin microchanneling as a new way for electrically assisted transdermal delivery of hydrophilic drugs. *Journal of Controlled Release*, **89**:311-20.

Smith, G.D., Pangborn, W.A., dan Blessing, R.H., 2003. The structure of T6 human insulin at 1.0 A resolution. *Acta Crystallographica Section D Biological Crystallography*, **59**:474-82.

Soderholm, J.D., Hedman, L., Artursson, P., Franzén, L., Larsson, J., Pantzar, N., dkk., 1998. Integrity and metabolism of human ileal mucosa *in vitro* in the Ussing Chamber. *Acta Physiology Scandinavia*, **162**:47-56.

Sonaje, K., Lin, Y., Juang, J., Wey, S., Chen, C., dan Sung, H., 2009. In vivo evaluation of safety and efficacy of self-assembled nanoparticles for oral insulin delivery. *Biomaterials*, **30**:2329-39.

Staggers, J.E., Hernell, O., Stafford, R.J., dan Carey, M.C., 1990. Physical-chemical behavior of dietary and biliary lipids during intestinal digestion and absorption. 1. Phase behavior and aggregation states of model lipid systems patterned after aqueous duodenal contents of healthy adult human beings. *Biochemistry*, **29**: 2028–2040.

Suresh, P. dan Sharma, S., 2011. Formulation and *In vitro* Characterization of Self-Nanoemulsifying Drug Delivery System of Cinnarizine. International. *Journal of Comprehensive Pharmacy*, **2**:1-9

Takatsuka, S., Kitazawa, T., Morita, T., Horikiri, Y., dan Yoshino, H., 2006. Enhancement of intestinal absorption of poorly absorbed hydrophilic compounds by simultaneous use of mucolytic agent and non-ionic surfactant. *European Journal of Pharmaceutics and Biopharmaceutics*, **62**: 52–58.

Talegaonkar, S., Azeem, A., Ahmad, F.J., Khar, R.K., Pathan, S.A., dan Khan, Z.I., 2008. Microemulsions: a novel approach to enhanced drug delivery. *Recent patents on drug delivery & formulation*, **2**: 238–257.

Ten 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.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Thomas, N., Holm, R., Garmer, M., Karlsson, J.J., Müllertz, A., dan Rades, T., 2013. Supersaturated self-nanoemulsifying drug delivery systems (Super-SNEDDS) enhance the bioavailability of the poorly water-soluble drug simvastatin in dogs. *AAPSJ*, **15**:219-227.

Todo, H., Okamoto, H., Lida, K., dan Danjo, K., 2001. Effect of additives on insulin absorption from intratracheally administered dry powders in rats. *International Journal of Pharmaceutics*, Vol **220**:101-110.

Toschi, E., Camastra, S., Sironi, A.M., Masoni, A., Gastaldelli, A., Mari, A., dkk., 2002. Effect of acute hyperglycemia on insulin secretion in humans. *Diabetes*, Suppl **1**:S130-3.

Touitou, E., 1992. Enhancement of intestinal peptide absorption. *Journal of Controlled Release,* Vol **21**:139-144.

Tozaki, H., Odoriba, T., Iseki, T., Taniguchi, T., Fujita, T., Murakami, M., dkk., 1998. Use of protease inhibitors to improve calcitonin absorption from the small and large intestine rats. *Journal of pharmacy and Pharmacology*, **50**:913-20.

Wadhwa, J., Nair, A., dan Kumria, R., 2012. Emulsion forming drug delivery system for lipophilic drugs. *Acta Poloniae Pharmaceutica*, **69**: 179–91.

Walker, J.M., 2002. *The protein protocols handbook*, 2nd ed. Humana Press, New Jersey, pp:15-21.

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.

Warshaw, A.L., Walker, WA., dan Isselbacer, K.J., 1971. Small intestinal permeability to macromolecules. Transmission of horseradish peroxidase into mesenteric lymph and portal blood. *Laboratory Investigation*, **25**:675-84.

Warshaw, A.L., Walker, WA., dan Isselbacer, K.J., 1974. Protein uptake by the intestine:evidence for absorption of intact macromolecules. *Gastroenterology*, **66**:987-92.

Watnasirichaikul, S., Davies, N.M., Rades, T., dan Tucker, I.G., 2000. Preparation of Biodegradable Insulin Nanocapsules from Biocompatible Microemulsions. *Pharmaceutical Research*, **17**: 684–689.

Watnasirichaikul, S., Rades, T., Tucker, I.G., dan Davies, N.M., 2002. *In vitro* release and oral bioactivity of insulin in diabetic rats using nanocapsules dispersed in biocompatible microemulsion. *Journal of Pharmacy and Pharmacology*, **54**: 473–480.

Weerapol, Y., Limmatvapirat, S., dan Sriamornsak, P., 2014. Self-nanoemulsifying drug delivery system of nifedipine: impact of hydrophilic-lypophilic balance and molecular structure of mixed surfactants. *AAPS PharmSciTech*, **15**;435-443.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Weiss, R.B., 1982. Streptozotocin: a review of its pharmacology, efficacy, and toxicity. *Cancer Treatment Reports*, **66**:427-38.

Weiss, M., Steiner, D.F., dan Philipson, L.H., 2000. Insulin Biosynthesis, Secretion, Structure, and Structure-Activity Relationships, dalam: De Groot, L.J., Chrousos, G., Dungan, K., Feingold, K.R., Grossman, A., Hershman, J.M., dkk. (Eds.), *Endotext*. MDText.com, Inc., South Dartmouth (MA).

Weyer, C., Heise, T., dan Heinemann, L., 1997. Insulin aspart in a 30 70 premixed formulation. Pharmacodynamic properties of a rapid-acting insulin analog in stable mixture. *Diabetes Care*, **20**:1612-4.

Wilson, G.L. dan Leiter, E.H., 1990. Streptozotocin interactions with pancreatic beta cells and the induction of insulin-dependent diabetes. *Current Topic Microbiology Immunology*, **156**:27-54.

Winarti, L., Suwaldi, Martien, R., dan Hakim, L., 2016. Formulation of self-nanoemulsifying drug delivery system of bovine serum albumin using HLB (hydrophilic-lypophilic balance) approach. *Indonesian Journal of Pharmacy*, **27**:117-127.

Woodley, J.F., 1994. Enzymatic barriers for GI peptide and protein delivery. *Critical Reviews in Therapeutic Drug Carrier Systems*, **11**: 61–95.

Woodrow, K.A., Bennett, K.M., dan Lo, D.D., 2012. Mucosal vaccine design and delivery. *Annual Review of Biomedical Engineering*, **14**: 17–46.

Wu, W., Niu, M., Lu, Y., dan Hovgaard, L., 2011. Liposomes containing glycocholate as potential oral insulin delivery systems: preparation, *in vitro* characterization, and improved protection against enzymatic degradation. *International Journal of Nanomedicine*, 1155.

Xi, J., Chang, Q., Chan, C.K., Meng, Z.Y., Wang, G.N., Sun, J.B., dkk., 2009. Formulation development and bioavailability evaluation of a self-nanoemulsified drug delivery system of oleanolic acid. *AAPS PharmSciTech*, **10**:172-182.

Xia, C., Wang, J., dan Shen, W., 2000. Hypoglycemic Effect of Insulin-Transferrin Conjugate in Streptozotocin-Induced Diabetic Rats. *Journal of Pharmacology and Experimental Therapeutics*, **295**:594-600.

Yamamoto, A., Taniguchi, T., Rikyuu, K., Fujita, T., Murakami, M., dan Muranishi, S., 1994. Effects of various protease inhibitors on the intestinal absorption and degradation of insulin in rats. *Pharmaceutical Reserach*, **11**:1496-500.

Yang, Y., Hua, Q.X., Liu, J., Shimizu, E.H., Choquette, M.H., Mackin, R.B., dkk., 2010. Solution structure of proinsulin:conecting domain flexibility and prohormone processing. *Journal of Biology and Chemistry*, **285**:7847-51.

UNIVERSITAS
GADJAH MADA
FORMULASI SELF NANO-EMULSIFYING DRUG DELIVERY SYSTEM (SNEDDS) UNTUK PENGHANTARAN PROTEIN PER-ORAL
LINA WINARTI, Prof.Dr.Suwaldi, M.Sc., Apt; Prof.Dr. Lukman Hakim, M.Sc., Apt; Dr.rer.nat Ronny Martien, M.Si
Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Yoo, J., Baskaran, R., dan Yoo, B.-K., 2013. Self-Nanoemulsifying Drug Delivery System of Lutein: Physicochemical Properties and Effect on Bioavailability of Warfarin. *Biomolecules & Therapeutics*, **21**: 173–179.

Yorde, D.E., Sasse, E.A., Wang, T.Y., Hussa, R.O., dan Garancis, J.C., 1976. Competitive enzyme-linked immunoassay with use of soluble enzyme/antibody immune complexes for labeling.I. measurement of human choriogonadotropin. *Clinical Chemistry*, **22**:1372-1377.

Yu, L., Bridgers, A., Polli, J., Vickers, A., Long, S., Roy, A., dkk., 1999. Vitamin E-TPGS increases absorption flux of an HIV protease inhibitor by enhancing its solubility and permeability. *Pharmaceutical Research*, **16**: 1812–1817.

Zhang, Q., Na, H., Zhang, L., Zhu, P., Chen, Q., Qiu, Y., dkk., 2012. The *In vitro* and *In Vivo* Study on SNEDDS Based on Insulin-Phospholipid Complex. *Journal of Biomedical Nanotechnology*, **8**:90-7.

Ziv, E., Kidron, M., Raz, I., Krausz, M., Blatt, Y., Rotman, A., dkk., 1994. Oral administration of insulin in solid form to nondiabetic and diabetic dogs. *Journal of Pharmaceutical Science,* **83**(6):792-4.

Zu, Y., Meng, L., Zhao, X., Ge, Y., Yu, X., Zhang, Y., dkk., 2013. Preparation of 10-hydroxycamptothecin-loaded glycyrrhizic acid-conjugated bovine serum albumin nanoparticles for hepatocellular carcinoma-targeted drug delivery. *International Journal of Nanomedicine*, **8**: 1207–1222.